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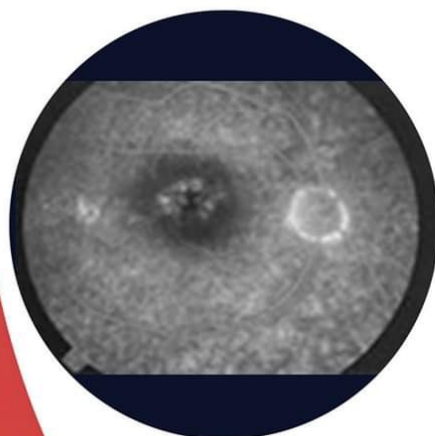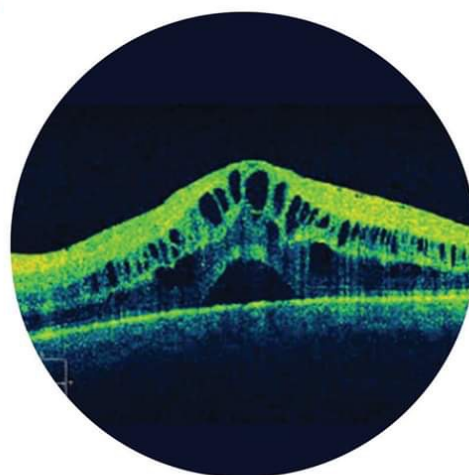These requirements are in accordance with the uniform requirement of manuscript submissions to Misurata Medical Journal.

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The content of abstracts should give a complete information to the reader of the paper.

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Type tables double-spaced, provide a table number and title for each. Provide a footnote to each table identifying all abbreviations used. Do not embed tables as graphic file, document object or pictures.

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For graphic, diagram, line drawing … etc. artwork should be done professionally. Labeling should allow for legibility following reduction to column width.

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B-Case Report:

Case report will be considered for publication only if it concern unorganized condition or offer new insight into pathophysiology, diagnosis or treatment of a disease. The abstract of case reports should not exceed 100 words and the overall text should not exceed 2000 words including tables, figures and references.

C-Letter to the editor:

A letter to the editor may be a response to a published article or may comment on a controversial issue. Letters should be brief, less than 250 words and undergo peer review.

Contents

Management of Developmental Dysplasia of Hip in First 6 Months of Age current experience at Misurata medical center

By
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ABSTRACT:

The term developmental dysplasia or dislocation of the hip (**DDH**) refers to the complete spectrum of abnormalities involving the growing hip, with varied expression from dysplasia to subluxation to dislocation of the hip joint. Unlike the term "congenital dysplasia or dislocation of the hip," **DDH** is not restricted to congenital problems but also includes developmental problems of the hip. It is important to diagnose these conditions early to improve the results of treatment, decrease the risk of complications, and favorably alter the natural history. Careful history taking and physical examination in conjunction with advances in imaging techniques, such as ultrasonography, have increased the ability to diagnose and manage **DDH**. Use of the Pavlik harness has become the mainstay of initial treatment for the infant. The objectives of our study is to assess our current experience regarding the effectiveness and safety of using Pavlik harness in babies ≤ 6 months of age in treating developmental hip dislocation, in terms of hip reduction rate and AVN rate and other possible complications in comparison with previous studies. Retrospective study evaluating outcome of 40 cases (50 Hips) of **DDH** in infant ≤ 6 months of age who were primarily treated using the Pavlik harness splint in outpatient department in Misurata central hospital in the year 2016. Apart from coexisting neuromuscular disorders, congenital abnormalities, or syndromes was our inclusion criteria. The data of the study include 40 cases (50 hips), 30 girls (75%) and 10 boys (25%), 30 of them was unilateral **DDH** and 10 cases was bilateral.Finally at the end of study the total successful rate was in 29 infants (72.5%), 5 infants (12,5%) failed redaction, 3 of them was bilateral and 2 was unilateral and 6 (15%) infant end with residual dysplasia, acetabular index more than 30 degree.

The highest success rate was obtained in children younger than age 3 months and the lowest one older than age 5 months , also Graf Type 3and 4 hips had the lowest rate of treatment success. **DDH** still constitutes one of the major orthopedic disorder in children in our country, early diagnosis ussing ultra sonography screen in newborns with risk factors at 4- 6 Wks of age, and early treatment by Pavlik harness still remains the gold standard for treatment of the infants ≤ 6 monthes, National Screening Committee with National Screening Program Should be established all over the country.

KEY WORDS: Dysplasia, Subluxation, Dislocation.

INTRODUCTION :

Developmental dysplasia of the hip (**DDH**) is defined by acetabular dysplasia, which can lead to hip dislocation. Now adays for children from one day to 6 months old with a confirmed **DDH**, it is recognized that Pavlik Harnesss is the gold standard for treatment of these childre[1-4]. The device was developed by Arnold Pavlik in 194[5] were he published his experience in treating developmental dysplasia of the hip with his harness[6].

The principle of the Pavliks method is to bring the child's lower limbs to flexion in the hips and knees, using stirrups. It is well-known that neither child nor adult is able to keep the lower limbs adducted in flexion,this is non-physiological, the muscles become tired quickly and the limbs go into abduction, and this what the hip joint needs for the treatment of dysplasia.

In our country, we still have many cases with **DDH**, the literature documents that Pavlik Harness treatment of dislocated hips has a success rate 66-99%[7].

In this study we express our experience regarding the use of Pavlik Harness.

MATERIALS AND METHODS :

A retrospective review of the medical records of babies ≤ 6 months old at diagnosis with clinically and or by imaging confirmed to have **DDH** and was treated In paediatric orthopedic outpatient clinic, at Misurata Medical Centre during the the year 2016, using pavlik harness orthosis. No other methods were used as first-line treatment in this group of infants and the followup period was for at least 1 year after the beginning of treatment. Infants with hip dislocation secondary to neurological, myopathic, or connective tissue .

diseases were excluded, three other patients were excluded because of incomplete data .

All the patients had been treated by the same orthopaedic team, and the Ultrasound evaluations had been performed by three well trained radiologists.in the same hospital.

We looked at 40 infants of **DDH** affecting 50 hips, 30 girls (75%) and 10 boys (25%), 30 of them was unilateral **DDH** and 10 infantes was bilateral.Systematic clinical assessment of the hips was performed at birth for the babies whom was refereed from paediatrician in Misurata Medical Centre concerning **DDH** evaluation .A negative clinical examination and without risk factors, leads to the routine clinical follow-up at 6 weeks old, while in case of a positive risk factor (positive family history, breech delivery, oligohydramnios, and twins), clinical reevaluation plus US. assessment at 4–6 weeks old and final diagnosis was made.

In cases of positive clinical findings for hip instability, hips were splinted at this time and were controlled clinicaly every 1-2 weeks and with US follow-up at 4–6 weeks later. Treatment was only initiated in confirmed **DDH**. The US diagnosis of **DDH** was based on the Graf hip classification, which uses α and β angles, and our decisions to treat **DDH** with an abduction brace were based on both clinical evaluation and results of the US. The Pavlik harness had been used as a primary treatment, once the diagnosis was

established , the Pavlik harness orthosis was applied on the same day of diagnosis and follow up was on outpatient basis.

The pavlick harness orthosis was used as described by Arnold Pavlik[8]. Its adjusted and checked by one of our pediatric orthopedic team . Instructions were given to parents on how to take care of the pavlik harness orthosis and how to deal with the baby while it is applied. Clinical re-assessment for the baby & the pavlik harness orthosis position done one week later. By the end of the sixth weeks, clinical and US assessments of the hip position were done while maintaining the pavlik haress orthosis applied on the patien,if the hip is relocated by US assessment with a wide safty zone on clinical examination, Pavlik harness treatment will be continued untill acetabular index recovery. On the other hand, those who failed to do so after 6 weeks from first application., other modality of treatment need to be started.

Other data was obtained about each case, such as the age of the patient, sex, side of pathology, unilateral or bilateral dislocation, family history and other risk factors for developmental dysplasia of the hip. Data were analyzed using SPSS software version 13.

RESULTS :

This study was done for the cases following paediatric orthopedic outpatient unit seeking medical advice concerning **DDH** on 2016, whom was refereed from paediatrician in Misurata central hospital.

The data of the study include 40 cases (50 hips), 30 girls (75%) and 10 boys (25%) with girls/boys ratio (3/1). There is a significant predominance of cases among girls than boys.

Of the 40 cases, 30 was unilateral **DDH** and 10 cases was bilateral, the ratio between them is 3:1. 20 of 40 cases had left-hip involvement and 10 had right hip involvement and the other 10 had bilateral involvement.

The age at diagnosis ranged from one week to 24 weeks, with a mean age of 8 weeks. **DDH** was diagnosed before the age of 4 weeks in13 infants, (32.5%) and between the ages of 4 and 18 weeks in 21 infants (52.5%), and in 6 (15%) cases was dignosed ≥ 5 monthes.

Table 1 shows the distribution of risk factor in the 40 cases, there is no risk in 15 cases (37%) while positive family histoty is the most significant risk facter represented (25%).

Table 1: Show risk factor of case

No risk factor	15	(37%)
Breech presentation	5	(12.5%)
Postive family history	10	(25%)
Limitation of abdaction	2	(5%)
Positive Ortolani	5	(12.5%)
Twins	1	(2.5%)
Oligohydrmins	2	(5%)
Malformation	0	(0%)

The age at diagnosis ranged from one week to 24 weeks , with a mean age of 8 weeks. DDH was diagnosed before the age of 4 weeks in13 infants, (32.5%) and between the ages of 4 and 18 weeks in 21 infants (52.5%), and in 6 (15%) cases was dignosed ≥ 5 monthes. The treatment

was begun at the time of diagnosis. The mean age at brace introduction was 3.1 months (range from , one weeks old to 24 weeks old). The wearing time was full-time (23 h/day) during a mean 3.6-month period (range: 2 months to 5 months old), except for the five infants undergoing a secondary reduction. The brace was worn for a total mean period (first full-time, then part-time at night) of 5.3 months (range, 3 months to 8 months). This treatment had to be interrupted and replaced in 5 infants out of 40 infants. The highest success redaction rate was obtained in infants younger than age 4 months 27 of 34 infants, (79,4%) and the lowest one older than age 5 months 2 of 6 infants (33%). Ultrasound studies revealed spontaneous evolution towards normal bone coverage in 29 infants (72.5 %), while in 5 infants (12.5%) was failed redaction. In 6 infants (15%) ends with residual dysplasia, acetabular index more than 30 degree after the end of one year.

Figure 1 shows the distribution of cases according to the method described by Graf for the 30 cases of unilateral hips.
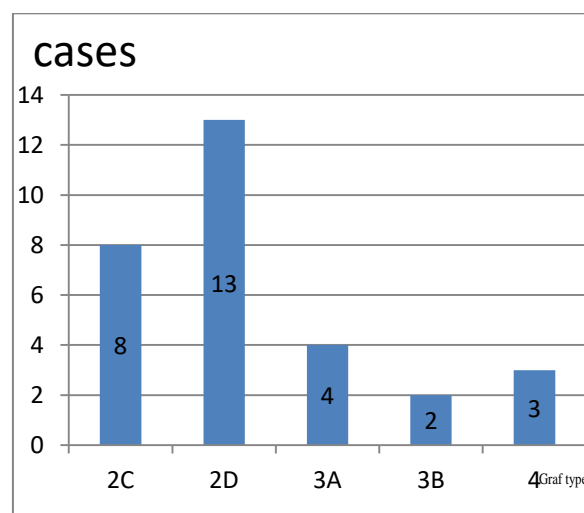
Figure 1: Distribution of cases according to the method described by Graf for

Table 2 shows distribution of cases according to the method described by *Graffor* for the 10 cases of bilateral hips.

Table 2: Shows distribution of cases according to the method described by Graf for

Graf type	RT	LT	No
2B	1	0	1
2C	3	2	5
2D	3	1	4
3A	2	4	6
3B	0	2	2
	4	11	2

Table 3 explain details of 30 cases of unilateral **DDH** including, side type of *Graf for*, failure of redaction (FR) and residual dysplasia at one year (RD), gender and AVN.

Table 3: Values of unilateral DDH cases

ID	GRAF	Side	R.D	FR	Sex	AVN
1	2C	RT	0	0	F	0
2	2C	LT	0	0	F	0
3	2C	LT	0	0	F	0
4	2C	LT	0	0	M	0
5	2C	RT	0	0	F	0
6	2C	LT	0	0	F	0
7	2C	LT	0	0	F	0
8	2C	LT	0	0	F	0
9	2D	RT	0	0	F	0
10	2D	LT	0	0	M	0
11	2D	LT	0	0	F	0
12	2D	RT	0	0	F	0
13	2D	LT	0	0	F	0
14	2D	LT	0	0	F	0
15	2D	LT	0	0	M	0
16	2D	RT	0	0	F	0
17	2D	LT	0	0	F	0
18	2D	RT	0	0	M	0
19	2D	LT	0	0	F	0
20	2D	LT	0	0	F	0
21	2D	RT	0	0	M	0
22	3A	LT	1	0	F	0
23	3A	LT	0	0	F	0
24	3A	RT	0	0	F	0
25	3B	LT	0	0	F	0
26	3B	LT	1	0	F	0
27	3B	RT	0	1	F	0
28	4	RT	0	1	M	0
29	4	LT	1	0	F	0
30	4	LT	0	1	M	0

Table 4, explain details of 10 cases of bilateral **DDH** including side,type of graf, failure of redaction and residual dysplasia , gender and AVN.

Table 4: Values of biilateral DDH cases

ID	G.R	G.L	R.R	R.L	F.R	Sex	AVN
1	2C	3A	0	0	0	F	0
2	2D	2D	0	0	0	F	0
3	3A	2C	1	0	0	M	0
4	4	3A	0	0	1	F	0
5	2B	3B	0	1	0	F	0
6	2C	3A	0	0	0	F	0
7	2D	4	0	0	1	M	0
8	2C	2C	0	0	0	F	0
9	3A	3B	0	1	0	F	0
10	2D	3A	0	0	0	M	0

Finally at the end of this study out of 40 cases, 5 cases failed redaction (12,5%), 3 of them was unilateral **DDH**, and 2 was bilateral **DDH**. Out of these 7 hips ,4 hips were Graf type 4.

In these cases static brace or a closed reduction and spica cast became the next treatment options.

Six cases end with residual dysplasia at the end of one year, acetabular index more than 30 degree, all of them were Graf type 3 and 4. And no case of AVN was documented at one year followup.

DISCUSSION:

Pavlik's harness is currently the favored device used to treat **DDH**.In literature, reduction rates obtained with this device range from 66% to 100% [7-9, 10, 11, 12].

In our study the brace was effective in Graf types 2 b,c and d, with a (100%) success ratio for unilateral dysplasia, while with type 3 dysplasia, this ratio dropped to (60 %), however, the redaction rate of the Graf type IV cases was low (30%), as for some other studys[13-14], while better results were also obtained with 50%[15] and 62%[16] of successful reduction rates. The second important outcome is the AVN rate after treatment. In literature, commonly reported AVN ratios are between 0% and 8%[12-13-17-18], while in our study was a 0% ratio of AVN. The ratio of residual dysplasia at 1-year old was (17.5%) incliding 6 infants. We had no reports of other complications like femoral nerve palsy or skin lesions. The identification of groups at risk for developmental dysplasia of the hip has been addressed in several studies[19]. In our study,family history of developmental dysplasia of the hip was not the most frequent risk factor, we observed that most frequently DDH was without risk factor, in agreement with a recent reviews, also future identification of susceptibility genes for developmental dysplasia of the hip might help improve the validity of methods and their effectiveness in guiding management decisions[20-23]. The strengths of this study include standardized and unchanged protocols for clinical and US screening and management throughout the study period, and a prospective collection of data. Well-trained physicians performed the clinical screening. as well as three experienced radiologists, performed all the US examinations using a combined US technique,as well as all the radiographic interpretations at ≥5 monthes.

CONCLUSION :

Dysplasia of the hip constitutes one of the major orthopedic disorders. over the last 20 years[24], ultrasonographic techniques has radically changed the prognosis of DDH . Ultrasonography is the only procedure capable of identifying dysplastic and unstable hips at an early age, thus allowing timely treatment[25,26].

On other hand in our community still we had high incidence of late diagnosis because of absence of national screening programme, as well as the family neglicance and poor education of family about DDH.

The normal development of the child's hip relies on congruent stability of the femoral head within the acetabulum, early diagnosis and treatment of DDH is critical to provide the best possible functional outcome.

The traditional risk factors for **DDH** were questioned and new ones were explored,and consequently we have a better understanding of the factors that are associated with this condition. In the future, genetic research may give us better

uderstanding on the molecular mechanisms that lead to this condition. there is still much clinical research to be done in order to convert all of our knowledge in to clinical practice. As early diagnosis and treatment is critical in order to achieve best functional outcome, there is much interest in the search for the best screening program. Despite best efforts many young adolescent with dysplasia are not detected at birth.

Although ultrasonography is the technique of choice for visualization of acetabular changes in children up to 4 months of age, also we recommend performing ultrasonographic screening to all newborns with risk factors at 4 to 6 Wk. of age.

Ultrasonography was established as the best imaging modality for screening and follow up of infants suspected for DDH up to the age when the proximal ossific nucleus appears, after that we perform radiographs to evalut ossified center of head of femur and to rule out other conditions.

The Pavlik harness still remains the main treatment for the younger infant ≤ 6 monthes, Patients that failed to achieve stable fixation with the Pavlik harness need either static brace or closed reduction and spica casting.

It is well noted that every strategy that aims to reduce developmental dysplasia should begin in post natal assessment with neonatologist for any child before discharge and by orthopedist assessment at4 to 6 weeks of age ,and orthopedist assessment for any child with risk factor especially positive family history and breech presentation as early as possible.

We there for acknowledge that good clinical education and well organized national clinical screening at birth performed by experienced doctors is essential for success and with this selective US strategy is needed.

RECOMMENDATIONS:

The condition should be an important health problem , National Screening Committee with National Screening Program should be established all over the country. Learning proper examination methods, with Dr's awareness and health education for our community regarding the condition is mandatory, with the aim of enhancing early diagnosis and treatment of the disorder and try to reduce incidence of adolescent hip dysplasia

REFERENCES :

1- von Kries R, Ihme N, Altenhofen L, Niethard FU, Krauspe R, et al. (2012)General ultrasound screening reduces the rate of first operative procedures for developmental dysplasia of the hip: a case-control study. Pediatr 160:271-27

2- Graf R (1980) The diagnosis of congenital hip-joint dislocation by the ultrasonic Combound treatment. Arch Orthop Trauma Surg 97: 117-133.

3-Aronsson DD, Goldberg MJ, Kling TF, Roy DR. Developmental Dysplasia of thehip. *Pediatrics* 1994; 94: 201-208 [PMID:8036074]

4-Vitale MGSkaggs DL. Developmental dysplasia of the hip from 401-411 [six months to four years of age. *J Am AcadOrthopSurg*2001; 9: PMID: 11730331]

5-.GuilleJT,Pizzutillo PD, MacEwen GD. Development dysplasia ofthe hip from birth to six months. *J Am AcadOrthopSurg*2000; 8:232-242 [PMID: 10951112

6-American Academy of Pediatric Clinical practice guideline:early detection of developmental dysplasia of the

hip. Committee on Quality Improvement, Subcommittee on Developmental Dysplasiaof the Hip. American Academy of Pediatrics. *Pediatrics* 2000; 105:896-905 [PMID: 10742345 DOI: 10.1542/peds.105.4.896]

7-Schwend.RMShaw BA, Segal LS. Evaluation and treatment ofdevelopmental hip dysplasia in the newborn and infant. *PediatrClinNorth Am* 2014; 61: 1095-1107 [PMID: 25439013 DOI: 10.1016/j.pcl.2014.08.008]

8-Luhmann SJ, Bassett GS, Gordon JE, et al. Reduction of a dislocation of the hip due to developmental dysplasia. Implications for the need for future surgery. J Bone Joint Surg Am 2003; 85-A:239.

9- K. Iwasaki, "Treatment of congenital dislocation of the hip by the Pavlik harness. Mechanism of reduction and usage," The Journal of Bone and Joint Surgery—American Volume, vol. 65,no. 6, pp. 760–767, 1983.

10- D. Atar, W. B. Lehman, Y. Tenenbaum, and A. D. Grant, "Pavlik harness versus Frejka splint in treatment of developmental dysplasia of the hip: Bicenter Study," Journal of Pediatric Orthopaedics, vol. 13, no. 3, pp. 311–313, 1993.

11- V. Bialik, "Pavlik's method in developmental dysplasia of thehip," Acta Orthopaedica et Traumatologica Turcica, vol. 41‹supplement 1, pp. 19–24, 2007.

12- JonesDA,Hip screening in the Newborn ,A Practical Guide. Pub Butterworth and Heinemann 1998 .ISBN 0-7506-2764-5NHS Newborn and Infant Physical examination Programme updated 25/11/2010.

13- Mulcahy H, Day MR, Coleman C, O'Dwyer P, Leahy-Warren P (2016)Developmental Dysplasia of the Hip: A Case Study to Illustrate Public HealthNursing practice. Adv Practice Nurs 2:106. doi:10.4172/apn.100010 .

14- H. Malkawi, "Sonographic monitoring of the treatment of developmental disturbances of the hip by the Pavlik harness," *Journal of Pediatric Orthopaedics Part B*, vol. 7, no. 2, pp. 144–149, 1998.

15- K. Iwasaki, "Treatment of congenital dislocation of the hip by the Pavlik harness. Mechanism of reduction and usage," *TheJournal of Bone and Joint Surgery—American Volume*, vol. 65, no. 6, pp. 760–767, 1983.

16- D.Atar, W. B. Lehman,Y. Tenenbaum, and A. D. Grant, "Pavlik harness versus Frejka splint in treatment of developmental dysplasia of the hip: Bicenter Study," *Journal of PediatricOrthopaedics*, vol. 13, no. 3, pp. 311–313, 1993.

17- V. Bialik, "Pavlik's method in developmental dysplasia of the hip," *ActaOrthopaedica et Traumatologica Turcica*, vol. 41, supplement 1, pp. 19–24, 2007.

18- H. Atalar, U. Sayli, O. Y. Yavuz, I. Uras¸, and H. Dogruel, "Indicators of successful use of the Pavlik harness in infants with developmental dysplasia of the hip," *International Orthopaedics*,vol. 31, no. 2, pp. 145–150, 2007.

19- ShipmanSA, Helfand M, Moyer VA, Yawn BP. Screening for developmental dysplasia of the hip: a systematic literature review for the US Preventive Services Task Force. *Pediatrics* 2006; 117:e557-e576 [PMID: 16510634 DOI: 10.1542/peds.2005-1597] .

20- MahanST, Katz JN, Kim YJ. To screen or not to screen? Adecision analysis of the utility of screening for developmental dysplasia of the hip. *J Bone Joint Surg Am* 2009; 91: 1705-1719.

21- Neonatal&Gynaecology Community of PracticeEndorsedby: South Australian Maternal Neonatal ,Hip Screening and Management of Developmental

Dysplasia of the Hip Flowchart ISBNnumber: 978-1-74243-844-3 Community of Practice LastRevised: 20/6/2017

22- E. Peled, V. Bialik, A. Katzman,M. Eidelman, and D. Norman, "Treatment of Graf 's ultrasound class III and IV hips using Pavlik's method," *Clinical Orthopaedics and Related Research*, vol. 466, no. 4, pp. 825–829, 2013

23- M. Eidelman, A. Katzman, S. Freiman, E. Peled, and V. Bialik, "Treatment of true developmental dysplasia of the hip using Pavlik's method," *Journal of Pediatric Orthopaedics Part B*, vol. 12, no. 4, pp. 253–258, 2012.

24- S. Suzuki, N. Kashiwagi, Y. Kasahara, Y. Seto, and T. Futami,"Avascular necrosis and the Pavlik harness. The incidence of avascular necrosisin three types of congenital dislocation of the hip as classified by ultrasound," *The Journal of Bone and JointSurgery—British Volume*, vol. 78, no. 4, pp. 631–635, 1996.

 25- A. K. Mostert, N. J. A. Tulp, and R. M. Castelein, "Results of Pavlik harness treatment for neonatal hip dislocation as related to Graf 's sonographic classification," *Journal of PediatricOrthopaedics*, vol. 20, no. 3, pp. 306–310, 2000.

26- PavelKotlarsky, Reuben Haber, Victor Bialik, Mark Eidelman developmental dysplasia of hip what has changed in the last 20 years *World J Orthop*2015 December, pp 886-901.

CLINICAL SPECTRUM AND EPIDEMIOLOGICAL PROFILE OF PATIENTS ADMITTED TO PAEDIATRIC INTENSIVE CARE UNIT AT MISURATA MEDICAL CENTRE

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ABSTRACT:
The knowledge of clinical spectrum and epidemiological profile of critically ill children plays a significant role in providing essential health care. The data collected enable prospective comparisons to be made with measure standards to improve the quality of patient care. The aim of this study is to clarify the clinical spectrum and epidemiological profile of the critically ill children admitted to the paediatric intensive care unit at a Misurata Medical centre. Descriptive data were collected prospectively from the **PICU** admissions over 2-years between January 2017 and December 2018. A total of 452 patients were analysed during the 2-year period, of which 257 (56.9%) were males and 195 (43.1%) were females. The majority of patients are below one year of age 252 (55.9%), mean duration of stay in **PICU** was 6.3 ± 5.1 days. Respiratory system was the leading systemic cause for both admission and death 166 (36.7 %). mortality rate was 41.1 %, with no association with sex but it was highest in infants below 1-year of age (63.4%). This study analyses the epidemiological pattern and clinical spectrum of patients admitted to **PICU** in Misurata Medical Centre, which showed slightly different characteristics as those reported in different relevant studies specially regarding mortality rate. This can serve as the basis for developing dedicated effort to improve the outcome and quality of care for critical illnesses.

KEY WORDS: Epidemiology, Infant, Intensive care units, Patient admission, Paediatrics, Comorbidity.

INTRODUCTION:
The care of critically ill children remains the most demanding and significant aspect in the field of paediatrics. Optimum care in the paediatric critical care unit depends on the level of training and expertise of the health-care personnel, the availability of the resources, and evidence based management protocols. The principal objective of paediatric critical care is not only to decrease the mortality but also to restore the child who is suffering from a life threatening condition to health with a minimum pain, anxiety, and complications and to provide comfort and guidance to the child's family[1]. It is well documented that the reduction in childhood morbidity and mortality was a key factor for the change in the age distribution of mortality and the increase of life expectancy experienced in the developed world during the 20th century, as life expectancy is particularly sensitive to mortality reductions at younger ages[2].

Since, about 5.9 million children under age five died in 2015[3] i.e., 16,000 every day, these are the figures given by global health observatory data, WHO. Providing basic paediatric intensive care services such as intravenous access and fluid resuscitation, basic antibiotic support, oxygen and invasive and non-invasive ventilator support, one can save the lives of million children every year. These interventions are low cost and easy to implement in developing countries on a large scale to decrease mortality. So, the knowledge of clinical spectrum and epidemiological profile of critically ill children plays a significant role in the planning of health policies that would alleviate various factors related to the evolution of most of the prevalent diseases and identifies the most vulnerable population subgroups.

The first objective of this study was to report the clinical spectrum, epidemiological profile, and outcomes of critically ill children admitted to a paediatric intensive care unit at a Misurata Medical Centre. And the second objective is to assess the mortality rate which depends on many factors such as demographics, clinical and management characteristic, admission practice, and well-equipped and well-staffed intensive care units

MATERIALS AND METHODS:
This descriptive study reviewed the admissions to **PICU** at Misurata Medical Centre from January 2017 to December 2018 (2 years period). The hospital operates 8 beds, which admits paediatric patients ≤14 years of age, from both medical and sometimes post-surgical patients who are critically ill and need care other than that available in the general wards.

Data collection:
The following data was collected Prospectively:
1-Demographic characteristics: age, sex, and admission date, residence, admission sources.
2-Clinical characteristics: length of stay (LOS), final diagnosis, the Paediatric Risk of Mortality PRISM III (12) during the initial 12 hours of admission, and Comorbidity.
3-Treatment characteristics; the need for mechanical ventilation (MV) and MV days, vasoactive drugs, Invasive procedures (Chest tube, Central venous line, CRRT, Bronchoscopy)
4-The outcome: which is classified as transfers to other tertiary hospitals for further care, discharges to general paediatric ward (Operating capacity taken in consideration), discharge home, discharges against medical advice and death. For age analysis, we adopted the following stratification: < 1 month, > 1 month – 1years, >1 - 5 years, > 5 -10 years, and >10 - 14 years. patients excluded from the study were, those who died on arrival (within 2 hours of admission); this is not

sufficient time to give optimal care in the ICU, and because the outcome of these patients is related to the emergency care.

Data analyses:
The SPSS Statistics (version 18) was used. Results were expressed as the means with ranges. Categorical data were tested using Fisher's exact test, and continuous data were tested using the t-test. P < 0.05 were considered significant.

RESULTS:
Our PICU consists of 8 beds, A total of 452 patients were analysed during the 2-year period, of which 257 (56.9%) were males and 195 (43.1%) were females, giving a male: female ratio of 1.3 : 1. Of the total patients admitted 253(55.9%) were infants, patients aged > 1-5 years were 100 (22.1%), age group of > 5-10 years constituted 55 (12.1%), and patients aged > 10 years to ≤14 years were 44 (9.7%). Figure 1 elaborates the sex and age wise distribution of cases admitted in PICU.
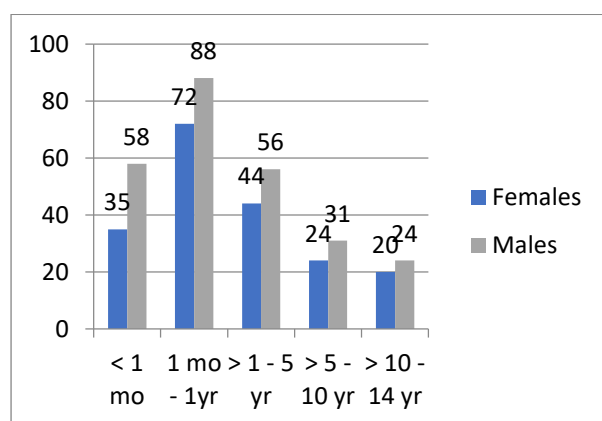

F*igure 1: Sex and age wise distribution of the study group.*

The mean duration of stay in **PICU** was 6.3 ± 5.1 days ranging from 1 to 28 days, The majority of the patients (71.5%) were admitted for 1 – 7 days. Regarding the relationship between the different age groups and the LOS, majority of those who stayed 1 - 7 days or > 14 days were aged below 1year (Table 1).

Table 1: Length of stay of the study groups.

Length of Stay days	Age / years				
	< 1 /12	1/12 – 1	>1 – 5	>5 – 10	> 10 – 14
1 – 7	64	102	76	34	323
7 – 14	24	33	15	7	84
> 14	10	23	7	2	45
Total	98	158	98	43	452

With regard to patient origin, most admissions 291 (64.3%) were referred by the general paediatric ward, 116 (25.8%) directly from emergency room, and 45 (9.9%) from other private and distant hospitals, as our hospital is the only regional reference hospital. Respiratory system was the most common system affected 166 (36.7 %), Pneumonia, acute

bronchiolitis, hyperactive airway disease (57.8%, 31.9%, 5.4% respectively) were the three most common respiratory causes for hospitalization. The second major system involved was central nervous system (CNS) 59 (13%), Intractable seizure (Febrile seizure, seizure disorder) constituted most of the CNS cases 27 (13.7%). Cardiac causes 8.5%, diabetic ketoacidosis 5.5%, Trauma-related or post-surgical cases (for postoperative care) constitute a small proportion 3.5% of all admissions, which mostly neurosurgical. Acute poisoning constituted 3.3% of all admissions, It mainly consisted of accidental drug ingestion, and the other causes are listed in (Table 2).

Highest PICU admissions was during winter and early spring months 51% (December- April), with the peak in January (15%), reflecting the possibility of respiratory infection predominance (Figure 2).
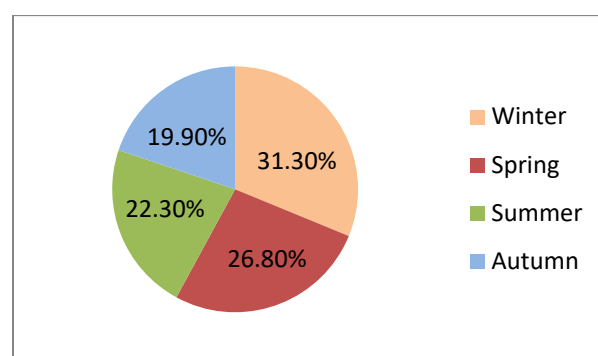
Figure 2: Seasonal Distribution of admissions of critically ill patients.

Approximately 66 (14%) patients exhibit comorbidities, mostly due to congenital heart disease. Apart from neurological cases were admitted commonly because of deteriorating GCS or GCS initially was less than 8, hypoxia and severe respiratory distress were the two common indications of ICU admission. Regarding the clinical outcome, 241 (53.4 %) patients improved and discharge either to home 19 (4.2%) or to paediatric general ward 211 (46.8%), of whom 10 was discharged due to operating capacity, 4 of which are readmitted again. Eleven (2.4%) were transferred to other tertiary paediatric hospitals for further specialized care after clinically improved; 25 (5.5 %) left against medical advice; and 186 (41.1 %) patients died; with no association to sex, but it was highest in infants (50%), and all patients who presented post- Cardiopulmonary arrest, and patients with PRISM III (12) > 25 were died. About 332 patients (73. 5%) were from Misurata, and 120 (26.5%) from outside, 66 of them were died, which constitutes 35.5% of all mortality. Table 3 elaborate the number of mortality in various age groups and sex.

Table 3: Sex and age wise distribution of the deceased cases

Sex	< 1/12	1 month – 1year	>1 – 5 years	>5 – 10 years	> 10 – 14 years
F	20	39	17	8	7
M	26	31	21	12	5
Total	46	70	38	20	12

Table 2: System wise distribution of the patients admitted in PICU.

System		Frequency	%
Respiratory 166	Acute bronchiolitis	53	37.5
	Asthma	9	
	Viral croup	3	
	Pneumonia	96	
	Pertussis	4	
	Acute sinusitis	2	
	Congenital lobar emphysema	1	
	Foreign Body Aspiration	6	
Cardiac 39	Cyanotic CHD	11	8.6%
	CHD, HF	22	
	Atrial myxoma, HF	1	
	Arrhythmia (SVT /Complete heart block)	2	
	Myocarditis / DCM	3	
CNS 59	Bacterial Meningitis	5	13%
	Encephalitis	12	
	Encephalopathy	8	
	Meningococcemia	2	
	Intractable convulsion	27	
	Gillian Barre syndrome	5	
Endocrine 25	DKA	23	5.5%
	Panhypopituitrism	2	
GIT / Liver 23	AGE, sever dehydration	12	5%
	Bacterial GE, HUS	3	
	Intractable diarrhoea and Shock.	2	
	UGIT Bleeding	1	
	Fulminant hepatic failure	5	
Renal, Genitourinary 15	AKI	6	3.3%
	Emergency hypertention	5	
	Proximal RTA, Shock state	2	
	PUJ obstruction, nephrostomy, Sepsis	1	
	Perinephric Abscess, MOF	1	
Poisonig 14	Accidental drug ingestion	10	3.1%
	Suicidal attempt	1	
	Scorpion bite	3	
Surgery (postoperative care) 13	Meningomyelocele repair, VP shunt	8	2.8%
	Obstructed inguinal hernia	2	
	Diaphragmatic hernia	1	
	Omphalocele repair (BWS)	1	
	Malrotation	1	
Cardiopulmonary Arrest (CPA)		10	2.5%
Septic Shock, Sepsis:		30	6.7%
Neonates (for further Care)		30	6.7%
Miscellaneous		9	2.8%
Malignancy		4	2.8%
Post- Trauma		3	2.8%
Others		6	2.8%
IEM		15	3.3%

Regarding the treatment characteristics, 286 patients (63.3%) received mechanical ventilation (either Invasive 53.9% or Non-Invasive 9.4%), and 229 (50.6%) received vasoactive drugs. Central Venous line done for 110 patients (24.3%), Chest tube for 6 patients with complicated pneumonia and CRRT for 5 patient with AKI, Bronchoscopy was done for all patient with suspected or witnessed Foreign body Aspiration. Epidemiological Profile, clinical and treatment characteristics of patients are summarized in Table 4.

Table 4: Epidemiological Profile, clinical and treatment characteristics of critically ill Patients.

Parameter	No.	%
Sex		
Females	195	43.1%
Males	257	56.9%
Residence:		
Inside Misurata	332	73.5%
Outside Misurata	120	26.6%
Source of admission:		
Emergency	11	25.8%
General paediatric ward	291	64.3%
Other hospital	45	9.9%
Length of stay:		
1– 7 days	323	71.5
>7 – 14 days	84	18.6
>14 day	45	9.9
Outcome:		
Discharge home	19	4.2%
Discharge to general ward	211	46.8%
LAMA	25	5.5%
Died	186	41.1%
Transfer to other hospital	11	2.4%
Treatment Characteristics:		
Mechanical Ventilator support	286	63.2%
Vasoactive Drugs	229	50.6%
Chest tube drainage	110	24.3%
Central venous line	6	1.3%
CRRT	5	1.1%
Bronchoscopy	6	1.3%
Comorbidity:		
Congenital Heart Disease.	13	40%
Down Syndrome, CHD.	12	18.2%
Cerebral Palsy	9	13.6%
Brain Degenerative Disease/IEM	14	10.6%
IDDM.	7	10.6
Others	11	16.6%

DISCUSSION:
The **PICU** is a special unit primarily concerned with the care of patients with critical illness and demands a broad based knowledge to cater for all aspects of management of these patients to achieve good outcome. The main purpose of PICU is to prevent mortality, restoring health and minimizing pain and suffering by intensively monitoring and treating critically ill children who are considered at high risk of mortality. This study addressed these issues and revealed that Children less than 1-year of age were the most vulnerable group who presented to the PICU 253 (55.9%), this was similar to that reported by El Halal MG et al[4], and a study conducted by Abhulimhen-Iyoha BI et al[5] revealed that 50.7% constituted

infants which is comparable to this study and also similar to that published in journal of college of physicians and surgeons Pakistan by Haque A et al[6], most children (62.5%) were under 5 years of age.

In our study, males constituted 56.9% of admission (257), and male: female ratio was 1.3: 1, it was similar to that reported by Batista et al[7]. (56%) and Einloft et al[8]. (58%), and to a study published by Haque A et al[6], also found that majority (60.9%) of patients were males. Another study from Nepal by Shah GS et al[9] found the male to female ratio to be 1.7:1. In this study, the mean length of stay in **PICU** was found to be 6.3 ± 5.1 days, similar finding to a study conducted in Brazil by Batista et al[7]. LOS in **PICU** was 6.9 ± 5.5 days. Some patients remained in the unit for as long as 28 days either because they required critical care for the period or for logistic reasons in which case there may be no step-down ICU to enable their transfer, this resulted in full recovery of some patients in PICU necessitating discharge home directly from the ICU amounting to an improper use of the ICU, and also, The absence of a high-dependency unit at our centre led to the admission of some patients who were not ill enough to require ICU admission into PICU. The aforementioned situations need to be checked to enhance cost–effective management of patients and avoid unnecessary stretch of the ICU facilities.

Respiratory and neurological diseases were the major causes of admission to the PICU in Misurata Medical Centre. It was similar to that reported by Draper et al[10], Shah GS et al[9] studies. But contradictory to the AIIMS Delhi study where septicaemia was the commonest diagnosis, and that reported by Abhulimhen-Iyoha et al[5], in which cardiovascular disease entity constitutes the most common (41.1%) cause of admission. This shows that paediatric intensive care admissions vary in different countries and one should be aware of the prevalent conditions to develop the facilities and prepare treatment protocols accordingly. Highest **PICU** admissions was during winter and early spring months 51% (December- April), with the peak in January (15%), reflecting the possibility of respiratory infection predominance, similar findings were reported by Rady HI[11].

Approximately 66 (14%) patients exhibit comorbidities, mostly due to congenital heart disease, cerebral palsy and Neurometabolic disorders, which is contributed to the high mortality in our study, findings similar to that reported in Japan by Ishihara T et al[12]. Apart from neurological cases were admitted commonly because of deteriorating GCS or GCS initially was less than 8, Hypoxia and severe respiratory distress was the two common indications of ICU admission. Regarding the clinical outcome, 241 (53.4 %) patients improved and discharge either to home 19 (4.2%) patients or to paediatric general ward 211(46.8%) patients, of whom 10 was discharged due to operating capacity, 4 of them are readmitted again. Eleven (2.4%) were transferred to other tertiary paediatric hospitals for further specialized care after clinically improved, 25 (5.5 %) left against medical advice, and 186 (41.1 %) patients died; with no association to sex, but it was highest in infants (50%), and all patients who presented with post-arrest died. About 332 patients (73. 5%) were from Misurata, and 120 (26.5%) from outside, 66 of them were died, which constitutes 35.5% of all mortality, It is considered as Significant numbers as critically ill children

need to be transferred between hospitals supported by a well-organized transfer system that guarantees the safety of the patient. Regarding the treatment characteristics, the majority of our patients 286 (63.3%) received mechanical ventilation (either Invasive 53.9% or Non-Invasive 9.4%), and 229 (50.6%) received vasoactive drugs. Central Venous line done for 110 (24.3%), Chest tube for 6 patients with complicated pneumonia and CRRT for 5 patient with AKI, Bronchoscopy was done for all patient with suspected or witnessed Foreign Body Aspiration.

The observed mortality rate in our study was high (41. 1%), this observation was similar to that reported by Abebe et al[13]. (40%) and higher in contrast to Batista et al[7]. (15.6%), Halal MG et al[4] (10.3%), and more higher than that reported from Abhulimhen-Iyoha BI et al[5], found that mortality in their centre was as low as 2.1%. Also, we found that the mortality was the highest below 1-year of age (50%) and it was similar to that reported by Rady H et al[12] (43.9%) and Batista et al[7]. These findings with the observed mortality necessitates provision of Important factors that may have contributed to higher mortality in our patients includes our fragile components of the health care system; inadequate transportation of critically ill patients, lack of resources and insufficient number of well trained and qualified nurses, also need to be overemphasized.

The severity of illness using tools like the Paediatric Risk of Mortality (PRISM) and the Paediatric Index of Mortality (PIM), found to be important independent predictors of mortality in many studies[5,6].

Each patient has to be examined and investigated to get the four Subscores as below:

-Vital signs has 5 measures: Systolic blood pressure, HR, GCS, Temperature, Pupillary response.

-Acid-base and blood gas has 5 measures: Acidic or Alkaline pH, PCO_2, Total CO_2, PaO_2.

-Biochemical tests have 4 measures: Plasma Glucose, Potassium, Creatinine, Blood urea nitrogen.

-Haematology tests have 3 measures: white blood cell count, platelet count, PTT.

After assessment of child and details of various investigations we have to give score as per age of patient for various variables and sum up all sub scores to get final score for PRISM III of that child within 12 hour of admission. total score: 0 - 74, The higher the total score, the worse the prognosis.

In table 5 we have correlated PRISM III score at the end of 12 hours with the outcome in our patients as mortality rate. It was applied only on 142 patients and was not completed as a part of the medical records of remainders of our PICU admissions. We have made few groups of total PRISM III score such as 6-10, 11-15, 16-20, 21-25, 26-30, 31-35, 36-40 and 40 above. In first group of PRISM III score" 6-10" there were 55 patients, 25 patients of them were died gives 45.4% mortality. In the next group of "11-15", there were 28 patients with 10 deaths, 35.7% mortality. In the group of "16-20" there were 15 patient and 12 of them died, 80% was the mortality. In group of "21-25" patients were 16 and mortality was 15 (94%). All patients were in groups of "26-30", "31-35", "36-40" all were died and observed mortality was 100%. In the last group with PRISM III score "41 and above", there were 0 patients. This suggests that with increasing PRISM III

score there is increase in mortality and indicates that, overall performance of the PRISM III score is good and needs application regularly with more search to show reasonable agreement between observed and expected mortality.

Table 5: PRISM III and the Outcome

PRISM III	Outcome			Mortality rate
	Died	Alive	Total	
6 - 10	25	30	55	45.4%
11 - 15	10	18	28	36.7%
16 - 20	12	3	15	80%
21 - 25	15	1	16	94%
26 - 30	6	0	6	100%
31 - 35	10	0	10	100%
36 – 40	12	0	12	100%
Above 40	0	0	0	0

The ability to assess patient risk of death is very important since such estimate would be beneficial in realizing many different goals such as assessing patient's prognosis, ICU performance, and ICU resource utilization, and also evaluating therapies, controlling, and matching severity of illness in clinical studies[7]. Quantitative clinical scoring systems have been developed to overcome the lack of consistency, reliability, and accuracy in physician's subjective opinions concerning patient status as well as in response to increasing emphasis on the evaluation and monitoring of health services as recent studies for countries that achieved the MDG-4 targets (Millennium Development Goal 4 that called for a reduction of under-5 mortality rates by two-thirds between 1990 and 2015) revealed important insights in to the determinants of change, coverage, intervention, and implementation of policies that have succeeded in specific contexts[3].

CONCLUSION:

This study analyses the epidemiological pattern and the clinical spectrum of patients admitted to **PICU** in Misurata Medical Centre which showed slightly different characteristics as those reported in different relevant studies specially regarding mortality rate. This can serve as the basis for developing dedicated and new protocols for the caregivers in an effort to improve the outcome of critical illness and stresses on the need for a step-down unit and redistribution of resources to cater for the needs of patients not ill enough to require ICU admission. This not only reduces the burden on the intensive care personnel but also increasing needed intensive care and invasive monitoring of critically ill patients in lack of optimum resources and insufficient number of well trained nurses which in turn significantly reduces the mortality.

REFERENCES:

1- Earan SK, Dhandapani L, Arunagirinathan A, Kantamneni S. Clinical Spectrum and Epidemiological Profile of Patients Admitted to Pediatric Intensive Care Unit at a Tertiary Care Centre in South India. Int J Sci Stud 2016;4(3):187-191.

2- You D, Hug L, Ejdemyr S, Idele P, Hogan D, Mathers C, et al. Global, regional, and national levels and trends in under-5 mortality between 1990 and 2015, with scenario-based projections to 2030: A systematic analysis by the UN Inter-agency Group for Child Mortality Estimation. Lancet 2015;386: 2275-86.

3- Mejia-GuevaraI, Zuo W, Bendavid E,Li N, Tuljapurkar S (2019) Age distribution, trends, and forecasts of under-5 mortality in 31 sub-Saharan African countries: A modeling study. PLoS Med 16 (3): e1002757. https: //doi.org/10.1371/ journal. pmed.1002757.

4- El Halal MG, Barbieri E, Mombelli Filho R, de Andrade Trotta E, Carvalho PR. Admission source and mortality in a pediatric intensive care unit. Ind J Crit Care Med. 2012 Apr;16(2):81-86.

5- Abhulimhen-Iyoha BI, Pooboni SK, Vuppali NK. Morbidity pattern and outcome of patients admitted into a pediatric intensive care unit in India. Indian J Clin Med 2014; 5:1.

6- Haque et al. Clinical profile and outcome in a paediatric intensive care unit in Pakistan. J Coll Physicians Surg Pak. 2009 Aug;19(8):534-35.

7- Batista NO, de Rezende Coelho MC, Trugilho SM, Pinasco GC, de Sousa Santos EF, Ramos-Silva V. Clinical-epidemiological profile of hospitalised patients in paediatric intensive care unit. J Hum Growth Dev 2015;25 :187-93.

8- Einloft PR, Garcia PC, Piva JP, Bruno F, Kipper DJ, Fiori RM. Epidemiological profile of sixteen years in a pediatric intensive care unit. Rev Public Health 2002; 36:728-33.

9- Shah GS, Shah BK, Thapa A, Shah L, OP M. Admission patterns and outcome in a paediatric intensive care unit in Nepal. Br J Med Res. 2014;4(30):4939-45.

10- Draper E, Fleming T, McKinney P, Parslow R, Thiru K, Willshaw A. National Report of the Paediatric Intensive Care Audit Network: January 2004-December 2006. Universities of Leeds and Leicester; 2007.

11- Rady HI. Profile of patients admitted to paediatric intensive care unit, Cairo University Hospital: 1-year study. Ain-Shams J Anaesthesiol 2014;7 :500.

12- Ishihara T, Tanaka H. Causes of death in critically ill paediatric patients in Japan: a retrospective multicentre cohort study. BMJ Paediatrics Open 2019;3: e000499.

13- Abebe T, Girmay M. The epidemiological profile of pediatric patients admitted to the general intensive care unit in an ethiopian university hospital. Int J Gen Med 2015;8 :63.

Effects of Immunotherapy Protocols on some Laboratory Parameters
in Libyan Renal Transplant Recipients

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ABSTRACT:
The availability of more potent immunosuppressive drugs has reduced the risk of acute rejection, and although it has increased the risk of adverse reactions as kidney dysfunction, and blood disorders. This study aimed to analyze the impact of immunotherapy on four laboratory parameters among transplanted patients visiting the outpatients department of Organ Transplant Centre, Tripoli-Libya. This cross-sectional and cohort study that conducted from January - June 2014 and included 117 renal transplant recipients. The results of this work showed the mean age of the patients was 41±14 years. The immunotherapy had significant effect on **TWBC** and serum urea but had no significant impact on serum creatinine and hemoglobin. We conclude significant effects of immunotherapy protocols should be considered during routine outpatient follow-up for patients.

KEY WORDS: Libyan renal transplant recipients, immunosuppressive protocols, laboratory parameters.

INTRODUCTION:

Renal transplantation is the preferred method for treating patients with end stage renal disease[1-3]. Furthermore, the quality of life and survival rates following organ transplantation have greatly improved due to advances in surgical technique, immunosuppressive therapy, and medical management. However, complications such as infection and allograft rejection, which are related to immunosuppressive therapy, remain major causes of morbidity and mortality following solid organ transplantation. Therefore, dose, duration, and temporal sequence in which immunosuppressive medications are administered must be considered[4]. Earlier drugs were non selective, and patients frequently succumbed to infection due to suppression of both the antibody mediated and cell mediated arms of immune system. Today, the principle approach to immunosuppressive therapy is to alter lymphocyte function using drugs, or antibodies against immune proteins[5]. Because of their sever toxicities when used as monotherapy, a combination of immunosuppressive agents, usually is employed at lower doses[6,7]. Their types as following: Firstly, antimetabolites which include azathioprine which is considered the cornerstone of immunosuppressive therapy during the last several decades. It inhibit DNA synthesis and block the growth of T cell; mycophenolate mofetil is used instead of azathioprine because of the latter ̓s safety and efficacy in prolonging graft survival with relatively few toxic side effects. It has been successfully used in combination with cyclosporine to prevent acute rejection[8]. Secondly, cytokine inhibitors which include cyclosporine that decrease interleukin 2 which is the primary stimulus for increasing the number of T cells and block calcineurine. Although cyclosporine can be used alone, it is more effective when glucocorticoids are also administered[9,10]; sirolimus (Rapamycin)®: It is equipotent to cyclosporine to be used with glucocorticoids and cyclosporine, thereby allowing lower doses of these drugs to be used and thus lowering their toxicities.

sirolimus or the related drug is generally not used in the early post transplant period[9,10]; tacrolimus (FK 506®): It is a macrolid that block calcineurine and inhibits IL2 synthesis. This drug has found favor over cyclosporine, not only because of its potency but because lower dose of glucocorticoids can be used[9]. Thirdly, antibodies which include antithymocyte globulin (ATG): They are polyclonal antibodies, employed together with other immunosuppressive agent to treat the hyperacute of allograft rejection by destruction of T- cells[9,11]; Anti-CD25 (Basiliximab): it has been approved for prophylaxis of acute rejection by block IL2 receptor. They are used with cyclosporine and corticosteroids[12];anti-CD3 (Orthoclone OKT3): monoclonal antibodies are used for treatment of acute rejection of renal transplant by destruction of T cells[9,11]. Finally, adrenocorticoids which include: methyl prednisolone, prednisolone and prednisone are used with other immunosuppressive agents in maintenance of allograft[13]. However, in the immediate post transplant period with its attendant risk of acute rejection, a combination of three drugs is used for immunosuppression: a cyclosporine or tacrolimus plus an antilmetabolite plus a corticosteroid[14,15]. Anyhow, the availability of more potent immunosuppressive drugs has reduced the risk of acute rejection, but increased the risk of drug related adverse effects including: Firstly, infections: infections occurring after transplantation are most common during the first few months, when levels of immunosuppression are at their highest, and may be life threatening in patients who are already critically ill prior to transplantation[16]. Therefore, antimicrobial therapy is routinely given during the first few months after transplantation[17]. Although, infections continue to be a bugbear though the pattern of infections has changed over the years[18]. Secondly, malignancy: immunosuppression is associated with an increase risk of malignancy, because T-cell suppression results in failure to control viral infections. In this regard, virus associated tumours include lymphoma (associated with EBV), Kaposi sarcoma (associated with HHV8) and skin tumours (associated with human

papilloma virus)[19]. Thirdly, cardiovascular disease and diabetes where corticosteroids and calcineurine blockers increase blood pressure, while sirolimus and everolimus contribute to hypercholesterolemia; and tacrolimus is associated with diabetes[20-22]. Lastly, Hematological disorders involve: leukopenia is associated with mycophenolate mofetil, tacrolimus, sirolimus, everolimus, and azathioprine[23], leukocytosis is demargination of leukocytes by corticosteroids[24], and iron deficiency anemia is common after renal transplantation, and decreased it is a more important cause of allograft dysfunction, particularly when the Serum creatinine level rises above 2 mg/dL, and erythropoietin production decrease. Although sirolimus, azathioprine, and mycophenolate mofetil had significantly higher incidences of anemia due to their ability to cause bone marrow suppression[25].

OBJECTIVE:
The objective of this study is to analyze the impact of immunosuppressive regimen on serum creatinine and urea, hemoglobin, and white blood cells.

METHODOLOGY:
Study Design: This study is a cross-sectional and cohort that conducted on 117 patients who underwent kidney transplantation between January –June 2014 at the Organ Transplant Center, Tripoli Central Hospital (TCH). Complete blood count (CBC) analysis, and Renal function test (RFT) were performed for all recipients.
Methods: RFT was measured from a morning blood sample using an automatic analyzer (Cobas integra 400 plus, Roche, Basel, Switzerland) to measure serum creatinine, and urea. In analytical unit precise temperature controlled reaction rotor ensure stable test conditions and reliable result[26]. Graft dysfunction was defined as more than 20% rise in the Serum creatinine[27,28]. CBC was measured by an automated hematology analyzer counter (Sysmex, Kobe, Japan) and hemoglobin analysis was also performed by using high-performance liquid chromatography (HPLC). It uses fluorescent flow cytometry and cell counting method to reliably detect abnormal samples and reduce false positive results[29,30]. Reading of at least three replicates were collected for each factor during the time of study.
Analysis: All data were collected then analyzed by Statistical Package for Social Sciences (SPSS) version 20 using Pearson correlation, one way Anova, and post hoc test (Brown-Forsythe and Welch).

RESULTS AND DISCUSSION:
A total of 117 renal transplant recipients, attending the nephrology outpatient clinic at TCH during the period from January to June 2014 who satisfied the inclusion criteria, were studied. Seventy three (62.4%) were males and 44 (37.6%) were females, their ages ranged between 9 and 76 years with a mean age of 41±14 years. It was the first transplant for 116 patients while 1 patient had a second transplant. The immunosuppressive regimen was triple in 86 patients (74%) and double in 31 patients (26%). Patients were categorized as shown in (Table 1).
To the best of our knowledge, this is the first study in Libya to analyze the significance of some laboratory parameters associated with immunotherapy receiving by renal transplant recipients. To address the correlation of Hb with

Serum creatinine, serum urea, and **TWBC**, we used the Pearson correlation analysis as shown in (Table 2). The analysis revealed significant negative correlation between Hb concentration and Serum creatinine ($P = 0.011$), serum urea ($P = 0.000$), and WBC count ($P= 0.030$) among RTRs, as shown in Table 2.

Table 1: Demographic Characteristics of Renal Transplant Recipient.

Parameters			No	%
Mean age ± Stranded deviation			41± 14	
Sex	Male		73	62
	Female		44	38
Immuno-suppressive regimens	Double	FK+MMF	17	14.5
		CyA+MMF	14	12
	Triple	CyA+MMF+Pred	45	38.5
		FK+MMF+Pred	38	32.5
		RAP+MMF+Pred	3	2.6

CyA: Cyclosporine MMF: Mycophenolate mofetil Pred: Prednisolone FK: Tacrolimus RAP: Sirolimus.

This means the anemic patients are significantly more exposed to renal dysfunction and leukocytosis, respectively. In agreement to our results, previous studies done by Brennan *et al*, Saito *et al*, and Marcen *et al* have concluded that the most important cause of iron deficiency anemia post renal transplantation is renal allograft dysfunction1[19,31,32]. Likewise, creatinine clearance ($P = 0.002$) and WBC count ($P = 0.004$) correlated with anemia in RTR reported by Yorgin *et a l*[33].
Then, we addressed the effects of immunosuppressive regimens on laboratory parameters as shown in (Table 3).

Table 2: Correlation between Hb and other laboratory parameters among RTR.

Parameters	r*	P
Serum creatinine	- 0.239	0.011 [a]
Serum urea	- 0.332	0.000 [a]
WBC	- 0.178	0.030 [a]

* *Correlation coefficient [a] Significant P <0.05.*
There was no significant effect of immunosuppressive therapy on Serum creatinine value (F 1.195; P 0.317> 0.05) and Hb value (F 2.130; P 0.082 >0.05), while there was significant effect on serum urea value (F 2.896; P 0.026 < 0.05) and total WBC count (F 3.589; P 0.009 <0.05) by using ANOVA test. Then we used a "post hoc" (Brown-Forsythe and Welch) test to determine which immunosuppressive regimen responsible for the significant effects on the total WBC count and serum urea.

Table 3: Effects of immunosuppressive therapy on laboratory parameters.

Parameters	F*	P
Serum creatinine	1.195	0.317
Serum urea	2.896	0.026 [a]
WBC	3.589	0.009 [a]
Hb	2.130	0.082

*ANOVA test ^{a} Significant P <0.05.

From Figure-1 which represents the mean urea among 5 groups of immunosuppressive therapy, we noted clearly that the mean urea was significantly high in CyA + MMF group (57.23±29.63; *P* 0.049) and in CyA + MMF + Pred group (55.59±31.14; *P* 0.012). Therefore, RTRs who receive CyA + MMF or CyA + MM F+ Pred were significantly associated with a greater risk of increasing urea level than other drugs. Our results is agreed with other study done by Herrero *et al* who shown that the combination of cyclosporine and mycophenolate mofetile has greater risk on serum urea than mycophenolate mofetile alone and has no significant effect on serum creatinine[34]. Similarly, Laskow *et al* study found cyclosporine confers a significant risk of nephrotoxicity via increasing blood urea nitrogen and significant decreases in creatinine clearance[35]. Thereby, our study confirms the combination of cyclosporine and mycophenolate mofetile predispose nephrotoxicity by rise in urea in RTR.
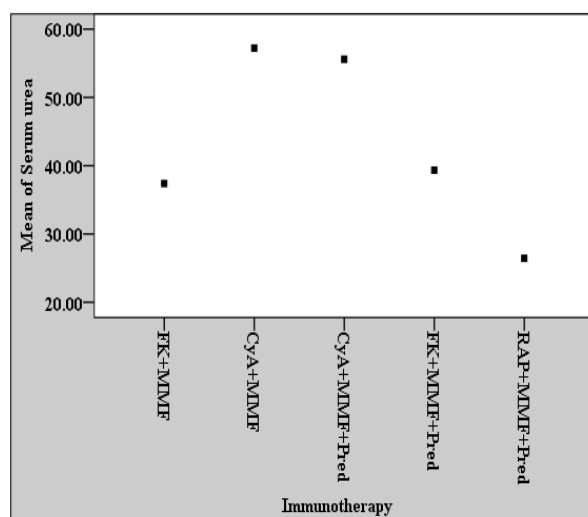

Figure 1: Comparison of mean urea between immunotherapy groups among RTR.

From figure 2, that represents the mean WBC count among 5 groups of immunosuppressive therapy.

Our results have noted that the mean WBC count was significantly high in CyA + MMF+Pred group (8.6±2.4; *P* 0.004) and in FK + MMF + Pred group (8.7±1.8; *P* 0.003). Therefore, RTRs who receive CyA + MMF + Pred or FK + MMF + Pred were significantly associated with a greater risk on elevation of total white blood cells. In according to our results, an early study done by Richard *et al* has shown that the mean WBC count had increased significantly (from 2,400 to 8,000) after 3hours from steroid therapy in RTR[36]. Additionally, Rohdewald *et al* study has shown leukocytosis are at minimum between 4 and 8 hours and maximum at 24hr[37]. Lastly, Giessing *et al* has concluded that as the recipient is under immunosuppression with cortisone, symptoms of UTI can be masked, especially in older recipients, and elevated leukocyte levels are apparent in blood samples. Because of the clinical importance of the WBC count in the RTR and the potential for large and unpredictable changes in WBC count in response to steroids, WBC and differential cell count should be obtained before the morning steroid dose[38]. Ultimately, immunotherapy had negative impact on serum urea and WBC and had no impacts on Serum creatinine and Hb.

CONCLUSION:

We conclude significant effects of immunotherapy protocols on laboratory parameters. Subsequently, patients should be evaluated during routine outpatient follow-up, particularly, those with anemia, considering the effects of immunotherapy protocol.
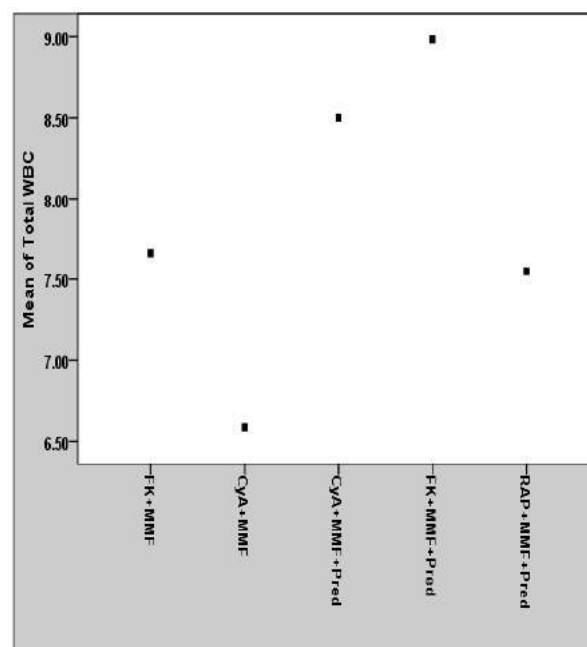
Figure 2: Comparison of mean WBC between immunotherapy groups among RTR.

REFERENCES:

1- Girlanda, R. (2013).Complications of post transplant immunosuppression. *INTECH*. 33: 831-92.

2- Schmaldienst, S., E. Dittrich, and W.H. Horl,(2002). Urinary tract infections after renal transplantation.*Current opinion in urology*, 2: p. 125-130.

Schmaldienst, S. and W. Horl,*Bacterial infections after renal transplantation.Contrib Nephrol*,1998.

3- Kosieradzki, M., Lisik, W., Rowinski., W., and Malkowski., P. (2011). Progress in abdominal organ transplantation. *Med. Sci. Monitt.*12:282-91.

4- Munoz, P.(2001). Management of urinary tract infections and lymphocele in renal transplant recipients.*Clinical infectious diseases*. 33: 53-57

5- Iqbal, T., Naqvi, R., and Akhter, S.F. (2010). Frequency of urinary tract infection in renal transplant recipients and effect on graft function.*Journal of the Pakistan Medical Association*. 60: 826.

6- Harvey, R.A., Howland, D. R., Mycek, J.M., and Champe, C.P. (2006).Lippincott's illustrated reviews: Pharmacology: Philadelphia: Wolters Kluwer.

7- Halloran, P.F. (2004). Immunosuppressive drugs for kidney transplantation.*New England Journal of Medicine*, 351:2715-2729.

8- Kasiske, B.L., Zeier ,M.G., Chapman, J.R., and Graig, G.C. (2010). KDIGO clinical practice guideline for the care of kidney transplant recipients: *a summary.Kidney international*. 77: 299-311.

9- Malhotra, P., Malu, S., and Kapur, S. (2000). Immunology of transplant rejection. Medscape.

10- Harvey, R.A., Mycek, M., and Champe, P.C. (1998). Lippincott's Illustrated Reviews: Pharmacology.*Trends in Pharmacological Sciences*. 19:28-38.

11- Anderson, J.K., Kabalin, J. and Cadeddu, J.(2007). Surgical anatomy of the retroperitoneum, adrenals, kidneys, and ureters. *Campbell-Walsh Urology*,1: 34-37.

12- Zhao, J., Wang, K., and Gao, Z. (2011). The transplantation operation and its surgical complications. INTECH Open Access Publisher.

13- Rubin, R.H.(1993). Infectious disease complications of renal transplantation.*Kidney international*, 44:221-236.

14- Pelle, G., Vimont, S., Levy, P.P., Hertig, A., Ouali, N., Chassin, C., Arlet, G., Rondeau, E., and Vandewalle, A. (2007). Acute pyelonephritis represents a risk factor impairing longterm kidney graft function. *American Journal Transplantation*, 7:899-907.

15- Rubin, R.H., Wolfson, J.S., Cosimi, A.B., and Tolkoff-Rubin, N.E,(1981). Infection in the renal transplant recipient. *The American journal of medicine,* 70:405- 411.

16- Soave, R. (2001). Prophylaxis strategies for solid-organ transplantation.*Clinical infectious diseases,* 33: 26-31.

17- O'Shaughnessy, E.A., Dahl, D., Smith, C., and Kasiske, B. (2002). Risk factors for fractures in kidney transplantation. Transplantation,7:362-366.

18- Brennan, D.C. (2006). Long-term trends in allograft survival. *Advances in chronic kidney disease*, 13:11-17.

19- Snydman, D.R. (2001). Epidemiology of infections after solid-organ transplantation. *Clinical infectious diseases*, 33: S5-S8.

20- Venkat, K., and Venkat, A. (2004). Care of the renal transplant recipient in the emergency department. *Annals of emergency medicine*. 44: 330-341.

21- Marty, F.M., and Rubin, R.H.(2006).The prevention of infection posttransplant: the role of prophylaxis, preemptive and empiric therapy. *Transplant international*, 19:2-11.

22- Fishman, J.A. (2007). Infection in solid-organ transplant recipients. *New England Journal of Medicine*, 357:2261-2614.

23- Christopher,H., Boon, N.A., Colledge, N. A., and Walker, B. R.(2002). Davidson's principles and practice of medicine. Churchill Livingstone. pp 525.

24- Fishman, J.A., and Rubin, R.H. (1998). Infection in organ-transplant recipients.
New England Journal of Medicine, 338:1741-1751.

25- Becker-Cohen, R., Nir, A., Rinate, C., Fienstein, S., Algur, N., Farber, V., and Frishberig, Y. (2006). Risk factors for cardiovascular disease in children and young adults after renal transplantation.*Clinical Journal of the American Society of Nephrology*,1:1284-1292.

26- Buttarello, M., and Plebani, M. (2008). Automated blood cell counts. *Americanjournal of clinical pathology*, 130:104-116.

27- Adly, A.A., Toaima, D.N., Mohamed,N.R., and Abu El Seoud, K.M. (2014). Subclinical renal abnormalities in young thalassemiamajor and intermedia patients and its relation to chelation therapy.*Egyptian Journal of Medical Human Genetics*, 15:369-377.

28- Munoz, P. (2001). Management of urinary tract infections and lymphocele in renal transplant recipients.*Clinical infectious diseases*. 33: 53-57.

29- Iqbal, T., Naqvi, R., and Akhter, S.F. (2010). Frequency of urinary tract infection in renal transplant recipients and effect on graft function.*Journal of the Pakistan Medical Association*. 60: 826.

30- Saito, S., Fugiwara, T., Sakagami, K., Matsuno, T., and Tanaka,N. (1998). Anemia following renal transplantation.*Transplantation proceedings*: 30:2901-32.

31- Marcan, R.,Galeano, C., Fernandez-Rodriguez, A., Jiménez, S., Teruel, J.L, Burgos, F.J., and Quereda, C.(2009).Achieving chronic kidney disease treatment targets in renal transplant recipients: results from a cross-sectional study in Spain. *Transplantation*, 87:1340-1346.

32- Yorgin, P.D., Belson, A., Sanchez, J., Al Uzri AY, Sarwal, M., Bloch, D.A., Oehlert, J., Salvatierra, O., and Alexander, S.R.(2002).Unexpectedly high prevalence of posttransplant anemia in pediatric and young adult renal transplant recipients. *American journal of kidney diseases*, 40:1306-1318.

33- Herrero, J.I.,Quiroga, J., Sangro, B., Pardo, F., Rotellar, F., Cienfuegos, J.A., and J. Prieto. (2003). Conversion from calcineurin inhibitors to mycophenolate mofetil in liver transplant recipients with diabetes mellitus. *Transplantation proceedings*, 1345: 644-4.

34- Laskow, D.A., Curtis, J.J., Luke, R.G., Julian, B.A., Jones, P., Deierhoi, M.H, Barber, W.H, and Diethelm, A.G.(1990). Cyclosporine-induced changes in glomerular filtration rate and urea excretion.*The American journal of medicine*, 88: 497-502.

35- Breitenfield, R.V., Pachucki,L. C., Hebert,L.A., and Walter, F. (1978). Effect of glucocorticoids on WBC counts in splenectomized renal transplant recipients.*Archives of internal medicine*, 138:583-585.

36- Rohdewald, V., Rehder, J., Mollmann,H ., Barth, J., Derendorf, H. (1987). Pharmacokinetics and pharmacodynamics of prednisolone following extremely high dosage as prednisolone hemisuccinate.*Arzneimittel-Forschung*, 37:194-198.

37- Giessing, M.(2012). Urinary tract infection in renal transplantation.*Arab journal of urology*, 10: 62-168.

RELIABILITY OF CLINICAL EXAMINATION AND MAGNETIC RESONANCE IMAGINING FINDINGS VERSUS ARTHROSCOPIC FINDINGS IN MENISCAL AND ANTERIOR CRUCIATE LIGAMENT ACUTE INJURIES

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ABSTRACT:
The traumatic injury of the knee requires certain investigations for the establishment of diagnosis, in addition to clinical history and a thorough physical examination. The use of arthrography and arthroscopy improves the accuracy of the diagnosis. **MRI** scanning of the knee joint has often been regarded as the noninvasive alternative to diagnostic arthroscopy. This study was established to compare the accuracy of the clinical examination and **MRI** versus arthroscopic findings in acute knee injuries. This is a prospective analytical study done from December 2016 to July 2017 in orthopedic department of Misurata Central Hospital for 42 patients who suffer from acute knee injury. Only patients who underwent an arthroscopy within 2 months following clinical examination (history, mode of trauma, Mc Muarry, anterior drawer and Lachmann's tests) and **MRI**. Arthroscopy was considered as gold stander for the diagnosis of knee injury. The resulting population consisted of 42 patients, 32 (76.2 %) males and 10 (23.8 %) females. Their ages ranged from 19 to 62 years, with a mean age of 31.9 years at the time of the arthroscopic surgery. The sensitivity, specificity, diagnostic accuracy of clinical examination were 84.6%, 75% and 80.95% respectively for McMurray test; 44.5%, 91.6% and 71.4% respectively for Anterior drawer test; 77.8%, 91.7% and 85.7% for Lachman test. The sensitivity, specificity, diagnostic accuracy of **MRI** were 91.7%, 80% and 95.2% for medial meniscal tear; 33.4%, 25% and 57.6% respectively for lateral meniscal tear; 90.1%, 90% and 95.3% for anterior cruciate ligament (**ACL**) tear. The accuracy of predicting of acute knee injury depends on the level of the skilled orthopedics or trauma surgeon's hand, **MRI** is accurate modality that can be used in uncertain indication for arthroscopy. The accuracy of clinical examination was relatively better in isolated knee injury.

KEY WORDS: Magnetic Resonance Imagining, Arthroscopy, Medial meniscus Anterior Cruciate Ligament.

INTRODUCTION:

The purpose of history and clinical examination is to make a correct diagnosis. A thorough physical examination is the first step in evaluating a patient with knee pain[1]. Approximately 28% of patients were present in orthopedic OPD with complaints of knee pain[2].

The McMurray test is the most common clinical test used to diagnose meniscal tears. Anterior drawer (AD) sign and Lachman's test are commonly used to diagnose **ACL** injury. There is no uniformity in the results published about the accuracy of these tests[3], The sensitivity and specificity of the tests used to diagnose **ACL** and meniscus injury range from 2 to 100%[1, 4-7]. Qualified orthopedic surgeons can safely diagnose **ACL** and meniscal injuries through physical examination, while reserving **MRI** for complicated and confusing cases. This practice is not recommended initially, and it impairs the surgeon's training[1, 8, 9]. **MRI** scanning of the knee joint has often been regarded as the noninvasive alternative to diagnostic arthroscopy. In the 1980's Kean et al. began using magnetic resonance imaging in the diagnosis of knee disorders[10]. The sensitivity of this examination can be raised according to the methods used by radiologists[11]. **MRI** has high applicability to the knees, in comparison with other joints, and it provides excellent diagnostic capacity for evaluating lesions of different types, such as ligament, meniscal, tendon, bone and chondral injuries[12]. Injuries to the meniscus occur frequently and are often followed by arthroscopic surgery, which is the most commonly performed procedure in knee joint surgery[13]. The rate of complications during a diagnostic arthroscopy is low, but still existent with 3 %[14].

Arthroscopy is regarded as the gold standard among the investigative modalities[15-17].

The progress of arthroscopic surgery over recent decades, together with clinical and complementary examinations, in association with the low morbidity of the surgical procedure, has encouraged its use for diagnosing, treating and making prognoses in relation to intra-articular knee injuries[18].

AIM OF THE STUDY:

The aim of the present study was to determine the accuracy, sensitivity, specificity, positive predictive value examinations and **MRI** on the acute knee injuries regarding meniscal and **ACL** injury, taking arthroscopic finding on this joint to be the gold standard.

PATIENTS AND METHODS:

Between December 2016 to June 2017 a prospective study was conducted on 42 patients with acute knee injuries (22 Lt Knee and 20 Rt knee) of mean age 31.9 range from (16 - 62 years). Distribution according to sex was 32 male (76.2%) and 10 female (23.8%), pain was present in 18 patients (42.8%), pain and instability were in 16 patients (38.1%), joint effusion was in 20 patients, locking only in 12 patients (28.6%), instability only in 6 cases (14.3%).

The mode of injury were sport related injuries in 16 patients (38.09%), trauma other than sport was in 26 patients.

Forty two cases of acute knee injury with suspicion of meniscal or **ACL** injuries were identified clinically and subjected to both **MRI** study and arthroscopy. Exclusion criteria was any patient with degenerative changes or evidence of loose bodies in plain radiograph, any prior

surgery for the index of diagnosis or patient treated non operatively.

Clinical criteria used were history, tender joint line, and positive McMurray's test for meniscal injury. Lachman test and anterior drawer test were considered to be essential for clinical diagnosis of anterior cruciate ligament injury.

Both physical and arthroscopic surgeries were performed by 1 of 2 expert orthopedic surgeons with more than 5 year experience.

We take in our consideration the report of **MRI** that was read and written by expert radiologist with more than 5 years experience and not the interpretation of the images.

A standardized grading of the meniscal tears was used, ranging from I to IV (Table 1). In this study grade III and IV ruptures were considered to be positive.

Table 1: Classification of meniscus rupture in MRI.

Stage	Description
I	globular intensity, not adjacent to either articular surface
II	linear signal within the meniscus
III	linear signal that extends to either the superior or inferior articular surface
IV	meniscus fragmentation

Record of clinical evaluation, **MRI**, and arthroscopic findings were collected and compared. Arthroscopic findings were regarded as the gold standard.

The data were analyzed using SPSS software version 13 and the sensitivity, specificity, accuracy, positive predictive value, negative predictive value were evaluated.

Some of the concepts used in this study are defined below (Table 2):

-True positive (TP): physical examination or **MRI** showing lesion, and arthroscopy showing lesion.

-True negative (TN): physical examination or **MRI** normal, with arthroscopy normal.

-False positive (FP): physical examination or **MRI** showing lesion, with arthroscopy normal.

-False negative (FN): physical examination or **MRI** negative, and arthroscopy showing lesion.

-Sensitivity - this demonstrated the efficiency of **MRI** and the physical examination for diagnosing lesions through arthroscopy TP/TP+TN.

-Specificity - this demonstrated the efficiency of the parameters for diagnosing the absence of lesions through arthroscopy TN/TN+FP.

Table 2: Data analysis.

	Arthroscopy positive	Arthroscopy negative
Clinically or arthroscopy positive	TP	FP
Clinically or arthroscopy negative	FN	TN

-Accuracy - this demonstrated the capacity of the physical examination or **MRI** to correctly define the presence or

absence of lesions through arthroscopy TP+TN/number of examinations.

-Positive predictive value (PPV) - this was the likelihood that the lesion diagnosed on **MRI** or in the physical examination would be present through arthroscopy TP/TP+FP.

-Negative predictive value (NPV) - this was the likelihood that there would not be any lesion when the physical examination or **MRI** was normal TN/TN+FN.

RESULTS:
The study group of 42 patients consisted of 32 men (76.2%) and 10 women (23.8%). All underwent arthroscopic knee surgery. The average age was 31.9 years(range: 16–62 years).Youngest patients age is 16years and oldest age is 62 years. Maximum number of patients (n=20) who suffered knee injury were in the age group of 21-30 years (Table 3).

Table 3: Age distribution of patients.

Age / years	No.	%
11 -20	4	9.5
21- 30	20	47.6
31 – 40	10	23.8
41 – 50	6	14.3
51 – 60	0	0
61 – 70	2	4.7

Maximum number of patients is complaining of pain only (n=18) and positive with McMurray's test (n=26) is show in table 4 (a and b).

Table 4-a: clinical history.

Complain	No.	%
Pain	18	42.8
Instability	6	14.3
Locking	12	28.6
Pain and instability	16	38
Joint effusion	20	47.6
Sport injury	16	38
Trauma other than sport	26	62

Table 4-b: physical examination.

Sign	No.	%
McMurray's test	26	67
Anterior drawer test	10	23.8
Lachman test	16	38

Maximum numbers of patients according to **MRI** reports are with **ACL** tear (n=28) and lowest with lateral meniscus lesion (n=6) are shows in table 5.

Table5 : Results of MRI reports.

MRI	No.	%
ACL lesion	28	66.7
Medial meniscus lesion lesion	16	38
Lateral meniscus lesion lesion	6	14.3

Maximum numbers of patients according to Arthroscopic examinations are those patients who suffer from **ACL** tears (n=28) show in table 6.

Table 6: Results of arthroscopic examination.

Arthroscopy	No.	%
ACL lesion	28	66.7
Medial meniscus lesion lesion	12	28.6
Lateral meniscus lesion lesion	9	21.4

Comparison of the arthroscopic and physical examinations findings yielded the following results:
1. McMurray's test findings yielded 22 true-positives (were confirmed on Arthroscopy) and 12 true-negatives (without evidence of meniscal lesions) with 4 false positive (were miss interpreted to have meniscal lesions) and 4 false negative (were not diagnosed by McMurray's test) (table7), which resulted in 84.6% sensitivity, 75% specificity, 84.6% positive predictive value, 25% negative predictive value and 80.95% accuracy.

Table 7: number of patients according to anterior drawer sign.

	Arthrosc. positive	Arthrosc. negative	Total
Drawer positive	8 (TP)	2 (FP)	10
Drawer negative	10 (FN)	22 (TN)	32
Total	18	24	42

2. Anterior drawer test yielded 8 true-positives (were confirmed on arthroscopy) and 22 true-negatives (without evidence of **ACL** laxity by test) with 2 false positive (were miss interpreted to have **ACL** laxity) and 10 false negative (were not diagnosed by test) (table 8), which resulted in 44.5% sensitivity, 91.6% specificity, 80% positive predictive value, 68.7% negative predictive value and 71.4% accuracy.

Table 8: number of patients according to anterior drawer sign.

	Arthrosc. positive	Arthrosc. negative	Total
Drawer positive	8 (TP)	2 (FP)	10
Drawer negative	10 (FN)	22 (TN)	32
Total	18	24	42

3. Lachman's test yielded 14 true-positives (were confirmed on arthroscopy) and 22 true-negatives (without evidence of **ACL** tear) with 2 false positive (were miss interpreted to have **ACL** tear) and 4 false negative (were not diagnosed by test) (table 9), which resulted in 77.8% sensitivity, 91.7% specificity, 87.5% positive predictive value, 84.6% negative predictive value
And 85.7% accuracy.

Table 9: number of patients according to Lachman's test.

	Arthroscopic positive	Arthroscopic negative	Total
Lachman positive	14 (TP)	2 (FP)	16
Lachman negative	4 (FN)	22 (TN)	26
Total	18	24	42

Comparison of the arthroscopic and **MRI** reports finding yielded the following results:
1. MRI findings for the medial meniscus lesions yielded 22 true-positives (were confirmed on arthroscopy) and 8 true-negatives (without evidence of MM lesions) with 10 false positive (were miss interpreted to have MM lesions) and 2 false negative (table 10), which resulted in 91.7% sensitivity, 80% specificity, 68.8% positive predictive value, 80% negative predictive value and 95.2% accuracy.

Table 10: number of patients according to MRI findings for the medial meniscus lesions.

	Arthroscopic positive	Arthroscopic negative	Total
MRI positive	22 (TP)	10 (FP)	32
MRI negative	2 (FN)	8 (TN)	10
Total	24	18	42

2. MRI findings for the lateral meniscus lesions yielded 6 true-positives (were confirmed on arthroscopy) and 18 true-negatives (without evidence of LM lesions) with 6 false positive (were miss interpreted to have LM lesions) and 12 false negative (table 11), which resulted in 33.4% sensitivity, 25% specificity, 50% positive predictive value, 40% negative predictive value and 57.2% accuracy.

Table 11: number of patients according to MRI findings for the lateral meniscus lesions.

	Arthroscopic positive	Arthroscopic negative	Total
MRI positive	6 (TP)	6 (FP)	12
MRI negative	12 (FN)	18 (TN)	30
Total	18	24	42

3. MRI findings for the ACL yielded 20 true-positives (were confirmed on arthroscopy) and 18 true-negatives (without evidence of **ACL**) with 2 false positive (were miss interpreted to have **ACL**) and 2 false negative (were not diagnosed by **MRI**) (table 12), which resulted in 90.1% sensitivity, 90% specificity, 90.1% positive predictive value, 90% negative predictive value and 95.3% accuracy.

Table 12: number of patients according to MRI findings for ACL.

	Arthroscopic positive	Arthroscopic negative	Total
MRI positive	20 (TP)	2 (FP)	22
MRI negative	2 (FN)	18 (TN)	20
Total	22	20	42

Sensitivity, specificity, positive predictive value, negative predictive value and accuracy aspects of clinical examination, **MRI** and arthroscopic diagnosis of **ACL**, medial meniscus lesions, lateral meniscus lesions are summarized in table 13.

DISCUSSION:

Ligament and meniscal injuries of the knee are generally diagnosed by orthopedic surgeons by means of physical examinations, with complementary aid from **MRI**. In this study, the concordance between these two types of diagnostic method was investigated in comparison with the arthroscopic findings from the knee.

In acute injuries in which physical examination may be inconclusive, **MRI** helps in the diagnosis in this population and may guide the surgical indication, according to Munshi et al [19].

Table 13: summarized the results of study.

	McM	Ante. Draw.	Lac.	MRI MM	MRI LM	MRI ACL
Sens- itivity	84.6	44.5	77.8	91.7	33.4	90.1
Spec- ificity	75	91.6	91.7	80	25	90
PPV	84.6	80	87.5	68.8	50	90.1
NPV	25	68.7	84.6	80	40	90
Accu- racy	80.95	71.4	85.7	95.2	57.2	95.3

McM=McMurray's, Lac= Lachman

Combined methods for diagnosing knee injuries consisting of physical examination and **MRI** were found to be capable of diminishing the number of negative arthroscopy procedures by 5%, as demonstrated by Munk et al [20]. De Smet and Graf analyzed 400 records and concluded that sensitivity of **MRI** scans was reduced for meniscal tears in the presence of **ACL** injury [23].

In a double-blind study done by Rappeport et al. [21] commented that knee arthroscopy was performed without prior knowledge of the **MRI** data. The accuracy of the **MRI** was greater than arthroscopy as the gold standard for diagnosis, and when **MRI** was used as the standard, the accuracy of the arthroscopy was lower, given that in a certain small number of patients, some injuries found on **MRI** were not shown during arthroscopy. It was suggested that **MRI** should be used initially for diagnosing knee injuries, which would also diminish the number of negative arthroscopy procedures.

MRI was an appropriate method for complementing the physical examination in cases of ligament and meniscal injuries of the knee and demonstrated sensitivity and

specificity values for **MRI** for injuries of the **ACL**, medial meniscus and lateral meniscus of respectively 82% and 96%, 96% and 66%, and 87% and 88%, in comparison with arthroscopy [22].

Previous studies comparing low-field **MRI** to surgical findings have shown near similar results for the medial meniscus (sensitivity 75% - 96% & specificity 69% - 100%), but lateral meniscus findings have (sensitivity 56.2% - 93% & specificity 88.23% - 100%) [4, 10, 24-28]. We are also unaware of any reason why such differences would exist between the medial and lateral menisci. Because of greater fixation, less mobility, and its function as a secondary stabilizer of anterior translation, medial meniscus tears tend to be more prevalent and more symptomatic [29, 30].

Fischer et al [4] considered the fact that because of high incidence of medial meniscus tears may have caused the radiologists to anticipate findings and therefore "over-read" tears of the medial meniscus and "under-read" those of the lateral meniscus.

In our study **MRI** had an accuracy of 95.2% - 57.2% for diagnosing medial and lateral meniscal tears respectively. Differences in accuracy could also result from differences in scanning protocols. Most probably using one radiologist would have improved the consistency of radiological diagnoses [29, 30]. Of course, various examiners do not all have the same level of experience, therefore the accuracy varies.

Although magnetic resonance imaging and arthroscopy have become more and more important in the treatment of meniscal and **ACL** disorders, a carefully performed physical examination and an exactly taken history remains essential and is the first diagnostic step taken. Depending on the results of the clinical examination the surgeon will decide if an **MRI** examination is necessary, or the patient can be admitted to surgery relying on the clinical examination.

CONCLUSION:

By obtaining correlation between clinical examination, **MRI** scan, and arthroscopy for meniscal and **ACL** injuries, we conclude that carefully performed clinically examination can give idea about diagnosis of meniscal and **ACL** injuries in comparison to **MRI** scan. When clinical signs and symptoms are inconclusive, performing an **MRI** scan is likely to be more beneficial in avoiding unnecessary arthroscopic surgery.

RECOMMENDATIONS:

The clinical examination is an important and accurate diagnostic modality for evaluation of traumatic derangement of the knee injury. It is noninvasive, easy available and valuable diagnostic modality.

MRI is a noninvasive, radiation free useful and reliable diagnostic tool for evaluating knee pathology and it can be used as a first line investigation in diagnosing meniscal and cruciate ligament injuries. The diagnostic yield is increased with appropriate use of sequences and proper analysis of images in all planes with high technical and expert radiologist.

Almost all the ligamentous and meniscal injuries can be diagnosed with high level of confidence. Pathological entities should be carefully differentiated from normal variants, pitfalls and artifacts of imaging.

In traumatic setting in post-traumatic knee, **MRI** evaluation before arthroscopy has been proved as cost-effective and

has to be kept in mind especially in patient with low socio-economic status.

Despite the fact that arthroscopy has altered the management of knee pathologies, most orthopeadicians admit the limitations of the procedure in the evaluation of extra-articular pathology, its invasiveness, cost and uncommon but possible complications associated with it. Arthroscopy still remains gold standard for definitive diagnosis.

REFERANCES:

1- Kocabey Y, Tetik O, Isbell W, Atay O, Johnson D. The value of clinical examination versus magnetic resonance imaging in the diagnosis of meniscal tears and anterior cruciate ligament rupture. Arthroscopy 2004; 20:696-700.

2- Peat G, McCarney R, Croft P. Knee pain and osteoarthritis in older adults: A review of community burden and current use of primary health care. Ann Rheum Dis 2001; 60:91-7.

3- Jain DK, Amaravati R, Sharma G. Evaluation of the clinical signs of anterior cruciate ligament and meniscal injuries. Indian J Orthop 2009; 43:375-8.

4- Fischer SP, Fox JM, Del Pizzo W, Friedman MJ, Snyder SJ, Ferkel RD. Accuracy of Diagnoses from magnetic resource imaging of the knee: A multicentre analysis of one thousand and fourteen cases J Bone Joint Surg Am 1991;73:2-10.

5- Benjaminse A, Gokeler A, Van der Schans CP. Clinical diagnosis of an anterior cruciate ligament rupture: A meta-analysis. J Orthop Sports Phys Ther 2006; 36:267-88.

6- Ostrowski JA. Accuracy of 3 diagnostic tests for Anterior cruciate ligament tears. J Athl Train. 2006;41(1):120-1.

7- Katz JW, Fingeroth RJ. The diagnostic accuracy of ruptures of the anterior cruciate ligament comparing the Lachman test, the anterior drawer sign, and the pivot shift test in acute and chronic knee injuries. Am J Sports Med 1986; 14:88-91.

8- Kostov H1, Arsovski O, Kostova E, Nikolov V. Diagnostic assessment in anterior cruciate ligament (**ACL**) tears. 2014;35(1):209-18.

9- Khan HA, Had H, Sharma P, Bajaj P, et al. Correlation between magnetic resonance imaging and arthroscopic findings in the knee joint. 2015 Feb;20(1):e18635. doi: 10.5812/traumamon.18635. Epub 2015 Jan 7.

10- Mandelbaum BR, Finerman GAM, Reicher MA, et al. Magnetic resonance imaging as a tool for evaluation of traumatic knee injuries. Am J Sports Med 1986; 14: 361.

11- Magee T, Shapiro M, Williams D. MR accuracy and arthroscopic incidence of meniscal radial tears. Skeletal Radiol. 2002;31(12):686-9.

12- Sanders TG, Miller MD. A systematic approach to magnetic resonance imaging interpretation of sports medicine injuries of the knee. Am J Sports Med. 2005;33(1):131-48.

13- Small NC. Complication in arthroscopic surgery performed by experienced arthroscopist. Arthroscopy 1988; 4: 215–221.

14- Crawford R, Walley G, Bridgman S, Maffulli N. Magnetic resonance imaging versus arthoscopy in the diagnosis of knee pathology, concentrating on meniscal lesions and **ACL** tears: A systematic review. Br Med Bull 2007; 84:1-4.

15- Kim SJ, Shin SJ, Koo TY. Arch type pathologic suprapatellar plica. Arthroscopy 2001; 17:536-8.

16- Khan Z, Faruqui Z, Oguynbiyi O, Rosset G, Iqbal J. Ultrasound assessment of internal derangement of the knee. Acta Orthopaedics Belg 2006; 72:72-6.

17- Barry BP. General principles of arthroscopy. In: Terry SC, editor. Campbell's operative orthopaedics. 9 ed. Philadelphia: Mosby Inc; 1999, 2. 364-73.

18- Munshi M, Davidson M, MacDonald PB, Froese W, Sutherland K. The efficacy of magnetic resonance imaging in acute knee injuries. Clin J Sport Med. 2000;10(1):34-9.

19- Munk B, Madsen F, Lundorf E, Staunstrusp H, Schmidt SA, Bolvig L, et al. Clinical magnetic resonance imaging and arthroscopic findings in knees: a comparative prospective study of meniscus anterior cruciate ligament and cartilage lesions. Arthroscopy. 1988;14(2):171-5.

20- Rappeport ED, Wieslander SB, Stephensen S, Lausten GS, Thomsen HS. **MRI** preferable to diagnostic arthroscopy in knee injuries. A double- blind comparison of 47 patients. Acta Orthop Scand. 1997;68(3):277-81.

21- Severino NR, Camargo OPA, Aihara T, Cury RPL, Oliveira VM, Vaz CES, et al. Comparação entre a ressonância magnética e a artroscopia no diagnóstico de lesões do joelho. Rev Bras Ortop. 1997;32(4):275-8.

22-Smet AA, Graf BK. Meniscal tears missed on MR imaging: relationship to meniscal tear patterns and anterior cruciate ligament tears. AJR Am J Roentgenol. 1994;162(4):905–911.

23- Cotten A, Delfaut E, Demondion X, et al. MR imaging of the knee at 0.2 and 1.5 T: correlation with surgery. AJR Am J Roentgenol. 2000; 174:1093–1097.

14-Lokannavar HS, Yang X, Guduru H. Arthroscopic and low-field **MRI** (0.25 T) evaluation of meniscus and ligaments of painful knee. J Clin Imaging Sci. 2012; 2:24.

25- Naranje S, Mittal R, et al. Arthroscopic and magnetic resonance imaging evaluation of meniscus lesions in the chronic anterior cruciate ligamentdeficient knee. Arthroscopy.2008 Sep;24(9):1045-51. doi: 10.1016 / j.arthro. 2008.03.008. Epub 2008 May 15.

26- Ahmad N, Khanda GE, et al. Assessment of menisci and ligamentous injuries of the knee on magnetic resonance imaging: correlation with arthroscopy. J Pal Med Assoc. 2008 Oct;58(10):537-40.

27- Gupta MK, Raunlyar MK, Kam NK, Ahmad K, et al. **MRI** evaluation of knee injury with arthroscopic correlation. J Nepal Health Counc.2014 Jan;12(26): 63-7.

28- Greis PE, Bardana DD, Holmstrom MC, Burks RT. Meniscal injury: I. Basic science and evaluation. J Am Acad Orthop Surg. 2002; 10:168–176.

29- Fan RS, Ryu RK. Meniscal lesions: diagnosis and treatment. MedGenMed. 2000.

INCIDENCE OF POST-PHACO CYSTOID MACULAR OEDEMA AND ITS RISK FACTORS

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ABSTRACT:
Cataract surgery is the most common ocular surgery done nowadays. Cataract leads to anatomical as well as physiological changes in the lens. Most of the surgeries done to improve the visual outcome. The surgery disturb the anatomy and the refraction of the eye. Day by day the quality of cataract surgery improves due to improvement in instrumentations and skills. This goes hand by hand in improvement of visual outcome. Although the complications of cataract surgery is markedly reduced with those advancements, still some complications do occur leading to poor post-operative vision. Cystoid macular oedema (**CME**) is a common cause of decreased vision after cataract surgery (originally known as Irvine-Gass syndrome).

KEY WORDS: Cataract, Cystoid macular oedema, Phcoemulcification, Maculopathy.

INTRODUCTION:

Cystoid macular oedema (**CME**) is a common cause of decreased vision after cataract surgery (originally known as Irvine-Gass syndrome). The pathogenesis of **CME** is unknown, the final common pathway appears to be increased perifoveal permeability with accumulation of fluids in the inner nuclear and outer plexiform layers. **CME** is often associated with intraocular inflammation and may be mediated through the release of prostaglandins and leukotrinese. Different methods have been used to diagnose **CME**. It has been determined from angiographic findings by fluorescein angiography, from clinical findings by fundoscopy, by deterioration in visual acuity and optical coherence tomography (OCT) findings of central subfield macular thickening. The incidence rates of postoperative **CME** (**PCME**) vary essentially according to the method of diagnosis, moreover, its incidence has decreased with less invasive and less traumatic cataract surgery techniques (Table 1).

Table 1: Incidence of PCME in different cataract extraction techniques in uncomplicated cataract operations.

Cataract extraction technique	Clinically significant PCME	PCME defined by FA	PCME defined by OCT
Intracapsular cataract extraction	8%[1]	36%–60%[5]	Not available
Extracapsular cataract extraction	0.8%–20%[2]	16%–32.2%[6,7]	Not available
Phacoemulsification	0.1%–2.35%[3]	20%–54.7%[8,9]	3%–41%[10,11]
Femtosecond-assisted cataract surgery	1.18%[4]		1.18%[4]

REFERENCE STUDY:

- Recently, Some of risk factors, including diabetes, capsule rupture, previous diagnosis of epiretinal membrane, uveitis, retinal vein occlusion, and retinal detachment repair, were confirmed in a retrospective database study based on 81,984 surgeries[12].

- The same study showed that high myopia, age-related macular degeneration, or the use of a PG analogue did not increase the risk of **PCME** and that the risk increased proportionally with increasing severity of diabetic retinopathy.

- In this study the eyes was distributed into 3 analysis groups:

**1.** Group 1: eyes with no risk factors and no diagnosis of diabetes at the time of surgery, the incidence of PME was 1.17%.

2. Group 2: eyes with at least a single risk factor and no diagnosis of diabetes at the time of surgery, the overall incidence of this group was 1.56%.
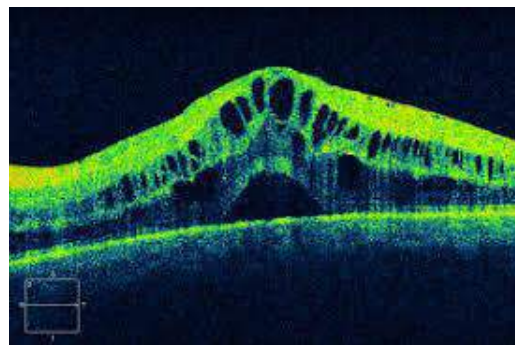
3. Group 3: eyes of patients who had a diagnosis of diabetes at the time of surgery, the incidence was 4.04%.

CME: Funduscopy appearance.
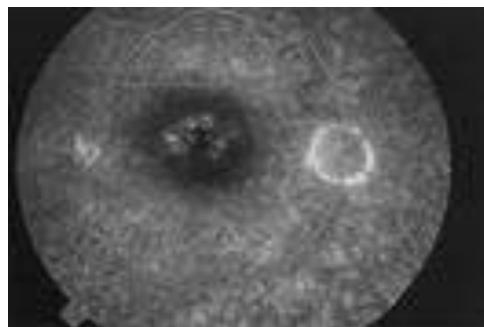
CME: Angiografic appearance.

METHODS:
- Retrospective database study of electronic medical records (EDMS).
- A total of 917 underwent phacoemulsification with intra-ocular lens implantation between 01/10/2016 and 31/03/2017.
- A study period of 6 months was selected to provide a adequate number of cases with sufficient postoperative follow-up information.
- All patients who were recorded on the EDMS to have had any phacoemulsification and intraocular lens implantation procedure during this period of time were analysed.
- Those patients who underwent a cataract surgery in the second eye during the study period had both eyes included, and data on individual eyes were treated as independent units for the purpose of this analysis.
- The presence of postoperative macular oedema was defined as a recorded clinical finding or diagnosis of cystoid macular oedema within 90 days of surgery.
- It is not routine practice to perform OCT or fluorescein angiography after surgery unless the visual acuity outcome is not as expected. Therefore, the figures are more likely to reflect visually significant macular oedema, rather than subclinical disease only detectable using these investigations.
- Data which was extracted on all eyes included:
1- Surgeon experience (consultant or trainee).
2- presence or absence of intraoperative (posterior capsule rupture, Zonular dialysis, iris trauma, iris prolapse) or postoperative complications (post-operative uveitis, retained lens fragment).
3- Presence or absence of any risk factors: Diabetic retinopathy and maculopathy, Age related macular degeneration (wet or dry), Epiretinal membrane, Vitreo-macular traction, Retinal vascular occlusions (RVO), previous retinal detachment surgery, recurrent uveitis, high myopia and the usage of prostaglandin analogue.
4- Has the eye received a prophylactic non-steroidal anti-inflammatory (NSAIDs) treatment or not.

RESULTS:
- Data collected from 917 eyes who underwent Phcoemulcification and IOL implantation, 34 eyes developed **CME** within 3 months post-operatively.
- The incidence rate of **CME** is 3.7%.
- 26 (76.4%) eyes out of 34 was done by consultants, and 8 (23.5%) eyes was done by trainees. Twenty fife (73.5%) eyes with **CME** have not had any intraoperative or postoperative complications. The most common operative complication in eyes with **CME** was the postoperative uveitis 7 (20%) eyes (Table 2).

CME: OCT appearance.

Table 2: Number of eyes with CME in relation to different operative complications.

	N0.	%
None	25	%73
PCR-With Vitreous Loss	1	%3
Lens Trauma	0	%0
Post-Operative Uveitis	7	%20
Retained Lens Fragment	0	%0
Choroidal Effusion	1	%3

No risk factor was detected in 16 (47%) eyes with **CME**, previous **CME** in the fellow eye was the most common risk factor seen in 7 eyes (20.5%). ERM in 6 eyes (17.6%), Prostaglandin analogue and diabetic retinopathy (non with diabetic maculopathy) with 4 eyes each (11.7%) (Figure 1). The majority of the eyes with **CME** do not receive any prophylactic NSAIDs (31 eyes). On the other hand, 3 eyes only had **CME** while receiving prophylactic NSAIDs postoperatively, all of them had previous **CME** in the other eye (Figure 2).
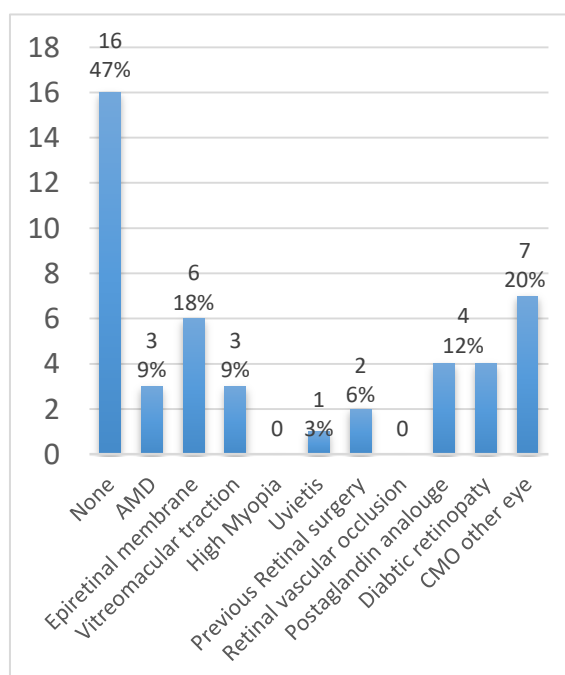
Figure 2: Percentage of NSAIDs usage in eyes with CME.
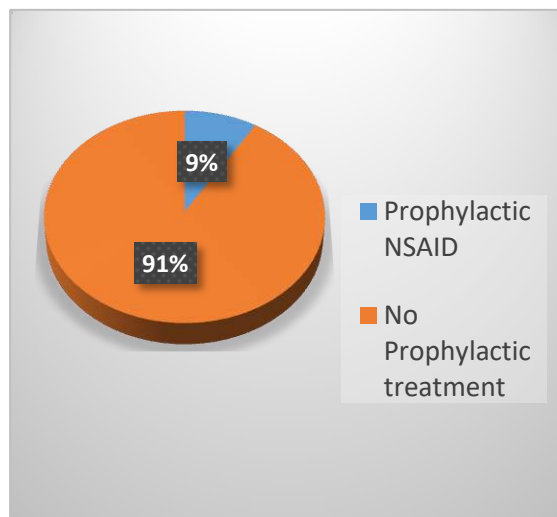
Figure 2: Percentage of NSAIDs usage in eyes with CME

DISCUSSION:
- This clinical audit is to determine the incidence of CME in routine real world clinical practice, based on structured data extraction from 917 consecutive phacoemulsification cataract operations performed at St Helens hospital over 6 months.

- The eyes which developed **CME** after phacoemulsification surgery are 34 eyes with incidence rate 3.7%. This incidence is slightly above than that on the reference study which is 1.17% in eyes with no risk factors and 1.56% in eyes with at least one risk factor but no DR.

- Most of the eyes with **CME** have not had any intraoperative or postoperative complications, 25 (73.5%) eyes. The most common operative complication in eyes with **CME** was the postoperative uveitis, 7 (20%) eyes. Only one (2.9%) eye had posterior capsule rupture (PCR) with vitreous loss.

- No risk factors detected in 16 (47%) eyes with **CME**, previous **CME** in the fellow eye is the most common risk factor, 7 (20.5%) eyes. ERM 6 (17.6%) eyes, Prostaglandin analogue and diabetic retinopathy (non with diabetic maculopathy) with 4 eyes each (11.7%).

- The majority of the eyes with **CME** do not receive any prophylactic NSAIDs, 31 eyes. On the other hand, 3 eyes only had **CME** while receiving prophylactic NSAIDs postoperatively, all of them had previous **CME** in the other eye.

CONCLUSION:
Cystoid macular oedema (**CME**) is a common cause of decreased vision after cataract surgery. Although its occurrence is not that common, most of the cases show no risk factor, the most common risk factor is the history of the same illness in the other eye. Postoperative inflammation is a significant risk factor. The use of prophylactic NSAIDs seems to reduce the rike of postoperative CME.

RECOMMENDATIONS:
- Detailed fundus examination prior to listing any patient to have a cataract extraction to detect any risk factors.
- Prophylactic NSAIDs postoperatively to any eye with at least one common risk factor such as previous history of **CME**, ERM and diabetic maculopathy.
- Routine postoperative NSAIDs to be discussed??

REFERENCES:
1- Bradford JD, Wilkinson CP, Bradford RH Jr. Cystoid macular edema following extracapsular cataract extraction and posterior chamber intraocular lens implantation. *Retina*. 1988;8(3):161–164.
2- Mentes J, Erakgun T, Afrashi F, Kerci G. Incidence of cystoid macular edema after uncomplicated phacoemulsification. *Ophthalmologica*. 2003;217(6):408–412.
3- Wetzig PC, Thatcher DB, Christiansen JM. The intracapsular versus the extracapsular cataract technique in relationship to retinal problems. *Trans Am Ophthalmol Soc*. 1979; 77:339–347.
4- Levitz L, Reich J, Roberts TV, Lawless M. Incidence of cystoid macular edema: femtosecond laser-assisted cataract surgery versus manual cataract surgery. *J Cataract Refract Surg*. 2015;41(3):683–686.
5- Yoshioka H, Kawashima K, Sugita T. [Cystoid macular edema following cataract extraction 2]. *Nippon Ganka Gakkai Zasshi*. 1972;76: 1118–1124.
6- Solomon LD. Ef cacy of topical flurbiprofen and indomethacin in preventing pseudophakic cystoid macular edema. Flurbiprofen-**CME** Study Group I. *J Cataract Refract Surg*. 1995;21(1):73–81.
7- Warren KA, Fox JE. Topical nepafenac as an alternate treatment for cystoid macular edema in steroid responsive patients. *Retina*. 2008; 28(10):1427–1434.
8- Wright PL, Wilkinson CP, Balyeat HD, Popham J, Reinke M. Angiographic cystoid macular edema after posterior chamber lens implantation. *Arch Ophthalmol*. 1988;106(6):740–744.
9- Miyake K, Masuda K, Shirato S, et al. Comparison of diclofenac and fluorometholone in preventing cystoid macular edema after small incision cataract surgery: a multicentered prospective trial. *Jpn J Ophthalmol*. 2000;44(1):58–67.
10- Ching HY, Wong AC, Wong CC, Woo DC, Chan CW. Cystoid macular oedema and changes in retinal thickness after phacoemulsi cation with optical coherence tomography. *Eye (Lond)*. 2006;20(3):297–303.
11- Chu CJ, Johnston RL, Buscombe C,etal. Risk factors and incidence of macular edema after cataract surgery: a database study of 81984 eyes. *Ophthalmology*. 2016;123(2):316–323.

SURVIVAL RATE OF VERY LOW BIRTH WEIGHT

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ABSTRACT:

Case series study for all infants admitted to neonatal intensive care at Aljala Maternity Teaching Hospital, Tripoli, Libya. All medical records for infant with birth weight equal or less than 1500 grams were reviewed to determine their survival rate. The result present survival rate for very low birth weight was 72.1% and for ELBW 19.1%. The most important factors affecting outcome were birth weight, gestational age, sex, mode of delivery and Apgar score.

KEY WORD: Survival rate, Very low birth weight, Apgar score.

INTRODUCTION:

Very low birth weight infants (**VLBW**) represent a vulnerable group of neonates with high mortality rate[1], **VLBW** is defined as birth weigh less than 1500 gm and they are predominantly premature, have higher mortality and morbidity than normal new born and more likely to suffer of some types of long term handicap, in the United States in 2003 the **VLBW** was approximately1.4% - 3.1% among black and 1.2% among whites[2]. Prematurity is the most common cause of neonatal deaths worldwide and it causes 60 to 80%of deaths without congenital anomaly[3]. Implementation of neonatal intensive care units, use of mechanical ventilation and exogenous surfactant has been reported to improve the outcome especially for extremely low birth weight infant; the survival rate has been well documented in developed countries with an increasing survival trend especially in extreme low birth weight (ELBW) infants[4 5]. Their survival rate is directly related to birth weight, with approximately 20% of those between 500 -600 gm and over 90% of those between 1250 -1500 gm[2]. The survival rate of **VLBW** infant's worldwide range between 43% in developing countries such as Jamaica, to more than 90% in developed countries such as the Netherlands[6,7]. Aljala Maternity Hospital provided maternal and neonatal services for population of Tripoli and surrounding areas. All live born **VLBW** infants admitted to level III intensive care baby unit despite shortens in mechanical ventilation and exogenous surfactant.

AIME OF STUDY:

This study aimed to determine the survival rate of **VLBW** infants admitted to Aljala maternity hospital Tripoli/ Libya and factors affecting on it.

MATERIAL & METHODS:

Case series study was conducted in neonatal intensive care, Aljala Maternity Hospital , Tripoli, Libya over 12 months period (JAN – DEC 2010). Aljala Maternity Hospital is one of main teaching hospital in Tripoli; with a capacity of 250 beds. 14000 deliveries registered during the study period.
Data collected by reviewing medical records for infants admitted to NICU with birth weight 1500 grams or less, data collected in a predesigned case sheet (**VLBW**) infants data collection sheet.), that includes:

1- Identification: File number, date of admission.
2- Demographic data: Date of birth, antenatal care.
3- Neonatal data: Birth weight, sex, mode of delivery, Apgar score at 1 min (equal or less than 5, more than 5), Apgar score at 5 min (equal or less than 5, more than 5), need for mechanical ventilation, surfactant administration, intraventricular haemorrhage, pulmonary haemorrhage, Necrotizing enterocolitis, Retinopathy of prematurity, duration of hospitalization, outcome, cause of death.
Very low birth weight infant were defined an infant with birth weight equal or less than 1500 grams, ELBW were defined an infants with birth weight equal or less than 1000 grams.
All Data were analysed using the SPSS software version 19, p<0.05 considered to be significant, chi-square Test was used to test an association between risk factors and survival outcome.

RESULTS:

Of all 110 **VLBW** and ELBW infants admitted to NICU, at Aljala Maternity Hospital Tripoli, Libya 2010. Two cases were transferred to Tripoli Medical Centre (Tertiary level) because they need surgical intervention, so both of them were excluded from the study. Among **VLBW** infants 43.5% were ELBW their survival rate was 19.1%, 56.5% was **VLBW** their survival rate 72.1%.
The mean birth weight 1080 ± 309.7 gms , rang from 300 -1500 grams, the survival rate increased by increasing birth weight (fig. 1 & table 1).
Regarding the gestational age it ranges from 23 to 38 weeks gestation, mean gestational age for survival 31.9±3.1 weeks, while the mean gestational age for patients who did not survive were 27.4 ± 3.07 weeks also the survival rate increased by increasing the gestational age (p=0.001) except for one infant who delivered at 38 week gestation and admitted as a case of intrauterine growth retardation (IUGR) with multiple congenital anomaly. Concerning the sex of the infant we found that about 63% of the female patients survive against 33.3% for the males (p=0.002). Mode of delivery also made sense in the distribution of survival and non-survival where 53 infants delivered via normal vaginal delivery, 53 via emergency C/S, and 2 infants by elective C/S, their survival rate were 32%, 65%, and 100% respectively (p=0.001). Congenital anomalies detected in7 patients (6.5%) their survival rate was 42.8% (p = 0.734) (table 1 & figure 2).
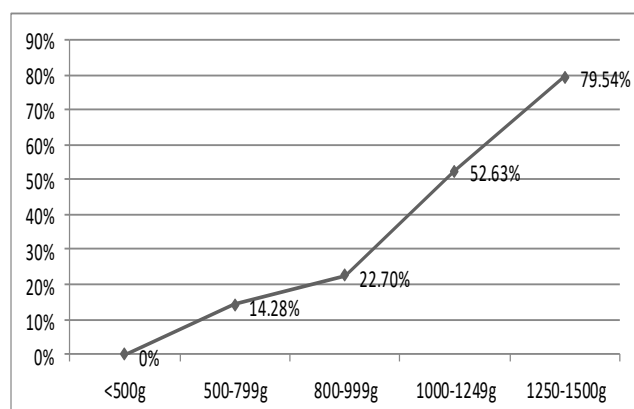
Figure 1: Survival rate according to birth weight.

Regarding the gestational age it ranges from 23 to 38 weeks gestation, mean gestational age for survival 31.9±3.1 weeks, while the mean gestational age for patients who did not survive were 27.4 ± 3.07 weeks also the survival rate increased by increasing the gestational age (p=0.001) except for one infant who delivered at 38 week gestation and admitted as a case of intrauterine growth retardation (IUGR) with multiple congenital anomaly. Concerning the sex of the infant we found that about 63% of the female patients survive against 33.3% for the males (p=0.002). Mode of delivery also made sense in the distribution of survival and non-survival where 53 infants delivered via normal vaginal delivery, 53 via emergency C/S, and 2 infants by elective C/S, their survival rate were 32%, 65%, and 100% respectively (p=0.001). Congenital anomalies detected in 7 patients (6.5%) their survival rate was 42.8% (p = 0.734) (table 1 & figure 2).

Table 1: Factors affecting survival rate.

factors	No. of survives	%	No. of Deaths	%	Total	P value
Birth weight: <500gm	Zero	Zero	2	100	2	0.001
500-799 gm	3	14.3	18	85.7	21	
800-999 gm	5	22.7	17	77.3	22	
1000-1249 gm	10	52.6	9	47.4	19	
1250-1500 gm	35	79.5	9	20.5	44	
Gestational age: <28 weeks	2	5.9	2	47.1	34	0.001
28-30 weeks	18	52.9	16	47.1	34	
31-33 weeks	17	77.3	5	22.7	22	
34-36 weeks	9	90	1	10	10	
37-40 weeks	7	87.5	1	12.5	8	
Sex: Female	36	63.2	21	36.8	57	0.002
Male	17	33.3	34	66.7	51	
Mode of delivery: NVD	17	32.1	36	67.9	53	0.001
Elective c/s	2	100	0	0	2	
Emergency c/s	34	64.2	19	35.8	53	
Congenital anomaly: Yes	3	42.9	4	57.1	7	0.734
No	50	49.5	51	50.5	101	
Apgar score at 1min: ≤5	10	25	30	75	40	0.001
>5	36	66.7	18	33.3	54	
Apgar score at 5 min: ≤5	2	15.4	11	84.6		0.015
>5	48	55.2	39	44.8	13	
					87	

(Apgar score at 5 min not recorded for 8 infants)

As regards to Apgar score 40 infants their Apgar scores were equal or less than 5 at 1 minute, 10 (25%) survive, 30 (75%) were died, 54 infants their Apgar score more than 5 in first minute, 36 (66.7%) survival, 18(33.3%) died (p=0.001), Apgar at 1 minute not recorded for 14 infants. Compared with Apgar score at 5 minute   from the 13 infants with Apgar score equal or less than 5 at 5 minute two (15.4%) survive and 11 (84.6%) died beside 87 infants their Apgar more than 5. 48 infants (55.2%) survive, and 39 (44.8%) died, P= 0. 015 Regarding the morbidity among **VLBW**; respiratory distress syndrome (RDS) was the most common and presented in 86 infants (79.6%), mechanical ventilation was used in 66 infants (61.1%), positive air way pressure was used in 45 infants (41.7%), surfactant therapy was used in 52 infants (48%), pulmonary haemorrhage (PH) diagnosed in 24 infants (22.2%), Intraventricular haemorrhage (IVH) was present in 22 infants (20.3) and 73 of total admission were not screened for IVH , all infants admitted to neonatal intensive care unit were not screened for Retinopathy of prematurity during hospital stay, Necrotizing enterocolitis (NEC) diagnosed in 10 patient (9.25%), IUGR was diagnosed in 29 infants (26.85%) (table 2).

Table 2: Clinical diagnosis of very low birth weight infants.

Diagnosis	Number	Number of Survives	Survival %
RDS	86	35	40.7%
IVH	22 (73 not screened)	7	31.8%
NEC	10	7	70%
IUGR	29	22	75.8%
PH	24	6	25%

The most common cause of deaths were sepsis (11.8%), similar percentage of infants who died during this period without any record explaining the cause of death, 10 (9%) cases due to pulmonary haemorrhage, 9 (8.2%) infants died due to pneumothorax, 4 cases due to disseminated intravascular coagulopathy (DIC) (3.6%), 2 cases due to sever hyaline membrane disease (HMD), congenital anomaly (CA) (1.8%) and one case due to sever hypoxic ischemic encephalopathy (HIE). The duration of hospital stay of those infants was range from one hour to 67 days (table 3).

*Table 3: Causes of death among very low birth weight.*

Cause of death	Frequency	Percentage
Sepsis	13	11.8%
Pulmonary haemorrhage	10	9.1%
Pneumothorax	9	8.2%
DIC	4	3.6%
HMD	2	1.85%
HIE	1	0.9%
Congenital anomaly	2	1.8%
Insufficient data	13	11.8%
Extreme prematurity	1	0.9%

Regarding to the survival rate according to gestational age, it was 100% 1n the age group above 37 weeks, 0% in the age group less than 25 weeks and about 50% at 30 weeks of gestation (Figure 2).

DISCUSSION:

To our knowledge this is the first study that reports the survival rate of very low birth weight infants in Aljal maternity hospital, Tripoli, Libya. This study will provides essential information for health budgeting and planning, as well as a benchmark for comparison, intervention programs must be based on statistics applicable to the local setting.

The survival rate of **VLBW** infants in the present study 72.1% which is almost exactly the same as that reported from South America for 1997 and Thailand for 1996, which reflects the similarity in practice and disease profile between the two units, but is substantially below that of developed

countries[8-9]. The survival of ELBW infants is 19.1% was less than in other developing countries such as Jamaica and Thailand[10-7]. The present study shows similar picture of other study, there was a gradual decline in mortality with increasing birth weight, almost the survival rate 79.54% in the infants who birth weight between 1250-1500grams.
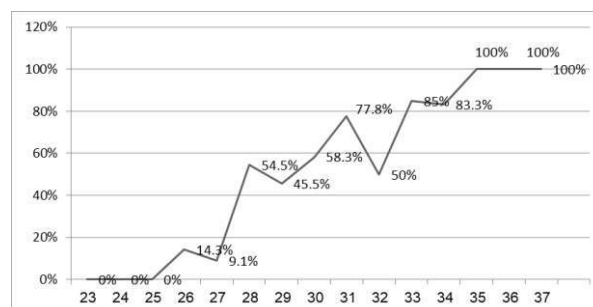
Figure 2: Survival rate according to gestational age (with exclusion of one patient with 38 weeks of gestation.

Similarly an increase in the gestational age of preterm neonates lead to a rapid decline in mortality rate, survival rate 90% among the infants of gestational age 34 - 36 weeks compared to 77.27% among gestational age 31 - 33 weeks, 50%for infants 28-30 weeks and 5.88% for infants below 28 weeks, this reflective of the fact that those with higher gestational age had more mature organs and were better equipped to with stand the transition from intrauterine to extra uterine life, so birth weight and gestational age have been shown to correlate with outcome[11-13].

The association of poor survival with vaginal delivery implies that caesarean section might be recommended for these infants, however this must be interpreted with caution, female gender has continued to show better survival rate[14,15].

When studying the cause of death for our patients, data was insufficient in 13 records this can be explained by absence of good filling system and no use of the international death certificate in our hospital, neonatal sepsis rank in first followed by pulmonary haemorrhage as the cause of death, then pneumothorax, DIC, sever HMD, extreme preterm infants and congenital anomaly.

Significant relation between Apgar score at 1 minute and survival rate was detected in our study which similar to Chanvitan study[16], 14 infants from our study population were without record of their Apgar at 1 minute and 8 infants without record at 5 minute, because the staff in the labor ward in our hospital still deal with them as miscarriage, which an area of concern.

CONCLUSION:

However our study shows that, despite the great improvement in neonatal care the **VLBW** survival in our unit still below that in developed countries, the limited health resources and high patient numbers make the provision of full tertiary support to every **VLBW** infant a difficult task, this problem has been addressed by limited number of nursing staff, ventilator machines and availability of total parenteral nutrition in our unit, allocating of the patients as miscarriage by the staff leads to the poor survival of ELBW

in our hospital. The low rate in hospital screening for Intraventricular haemorrhage is also an area of concern and need to be improved, no infants were screened for Retinopathy of prematurity, because the policy of our unite is to be screened after discharge which also another area of concern.

REFERENCES:

1- Daynia E Ballot, Tobias F Chirwa, Peter A Cooper. Determinants of survival in very low birth weight neonates in a public sector hospital in Johannesburg. BMC Pediatrics 2010, 10:30

2- Barbara J. Stoll and Ira Adams- Chapman. The high risk infants. Nelson textbook of paediatrics 18 th edition 7003-McCormick MC. The contribution of low birth weight to infant mortality and childhood morbidity. N Engl J Med.1985,312:82-90

4- Hack M, Wright LL, Shankaran S, Tyson JE, Horbar JD, Bauer CR, el al . Very low birth weight outcome of the national institute of child health and human development neonatal network, November 1989 to October 1990. Am J Obstet GYNECOL 1995,172:457-64

5- DaarlowBA, Cust AE, Donoghue DA. Improved outcomes for very low birth weight infants. Evidence from New Zealand national population based data. Arch Dis child fetal Neonatal Ed 2003,88:f23-8.

6- Trotman H, Bell Y: neonatal sepsis in very low birth weight infants at the university Hospital of the west indies. West Indian Med J 2006,55:165-9

7- Anthany S, Ouden L, Brand R, Verloovevanhorick P, Gravenhorst JB: Changes in perinatal care and survival in very preterm and extremely preterm infants in the Netherlands between 1983 and 1995 Eur J Obstet Gynecol Report Biol 2004,112:170-7

8- Grupo Colabarative Neocosur, Very low birth weight infant outcomes in 11 south America NICUs. J Perintal 2002, 22:27

9- TsouKI, Tsao PN: The mortality and survival of very low birth weight infants in Taiwan. Actapaediadr Taiwan 2003,44:349-33.

10- Sritipsukho S, Suarod T, Sritipsukho P: Survival and outcome of very low birth weight infants born in a university hospital with level ii NICU. J. Med Assoc Thai 2007, 90:1323-9

11- Hack M, Friedman H, Fanaroff AA. Outcomes of extremely low birth weight infants paediatrics 1996; 98:931-937.

12- Steven DK, Wright LL, Lemen JA, Korones SB, Papile LA, Bauer CR, Stoll BJ, Tyson JE, Shunkaran S, Fanaroff AA, Donovan EF, Ehrwnkranz RA, Verter J, Very low birth weight outcomes of the national institute of child health and human development neonatal research network, January 1993 through December 1994. Am J Obstet Gynecol 1998;179;1632-1639.

13- EL- Metwally D, Vohr B, Tucker R. Survival and neonatal morbidity at the limit s of viability in the mid 1990:22 to25 weeks . J Pediatr 2000; 137:616-622.

14- Cartlidge PHT, Sterrart JH. Survival of very low birth weight and very preterm infants in a geographically defined population. Actapaediatr 1997;86:105-110.

15- Stevenson DK, Verter J, Fanarooff AA, Ehrenkranz RA, Shankran S, Donovan EF, Wright LL, Lemon S, Tyson JE, Kovones SB, Bauer CR, Stoll BJ, Papile L-A   for the national institute of child health and human development neonatal research network. Difference in outcomes of very low birth weight infants: the new born male disadvantage. Arch Dis child fetal neonatal Ed 2000,f182-f185.

16- Chanvitan P, Ruangnapa K, Janjindamai W, Disaneevate S. Outcomes of very low birth weight infants in Songklanagarind Hospital. J Med Assoc Thai 2010 Feb; 93(2): 191-8

THE USE OF ITERATIVE RECONSTRUCTION FOR NOISE REDUCTION IN PAEDIATRIC HEAD CT: EXPERIENCE IN 20 PATIENTS

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ABSTRACT:
Computed tomography (**CT**) is one of the most used diagnostic modalities in paediatric populations, which is a concern as it also delivers a high patient dose. Recent research has focused on providing better image quality at lower dose. The iterative reconstruction algorithm was introduced as a new technique that reduces noise to increase image quality. The aim of this study is to assess the effectiveness of iterative reconstruction in reducing the radiation dose in paediatric patients performing head **CT** while preserving image quality. The dose in low dose group (**LD**) was around 20% lower than that of standard dose **CT** group (**SDCT**), subjective image quality parameters were significantly improved when iterative reconstruction (**IR**) was used in **SDCT** and **LD** groups while no significant change in the objectives image quality. Iterative reconstruction improves image quality in standard dose protocol as well as low dose protocol (20% dose reduction).

KEYWORDS: Iterative Reconstruction, Dose reduction, Paediatric head **CT**.

INTRODUCTION:

Computed Tomography (**CT**) is fast, precise and one of the most used modalities for diagnostic imaging[1]. It is considered the technique of choice both in adult and paediatric population, but it is also associated with high radiation exposure. Seven million paediatric **CT** scans were performed in 2007 in the USA and with this value rises almost 10% every year. Dose reduction for paediatric examinations has become a priority, since younger patients have a higher potential for an increased lifetime risk of radiation-induced complications[2]. However, the dose reduction should not compromise diagnostic image quality.

It is thought that, children receive a much higher radiation dose than necessary, so the Society for paediatric radiology practicing the as low as reasonably achievable (ALARA) concept, principle of the minimal radiation required for diagnostic imaging[3,4]. Different **CT** reconstruction algorithms have been developed over the years. Filtered back projection (FBP) is by far the most used today [5]. It is fast and applies different filters[6] and increases spatial resolution. It also increases image noise requiring a higher X-ray tube setting, resulting in a higher radiation exposure[7]. Iterative reconstruction (**IR**) techniques have been developed to reduce dose while maintaining or improving objective image quality by reducing noise and consequently improving Signal-to-Noise Ratio (SNR). However, these techniques initially required a high computing power and have been too time consuming, limiting its clinical application[8]. Recently developed an advanced iterative reconstruction techniques require less computing power and uses both FBP and raw data-based iterations to remove noise and improve image quality. The corrected image is compared with the original and the process is repeated several times[9].

PATIENTS AND METHODS:
Patient Selection:

The current study was conducted prospectively on 20 consecutive paediatric patients with an age ranging from two to eighteen years who were referred for non-contrast head **CT** examination. We excluded patients with suboptimal study quality due to motion artefacts, Patients below 1 year of age and Patients with significant **CT** abnormalities hindering quantitative or qualitative assessment.

CT Protocol Selection:

Patients were divided into three different dose groups for head **CT** protocols: By changing tube current and /or tube potential:

1st group (**SDCT**): 10 patients with standard paediatric head **CT** protocol; using 110KV and 190 mAs.

2nd group (**LD**): 10 patients with low dose head **CT** protocol; using 110KV and 140mAs.

CT Data Acquisition:

All studies performed on a 64-multidetector-row **CT** (perspective; Siemens Health Care, Erlangen, Germany) scanner, rotation time 0.6 second, pitch 1.2 and slice thickness 2mm **CT** image volumes were reconstructed for each group using standard filtered back projection FBP technique and iterative reconstruction (sinogram affirmed iterative reconstruction) SAFIRE with vendor recommended strength of 3/5, images were reconstructed with a smooth kernel, FBP images were reconstructed using the H30 kernel and SAFIRE images using the J30 kernel.

Radiation Dose Assessment:

Dose comparison between groups was done by dose–length product (DLP), that was automatically prepared by the scanner for each examination and by effective dose (ED) that was calculated by multiplying the DLP (in mGy × cm) by a region-specific normalized ED (EDLP) (in mSv × mGy-1 × cm-1).(10) Four different EDLP were reported for children(11): for 0 year, 0.011 mSv × mGy-1 × cm-1; for 1 year, 0.0067 mSv × mGy-1 cm-1; for 5 years, 0.0040 mSv × mGy-1 × cm-1; for 10 years, 0.0032 mSv × mGy-1 × cm-1. As Thomas K.E. and Wang B [12] used in their study, we used EDLP of 0 years for 0 days to 3 months, of 1 year for 4 months to 2 years, of 5 years for 3 to 7 years, of 10 years for 8 to 14 years, and of adult (0.0021 mSv × mGy-1 × cmj1) for 15 years or older.

Image Quality Analysis:

-Quantitative analysis: image noise, signal to noise ratio (SNR) were calculated. Noise measured in centrum semiovale and cerebellum white matter, It was defined in Hounsfield unit (HU) by SD of the mean density (MD) in

the region-of-interest (ROI) measurement. We obtained noise in white matter (Nwm) by averaging the SD of two 10-mm^2 circular ROI that were drawn at two different places in the white matter, on the same slice at the level of centrum semiovale and two 4 mm^2 circular ROI that were drawn at two different places in the white matter, on the same slice at the level of cerebellum (figure1).
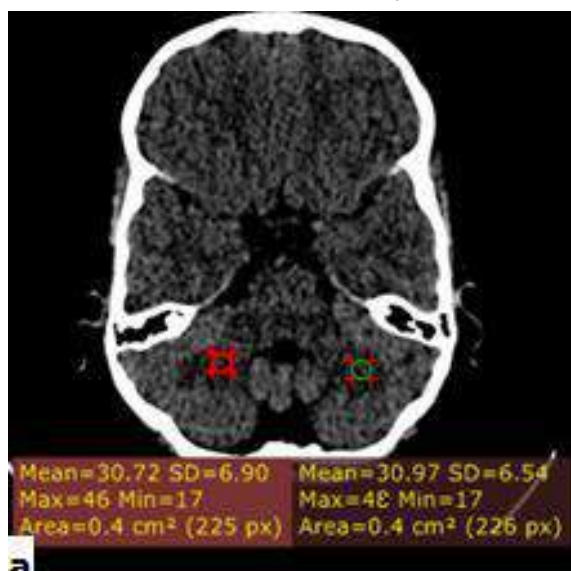
Figure 1a: Axial CT image at the level of cerebellar white matter to show the objective analysis using region of interests and measuring the average density.
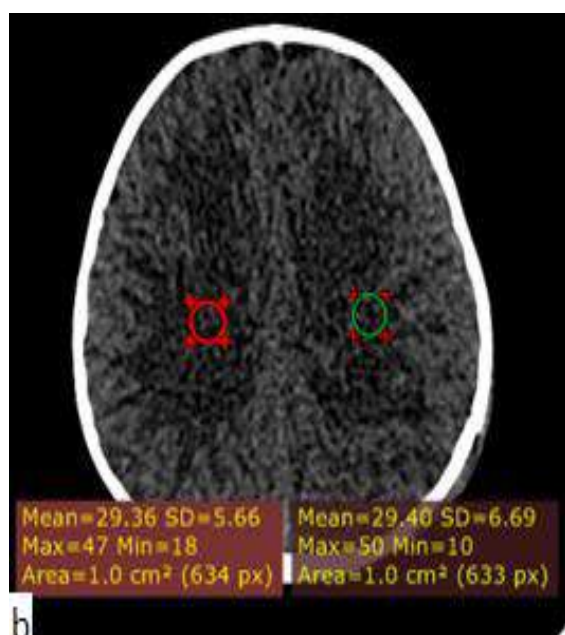
Figure 1b: Axial CT image at the level of centrum semiovale to show the objective analysis using region of interests and measuring the average density.

Signal-to-noise ratio was calculated by using the following

formula: $\text{SNR} = \dfrac{mean\ HU\ of\ tissue\ in\ ROI(MD)}{SD\ of\ HU\ in\ ROI}$

-Visual qualitative analysis: subjective image noise, image sharpness and diagnostic acceptability scored for each study by two blinded experienced radiologist (figure2) reviewers were blinded to dose level, and reconstruction kernel. **CT** image datasets were presented to the reviewer in random order, with images evaluated on a computer workstation (Syngo® Multimodality Workplace 20/0B-WE40A) (Table 1).

Table 1: The parameters of qualitative analysis.

Image Noise	Image Sharpness	Overall Quality
1=Non diagnostic	1= blurred /ill-defined	1= non diagnostic
2=Sub optimal	2= sub optimal	2= sub optimal
3=Average	3= diagnostic	3= average
4=Excellent	4= sharp contour/ well defined	4=Excellent
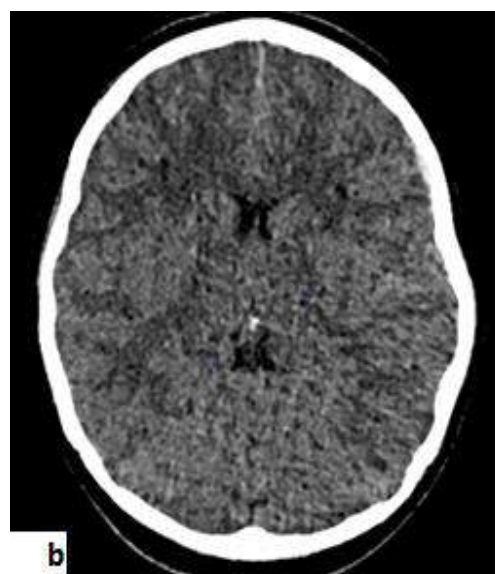
Figure 2: In group II examination, at the level of basal ganglia to demonstrate qualitative analysis with FBP (a) and with SAFIRE (b). No qualitative difference in image quality were identified.

RESULTS:
Quantitative Analysis:
The effective dose (ED) was insignificantly lower in low dose group than that in the standard dose **CT** group (p = 0.147) the difference was 19 (Table2). Noise measures of groups are shown in Tables 3 and 4 , the difference in the NWM of FBP and SAFIRE in each group was insignificant ,we found that NWM in **LD** group was insignificantly lower in FBP than that of SAFIRE (p = 0.066).

SAFIRE in **SDCT** and **LD** groups did not improve the SNR (p= 0.906, 0.177) respectively.

Table 2: Comparison between the different studied groups according to effective dose (mSv).

	Group I	Group II	F	P
Effective Dose				
Min. – Max.	1.20 – 2.50	0.50 – 2.0	30.726	<0.001
Mean ± SD	1.61 ± 0.35	1.30 ± 0.49		
Median	1.55	1.20		
% of reduction		19.3		

F: F test (ANOVA), Sig. bet. groups was done using Post Hoc Test (Tukey)

p_{con} : *p value for comparing between group I with each other groups*

Qualitative Analysis:
 In **SDCT** and **LD** groups the SAFIRE got significantly better scores in the image sharpness and overall quality regarding both viewers p<0.05, the image noise there was no significant difference regarding both viewers in **SDCT** group while 1st viewer gave better scores for SAFIRE in **LD** group (Tables 5,6).

Table 3: Comparison between NWM of FBP and SAFIRE in each group (HU).

NWM	FBP	SAFIRE	T	P
Group I				
Min. – Max.	4.45 – 6.37	4.21 – 6.06	0.102	0.921
Mean ± SD	5.48 ± 0.63	5.46 ± 0.60		
Median	5.46	5.64		
Group II				
Min. – Max.	4.67 – 11.41	5.09 – 11.67	2.090	0.066
Mean ± SD	6.62 ± 1.83	6.96 ± 1.77		
Median	6.36	6.62		

t: Paired t-test
*: Statistically significant at $p \leq 0.05$

Table 4: Comparison between S.N.R of FBP and SAFIRE in each group (HU).

S.N.R	FBP	SAFIRE	T	P
Group I				
Min. – Max.	4.58 – 6.65	4.94 – 6.58	0.122	0.906
Mean ± SD	5.58 ± 0.64	5.55 ± 0.55		
Median	5.46	5.39		
Group II				
Min. – Max.	2.88 – 6.01	3.19 – 5.71	1.465	0.177
Mean ± SD	4.72 ± 0.78	4.57 ± 0.63		
Median	4.75	4.59		

t: Paired t-test *: Statistically significant at $p \leq 0.0$

Table 5: comparison of visual scores between FBP and SAFIRE for SDCT group (n = 10).

	FBP				SAFIRE				P
	1	2	3	4	1	2	3	4	
	No., %	No., %	No., %	No., %	No., %	No., %	No., %	No., %	
1st Reviewer **Image noise**	0, 0.0	2, 20.0	6, 60.0	2, 20.0	0, 0.0	1, 10.0	4, 40.0	5, 50.0	0.102
I.S	0, 0.0	2, 20.0	5, 50.0	3, 30.0	0, 0.0	0, 0.0	3, 30.0	7, 70.0	0.034[*]
O.Q	0, 0.0	1, 10.0	6, 60.0	3, 30.0	0, 0.0	0, 0.0	3, 30.0	7, 70.0	0.025[*]
2nd Reviewer **Image noise**	0, 0.0	2, 20.0	6, 60.0	2, 20.0	0, 0.0	0, 0.0	8, 80.0	2, 20.0	0.157
I.S	0, 0.0	3, 30.0	5, 50.0	2, 20.0	0, 0.0	0, 0.0	3, 30.0	7, 70.0	0.005[*]
O.Q	0, 0.0	3, 30.0	5, 50.0	2, 20.0	0, 0.0	0, 0.0	7, 70.0	3, 30.0	0.046[*]

p: p value for Wilcoxon signed ranks test for comparing between FBP and SAFIRE. I.S: Image Sharpness, O.Q: Overall Quality, *: Statistically significant at $p \leq 0.05$

Table 6: comparison of visual scores between FBP and SAFIRE for LDCT group (n = 10).

	FBP				SAFIRE				p
	1	2	3	4	1	2	3	4	
	No., %	No., %	No., %	No., %	No., %	No., %	No., %	No., %	
1st Reviewer Image noise	0, 0.0	4, 40.0	5, 50.0	1, 10.0	0, 0.0	1, 10.0	6, 60.0	3, 30.0	0.025[*]
I.S	0, 0.0	3, 30.0	6, 60.0	1, 10.0	0, 0.0	0, 0.0	7, 70.0	3, 30.0	0.025[*]
O.Q	0, 0.0	3, 30.0	6, 60.0	1, 10.0	0, 0.0	0, 0.0	7, 70.0	3, 30.0	0.025[*]
2nd Reviewer Image noise	2, 20.0	1, 10.0	5, 50.0	2, 20.0	2, 20.0	1, 10.0	5, 50.0	2, 20.0	1.000
I.S	2, 20.0	1, 10.0	6, 60.0	1, 10.0	1, 10.0	1, 10.0	1, 10.0	7, 70.0	0.005[*]
O.Q	2, 20.0	1, 10.0	6, 60.0	1, 10.0	1, 10.0	2, 20.0	3, 30.0	4, 40.0	0.046[*]

p: p value for Wilcoxon signed ranks test for comparing between FBP and SAFIRE, I.S: Image Sharpness, O.Q: Overall Quality,
*: Statistically significant at p ≤ 0.05

DISCUSSION:

In the current study, it was found that in Standard dose group (**SDCT**) and low dose group (**LD**; SAFIRE compared to FBP reconstruction improved subjective image quality (image sharpness and overall quality parameters) for the same dose according to both reviewers while SAFIRE gave significant improvement in image noise parameter in group II according to 1st reviewer.

This was matching with studies done by **Korn et al.** [6] who evaluated different adult patients randomly assigned to a standard dose, and two low dose groups all reconstructed with FBP and iterative reconstruction. They found that for the same dose, iterative reconstruction improved subjective image quality, allowing for a 20% reduction in effective dose.

However, in the studies done by **Vorona et al** [13] decreased dose by 20% with a 20% iterative reconstruction for a small subset of paediatric head **CT** exams for shunt evaluations and compared them to older studies on the same patient without reduced dose and FBP. They found that there were no significant differences in subjective image quality in their study. **Kilic et al** [14]. Compared paediatric head **CT**s of 152 standard dose examinations reconstructed with FBP only versus 153 exams obtained with low dose reconstructed with FBP and 30% iterative and 70% FBP. The authors found no significant difference in subjective diagnostic quality between the standard dose group and low dose group reconstructed with 30% iterative reconstruction. **Ren et al** [15] compared objectively and subjectively the 300-mAs adult head **CT** examinations (DLP = 838 mGy × cm) with the 200-mAs ones (DLP = 559 mGy × cm, 33% dose reduction) that were reconstructed at various levels of Adaptive Statically Iterative Reconstruction (ASIR). They found subjective image quality of **LD** group with 30% ASIR was worse than or equal to that of the standard group.

Regarding objective measurements in standard dose group and low dose group; It was found WM measurements (noise and SNR) were better in the STD group with no

difference in the WMN and SNR between FBP and SAFIRE reconstruction within the same group, however, a reduction of ED around 20% in low dose group (group II) was achieved . Similarly, study by **Kilic et al** [14] WM measurements (noise and SNR) were better in the STD group. And in the study by **Ren et al.** [15] they found no marked difference in the noise between FBP and 30% ASIR images within the same group.

Corcuera-Solano et al [16] aimed to assess dose reduction for patients in the neurosurgical intensive care unit who undergo multiple head **CT** scans. While maintaining similar image quality and SNR levels, SAFIRE reconstruction low-dose **CT** (LDCT) offered higher image quality than FBP standard-dose **CT** with no differences in SNR at a 24% lower CTDIvol.

However, **Rapalino et al** [17] . In which they evaluated the effect of ASIR in reduced-dose adult head **CT** examinations. They found similar amount of SNR in the STD (FBP alone, DLP = 1270 mGy × cm) head **CT** examinations as in the **LD** examinations (20%-40% ASIR, 26.2% dose reduction, DLP = 932 mGy × cm).

These results were different from **Korn et al** [6] who stated that SAFIRE increases signal-to-noise by an average 48% while preserving objectively measured image sharpness at 20% dose reduction. When compared to standard dose FBP, SNR and CNR in the reduced dose SAFIRE scan were even improved.

We acknowledge several study limitations. First, **SDCT** and LDCT scans were all obtained in different groups of patients to ovoid exposing children to unnecessary radiation; instead we preferred to compare the means of different matched patient groups. Second, sample size of the groups was small to address the discordant finding. Larger series are warranted to find out whether this finding is due to a statistical error caused by small sample size or to the effect of SAFIRE on the paediatric brain. Third, our objective data is limited as measurements of noise were only obtained in the centrum semiovale and cerebellar hemispheres. Fourth we did not evaluate the effect of

different SAFIRE strength. Fifth, radiologists experience with the appearance of SAFIRE images (particularly at the higher levels) can readily differentiate them from traditional FBP images.

Finally we concluded that SAFIRE reconstruction in pediatric head **CT** scan improves subjective image quality at standard dose as well as low dose (20% dose reduction) while preserving objectively measured image quality.

CONCLUSIONS:

There was no statistically significant difference regarding quantitative analysis in the use of SAFIRE and FBP on all groups.

Uses of SAFIRE compared to FBP gave statistical significant improvement in qualitative   parameters in standard dose and low dose (20% dose reduction) group.

We recommend using Iterative Reconstruction in pediatric head **CT** scan to improve image quality in standard dose protocol as well as low dose protocol (20% dose reduction).

REFERENCES:

1- Chang RC, Yu CC, Hsu FY, Chen TR, Hsu SM, Tyan YS. Dose assessment of the patient and the helper in emergency head computed tomography. Radiat Meas. 2011; 46(12):2048-51.

2- Brenner DJ, Elliston CD, Hall EJ, Berdon WE. Estimated risks of radiation-induced fatal cancer from pediatric **CT**. AJR Am J Roentgenol. 2001; 176(2):289-96.

3- Solvis T. The ALARA (as low as reasonably achievable) concept in pediatric **CT** intelligent dose reduction: multidisciplinary conference organized by the Society of Pediatric Radiology, August 18–19, 2001. Pediat Radiol 2002; 32:217–313.

4- Goske MJ, Phillips RR, Mandel K, et al. Image gently: a Web-based practice quality improvement program in **CT** safety for children. AJR Am J Roentgenol 2010; 194:1177-82.

5- Pickhardt PJ, Lubner MG, Kim DH, Tang J, Ruma JA, del Rio AM, et al. Abdominal **CT** with model-based iterative reconstruction (MBIR): initial results of a prospective trial comparing ultralow-dose with standard-dose imaging. AJR Am J Roentgenol. 2012; 199(6):1266-74.

6- Korn A, Fenchel M, Bender B, Danz S, Hauser TK, Ketelsen D, et al. Iterative reconstruction in head **CT**: image quality of routine and low-dose protocols in comparison with standard filtered back-projection. AJNR Am J Neuroradiol. 2012; 33(2):218-24.

7- Greffier J, Fernandez A, Macri F, Freitag C, Metge L, Beregi JP. Which dose for what image? Iterative reconstruction for **CT** scan. Diagn Interv Imaging. 2013; 94(11):1117-21.

8- Han BK, Grant KL, Garberich R, Sedlmair M, Lindberg J, Lesser JR. Assessment of an iterative reconstruction algorithm (SAFIRE) on image quality in pediatric cardiac **CT** datasets. J Cardiovasc Comput Tomogr. 2012; 6(3):200-4.

9- Grant K, Raupach R. SAFIRE: Sinogram Affirmed Iterative Reconstruction [Internet]. Siemens; 2012. Available from: https://www. healthcare. siemens.com/computed-tomography/ options-upgrades/ clinical-applications/safire

10- Bongartz G, Golding SJ, Jurik AG, et al. European guidelines on quality criteria for computed tomography.

11- EUR 16262 EN. 1999. Available at: http://www.drs.dk/guidelines/ct/quality/mainindex.htm. Accessed July 11, 2012.

12- Report of AAPM Task Group 23. The Measurement, Reporting, and Management of Radiation Dose in **CT**. AAPM Report No.96. Available at: http://www. aapm.org/pubs/reports/rpt_96.pdf. Accessed February 8, 2012.

13- Thomas KE, Wang B. Age-specific effective doses for pediatric MS**CT** examinations at a large children s hospital using DLP conversion coefficients: a simple estimation method. Pediatr Radiol. 2008; 38:645-645.

14- Vorona GA, Zuccoli G, Sutcavage T, Clayton BL, Ceschin RC, Panigrahy A. The use of adaptive statistical iterative reconstruction in pediatric head **CT**: a feasibility study. AJNR Am J Neuroradiol 2013 Jan; 34(1):205–11.

15- Kilic K, Erbas G, Guryildirim M, Konus OL, Arac M, Ilgit E, Isik S. Quantitative and qualitative comparison of standard-dose and low-dose pediatric head computed tomography: a retrospective study assessing the effect of adaptive statistical iterative reconstruction. J Comput Assist Tomogr 2013 May-Jun; 37(3): 377–81.

16- Ren Q, Dewan SK, Li M, et al. Comparison of adaptive statistical iterative and filtered back projection reconstruction techniques in brain **CT**. Eur J Radiol. 2012; 81:2597-2601.

17- Corcuera-Solano I, Doshi AH, Noor A, Tanenbaum LN. Repeated head **CT** in the neurosurgical intensive care unit: feasibility of sinogram-affirmed iterative reconstruction-based ultra-low-dose **CT** for surveillance. AJNR Am J Neuroradiol. 2014; 35(7):1281-7.

-tomography/ options-upgrades/clinical-applications/safire

10- Bongartz G, Golding SJ, Jurik AG, et al. European guidelines on quality criteria for computed tomography.

11- EUR 16262 EN. 1999. Available at: http://www.drs.dk/guidelines/ct/quality/mainindex.htm. Accessed July 11, 2012.

12- Report of AAPM Task Group 23. The Measurement, Reporting, and Management of Radiation Dose in **CT**. AAPM Report No.96. Available at: http://www.aapm.org/pubs/reports/rpt_96.pdf. Accessed February 8, 2012.

13- Thomas KE, Wang B. Age-specific effective doses for pediatric MS**CT** examinations at a large children s hospital using DLP conversion coefficients: a simple estimation method. Pediatr Radiol. 2008; 38:645-645.

14- Vorona GA, Zuccoli G, Sutcavage T, Clayton BL, Ceschin RC, Panigrahy A. The use of adaptive statistical iterative reconstruction in pediatric head **CT**: a feasibility study. AJNR Am J Neuroradiol 2013 Jan; 34(1):205–11.

15- Kilic K, Erbas G, Guryildirim M, Konus OL, Arac M, Ilgit E, Isik S. Quantitative and qualitative comparison of standard-dose and low-dose pediatric head computed tomography: a retrospective study assessing the effect of adaptive statistical iterative reconstruction. J Comput Assist Tomogr 2013 May-Jun; 37(3): 377–81.

16- Ren Q, Dewan SK, Li M, et al. Comparison of adaptive statistical iterative and filtered back projection reconstruction techniques in brain **CT**. Eur J Radiol. 2012; 81:2597-2601.

17- Corcuera-Solano I, Doshi AH, Noor A, Tanenbaum LN. Repeated head **CT** in the neurosurgical intensive care unit: feasibility of sinogram-affirmed iterative reconstruction-based ultra-low-dose **CT** for surveillance. AJNR Am J Neuroradiol. 2014; 35(7):1281-7.

PATTERN OF NEOPLASMS IN CENTRAL COASTAL LIBYA; REGISTERED AT THE HISTOPATHOLOGY DEPARTMENT, MISURATA CENTRAL HOSPITAL

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ABSTRACT:

This is a retrospective study of benign and malignant tumours based on microscopic reports in Department of histopathology, Misurata Central Hospital in the period of four years (December 1994 to December 1998). The total number of biopsies for the studied period was 15 755; The cases with neoplastic proliferations were 1 439(9,13%) and the benign tumour were twice more than the malignant. The materials are analysed according age, sex and localization, and the results might be used for regional medical care programming.

KEY WORDS:

INTRODUCTION

Epidemiological studies have brought to light a number of factors of indisputable in importance in the development and distribution of cancer[1]. In some studies there are significant regional differences[2] in frequency and distribution of neoplasms. Communal, social and familial and personal habits and traditions determine the structure of pathology[3]. These investigations and research are one of the principal means of obtaining knowledge about the causes of cancer[4-10]. This is possible only by connecting epidemiological data with the other fields of research [7]. The last decades have seen dramatic advances in our understanding of neoplasia, but also an acceleration list of un-answered questions[8]. Now it is clear that the pattern of diseases vary widely between social groups and between populations living in different environment[9]. When the health policymakers have seriously undertaken the evidence based medicine at the forefront of the decision making in an attempt to distribute the shrinking resources wisely[11], it is very important to use correct primary data. The aim of this study is to investigate the frequency, gender and age distribution of neoplastic diseases in Central Coastal Libya, and the data to be used for the optimal possible planning of prevention, early detection of the neoplastic diseases and adequate treatment of the patients.

MATERIAL AND METHODS:

All microscopically diagnosed cases of neoplastic diseases in the Department of Histopathology, Misurata Teaching Hospital, Misurata, Libya, from December 1994 to November 1998 were included in the study. From total number of 15755 biopsies, neoplastic cases were 1439 (9,13%). All the patients were indexed by registry number with following information: Name, Age, Sex, Nationality, location of the lesion and microscopic diagnosis. The microscopic diagnoses were according the WHO histopathological classifications. We studied age and sex frequency of all benign and malignant lesions.

R E S U L T S:

Of the all 1439 neoplasms 954 (67, 42%) were benign and 422 (29,82%) were malignant (Table 1).

Table 1: Microscopically diagnosed benign and malignant neoplasms.

Type of neoplasms	Number	%
Benign	954	67.42
Border line malignancy	39	2.76
Malignant	422	29.82
Total	1 415	

The most often diagnosed benign neoplasm was leiomyoma with predominantly myometrial location. On the second and third place were lipoma and haemangioma most often found in the skin and subcutaneous tissues, followed by breast fibroadenoma, squamous cell papilloma, adenoma, teratoma, fibroma histiocytoma and others (Table 2).

Table 2: Frequency of microscopically diagnosed benign neoplasms.

Type of neoplasms	Number	%
Leiomyoma	329	34.48
Lipoma	168	17.61
Haemangioma	101	10,58
Fibroadenoma	91	9.53
Squamous cell papilloma	60	6.29
Adenoma	58	6.07
Teratoma	38	3.98
Fibroma	53	5.55
Histiocytoma	17	1.78
Others	39	4
Total	954	

The neoplasms of border line characteristics were found mostly in the breast, salivary glands, skeleton, ovary and subcutaneous tissues (Table 3).

Table 3: Microscopically diagnosed border-line neoplasms.

Type of neoplasms	Number
Phylloid tumour of the breast	13
Pleomorphic salivary gland adenoma	7
Osteoclastoma	7
Border line ovarial tumours	5
Cylindroma	3
Others	4
Total	39

The most often microscopically diagnose malignant neoplasm in the region was carcinoma of different microscopic type and localization (Table 4), second malignancy was malignant lymphoma (non-Hodgkin and Hodgkin) followed by sarcoma, malignant melanoma and malignant histiocytoma.

The most frequent epithelial malignancy was adenocarcinoma, followed by squamous cell carcinoma (SCC), undifferentiated carcinoma and malignant melanoma. Non-Hodgkin malignant lymphomas were diagnosed twice often than Hodgkin disease (Table 5)

The age and sex distribution of the most frequently diagnosed benign neoplasms are presented in (Table 6).

Table 4: Relative frequency of diagnosed malignancies.

Type of malignancy	Number	%
Carcinoma	324	76.78
Malignant lymphoma	41	9.71
Sarcoma	31	7.34
Malignant melanoma	11	2.60
Malignant histiocytoma	8	1.89
Others	7	1.65
Total	422	

Table 5: Relative frequency of diagnosed malignant neoplasms.

Type of malignancy	No.	%
Adenocarcinoma	131	31
Squamous cell carcinoma (SCC)	54	12.8
Breast carcinoma	42	10
Transitional cell carcinoma (TCC)	26	6
Basal cell carcinoma (BCC)	13	3
Sarcoma	31	7
Non-Hodgkin malignant lymphoma	22	5
Hodgkin disease	14	3
Malignant melanoma	11	2.6
Teratocarcinoma	5	1
Choriocarcinoma	6	1.4
Malignant histiocytoma	8	2
Undifferentiated carcinoma	13	3
Total	422	

Table 6: Age distribution of the benign neoplasms.

Wswsw hgjgijj asws	LM	Lipoma		HA		FA	SCP		AT
		M	F	M	F		M	F	
0-5	-	2	2	3	3	-	2	-	-
6-10	-	2	1	4	2	-	1	1	-
11-15	-	1	-	4	2	-	1	1	-
16-20	1	-	7	5	4	36	1	1	5
21-25	15	3	9	5	5	22	3	4	4
26-30	61	5	14	1	4	18	2	4	16
31-35	85	8	7	1	4	1	4	4	5
36-40	70	11	18	2	1	3	3	4	4
41-45	35	1	14	1	3	-	3	2	2
46-50	34	1	18	4	1	-	1	2	-
51-55	5	2	2	-	1	-	1	-	-
56-60	-	3	8	-	2	-	3	-	-
61-65	-	5	-	-	-	-	2	2	-
>65	7	3	5	-	-	-	-	-	-
Total	294	47	105	32	37	80	27	25	36
Mean	37	41	39	22	26	23	36	35	27

LM; Leiomyoma, HA; Hemangioma, FA, Fibroadenoma; SCP; Squamous cell papilloma, AT; Adult teratoma

Leiomyoma was found mostly as a benign tumour of the uterus and predominantly in the reproductive age with only single cases in the group older than 50 years. Leiomyomas in the male population were mostly prostatic. Uterine leiomyoma was found more often in the women between 26 and 40 years. From the seven leiomyomas in the age group over 65 years four were prostatic, one ovarial and one of the stomach.

The lipoma was found more than two times often in the female population than in the male. The relation female:male lipomas was 3,23. This benign lesion was distributed in nearly all age groups with highest incidence in the reproductive age and only single cases in the pre and post reproductive years.

The haemangioma was found with nearly equal sex and age distribution and a little higher incidence in the age group between 11 and 25 years.

The fibroadenoma of the breast and adult teratoma of the ovary were found mostly in the reproductive years with higher frequency for fibroadenoma in the 16 – 20 years age group and for teratoma in the group 26 - 30 years.

The squamous cell papilloma was found with nearly equal sex distribution and higher incidence in the reproductive age, decreasing after the age of 50 years. Only single squamous cell papilloma were diagnosed in the prepubertal years.

The age and sex distribution of the most often diagnosed malignant epithelial neoplasms is presented on table7.

Table 7: Age and sex distribution of malignant epithelial neoplasms.

Malignant neoplasm/Age	21 25	26 30	31 35	36 40	41 45	46 50	51 55	56 60	61 65	66 70	71 75	76 80	81 85	86 90	Over 91	Total	Mean age
Adenocarcinoma																	
M	0	0	0	2	1	4	0	10	13	10	6	11	0	0	0	57	65,84
F	0	4	1	10	1	9	9	8	14	4	7	3	0	0	0	70	55,94
SC Carcinoma																	
M	0	0	0	1	1	1	1	3	7	3	0	1	0	0	0	18	60,78
F	0	0	4	5	1	4	1	6	1	1	0	3	0	0	0	26	52,08
Breast duct Ca																	
M	0	3	3	5	2	8	3	2	2	1	1	0	0	0	0	30	46,93
F	2	2	0	0	2	1	0	0	1	1	0	0	0	0	0	9	42,22
TCC M																	
F	0	0	2	0	0	5	3	1	2	2	2	1	0	1	0	19	58,68
	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	2	60,00
BC Carcinoma																	
M	0	0	1	0	0	1	0	0	2	1	1	2	0	1	0	9	66,11
F	0	o	0	0	1	0	1	2	1	0	1	0	0	0	0	6	59,16
Malig.Melanom																	
M	0	0	0	0	0	0	0	1	0	1	2	0	1	4	1	7	80,14
F	0	0	0	0	0	0	1	1	0	1	0	0	0	0	0	3	61,00

The adenocarcinoma was found more often in the female population, starting in the age group 26 – 30 years, but with most high frequency if 61 – 65 years old group. In the males this microscopic type of cancer was found to start 10 years later and nearly the same level of incidence from 56 to 80years.

The squamous cell carcinoma (SCC) was also found more often in the female population with approximately the same frequency from 31 to 80 years. In the male group this type of malignancy was found to start five years later with most high frequency in the age of 61 – 65 years. The breast carcinoma in its lobular variant was found in the most young cancer group 21 – 25 years, whereas the ductal type starting in the group 26 – 30 years, with highest frequency in the age 46 – 50 years.

The transitional cell carcinoma (TCC) was found nearly 10 times more often in the male population with highest frequency between 46 and 55 years.

The basal cell carcinoma (BCC) was found also more often in the males with nearly regular distribution between 31 and 75 years, and slightly more often found in the older age.The malignant melanoma (MM) was found in the oldest age groups from 51 to 106 years and more than two times often in the male population.

The mean age of the females with benign tumours and nearly all groups of epithelial malignancies is lower than that of corresponding male groups with exception of haemangioma and transitional cell carcinoma (Tables 6 and 7).

The age and sex distribution of the lymphomas and some of sarcomas is presented on table 8.

The Hodgkin disease and malignant lymphomas were found more often in the male population with the highest frequency in the both sex groups in the age of 16 to 25 years. In the group of malignant lymphomas was found higher incidence in the ages 46 – 50 and 66 – 70 years. The female patients with Hodgkin disease are twice younger than the male patients, whereas non-Hodgkin's lymphoma female patients are around five years older than the males.

The liposarcoma was also found more often in the male population with nearly equal distribution between 16 and 75 years.

In the studied period were diagnosed only four leiomyosarcomas of the uterus with mean age of the patients 45 years. The main localizations of malignant neoplasms are presented of Table 9.

Table 8: Age and sex distribution of Hodgkin disease, malignant lymphomas and some sarcomas.

Neoplasm/Age	00 05	06 10	11 15	16 20	21 25	26 30	31 35	36 40	41 45	46 50	51 55	56 60	61 65	66 70	71 75	76 80	81 85	86 90
Hodgkin M	-	-	-	3	1	1	-	1	-	-	-	1	-	-	-	-	-	1
Hodgkin F	1	-	1	2	2	-	-	-	-	-	-	-	-	-	-	-	-	-
Malig. lympho M	1	1	-	-	2	1	-	-	-	2	1	-	1	2	1	-	-	1
Malig. lympho F	-	1	-	-	-	-	-	-	1	2	-	1	1	2	-	-	-	-
Liposarcoma M	-	-	-	2	-	-	-	-	-	-	1	1	-	-	1	-	-	-
Liposarcoma F	-	-	-	-	-	-	1	-	-	-	1	-	-	1	-	-	-	-
Leiomyosarcoma	-	-	-	-	-	-	2	-	-	1	-	-	1	-	-	-	-	-

Most of the malignant neoplasms were found in the female genital tract, first of all in the uterine corpus, followed by the cervical and ovarian cancers.

On the second place were found malignant tumours of gastrointestinal tract, mostly arising in the colon and the stomach.

The frequency of the breast and skin cancers was found to take the third and fourth places with very slight difference. Relatively high number of malignant neoplasms were diagnosed on biopsies from lymph nodes, soft tissue, nasopharynx, effusions and urine.

Table 9: Main localizations of malignant tumours.

Main localization	O r g a n s					Total
Female genital tract	Vulva 1	Cervix 23	Endometrium 15	Uterine body 11	Ovary 17	67
GI Tract	Colon 35	Appendix 3	Sm. Intestine 1	Stomach 13	Oesophagus 3	54
Cytology	Effusions 11		Urine and lavage 30		Sputum 4	45
Nasopharinx	Nasopharinx 5		Larynx 11		Lung 3	19
Urinary system	Urinary tract 2				Kidney 29	
Male genital system	Prostate 5				Testis 4	9
Liver and pancreas	Liver 6				Pancreas 2	8
Bones						7
Breast						50
Skin						47
Peritoneal biopsie						7
Lymph nodes						29
Soft tissues						24

Most of the malignant neoplasms were found in the female genital tract, first of all in the uterine corpus, followed by the cervical and ovarian cancers.

On the second place were found malignant tumours of gastrointestinal tract, mostly arising in the colon and the stomach. The frequency of the breast and skin cancers was found to take the third and fourth places with very slight difference. Relatively high number of malignant neoplasms were diagnosed on biopsies from lymph nodes, soft tissue, nasopharynx, effusions and urine.

DISCUSSION:

To have reliable information about medico-social side of oncological problem it needs to collect as full as possible data about benign, premalignant and malignant lesions based on diagnoses in well-developed histopathology department using most of the classical and modern microscopic diagnostic methods. This is especially important when the aim is prevention, early diagnosis and adequate treatment of the neoplasms. The figures in this study are still far from such completeness, but many of them is possible to be used

in planning the medical care in oncology. Although it operates with relatively small number of malignancies, these are found between two times more benign neoplasms. The female predominance of the neoplasms is clearly presented and much different from reports studying the populations with nearly equal socio-economic and cultural conditions [2, 5]. Most probably it is a reflection of differentiated activities of Misurata Teaching hospital. The total distribution of the malignancies in this study is found to be very near to the data from some developed countries [6], where the epithelial malignancies are with most high frequency and immediately next to them are the primary malignant neoplasms of the lymphoid tissue.

In the studied period the benign neoplasms were diagnosed nearly three times more often in the female patients than in the males, only the squamous cell papilloma was found with slight male predominance. For leiomyoma, fibroadenoa and adult teratoma, which in this study were nearly completely female lesions were with very near age distribution. Nearly the same frequency distribution was found for lipoma and squamous cell papilloma which suggests something common in the condition of arising or causation of these benign neoplasms. The clear cut difference in the distribution of haemangioma predominantly in the age groups before 35 years most probably is resulted because the surgical removal of this type benign lesions is mostly cosmetically indicated.

Female prevalence was found in the group of malignant epithelial tumours with exclusion of transitional cell carcinoma of the urinary tract. Adenocarcinoma as a most frequent malignancy was found more often in the female population and as in other reports most of all localized in gastrointestinal tract [5, 6]. Although the age distribution of nearly all epithelial malignancies was approximately equal, the adenocarcinoma and the breast cancer in the female population are not only more often, but also starting in the younger age groups. For the male prevalence of transitional cell carcinoma (TCC) in this study there was no acceptable explanation, but it is not excluded to be connected with heavy smoking, whereas for the older age and male prevalence of malignant melanoma and basal cell carcinoma, most probably to be connected with prolonged sun expose.

In the group of malignant lymphomas higher was found in the male population as it is reported in the developed countries [6] and in some communities with the same environmental, socio-economic and cultural conditions [5]. Unexpected male predominance was found for liposarcoma in contrast with benign fat tissue tumour – lipoma, for which the frequency in the female population was more than twice often. In our study leiomysarcoma was found only in the female population with mean age nearly ten years higher than the leiomyoma female patients.

Although the highest frequency of malignant tumours was found in the female genital tract, there was difference in the distribution of this neoplasms compared with other reports [5]. In our study the frequency of cervical, uterine and ovarian malignancies was found nearly equal with very slight prevalence of malignant neoplasms of uterine corpus. This most probably seems to be related to communal habits of circumcision, regular sexual relations, early marriage,

no contraception and multi-parity. Nearly the same frequency of breast and skin cancer as in our study was already reported in communities with the same environmental, socio-economic and cultural conditions and habits [5].

Based on the data of this study it is possible to make some general conclusions:

1. The pattern of cancer in Central Coastal Libya diagnosed in the Department of Histopathology in Misurata Teaching Hospital shows the same structure as in the developed countries, and the same time for some localizations, mostly female genital tract, date very near to the communities with near or the same cultural, socio-economic and environmental conditions.

2. The age distribution of most malignant neoplasms is overlapping that of benign tumours.

3. The clear cut female predominance of benign and malignant neoplasms most probably is reflection of the specificity of the structure and activities of Misurata Teaching Hospital.

4. The relative frequency of malignancies of the female genital system might be accepted as real and have to be connected with social organization, cultural habits and environmental conditions of the population in this Libyan region.

5. As all the cases included in this study are IN or OUT patients, to pretend for early diagnosis of the neoplasms it needs: a). In the cities of Misurata type and size there should be oncological organized medical units with possibilities of diagnosis, post-diagnostic follow up and treatment of the patients. These units have to plan and execute screening programs for the risk groups of the population; b). As the basic diagnostic method for the neoplastic diseases now-days is the microscopic study, there must be active working histopathology departments in every central hospital with the possibilities of modern histopathological diagnosis.

Note: The results were reported on symposium "Early detection and prevention of cancer" 5th & 6th December 1998, Tripoli Medical Centre.

REFFERENCES:

1- Anderson, M., Premalignant and malignant diseases of the cervix, I: Obstetrical and Gynaecological Pathology, Ed. Fox, H., Churchil Livingstone, Edinburgh, London, Melbourne and New York, 1987, 255 – 301;

2- Akhtar, Sh., Reyes, L., Cancer in Al – Qassim, Saudi Arabia. A retrospective study (1987 – 1995), Annals of Saudi Medicine, 1997, 17, 6, 595 -600;

3- Cotran, R., Kumar, V., Robbins, S., Robbins' pathological bases of disease, W.B.Saunders Company, 4th edition, Philadelphia, London, Toronto, Mountreal, Sydney, Tokyo, 1989, 469 – 514;

4- Dall, R., Epidemiology of human neoplasia, In: Oxford textbook of pathology, Ed: McGee, J. and all, Oxford University Press, 1992, 679 – 694;

5- El – Helal, Th., Bener, A., Galadari, I., Pattern of cancer in the United Arab Emirates referred to Al - Ain Hospital, Annals of Saudi Medicine, 1997, 17, 5, 506 – 509;

6- Gusberg, S., Introduction. Cancer control, In: Female Genital Cancer, Ed. Gusberg S and all, Churchill Livingstone, New York, Edinburgh, London, Melbourne, 1988, 21 – 33;

7- Hoover, R., Fraumeni, J., The epidemiological method of research, In: Female Genital Cancer, Ed. Gusberg and all., Churchill Livingstone, New York, Edinburgh, London, Melbourne, 1988, 21 – 33;

8- Lieberman, M., Lebovitz, R., Neoplasia In: Anderson's Pathology, Ed: Kissane, J., 9th edition, Mosby, IE, St. Louis, Baltimore, Philadelphia, Toronto, 1990, 566 – 514;

9- Mc Leen, A., Wolf, S., Environmental pollution, In: Oxford textbook of pathology, Ed: McGee, J. and all, Oxford University Press, 1992, 725 – 746;

10- Newel, G., Epidemiology of Cancer, In: Cancer, principles and practice of oncology, Ed: De Vita, V. and all., Lippincott, London, Mexico City, New York, St. Louis, Sal Paolo, Sydney, 1985, 151 – 195;

11- Stewart, A., Evidence based medicine: A new paradigm for the teaching and practice of medicine, Annals of Saudi Medicine, 1999, 19, 1, 32 – 36.

ANALYSIS OF LOW FIELD MRI SCANNERS FOR EVALUATION OF KNEE PATHOLOGY BASED ON ARTHROSCOPY

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ABSTRACT:

Magnetic Resonance Imaging has emerged as the primary investigation for evaluation of the knee injury because of its high resolution and accuracy and it has often been regarded as the noninvasive alternative to diagnostic arthroscopy.

The objective of this study was to correlate the results with arthroscopy, and to establish the accuracy of **MRI** in detecting ligament and meniscal injury and deferent knee pathology. A prospective analytical study done from March 2014 to July 2017 in Misurata city (Central Misurata hospital, Asafwa hospital and Alhikma hospital) for 82 patients. Only patients who underwent an arthroscopy following **MRI** were included. The resulting population consisted of 82 patients 66 (80.4 %) males and 16 (19.6 %) females. Their ages ranged from 17 to 62 years, with a mean age of 33.7 years at the time of the arthroscopic surgery. Various types of lesion seen on **MRI** were as follows: anterior cruciate ligament (ACL) tear 20 (24.3%), medial meniscus (MM) lesions 29 (35%), lateral meniscus (LM) lesions 22 (26.8%), degenerative changes 11 (13.4%), patellar lateralization 1 (1.2%) and posterior cruciate ligament (PCL) tear 1 (1.2%). Sensitivity, specificity and accuracy of **MRI** in detecting meniscal and cruciate ligament injury were MM: 100%, 88.67%, 92.68%; for LM: 78.57%, 96.42%, 92.7%; for ACL: 95.23%, 96.72%, 96.34%; for PCL: 50%, 100%, 100%; for degenerative changes: 78.85%, 97.05%, 93.9% and for patellar lateralization 16.7%, 100%,93,9% respectively. **MRI** is a noninvasive, useful and reliable diagnostic tool for evaluating knee injury and it can be used as a first line investigation in patients with knee injury.

INTRODUCTION:

Magnetic resonance image (MRI) is a cross-sectional imaging technology that uses a magnetic field and radio frequency signals to cause hydrogen nuclei to emit their own signals, which then are converted to images by a computer. When hydrogen nuclei stimulated by radio frequency signals leading to energy emitted from it, MRI is based on measurements of that energy. The energy emitted varies depending on type of tissues from which the signals emanate. Which allow MRI to distinguish between different tissues.

There is imaging characteristic of normal tissue that can be seen as follow:

- Fat gives rise to high signal intensity on T1 weighted images and low to intermediate signal intensity on T2.
- Tendons, ligaments, and menisci show low signal intensity on all sequences.
- Cortical bone displays very low signal intensity on all sequences.
- Muscles exhibit intermediate signal intensity on both T1 and T2 weighted images, although the signal intensity is slightly lower on T2.
- Cartilage gives rise to intermediate signal intensity on both T1 and T2 weighted images.

Knee arthroscopy remains by far the most frequent arthroscopic procedure that is performed worldwide. This is due to its historical longevity and the large number of well trained surgeons, as well as the extensive amount of knee pathology that can be addressed arthroscopically and the ease of access to the articular structures, compared to other joints. In the beginning, diagnostic arthroscopy was fairly common, but now a days, with the advent of knee MRI as a routine investigation, there is a clear shift towards interventional use. Common procedures performed during arthroscopic surgery are meniscectomies, meniscal sutures, ACL reconstructions, cartilage debridement and less frequently PCL or multi ligament reconstructions, patellar subluxations and cartilage repairs.

AIM OF THE WORK:

knee problem is one of most common presenting symptoms that can be seen by orthopedic surgeon. It is varies from sport relate injuries, degenerative changes, domestic injuries. so many physician use **MRI** of knee as non-invasive radiation free with better ability to assess knee pathology. MRI scan is routinely used to support the diagnosis for meniscus or ligamentous injuries prior to recommending invasive arthroscopic examination and surgery.

MRI scanning is depend on image view, technical factors that is why our study was designed to identify correlation of **MRI** and it's finding with arthroscopic finding.

PATIENTS AND METHODS:

This is a prospective analytical study done from March 2014 to July 2017 in Misurata city (Misurata Medical center, Asafwa Hospital and Alhikma Hospital) for 82 patients. Only patients who underwent an arthroscopy following **MRI** were included (82 patients).

The standardized MR imaging protocol consisted of sagittal, coronal and axial sequences, in section thickness of 3-5 mm. ACL was considered normal when it appeared as a band of fibers of low to intermediate signal intensity on

both sagittal and coronal dual images. The ACL was considered to be partially torn when there was abnormal signal intensity within the ligament or when otherwise intact fibers appeared wavy on sagittal or coronal dual images. The ACL was considered to be completely torn if there was disruption of all fibers or if it was not discernible at all on MRI. The menisci was considered normal when it appeared as low signal intensity in all there plane evolution. according to changes in signal classification are done (table 1).

Table 1:Classification of meniscus rupture in MRI.

Stage	Description
I	globular intensity, not adjacent to either articular surface
II	liner signal within the meniscus
III	liner signal, the extend to either the superior or inferior articular surface
IV	meniscus fragmentation

These patients had arthroscopic knee surgery within a mean 70 days (range, 7- 345 days) after having the MRI performed. The arthroscopic surgeries were performed by one of 2 orthopedic surgeons with more than 5 years of experience. MRI images and reports were reviewed by the surgeons prior to surgery, and the MRI reports were available to the surgeons at the time of surgery. Operative reports were dictated independent of the MRI readings, and the two were later compared.

The composite data was tabulated and studied for correlation with MRI findings and grouped into four categories:

- True-positive (TP): if the **MRI** diagnosis was confirmed by arthroscopic evaluation.
- True-negative (TN): when **MRI** negative for lesion and confirmed by arthroscopy.
- False-positive (FP): when **MRI** shows lesion but the arthroscopy was negative.
- False-negative (FN): - result when arthroscopy was positive but the **MRI** showed negative finding.

Statistical analysis was used to calculate the sensitivity, specificity, positive predictive value (PPV) and the negative predictive value (NPV), accuracy, in order to analyze **MRI** results.

RESULTS:
The study group of 82 patients consisted of 66 men (80.4 %) and 16 women (19.6 %). All underwent arthroscopic knee surgery. The average age was 33.4 years (range: 17– 62 years). Maximum number of patients (n=30) who suffered knee pathology were in the age group of 21-30 years (Table 2).

Comparison of the arthroscopic and **MRI** findings yielded the following results:
MRI findings for the ACL yielded 20 true-positives (were confirmed on arthroscopy) and 59 true-negatives (without evidence of ACL) with 2 false positive (were miss interpreted to have ACL) and 1 false negative (were not

diagnosed by (**MRI**) (table 3), which resulted in 95.23% sensitivity, 96.72% specificity, 90.9% positive predictive value, 98.34% negative predictive value and 96.34% accuracy.

Table 2: Age distribution.

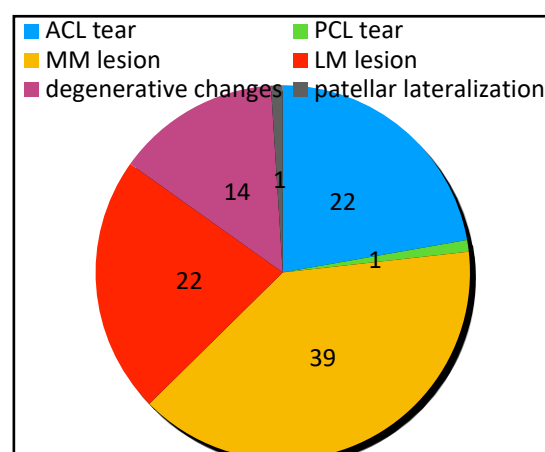| Age / Years	Number	%
11 -20	9	11
21 - 30	30	37
31 - 40	20	24
41 - 50	17	21
Above 50	6	7

Figure 1 a: Distribution number of knee pathology by MRI.
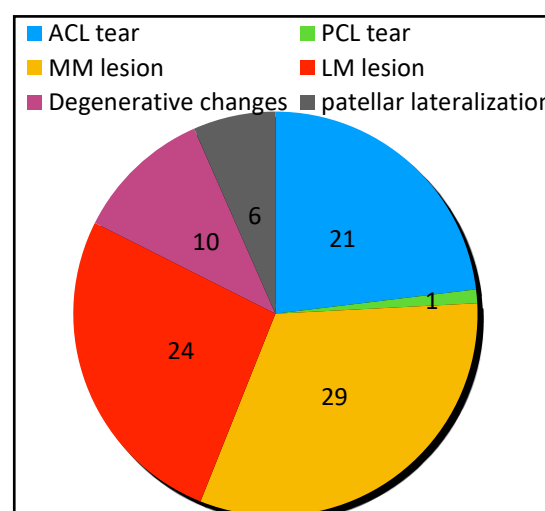

Figure 1-b: Distribution of knee pathology by arthroscopic evaluation.

Table 3: MRI findings for the ACL.

	Arthroscopic positive	Arthroscopic negative	Total
MRI positive	20 (TP)	2 (FP)	22
MRI negative	1 (FN)	59 (TN)	60
Total	21	61	82

MRI findings for the PCL yielded one true-positives (were confirmed on arthroscopy) and 81 true-negatives (without evidence of PCL) with 0 false positive and 0 false negative (table 4), which resulted in 50% sensitivity, 100% specificity, 100% positive predictive value, 100% negative predictive value and 100% accuracy.

Table 4: MRI findings for the PCL.

	Arthroscopic positive	Arthroscopic negative	Total
MRI positive	20 (TP)	0 (FP)	20
MRI negative	0 (FN)	81 (TN)	81
Total	1	81	82

MRI findings for the MM lesions yielded 29 true-positives (were confirmed on arthroscopy) and 47 true-negatives (without evidence of MM lesions) with 6 false positive (were miss interpreted to have MM lesions) and 0 false negative (table 5), which resulted in 100% sensitivity, 88.67% specificity, 82.85% positive predictive value, 100% negative predictive value and 92.68% accuracy.

Table 5: MRI findings for the MM lesions.

	Arthroscopic positive	Arthroscopic negative	Total
MRI positive	29 (TP)	6 (FP)	22
MRI negative	0 (FN)	47 (TN)	47
Total	29	53	82

MRI finding regarding LM lesions yielded 22 true-positives, 54 true-negatives and 2 false positive and 4 false negative (table 6) (sensitivity 78.57% - specificity 96.42%).

Table 6: MRI findings for the LM lesions.

	Arthroscopic positive	Arthroscopic negative	Total
MRI positive	22 (TP)	2 (FP)	24
MRI negative	4 (FN)	54 (TN)	58
Total	26	56	82

MRI findings for the degenerative changes yielded 11 true-positives (were confirmed on arthroscopy) and 66 true-negatives (without evidence of degenerative changes) with 2 false positive (were miss interpreted to have degenerative changes) and 3 false negative (were not diagnosed by MRI) (table 7), which resulted in 78.85% sensitivity, 97.05% specificity, 84.61% positive predictive value, 95.65% negative predictive value and 93.9% accuracy.

Table 7: MRI findings for the degenerative changes.

	Arthroscopic positive	Arthroscopic negative	Total
MRI positive	11 (TP)	2 (FP)	13
MRI negative	3 (FN)	66 (TN)	82
Total	14	68	82

Regarding patellar lateralization 67 cases were MRI and **arthroscopic** negative (Table 8).

Table 8: MRI findings for the patellar lateralization.

	Arthroscopic positive	Arthroscopic negative	Total
MRI positive	1 (TP)	0 (FP)	1
MRI negative	5 (FN)	76 (TN)	81
Total	6	76	82

DISCUSSION:

The role of **MRI** has steadily increased and now it has become the investigation of choice for most of the knee pathology. It is also used for pre and post-operative Meniscal injuries are a common cause of knee dysfunction and leads to one-third of all knee disturbances[1]. Similarly ACL tears also leads to significantly unstable knee joint that can leads to other knee problems. Despite being the most frequently injured ligament of the knee, its clinical diagnosis remains difficult. **MRI** a noninvasive and radiation free diagnostic modality is commonly used for these internal derangements[2].

Our study included 82 patients clinically suspected to have some form of internal derangement of knee. Maximum patients were young subjects in the age group of 21-30 years (37%). Also, 39% by **MRI** and 32% by Arthroscopy was diagnosed to have MM lesions all age groups of this study.

The low-field **MRI** scanner used in this study was a good predictor of MM lesions (sensitivity 100% - specificity 88.67%), but not for LM lesions (sensitivity 78.57% - specificity 96.42%). Previous studies comparing low-field **MRI** to surgical findings have shown similar results for the medial meniscus (sensitivity 75% - 96% & specificity 69%-100%), but lateral meniscus findings have (sensitivity 56.2% - 93% & specificity 88.23%-100%)[4-15].

We are also unaware of any reason why such differences would exist between the medial and lateral menisci. Because of greater fixation, less mobility, and its function as a secondary stabilizer to anterior translation, medial meniscus tears tend to be more prevalent and more symptomatic[16,17]. Fischer et al; considered the fact that because of high incidence of medial meniscus tears may have caused the radiologists to anticipate findings and therefore "over-read" tears of the medial meniscus and "under-read" those of the lateral meniscus[6].

We find also low-field **MRI** to be a good identifier of ACL tears (sensitivity 95.23% - specificity 96.72%), which is comparable with other low-field (sensitivity, 75%-98%; specificity, 81%-100%) [5-7, 9, 10, 12-15, 18].

There was only one patient with PCL tears were present in this study, so more information is needed to assess the accuracy of low-field **MRI** in identifying such pathology (specificity 100%).

We cannot conclude our results on patellar lateralization because of no similar research could be found in this area.

There is no doubt that the radiologist's experience, technical performance of MRI and training are very important factors in interpretation of MRI. At the same time, reliable statistical data of the diagnostic value of the MRI are also related to the independent base of reference. Regarding knee MRI, in most of the studies and in our study as well, the base of reference is arthroscopy[19, 20].

This presupposes that arthroscopy is 100% accurate allows for the diagnosis of every possible knee pathology. This is not always the case[21]. Arthroscopy is a technically demanding procedure and the results are varying according to surgeon's experience, especially in difficult cases[22].

The MRI is a useful tool for identifying the extent of knee pathology, but it is not without limitations.

CONCLUSIONS AND RECOMMENDATIONS:

MRI is a noninvasive, radiation free useful and reliable diagnostic tool for evaluating knee pathology and it can be used as a first line investigation in diagnosing meniscal and cruciate ligament injuries. The diagnostic yield is increased with appropriate use of sequences and proper analysis of images in all planes with high technical and expert radiologist. Almost all ligamentous and meniscal injuries can be diagnosed with high level of confidence.

Pathological entities should be carefully differentiated from normal variants, pitfalls and artifacts of imaging.

In traumatic setting in post-traumatic knee, MRI evaluation before arthroscopy has been proved as cost-effective. Despite the fact that arthroscopy has altered the management of knee pathologies, most orthopedic surgeons admit the limitations of the procedure in the evaluation of extra-articular pathology, its invasiveness, cost and uncommon but possible complications associated with it.

Arthroscopy still remains gold standard for definitive diagnosis.

REFFERANCE:

1- Bui-Mansfield LT, Youngberg RA, Warme W, Pitcher JD, Nguyen PL. Potential cost saving of MR imaging obtained before arthroscopy of the knee. Evaluation of 50 consecutive cases. AJR. 1997; 168:913–18.

2- Shahriaree, Heshmat, editors. O'Connor's Text book of arthroscopic surgery. Philadelphia: J.B Lippincott; 1984.

3-S.E.I, et al. Knee joint examination by **MRI**: the correlation of pathology, age and sex. N Am J Med Sci. 2010; 2(4):202–204.

4- Barnett MJ. MR diagnosis of internal derangements of the knee: effect of field strength on efficacy. AJR Am J Roentgenol. 1993; 161:115–118.

5- Cotten A, Delfaut E, Demondion X, et al. MR imaging of the knee at 0.2 and 1.5 T: correlation with surgery. AJR Am J Roentgenol. 2000; 174:1093–1097.

6- Fischer SP, Fox JM, Del Pizzo W, Friedman MJ, Snyder SJ, Ferkel RD. Accuracy of diagnoses from magnetic resonance imaging of the knee. A multi-center analysis of one thousand and fourteen patients. J Bone Joint Surg Am. 1991; 73:2–10.

7- Franklin PD, Lemon RA, Barden HS. Accuracy of imaging the menisci on an in-office, dedicated, magnetic resonance imaging extremity system. Am J Sports Med. 1997; 25:382–388.

8- Glashow JL, Katz R, Schneider M, Scott WN. Double-blind assessment of the value of magnetic resonance imaging in the diagnosis of anterior cruciate and meniscal lesions. J Bone Joint Surg Am. 1989; 71:113–119.

9- Kinnunen J, Bondestam S, Kivioja A, et al. Diagnostic performance of low field **MRI** in acute knee injuries. Magn Reson Imaging. 1994; 12:1155–1160.

10- Lokannavar HS, Yang X, Guduru H. Arthroscopic and low-field **MRI** (0.25 T) evaluation of meniscus and ligaments of painful knee. J Clin Imaging Sci. 2012; 2:24.

11-Mandelbaum BR, Finerman GA, Reicher MA, et al. Magnetic resonance imaging as a tool for evaluation of traumatic knee injuries. Anatomical and pathoanatomical correlations. Am J Sports Med. 1986; 14:361–370.

12- Riel KA, Reinisch M, Kersting-Sommerhoff B, Hof N, Merl T. 0.2-Tesla magnetic resonance imaging of internal lesions of the knee joint: a prospective arthroscopically controlled clinical study. Knee Surg Sports Traumatol Arthrosc. 1999; 7:37–41.

13- Naranje S, Mittal R, et al. Arthroscopic and magnetic resonance imaging evaluation of meniscus lesions in the chronic anterior cruciate ligament-deficient knee. Arthroscopy. 2008 Sep;24(9):1045-51. doi: **10-**1016/j.arthro.2008.03.008. Epub 2008 May 15.

14- Ahmad N, Khanda GE, et al. Assessment of menisci and ligamentous injuries of the knee on magnetic resonance imaging: correlation with arthroscopy. J Pal Med Assoc. 2008 Oct;58(10):537-40.

15- Gupta MK, Raunlyar MK, Kam NK, Ahmad K, et al. **MRI** evaluation of knee injury with arthroscopic correlation. J Nepal Health Counc.2014 Jan;12(26):63-7.

16- Fan RS, Ryu RK. Meniscal lesions: diagnosis and treatment. MedGenMed. 2000;2(2).

17- Greis PE, Bardana DD, Holmstrom MC, Burks RT. Meniscal injury: I. Basic science and evaluation. J Am Acad Orthop Surg. 2002; 10:168–176.

18- Kladny B, Gluckert K, Swoboda B, Beyer W, Weseloh G. Comparison of low-field (0.2 Tesla) and high-field (1.5 Tesla) magnetic resonance imaging of the knee joint. Arch Orthop Trauma Surg. 1995; 114:281–286.

19- Esmaili Jah AA, Keyhani S, Zarei R, Moghaddam AK. Accuracy of **MRI** in comparison with clinical and arthroscopic findings in ligamentous and meniscal injuries of the knee. Acta Orthop Belg. 2005;71(2):189–196.

20- Navali AM, Bazavar M, Mohseni MA, Safari B, Tabrizi A. Arthroscopic evaluation of the accuracy of clinical examination versus **MRI** in diagnosing meniscus tears and cruciate ligament ruptures. Arch Iran Med. 2013;16(4):229–232.

21- Khanda G, Akhtar W, Ahsan H, Ahmad N. Assessment of menisci and ligamentous injuries of the knee on magnetic resonance imaging: correlation with arthroscopy. J Pak Medical Association. 2008;58(10):537–540.

22- Hristijan Kostov, Slavcho Stojmenski, Elena Kostova. Reliability Assessment of Arthroscopic Findings Versus **MRI** in ACL Injuries of the Knee. Acta Inform Med. 2014 Apr; 22(2): 111–114. doi: 10,5455/aim, 2014.

Evaluation Of Drug Utilization In Medical Departments At Misurata Medical Center

By
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ABSTRACT:
Drug utilization studies on Medicine Department are an area of research where the data available is very limited. This study aimed to assess the drug prescribing trends and **WHO** core indicators for drug utilization in medicine department at Misrata Medical Center and to identify the common diseases among patients admitted in this department. A cross-sectional evaluation of the pattern of medications was conducted among 105 patients admitted in Medicine Department at Misurata Medical Center. The study found out Of 105 cases, 63.8% were male and 36.2% were female. Average age of patients was 59.3±19.6 years and average stay in the hospital was 3.6± 2.12 days. Maximum numbers of patients were admitted for diabetes mellitus (58%) as well as cardiovascular diseases (58%). Average number of drugs prescribed per prescription was 5.2 ± 2.1. Insulin 30/70 was the maximum utilized drug and among antibiotics, Amoxicillin / clavulanic acid was maximum utilized antibiotic. Finally, poly-pharmacy, over use of proton-pump inhibitors and some antibiotics are areas of concern. There is a need of more of such studies including larger number of patients and other departments; pharmacovigilance should be made more effective; and, hospitals should constitute drugs and therapeutics review committee to rationalize prescribing pattern.

KEY WARDS: Medicine department, drug utilization, **WHO** indicators core, prescribed drugs, antibiotics.

INTRODUCTION:

Drug utilization research was defined by **WHO** in 1977 as the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences[1].In this regard, rational prescribing of drugs is a skill for which proper knowledge about drugs, pharmacoeconomics, and pharmacovigilance[2,3]. Generally, drug utilization pattern varies from countries to countries and even among hospital within the same country and sometime within the same hospital at different point of time possibly because of changing disease trends over a period of time[4,5] and therefore, pattern of drug utilization is studied because it is necessary and essential to the role of community pharmacist in the pharmaceutical care through estimation of the prevalence of drug use, followed by analysis of the recommended guidelines for prescription are being followed or not[6]. If the drugs are overused, they increase occurrence of toxic reactions; if underused, there will be therapeutic failure and chances of development of resistant strain to antibiotics; if misused, will lead to unnecessary adverse drug effects, and drug interactions[5,6].At all events, an optimal pharmacotherapy is achieved when the right drug in the correct dosage and quality reaches the right patient at the right time point[7]. As **WHO** revealed more than 50 % of all medicines are prescribed, dispensed or sold inappropriately while 50 % of the patients fail to take them correctly[8]. These include mainly medications errors and adverse drug events which associated with increased costs for treatment[7,9]. In this regard, numerous issues are involved in the drug prescription error such as polypharmacy, lack of sufficient pharmacological knowledge, errors in patients' charts or documentation by nurses, inadequate pharmacy service, renal excretion of drugs, drugs with narrow therapeutic index, and the use of anticoagulants or diuretics[7,9].Therefore, evaluating the drug usage patterns in the Medical Department has the potential of determining the rationality of drug therapy through assessment of drug prescribing trends, average number of drug per prescription[4,10].

METHODOLOGY: A cross sectional and observational study was conducted on 105 consecutive medical files for patients who were admitted in the male and female medical wards at Misurata Medical Center to collect all demographic and treatment details per patients from day one of admission until the day of discharge during Marsh-April 2016. The study aimed to assess drug prescribing trends, average number of drug per prescription, and the WHO core indicators for drug utilization. All data were collected and analyzed using Statistical Package for Social Science (SPSS 20.0). For continuous variables, means and standard deviation were reported. For categorical variables, frequencies and percentage were reported, and Chi square test (χ^2) was used for comparison between categorical variables with *P*- value <0.05 was considered statistically significant.

RESULTS AND DISCUSSION:

Demographic characteristics of study population: out of 105 patients, 67(63.8%) were male and 38 (36.2%) were female, with age range between 15-90 years. Mean age in our study was 59.3±19.6, while mean age reported by Eshiet *et al* was 37.5 years[12] and by Meher *et al* was 48.12 years[13]. Distribution of our study population according to age and gender as shown below (Figure 1).
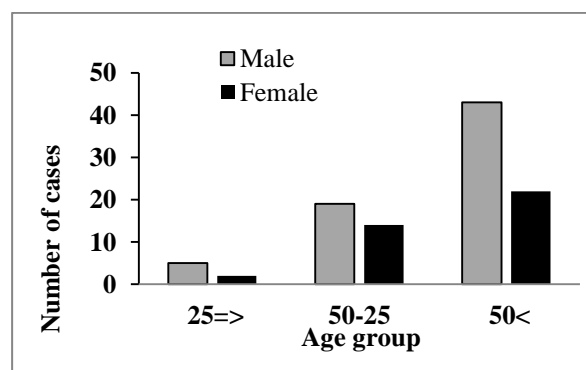

Figure 1: Age and sex distribution.

Age and gender distribution in the present study is approximately similar to that reported by Meena *et al*, and Choudhary *et al*.[6, 11].

Subsequently, our study demonstrated more males were admitted than females. Hence the majority of drug utilization was by males. Additionally, more prevalence of patients was observed in age group >50 years may be attributed to this population is vulnerable to many diseases and drug related problem.

Mean duration of hospital stay was 3.6 ± 2.12 days in our study while 7 days was observed in study by Chaudhary *et al*[11] and 3.38 days by Al Balushi *et al* [9] and subsequently average hospital stay of patients was less as compared to others studies and this indicate towards quality health services.

Common diagnosis among study population: In our study, patients were categorized by sex.. We observe all diagnosis were similar between both gender (*P*-value > 0.05) except in case of anemia was significantly higher in female than male due to anatomical causes (*P*- value < 0.05). Additionally, We found diabetes mellitus (58%) was

the more common morbidity pattern in medicine department as well as cardiovascular diseases (58%) followed by microbial infections(39%),anemia (37%), renal diseases (25.7%), gastrointestinal disease (23.8%), respiratory disease (17%), neurology disease (16%), and hypothyrodism (3.8%) (Table1) .Similarly to our finding, an Indian study that found the maximum number of patients were in hypertension and diabetes mellitus (49.69%) followed by chronic kidney disease, coronary artery disease, tuberculosis, COPD, liver disease, dilated cardiomyopathy, cancer, and arrhythmias[15].

Conversely to our study, the morbidity pattern in our patients was different to what is commonly found in other study that showed majority of the of drug per prescription was for patients presented with diseases of respiratory system followed by urinary tract diseases and the rest of the cases were related to other systems[16]. Anyway, the presence of co morbidities may lead to multiple and complex drug treatment and thus the chances of adverse drug reactions and drug interactions are greater[15].

Table 1: Diagnosis for study population.

Diagnosis	All cases (No.=105)		Male (No.=67)		Female (No. =38)		P-value*
	No.	%	No.	%	No.	%	
D.M	61	58	35	52.2	26	68.4	0.079
CVD	61	58	39	58.2	22	57.9	0.568
Microbial Infections	41	39	24	35.8	17	44.7	0.244
Anemia	39	37	20	29.9	19	**52.6**	**0.033****
Renal	27	25.7	18	26.9	9	23.7	0.454
GIT	25	23.8	14	20.9	11	28.9	0.243
Respiratory	18	17	13	19.4	5	13.2	0.318
Neurology	17	16	13	19.4	4	10.5	0.182
Hypothyroidism	4	3.8	-	-	4	10.5	-

* χ^2 test   ** Significant P <0.05.

Prescribing pattern of drug used:

In this study, we found a total number of drugs was 583; and the majority of drugs were administrated by the oral route (58%) followed by the parenteral route (36%) and then inhalation routes (6%). According to our finding, other study noted a total number of drugs administered by IV route was 737 (50.10%), oral route 631 (42.89%), IV + Oral route 58 (3.94%), inhalational route 26 (1.76%), IM route 12(0.8%) and by SC route 7(0.48%) [6] while, Choudhary *et al* study that found total number of drugs administered by injectable route 81%, by oral route 12%, and remaining 7% were used by both routes [11]. Analysis of prescriptions using **WHO** core indicators are shown in(Table 2).

Table 2: WHO prescribing core indicators.

Indicator	Value
Average number of drugs / prescription	5.2 ± 2.1
% prescription with antibiotics	(38/105)36%
prescription with injections	(38/105)36%
% from essential drug list	(213/385)36.5%

The most common route of administration was the oral drugs in our study. We observe among the most common drugs administered through oral routes was Acetyl Salicylic Acid 39 (37%) followed by lipid regulator as Atrovastatin 25(23.8%) and Simvestatin 24 (22.9) (Figure 2).
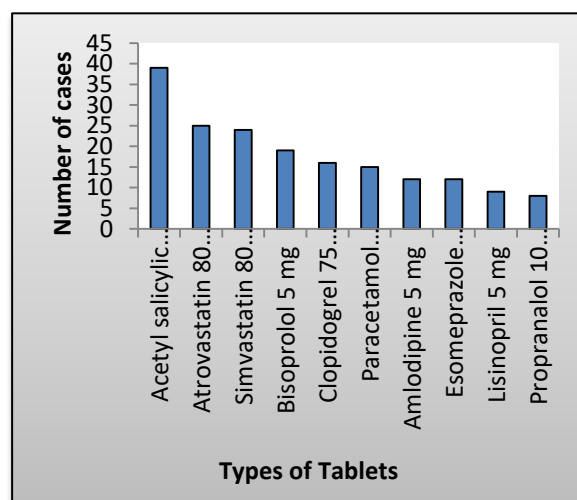

Figure 2: The top ten tablets prescribed to patients.

While, figure 3 addressed the most common injections in our study. We found Insulin30/70 - (59%) to top the list followed by Isotonic Sodium Chloride 38 (36%), Ranitidine 25 mg 36 (34%), Omeprazole 31(29.5%), and Paracetamol 27(25.7%). Conversely to our results, Jhaveri *et al* have found Ranitidine (58.14%), Metoclopromide (54.29%), Furosemide (41.12%), and Cefotaxime (23.37%) were the commonly prescribed parenteral drugs[18].
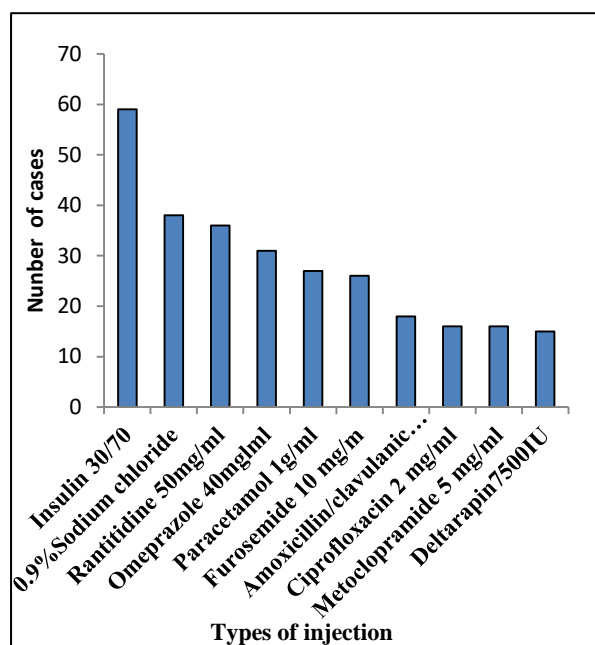

Figure 3: The top ten injections prescribed to patients.

In our study, mean number of drugs prescribed per patient was 5.4±2.1 which trends towards poly-pharmacy (≥5 drugs), while 4.01±2.24 was reported by Muzammil *et al* [14], 9.4± 0.31by Laurda *et al*[15]. Furthermore, we found no significant difference between patients needed poly-pharmacy and patients needed non polypharmacy at all age groups except at age group ≥50 years by using $\chi^{(2)}$ test as shown in (Table 3).

Table 3: Distribution of drug regimens prescribed to patients according to their age.

Age	Drug regimens		P*
	Polypharmacy	Non polypharmacy	
< 25	3	5	0.273
25-50	18	12	0.480
≥50	44	18	**0.001**

* Chi sequare

This means most of our study population visiting the hospital needed polypharmacy and this indicate chronic nature of their diseases and their tendency for comorbidity. Interestingly, ("Polypharmacy") is considered as a common type of irrational use of medicines, can have various consequences for the patients, the public, the health system, and even in the economy. This can lead to increased morbidity, mortality, wastage of resources, increased risk

of adverse drug reactions and the emergence of drug resistance[17]. Importantly, we observed 3 hypertensive patients had chest infection; one patient had Tuberculosis and treated with Lisinopril, while two had Pneumonia and treated with Captopril. Both Lisinopril, and Captopril induce bronchospasm, therefore, they contraindicated in these cases.

Antibiotics prescribed among patients:
In our study, we found total number of antibiotics prescribed was 71 (12.2%) in Medical Department where Amoxicillin/clavulanic acid 18 (25.4%%) followed by Ciprofloxacin 16 (22.5%) were present to top of antibiotics and the higher rate of antibiotics were prescribed for respiratory infection. Figure 4 illustrates all antibiotic regimens were received by 38 (36%) patients in our study. We observed 17 (44.7%) patients were treated with a monotherapy of antibiotic, which lead to very less chance of resistance of antibiotic and adverse reactions, while 6 (15.8%) cases received several antibiotic regimens and 15 (39.5%) patient treated by constant antibiotic regimens from admission until discharge. In this regard, other study done by Meena *et al* that noticed total number of patients to whom antibiotics were prescribed was (84%) and cephalosporins were the most commonly antimicrobial drug (28.91%), followed by Antimalarial drugs (21.38%), Penicilllins (12.34%), Fluroquinolones (9.03%), Antiprotozoal drugs (8.43%), Tetracyclines (8.13%), Clindamycin (7.22%), Aminoglycosides (1.80%), Macrolides (1.5%) and Vancomycin (1.2%)[6].In more details, the current study found that microbial cultures were not used as a guide for the prescription of antibiotics in 25/38 (65.8%)of the cases studied. Microbial cultures were requested in only 13/38 (34.2%) of the cases. Our findings is similar to the survey of the pattern of antibiotic use which revealed only about 1/5 of the patients **who** were studied had any form of microbiological investigation and out of these, less than 1/2 of the results were used as a guide for antibiotic prescription[19].Either, another study reported the selection of antibiotics were rational for most of the indications, bacteriological confirmation prior to institution of antibiotics were not done in any case. Furthermore, We found most antibiotics were prescribed in appropriate dose except Ceftriaxone which prescribed twice daily instead of once dosing for Respiratory infection and UTI in cases had renal dysfunction due to their elimination through both renal and biliary route. So, this drug has been used in higher doses, but as defined daily dose which represents maintenance dose of drug, Ceftriaxone may have been used for acute and emergency conditions in higher doses. Finally, we observed the empirical use of broad spectrum antibiotic treatment for most infections. However, it is recommended that samples for Microbial cultures should be obtained before the commencement of empirical treatment; a quick switch in antibiotic therapy from a broad spectrum antibiotic; and a narrow spectrum agent is important once the causative organism has been identified to limit the development of resistance because the antimicrobial resistance results in increased morbidity, mortality, cost of health care and ultimately a decrease in the rate of successful treatments[20].

CONCLUSION:
From the above results, we concluded relatively less number of patients was studied and very few similar studies available to compare; and poly-pharmacy and over use of some antibiotics are areas of concern.
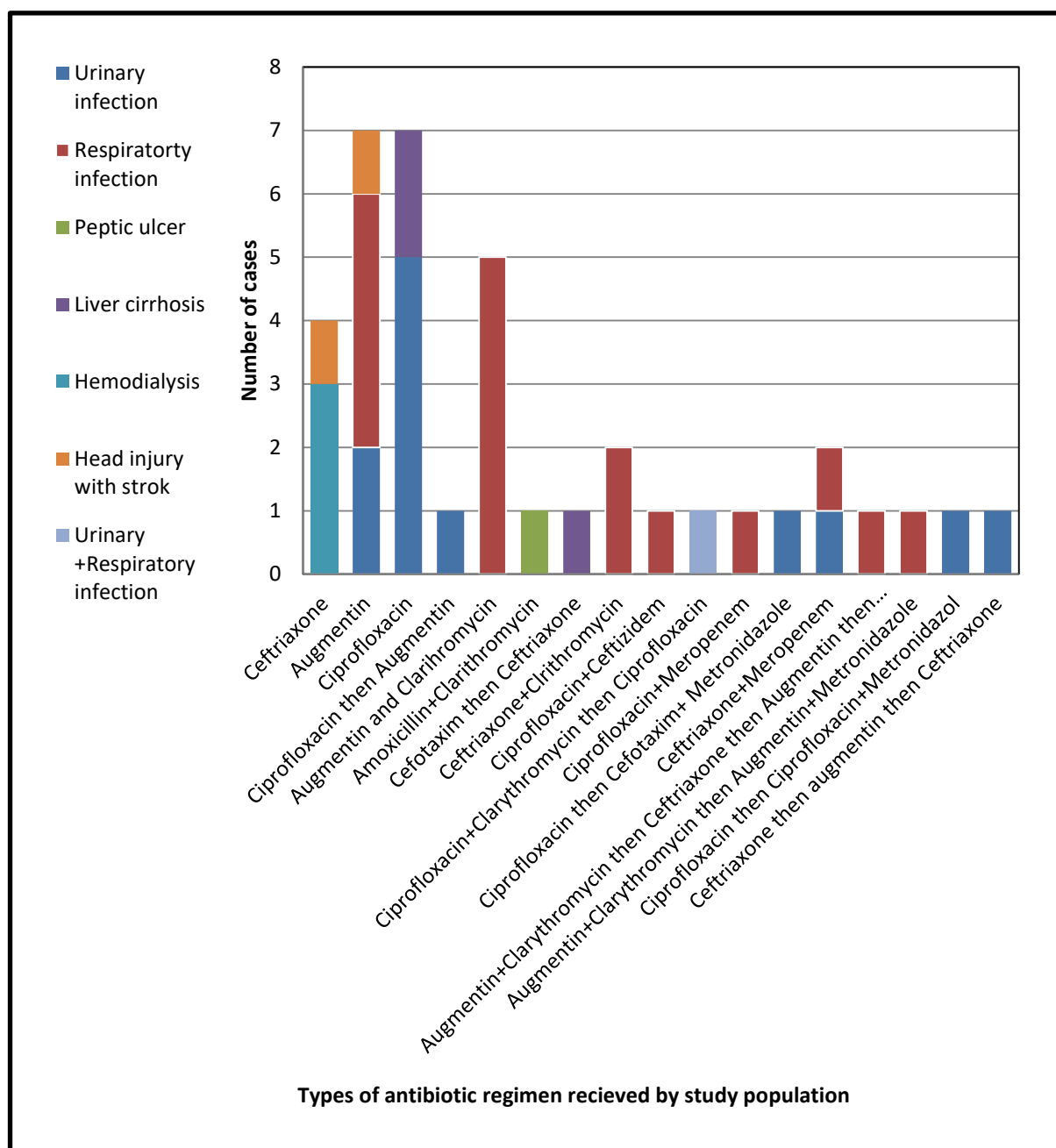
Figure 4 : Types of antibiotics regimens received by study population .

RECOMMENDATION:

We recommended more of such studies including larger number of patients and other departments should be performed; reference literatures such as British National Formulary (BNF) should be distributed at each ward to provide unbiased drug information; and adverse drug reactions reporting should be made where pharmacovigilance should be made more effective; and hospitals should constitute drugs and therapeutics review committee to rationalize prescribing pattern.

REFERENCES:

1-http://apps.**who**.int/medicinedocs/en/d/Js4876e/2.html. (Accessed on May 17, 2017).

2- Stanulovic, M., Kakovijevic, V., Roncevic, N. (1984). Drug utilization in paediatrics: non-medical factors affecting decision making by prescribers. *Eur S Clin Pharmacol*.;27:237-41.

3- Tognoni, G., Laporte, J.R. (1993). In: Drug utilization studies: Methods and uses. Dukes. MNG. Eds. From clinical trials to drug utilization studies. Copenhagen, **WHO** Regional office for Europe. 23-41.

4- Kaur S, Rajagopalan S, Kaur N, Shafiq N, Bhalla A, Pandhi P, *et al*. (2014) Drug utilization study in medical emergency unit of a tertiary care hospital in north India. *Emerg Med Int.*

5- Bergman, U., Christenson, I., Jansson, B.,Wiholm, B.E. (1980).Auditing hospital drug utilization by means of defined daily doses per bed-day. A methodological study.*Eur J Clin Pharmacol*.; 17:183-187.

6-Meena, V.K., Atray, M., Agrawal, A. (2016) Evaluation of Drug Utilization Pattern In Indoor Patients Of Medicine Department At Tertiary Care Teaching Hospital In Southern Rajasthan. *IJPSR*.;7:3835-40.

7-Krahenbuhl-Melcher,A., Schlienger,R., Lampert, M., Haschke, M., Drewe, J., Krahenbuhl,S. (2007). Drug-related problems in hospitals: a review of the recent literature. *Drug Saf.*; 30:379-407.

8-WHO. Promoting rational use of medicine: Core components. Geneva. 2002.

9-Al Balushi, K.A., Al-Shibli, S., Al-Zakwani, I.(2013). Drug utilization patterns in the emergency department: A retrospective study. *J Basic Clin Pharm.*; 5:1-6.

10-Bergman, U., Elmes, P., Halse, M., Halvorsen, T., Hood, H., Lunde, P.K, *et al*. (1975). The measurement of drug consumption- Drugs for diabetes in Northern Ireland, Norway and Sweden. *Eur J Clin Pharmacol.*;8:83-9.

11- Chaudhary PK, Maurya AK, Jain A, Pathak A, Sharma N. Drug utilization pattern in medicine department in a tertiary care teaching hospital in Uttar Pradesh. *Indo Am Journal of Pharmaceutical Research*, 2015 ISSN No: 2231-6876.

12-EshietUnyime Israel, Effiong Grace Sylvester*, Akwaowoh, Akpabio ElijahEshietUnyime Israel *et al.*: The Use of Antibiotics in a Nigerian Tertiary Health Care Facility. *American Journal of Biomedical Science and Engineering* 2015; 1(3): 25-31.

13-Meher, B.R., Mukharjee, D., Udayshankar. (2014). A study on antibiotic utilization pattern in a general medicine ward of a tertiary care teaching hospital. *Journal of Chem and Pharma Res.*; 6(7):1847-9.

14Najmi M,H., Hafiz, R.A., Khan, I., Fazli FRY.(1998) Prescribing practices: an overview of three teaching hospitals in Pakistan. *Jpak Med Asso.*; 48:73-76.

15-Lourdu, J.A., Venkata, N. Kumar P., Udhayalakshmi, T., Jayapriya, B. and Maruti, S, S. (2013). Drug utilization patterns of Geriatric patients admitted in the Medicine Department of a Tertiary Care Hospital. *Int. J. of Pharm.and Life Sci.* 4: 3087-3092.

16-Alkahtani, S.A. (2018). Drug Utilization Patterns in the Emergency Department of Najran University Hospital. *Journal of Pharmacy Practice and Community Medicine*, 4:12-15.

17-Shiva, H., Azadeh, N., Mehdi, R. (2013). "Irrational Antibiotic Prescribing": A local Issue or Global Concern? *Excl Journal*; 12: 395-issN1611-2156.

18-Jhaveri, B.N., Patel, T.K., Barvaliya, M.J., Tripathi, C.B.,(2014).Drug utilization pattern and pharmacoeconomic analysis in geriatric medical in-patients of a tertiary care hospital of India. *J Pharmacol Pharmacother*.5:15-20.

19-Jimoh, A.O., Etuk, E.U., Sani, Z., Shuaibu, H.A. (2011) The Pattern of Antibiotic use in a Family Medicine Department of Tertiary Hospital in Sokoto, North Western Nigeria. Journal of Clinical and Diagnostic Research, 5 (3):566569.

20-Goodman and Gilman's: The Pharmacological Basis of Therapeutics-11th Edi. 2006.

KELOID MANAGEMENT IN NATIONAL CANCER INSTITUTE/ MISURATA DURING 2011 - 2018

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ABSTRACT:

The difference between hypertrophic scars and keloids may be a difficult clinical challenge, where the Treatment options depend upon identifying the difference between both.

Therapeutic intervention should be undertaken with caution to minimize the possibility of recurrence or untoward effect of a larger resulting lesion especially with keloids. Efficacy of chemotherapeutic agent in treatment of keloid. Retrospective analysis of data of patients with keloid managed in national cancer institute/Misurata (NCI), In the period between (January 2011 to December 2018), patients were classified into two groups: 1st group (51 patients) underwent excision with 5-FU/steroid injections, and 2nd group (51 patients) underwent excision with steroid injections. A total of 102 patients with keloids were managed. Patients who underwent excision with the 5-FU/steroid combination had a 92% average reduction in lesion size compared to 73% in the group of patients who did receive only steroid, the side effects of treatment in 1st groups were higher 23% compared with the 2nd group 15%. Combination of 5-FU/triamcinolone may be superior in efficacy compared to intralesional steroid only therapy.

KEYWORDS: Keloid, 5FU, Steroid, Intralesional injections

INTRODUCTION

The distinction between hypertrophic scars and keloids may be a difficult clinical challenge, both lesions may be erythematous, raised, firm papules with a smooth surface. In general, hypertrophic scars remain within the confines of a wound and resolve spontaneously with time, Keloids extend beyond the original confines of the wound, persistently enlarge where Spontaneous resolution of keloids is unusual[1,2]. Histologically, hypertrophic scars and keloids are similar, in that both demonstrate whorls and collagen nodules, Hypertrophic scars demonstrate progressive flattening of these collagen nodules, whereas keloids have persistent disarray of these fibrous growths[1,2]. Treatment options depend upon identifying the difference between hypertrophic scars and keloids (if possible). Often, lesions may be treated with intralesional corticosteroid injection or surgical excision combined with other treatment to help minimize recurrence. Therapeutic intervention should be undertaken with caution to minimize the possibility of recurrence or untoward effect of a larger resulting lesion[3,4].

AIM AND OBJECTIVES OF THE STUDY

To identify the efficacy and the result of our new approach in the management of keloid by using chemotherapeutic agent (5FU) , instead of the ordinary method which was by intralesional steroid injection .

METHODS:

Retrospective analysis of data of patients with keloid managed in national cancer institute/Misurata(NCI), in the period between (January 2011 to December 2018). Patients were classified into two groups: 1st group (51 patient) underwent excision with 5-FU + steroid injections, and 2nd group (51 patient) underwent excision with only steroid injections.

Response (which mean no lesion recurrence during 6 months after management) and adverse effects

(telangiectasia, atrophy, hypopigmentation, and dehiscence) were considered. A mixture of 75% 5-FU 250mg\5ml and 25% Triamcinolone 40mg was used in 1st group and only Triamcinolone 40mg was used in 2nd group. Patients after undergoing excision, they received injections intraoperative then at 1, 2, and 3 months post-op.

RESULTS:

A total of 102 patient with keloids were managed. In the In 1st group 92% of them (47 patient out of 51) shows complete response (no lesion recurrence during 6 months Post-operative), compared to only 73% in patients in the 2nd group who did receive only steroid (37 patients out of 51) so, these results were statistically significant where (p = 0.05) (figure 1).
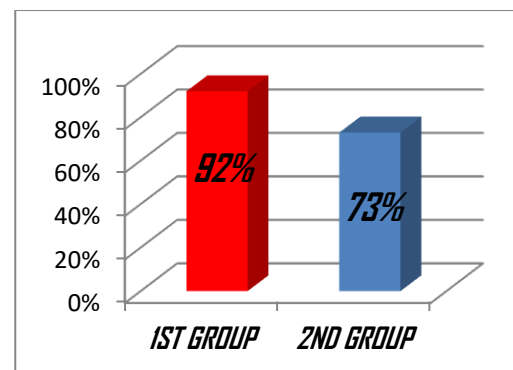

Figure 1: Response to treatment.

The side effects of treatment in 1st group were higher 23% (12 patients develop the adverse effect) in compared with the 2nd group where was only 15% (8 patients develop the adverse effect), these results statistically are not significant (p = 0.62) (figure2).

Keloid before and after treatment (A 12 year-old girl presenting with recurrent keloids treated by excision and intralesional injection of 5-FU+steroid (6 months post-operative).

The most common side effect was telangiectasia, also some patients shows Impaired wound healing, Sterile abscess, White marks, Localized or distant steroid acne, transient hyperpigmentation and subcutaneous lipoatrophy with different degree and proportions.
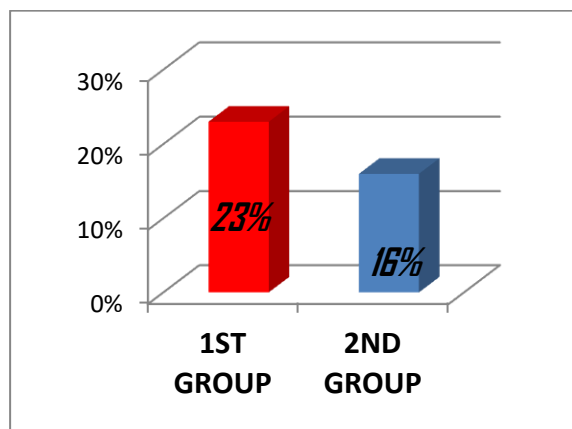

Figure 2: Side effect of treatment.

CONCLUSIONS:

Of course the retrospective method of this study is drawback point, also the duration of post management follow up was short, plus the lack of histopathological study of the keloid before and after therapy, but generally our results in this study and the supporting basic science data suggest combination of 5-FU/triamcinolone may be superior in efficacy compared to intralesional steroid only therapy[1-7].

The adverse effect profile was higher in the 5-FU group, despite the telangiectasia, atrophy, Impaired wound healing, Sterile abscess, White marks are known side effect of the steroid in general[8-13]. Side effects include transient hyperpigmentation and subcutaneous lipoatrophy which rarely appear in those patients are due to 5-FU component of therapy[12]. So, it will be beneficial to study the effects of 5-FU with a lower steroid component and also with using another anti-neoplastic agents.

REFERENCES

1- Broughton G, Janis JE, Attinger C. Wound healing: an overview. *Plast Reconstr Surg*. 2006;117:1e–S.

2- Al-Attar, A., Mess, S., Thomassen, J. M., et al. Keloid pathogenesis and treatment. *Plast Reconstr Surg* 117: 286-300, 2006.

3- Burton CS and Escaravage V. "Hypertrophic scars and keloids." In: Bolognia JL, *et al. Dermatology*. (second edition). Mosby Elsevier, Spain, 2008:1487-1502.

4- Daggett A, Congcharoen J, *et al*. "Top 10 things you need to know about keloids and their treatment." *J Miss State Med Assoc*. 2016;57(4):108-11.

5- Berman, B., Flores, F. Recurrence rates of excised keloids treated with postoperative triamcinolone acetonide injections or interferon alfa-2b injections. *J Am Acad Dermatol* 37: 755-757, 1997.

6- Griffith, B. H., Monroe, C. W., McKinney, P. A follow-up study on the treatment of keloids with triamicinolone acetonide. *Plast Reconstr Surg* 46: 145-150, 1970.

7- Tang, Y. W. Intra- and postoperative steroid injections for keloids and hypertrophic scars. *Br J Plast Surg* 45: 371-373, 1992.

8- Asilian, A., Darougheh, A., Shariati, F. New combination of triamcinolone, 5-Fluorouracil, and pulsed-dye laser for treatment of keloid and hypertrophic scars. *Dermatol Surg* 32: 907-915, 2006.

9- Apikian, M., Goodman, G. Intralesional 5-fluorouracil in the treatment of keloid scars. *Australas J Dermatol* 45: 140-143, 2004.

10- Benkhaial, G. S., Cheng, K. M., Shah, R. M. Effects of 5-fluorouracil on collagen synthesis during quail secondary palate development. *J Craniofac Genet Dev Biol* 13: 6-17, 1993.

11- Bulstrode, N. W., Mudera, V., McGrouther, D. A., et al. 5-fluorouracil selectively inhibits collagen synthesis. *Plast Reconstr Surg* 116: 209-221; discussion 222-203, 2005.

12- Gupta, S., Kalra, A. Efficacy and safety of intralesional 5-fluorouracil in the treatment of keloids. *Dermatology* 204: 130-132, 2002.

13- Nanda, S., Reddy, B. S. Intralesional 5-fluorouracil as a treatment modality of keloids. *Dermatol Surg* 30: 54-56; discussion 56-57, 2004.

TRENDS OF VASCULAR INJURIES DURING LIBYAN CRISIS

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ABSTRACT:
Misurata City had being a conflict zone having military attacks during Libyan Revolution in 2011. Most vascular traumas in military attacks occur from fragments from ballistic weaponry such as artillery, rockets, grenades, and bombs. Severe vascular injury is manifested by hemorrhage or ischemia and may harbor mortality or limb loss. The present study is to provide a review of war time vascular injuries experience on the observed injury patterns and current management strategies used in the care of unusual military attacks vascular injuries. A retrospective review was conducted of all war-related injured patients presenting to the emergency room (ER) with vascular injuries and treated at Misurata Central Hospital from March to October 2011. The recorded medical and demographic data were analyzed. Vascular injuries accounting for 7.5% of the total operated patients. 49.54% were of them were young age between16-29 years old. Nearly half of injuries (49.5%) were caused by shrapnel. Majority of patients had extremity injuries (73.4%); lower extremity including the thighs and legs was the most prevalent anatomical location (51.4%). While reversed interposition great saphenous venous grafts accounting for 35% of the injured vessels; synthetic grafts were used for 31.8% of repaired vessels. The mortality rate was 8.3%, amputations reported in 2.8% of cases as their immediate postoperative course was relatively uneventful. ascular injuries in our locality has a similar epidemiology and outcome to that previously reported, most vascular injuries in our study were seen in young men, frequently caused by shrapnel explosive weapons and in lower extremity. Femoral artery was the commonest injured vessel. Vascular reconstruction in the first hours after trauma may prevent many unnecessary and preventable amputation procedures.

Key wards: vascular war injuries, vascular repair, revascularization and secondary amputation.

INTRODUCTION:

The uprisings in Libya at 2011 took on a violent course quickly, and led to many casualties on both sides of the conflict. It had spread within weeks across the country to Maserati City which had being a conflict zone having military attacks during the crisis and become soon subject of mass violence at the hands of governmental armed forces. Combat-related vascular injuries are unlike civilian vascular injuries in terms of epidemiology, mechanism, pathophysiology, and outcome. Combat or military trauma is generally penetrating trauma because of high energy weapons which is associated with severe vascular injuries that is manifested by hemorrhage or ischemia and may harbor mortality or limb loss. Explosive weapons are designed to increase the number and energy of sleeve fragments leading to multiple penetrating wounds[1] . This is why vascular injuries are often associated with multiple traumas leading to high mortality unless prompt and appropriate surgical management is made. Exsanguination is perhaps the most significant cause of potentially preventable death after injury[2-3] . whereas ischemic tissue damage leads to high rates of amputation in a characteristically young and active population[4] . Regardless of the etiology of the vessel injury, the essential principles of treatment are emergency resuscitation at the scene, triage and rapid transport to an appropriate hospital, vigorous resuscitation, diagnosis, and definitive surgery. The management of military vascular trauma has changed considerably as a result of the wars of the 20th century and the significant contributions of Debakey, Hughes, Rich, and others[5-8] . Most of the changes in vascular trauma care were made out of necessity and adaptations to the casualties the surgeons were receiving as occurred, the Afghanistan war changed the way military surgeons treat vascular trauma patients[9] . The evacuation time, climate, and availability of medical resources will impact the outcome of surgical management of war-injured patients[10] .

AIM OF STUDY:

The present study reviews patients with vascular injuries treated at Misurata Central Hospital during the conflict in 2011 in Maserati City.
The objective of the present study is to provide a review of war time vascular injuries experience on the observed injury patterns and current management strategies used in the care of unusual military attacks vascular injuries.

METHODOLOGY:

A retrospective review was conducted of all war-related injured patients presenting to the emergency room (ER) with vascular injuries and treated at Misurata Central Hospital from March to October 2011. The recorded medical and demographic data were analyzed. Studied variables included age, gender, site of vascular injury, mechanism of injury, associated trauma, type of vascular repairs, and clinical outcome. Also the time between injury and arrival to hospital was recorded.
All patients were examined at ER clinically and documentation done regarding the pattern of injury whether penetrating or blunt, mechanism of vascular injury, and presence of nonvascular associated injury. Vascular injuries were characterized by type whether arterial, venous or a combination of both. Clinically the patients were categorized into 2 main categories; firstly is the soft signs such as history

of significant hemorrhage, injury proximity to major vessels (fracture pattern, dislocation, penetrating wound or blast injury), bruising or hematoma, or question regarding the presence or absence of a palpable pulse requiring Doppler ultrasound as another diagnostic test. Secondly; are the hard signs such as pulsatile hemorrhage, obvious ischemia, palpable thrill, or expanding hematoma requires immediate management in the operating room, and those were transferred to theatre for urgent intervention.

Intra-operatively; type of injury was documented whether partial tear, complete transection, contusion, pseudo-aneurysm or arterio-venous fistula. Similarly; type of vascular repair was documented including, simple ligation, reversed venous interposition graft, direct sutures, venous patch, and interposition PTFE (polytetrafluoroethylene graft). In majority of the cases vascular repair was attempted within the first hours from the time of admission to hospital. The great saphenous vein (GSV) was the conduit of choice of repair in both the upper and lower limbs if the patient's condition allowed. Temporary intraluminal shunting was indicated for patients with combined arterial, venous, and soft tissue injuries and concomitant long bone fractures when the decision was made to perform limb salvage.

The standard sterile system tubing was used as a shunt and concomitant venous injuries were repaired selectively. Following the procedure; time to revascularization is defined as the period from approximate time of injury to the time at which the patency of the injured vessel is restored at surgery. To reduce incidence of infection; prophylactic fasciotomy was avoided and patients monitored for developing early post revascularization compartmental syndrome within 12 hours that indicate associated fasciotomy. Arterial reconstruction was considered successful when the pulse distal to the reconstruction was present or if the continuity of the vessel was documented by Duplex study, due to absence of Angiography facility. Limb salvage is defined as the presence of a viable limb at one month after injury regardless of functional outcome.

RESULTS:

During the study period; a total of 218 patients with vascular injuries secondary to trauma by military attacks were included in the present study. Of the total operated patients at Misurata Central Hospital 2011, 7.5% were vascular injuries. Majority of them were males (209 men 95.9%); and 9 women (4.1%). Majority of them were revolutionaries (civilian) and their age was ranged between 2 and 60 years old (table1), half of them (49.54%) were young age belong to age group16-29 years old.

Regarding mechanism of vascular injuries; nearly half of injuries (49.5%) were caused by shrapnel while gunshot injuries were the second common cause of vascular trauma (37.6%). There were few (3.7%) stab injuries in this study as seen in table 2. Of the total injured patients 75.7% were presented in shocked state on their arrival to the hospital. Nearly one-fourth of the cases (24.5%) presented with external bleeding while one-third (29.1%) of them presented with absent pulses. The other clinical signs shown in table 3.

Regarding anatomical distribution of the vascular injuries; the lower limbs including the thighs, legs and feet were the most commonly affected area of the body. Majority of patients had

extremity injuries (73.4%). Further analysis showed that lower extremity vascular injury was the most prevalent anatomical location (51.4%), beside the abdomen and pelvis (16.1%). Only (3.2%) had chest trauma as seen in figure 1.

Table1 1: Vascular injuries according to Sex & age.

Parameter		Number	Percentage
Sex	Male	209	95.9%
	Female	9	4.1%
Age	≤ 15 years	14	6.42%
	16- 29	108	49.54%
	30- 44	80	36.7%
	≥ 45	16	7.34%
	Total	218	100%

Table1 2: Distribution of patients according to mode of vascular injury.

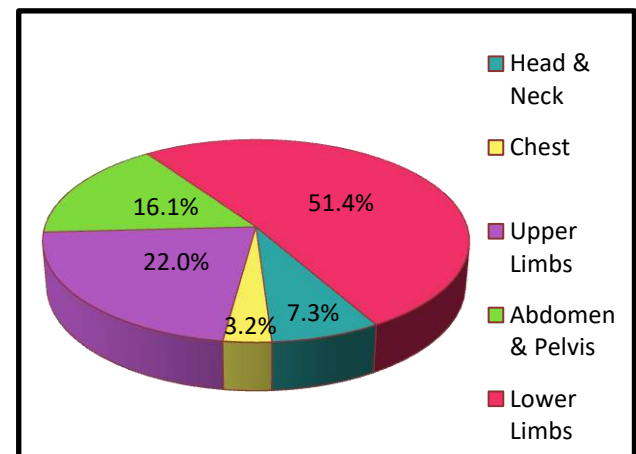| Mode of injury		Number	Percentage
Penetrating	Stab	8	3.7%
	Gunshot	82	37.6%
	Shrapnel	108	49.5%
	Landmine	6	3.2%
Blunt		13	6.0%
Total		218	100%

Fig. 1: Anatomical distribution of vascular injuries.

Concomitant injuries included vascular injury with bone and or nerve injury accounted for 52.3% of the cases, intra-abdominal vascular injury with concomitant injury to the liver, spleen and intestine accounted for 10.1%, while concomitant injury to thorax accounted for 6.9% as shown in table 4.

Two hundred eighteen patients underwent 280 vascular repairs that involved 139 arterial only, 24 venous only, and 55 involved both arterial and venous repair. Specific vascular injuries are listed in table 5 indicating that femoral artery was the commonest vascular injury during the study period and

accounting for 19.4%. Popliteal (11.4%) and brachial (10.0%) arteries were also common.

Regarding types of vascular injuries; complete transection (70.7%) was the commonest finding intra-operatively followed by contusion (18.6%) as seen in figure 2.

Table 3: Symptoms & signs of vascular injuries.

Symptoms / signs	Number
External bleeding	137
Absent pulse	163
Distal pallor & coldness	152
Pulsatile hematoma	14
Bruit or palpable thrill	10
Peripheral nerve deficit	84

Table 4: Distribution according associated injuries.

Associated injury	Number	Percentage
Vascular only	18	8.3%
Bone and or nerve injury	114	52.3%
Head & neck injury	12	5.5%
Thorax injury	15	6.9%
Abdominal injury	22	10.1%
Pelvic injury	9	4.1%
Associated soft tissue loss	28	12.8%
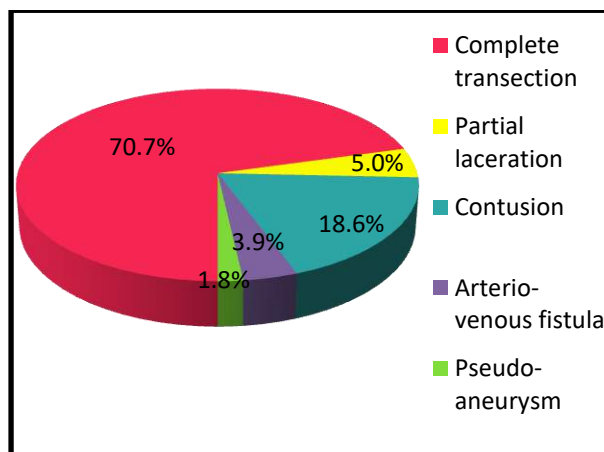
Fig.2: Types of vascular injury.

After control of bleeding, decision of method of repair is made depend on the inspected vessel, table 6 shows the vascular repair with regard to the type of vascular injury. While reversed interposition great saphenous venous grafts vascular repair with regard to the type of vascular injury. While reversed interposition great saphenous venous grafts accounting for 35% of the injured vessels; synthetic grafts were used for 31.8% of repaired vessels, and simple repairs are performed for 16.1% of them.

Because of the mass of wounded patient and limited number of beds; patients were evacuated to other local institutions or sent abroad for further management especially those who had neurological problems. Table 7 shows the outcome of vascular injuries. There were 18 deaths giving a mortality rate of 8.3%. 8 of them died from chest or abdominal vascular injury, 2 from hemorrhagic shock, 2 from adult respiratory distress syndrome, 2 from iliac vein injury, 2 head injury, 1 renal failure with infection, and 1 because of hemorrhagic shock with poor systemic condition. 6 patients (2.8%) underwent amputation of lower limb as their immediate postoperative course was relatively uneventful. There were 12 cases of thrombosis (5.5%) mostly treated immediately by a new synthetic interposition graft.

Table 7: Outcome of vascular injuries.

Complications	No.	%
Palpable pulse	172/200	86%
Absent pulse, compensated	16/200	8%
Absent pulse, not compensated	12/200	6%
Infection	26/218	11.9%
Renal failure	3/218	1.4%
Hemiplegia	2/218	0.9%
Death	18/218	8.3%
Amputation	6/218	2.8%
Thrombosis	12/218	5.5%

DISCUSSION:

The treatment of vascular injuries in war casualties is a challenging effort in a limited resource environment, and requires technical proficiency. Additionally; it requires hard judgment on when to perform temporizing maneuvers versus definitive repairs. Ideally, war injuries should be treated by surgeons having military surgery experience. In fact, civilian surgeons may find themselves trapped in wars practicing military surgery without prior training or experience in this field[11] . They must also therefore be experienced in the definitive surgical management of certain common and life or limb-threatening vascular injuries.

The observed high rate of vascular injuries (7.5%) in our study may be explained by explosive injury that frequently results in multiple penetrating wounds at various locations and levels and blunt force. Generally; in modern combat the rate is increased comparing to that reported in previous wars[12] .Our result was lower than reported in Iraqi (12%) but is comparable with results of Samy et al[13] .as they reported a rate of 7.6% of all casualties. Agrawal V. et al[14] .reported a lower rate of 3.8% of total causalities reaching hospital alive.

The battle field in the present study was almost exclusively male dominated. Women and children were not actively targeted, it is not surprisingly that majority of patients sustaining vascular injuries are male (95.9%) and young age as nearly 50% of them between 16-29 years old. Rich NM et al[5] and Agrawal V. et al[14] in their series also found that all the patients sustaining vascular injuries were males of 2nd to 3rd decade. Pediatric age with vascular injury represented 6.4% in our study which is higher than reported by Villamaria C. Y. et al [15] who are the first to report vascular trauma in a pediatric population at wartime in Iraq and Afghanistan, as

Table 6: Vascular injury and type of repair.

Vascular injury	Type of repair					Total	
	Direct repair	**Ligation**	**Reversed interposition GSV**	**Interposition PTFE**	**Venous patch**	**No.**	**%**
Complete transection	32	22	75	69		198	70.7%
Contusion		9	23	20		52	18.6%
Partial laceration	5				9	14	5%
Pseudo-aneurysm	**3**				2	5	3.9%
Arterio-venous fistula	5	3			3	11	1.8%
Total	**45 (16.1%)**	**34 (12.1%)**	**98 (35%)**	**89 (31.8%)**	**14 (5%)**	**280**	**100%**

PTFE: Polytetrafluoroethylene graft , GSV: Great saphenous Vein

3.5% of 4402 pediatric patients treated in United States military hospital between 2002 and 2011 had a vascular injury.

Similarly to all the wartimes[16-19] . In our study the penetrating injury was the most common mechanism of vascular injuries, as 50% of them were caused by explosions with shrapnel penetration whereas 37.6% were from gunshot wounds which is consistent with report in Afghanistan; 33%[12] . Patel et al[20] .reported higher penetrating vascular injuries accounting for 70% and 30% respectively. Agarwal et al[14] have observed that 56% of the patients having vascular injuries caused by gunshot injury.

The anatomic patterns of vascular injury in present study have similarities to those previously reported, most of them (73.4%) occurred in extremities which is consistent with results (72%) by Patel et al[20] . Correspondingly to previous studies [2,16,18,19] .lower extremity vascular injuries (51.4%) occurred more than two times that of upper extremity (22%), reflecting the relative length of axial vessels and the exposed position of lower extremity away from the protection of the trunk. However; Patel et al[20] .reported a lower rate (45%) of such injuries. The rarity of chest vascular injuries (3.2%) in this study is previously reported by Jawas et al[21] . Nearly, half of vascular injuries (52.3%) have associated orthopedic injuries, and 12.8% have soft tissue loss. Generally; the superficial femoral artery is most commonly injured represented 19.4% of the repaired vessels consistent with the incidence of femoral vessel injury that is reported in study by Joseph M. White et al[12] to be 17% of injuries. The second common repaired vessel was the popliteal artery (11.4%) followed by brachial artery in upper extremity (10%) of the total repaired vessels (280). Regarding the superficial femoral artery as the most commonly injured; a previous study[14] had similar results and even higher rate (33%–37%), than we observed followed by also by the popliteal (25%). Patients with hard or obvious signs of vascular injury are taken to the operating room for exploration, and there is often no time to perform a more detailed diagnostic evaluation, also high number of wounded patients arrived daily to hospital, CT angiography was not available at that time and sometimes sent to private hospitals. Therefore, the diagnostic evaluation concerns mostly to patients with soft signs of vascular injury. Duplex was used in diagnosing vascular injuries. Continuous

wave Doppler in this setting is quick and useful to confirm perfusion to an extremity on initial presentation. Ahanger AG et al[22] . had reported that laceration and transection of vascular injury comprises 80-85% of the vascular injuries, which is higher than our results including 70.7% transection injuries and 5% lacerated injuries of the repaired vessels. Because of shortage of facilities and inaccessibility of endovascular; all vascular injuries required open repair or ligation. Management of arterial repair with autologous vein graft remains the most durable and effective means of vascular repair[18-23] . in current study the most common applied method for vascular reconstruction was reversed interposition GSV which was used in 35% of the patients while PTFE graft was the second common procedure and used in 31.8% of the patients. The later development of prosthetic graft material made possible the routine use of prosthetic conduits as a substitute. Surgical experience suggests that PTFE is more resistant to infection than other prosthetic grafts and has acceptable patency rates when used in the above-knee position[24] .

Although ligation is an important damage control option; especially for minor or distal vessel injuries; our results revealed that ligation was carried out in 12.1% of selected injured vessels included ligation of the radial, ulnar and tibial arteries and did not cause ischemia of the involved limbs. Carole Y. Villamaria[15] reported that 31% of the cases managed by ligation, whereas Patel et al[20] reported ligation in 40.3% (395/981) of the cases as the initial management strategy. Furthermore; Joseph M. White et al[12] had a considerable observation that ligation (54%) and reconstruction (46%) are currently used in nearly equal proportions to manage vascular injury. So; ligation of arterial injuries might an important management strategy only in selective especially for minor or distal vascular injuries controlling the hemorrhage. In our study venous patch was used for repair in only 5% of injured vessels, venous repair remain a controversial issue in patients with vascular injuries. However, most would agree that venous repair by means, other than simple lateral suturing and end-to-end anastomosis, is a time consuming process with uncertain benefits especially in multiply injured patients[10] .

Vascular repair was independently associated with mortality[25] the complication rate following emergency

revascularization was 22% in current study which is comparable with international standards [26-27] . The most common postoperative morbidity was infection reached 11.9%. Secondary amputation was performed in 6 cases (2.8%) due to severe musculoskeletal injuries which were the most important prognostic factors in vascular injuries in extremities leading to uneventful postoperative course. This low rate of amputation might be explained that the study is focused mainly on the distribution of wounding requiring conventional management strategies and injuries associated with immediate or traumatic amputation were not included. Amputation rate is variable in different studies showing a rate of 2.6% to 56% [28-30] . A contemporary of 7-year analysis of vascular injury from the war in Afghanistan[20] mortality of the vascular injury was 5% which is lower than we observed (8.3%). Other previous reports had found the overall mortality resulting from vascular trauma is between 20 and 26% [31-34] .

Limitations in our data are related to mass casualty procedures, shortage of surgeons which has prevented the meticulous recording of wounding and surgical details in some patients in current study. Specific numbers and percentages are reported on the variables for which complete data are available.

CONCLUSION:
Vascular trauma in our locality has a similar epidemiology and outcome to that previously reported. Most vascular injuries in our study were seen in young men, frequently caused by shrapnel explosive weapons and in lower extremity. Femoral artery was the commonest injured vessel. Vascular reconstruction in the first hours after trauma may prevent many unnecessary and preventable amputation procedures. Vascular injuries wartime should be a focus of attention for definitive surgical management, prevention of limb loss, reducing mortality, training, innovative therapy research, and priority of care.

REFERENCES:
1- Champion HR, Holcomb JB, Young LA. Injuries from explosions: Physics, biophysics, pathology, and required research focus. J Trauma 2009, 66:1468–1477.

2- Woodward EB, Clouse WD, Eliason JL, et al. Penetrating femoropopliteal injury during modern warfare: experience of the Balad Vascular Registry. J Vasc Surg 2008; 47: 259–64.

3-Eliason JL, Cox MW, Bowser AN. In-theater management of vascular injury: 2 years of the Balad Vascular Registry. J Am Coll Surg 2007; 204: 625–32.

4- Rozycki GS, Tremblay LN, Feliciano DV, McClelland WB. Blunt vascular trauma in the extremity: diagnosis, management, and outcome. J Trauma 2003 Nov; 55(5):814e24.

5- Rich NM, Baugh JH, Hughes CW. Significance of complications associated with vascular repairs performed in Vietnam. Arch Surg 1970; 100: 646-51.

6- Rich NM, Hughes CW. Vietnam vascular registry: a preliminary report. Surgery 1969; 65:218-26.

7- Clouse WD, Rasmussen TE, Peck MA, et al. In-theater management of vascular injury: 2 years of the Balad Vascular Registry. Journal of the American College of Surgeons. 2007; 204(4):625-632.

8- Kauvar DS, Wade CE. The epidemiology and modern management of traumatic hemorrhage: US and international perspectives. Crit Care 2005; 9(Suppl. 5):S1e9.

9- Gruen RL, Jurkovich GJ, McIntyre LK, Foy HM, Maier RV. Patterns of errors contributing to trauma mortality: lessons learned from 2594 deaths. Ann Surg 2006 Sep; 244(3):371e80.

10- Hafez HM, Woolgar J, Robbs JV: Lower extremity arterial injury: Results of 550 cases and review of risk factors associated with limb loss. J Vasc Surg 2001, 33:1212–1219.

11- Behbehani A, Abu Zidan F, Hasaniya N, Merei J: War Injuries in the Gulf war: experience of a teaching hospital in Kuwait. Ann R Coll Surg Engl 1994, 76:407–411.

12- Joseph White; Adam Stannard; Gabriel Burkhardt; Brian Eastridge; Lorne Blackbourne; Todd Rasmussen. The Epidemiology of Vascular Injury in the Wars in Iraq and Afghanistan. Annals of Surgery. 253(6):1184–1189, JUN 2011.

13- Samy S. Nitecki, Tony Karram, Amos Ofer, et al. Management of Combat Vascular Injuries Using Modern Imaging: Are We Getting Better? Emergency Medicine International; Volume 2013, Article ID 689473, 6 pages.

14- Agrawal Vivek, Varinder Singh Bedi, Vembu Anand, Mukesh Kumar Garg. Management of vascular injury in counter insurgency area: A single-center study. Indian Journal of vascular & Endovascular surgery. 2018; 5 (1): 29-34.

15- Villamaria Carole Y., Jonathan J. Morrison, Colleen M. Fitzpatrick, et al. Wartime vascular injuries in the pediatric population of Iraq and Afghanistan: 2002–2011. March 2014; Volume 49 (3): 428–432.

16-Clouse WD, Rasmussen TE, Peck MA, et al. In-theater management of vascular injury: 2 years of the Balad Vascular Registry. Journal of the American College of Surgeons. 2007; 204(4):625-632.

17- Gawande A. Casualties of war – Military care for the wounded from Iraq and Afghanistan. N Engl J Med 2004; 351: 2471-5.

18- Fox CJ, Gillespie DL, O'Donnell SD, Rasmussen TE, et al. Contemporary management of wartime vascular trauma. J Vasc Surg 2005; 41: 638-44.

19- Fox CJ, Starnes BW. Vascular surgery on the modern battlefield. Surg Clin North Am 2007; 87: 1193-211, xi.

20- Patel JA, White JM, White PW, Rich NM, Rasmussen TE. A contemporary 7-year analysis of vascular injury from the war in Afghanistan. J Vasc Surg. 2018 Dec; 68(6):1872-1879.

21- Ali Jawas, Alaa K Abbas1, Munier Nazza, et al. Management of war-related vascular injuries: experience from the second gulf war. World Journal of Emergency Surgery 2013, 8:22.

22- Ahanger AG, Wani ML, Lone RA, Singh S, Hussain Z, Mir IA, et al.Missile vascular injuries: 19-year experience. Ulus Travma Acil CerrahiDerg. 2010; 16(2):135-8.

23- Rich NM, Rhee P: An historical tour of vascular injury management: from its inception to the new millennium. Surg Clin North Am 2001, 81:1199–1215.

24- Vaughan GD, Mattox KL, Feliciano DV, Beall AC Jr., Debakey ME. Surgical experience with expanded polytetrafluoroethylene (PTFE) as a replacement graft for traumatized vessels. J Trauma 1979; 19: 403-8.

25- Jeffrey J. Siracuse, Thomas W. Cheng, Alik Farber, Thea James, et al. Vascular Repair after Firearm Injury is Associated with Increased Morbidity and Mortality Boston University/Boston Medical Center, USA. Society of Clinical Vascular Surgery. Boc Raton; 47th Annual Symposium. 2019: march 16-20.

26- Hood DB, Weaver FA, Yellin AE. Changing perspectives in the diagnosis of peripheral vascular trauma. Semin Vasc Surg 1998; 11:255–260.

27- Starnes BW, Bruce JM. Popliteal artery trauma in a forward deployed Mobile Army Surgical Hospital: lessons learned from the war in Kosovo. J Trauma 2000; 48:1144–1147.

28- Ockert S, Winkler M, Richter A, Palma P, Post S. Vascular injuries after extremity trauma. Zentralbl Chir. 2002; 127(8):689–93.

29- Khan MI, Khan N, Abbasi SA, Baqai MT, Rehman B, Wayne A. Evaluation of emergency revascularisation in vascular trauma. J Ayub Med Coll Abbottabad. 2005; 17(2):40–3.

30- Fingerhut A, Leppaniemi AK, Androulakis GA, Archodovassilis F, et al. The European experience with vascular injuries. Surg Clin North Am. 2002; 82(1):175–88.

31- Barmparas G, Inaba K, Talving P, David JS, Lam L, Plurad D, et al. Pediatric vs adult vascular trauma: a National Trauma Databank review. J Pediatr Surg 2010 Jul; 45(7):1404e12.

32- Gupta R, Rao S, Sieunarine K. An epidemiological view of vascular trauma in Western Australia: a 5-year study. ANZ J Surg 2001 Aug; 71(8):461e6.

33- Loh SA, Rockman CB, Chung C, Maldonado TS, Adelman MA, Cayne NS, et al. Existing trauma and critical care scoring systems underestimate mortality among vascular trauma patients. J Vasc Surg 2011 Feb; 53(2):359e66.]

34- Sugrue M, Caldwell EM, Damours SK, Crozier JA, Deane SA. Vascular injury in Australia. Surg Clin North Am 2002 Feb; 82(1):211e9.

Distribution Of Cases By Stage At Diagnosis For Colorectal Cancer In National Cancer Institute Misurata

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ABSTRACT:
Colorectal cancer holds a significantly overwhelming health burden on a national and an international level and demands scrutinization from healthcare providers. Its survival rate is heavily associated with stage at diagnosis, which in turn is strongly affected by early detection. Thus, increasing early detection through colorectal cancer screening programs may have a grand impact on the stage at diagnosis and hence mortality rates. This is an effort to survey the colorectal cancer stage at diagnosis for the year 2018 at the National Cancer Institute (NCI) - Misurata, with estimation of the prevalence of patients diagnosed with an advanced stage of the disease. Data from the NCI - Misurata registry was used to thoroughly review a total of 174 colorectal cancer cases records. Identifying the stage at diagnosis using the Surveillance, Epidemiology, and End Results (SEER) summary stage. The summary stage provides the most basic way of categorizing how far a cancer has spread from its point of origin. Statistics attained from these records were compared with several developed countries' colorectal cancer reports to outline the radical differences in distribution of stage at diagnosis and its attribution. 39% (67) of patients presented at a distant-stage disease. Another 38% of patients were presented at a regional stage. Only 18.5% (32) presented at a localized stage. Histopathological results confirmed that 60% of the 89 patients operated on were lymph node positive. The male to female ratio was 1.13:1. Out of 28 cities: Misurata, Tripoli, and Khums represent more than half of the cases. When compared to developed countries (Canada and US) the distribution of stage at diagnosis was substantially less aggressive.
An alarming 77% (134) of cases were diagnosed at stage III or higher. When compared to lower prevalence of advanced stages at diagnosis in developed countries, it is believed that this is attributed to the lack of screening programs which have been proven to prevent this second leading cause of cancer-related deaths.

Keywords: Colorectal Cancer, Stage at diagnosis, Screening, National Cancer Institute, Misurata.

INTRODUCTION:
According to the WHO, colorectal cancer is the third most common cancer and the second leading cause of death among men and women[1]. Hence, colorectal cancer holds a significantly overwhelming health burden on a national and an international level and demands scrutinization from healthcare providers.

In all types of cancer, the disease stage provides invaluable information for healthcare providers and most importantly clinical decision-makers. Stage information is used by medical professionals to assess prognosis, plan treatment, and predict the course of the illness. At the population level, stage information can be important for understanding trends in cancer incidence over time[2]. Particularly, provide clinico-epidemiological reference to assess the effectiveness of screening programs, treatment efficacy, and adequate resources allocation.

Stage at diagnosis is strongly associated with survival for both colon and rectum cancers[3].For example, five-year relative survival for colon cancer is estimated to be 92% for cancers diagnosed at stage I compared with only 11% for stage IV; five-year survival for rectal cancer is estimated to be 87% for stage I and 12% for stage IV[3]. In addition, there are large differences in survival rates globally, and the international differences in survival are partially explained by differences in distribution of stage at diagnosis[4]. Thus, increasing early detection through cancer screening programs may have a drastic impact on mortality rate[2]. Almost 60% of colorectal cancer deaths could be prevented with screening[5], rendering this disease the leading preventable cause of death in the US.

OBJECTIVES:
-To survey the colorectal stage at diagnosis and prevalence of advanced stages among those diagnosed in 2018.
-To examine differences in stage presentation in NCI Misurata with high-income countries (developed countries)
-To provide medical professionals and researchers in Misurata National Cancer Institute (NCI) with statistics that could be used to make decisions and observe trends.

METHODS:
Conduction of this study was permitted under the NCI ethics committee. List of National Cancer Institute new colorectal cases was obtained from the statistics and registry office. The database contained 189 entries, only 174 colorectal cancer case files were retrieved rendering 15 entries missing. All cases diagnosed in the year 2018 were included regardless of sex, age, operated or not, and

outcome (dead or alive). Thorough review of each medical record was conducted to claim needed clinical data and information where possible. Patients were stratified based on stage at diagnosis according to the Surveillance, Epidemiology, and End Results (SEER) program summary stage. The SEER program is an authoritative source for cancer statistics in the United States to reduce the cancer burden, adopted by the National Institute of Health's NCI. It is the most basic way of categorizing how far a cancer has spread from its point of origin[6]. It uses all information available in the medical record; in other words, it is a combination of the most precise clinical and pathological documentation of the extent of disease[6]. It doesn't serve as substitute to other previously known staging tools, TNM or Duke staging, it merely unifies cases staged by different staging tools into one for conventional statistical purposes. In the case of colorectal cancer, the SEER summary stage is illustrated in table 1.

Table 1: SEER summary stage classification and equivalent TNM staging.

SEER	Description	Equivalent TNM
Localized	Invasive tumor confined to colon. Includes tumor extension through muscularis propria and subserosal tissue	Stage I and IIa. T1-3 N0 M0
Regional	Tumor extension outside the colon and/or invasion of regional lymph nodes. Includes local tumor extension into serosal surface, pericolic or mesenteric fat	Stage IIa, IIb and III. T3-T4 / Any N Any T / N1,2 M0
Distant	Tumor extends to distant organs or lymph nodes	Stage IV Any T

Adopted from SEER Program Coding and Staging Manual 2007

In addition, surgery specimen histopathology reports were examined for identification of the distribution of pathological TNM staging (pTNM) as outlined below (Table 2 and 3).

Finally, a review of literature for the latest American and Canadian colorectal cancer statistics and reports with a specific focus on distribution of stage at diagnosis for comparison with NCI - Misurata statistics.

RESULTS

The peak age of incidence was found to be 58.5 years with an SD value of 14.2. The median age of diagnosis for females was 55 and 61 for the males. Out of all the cases

surveyed it was discovered that 93 (53.4%) were males and 81 (46.6%) of the opposite gender. The incidence doesn't vary substantially by sex; male to female ratio was found to be 1.13:1.

Table 2: Pathological N stage (pN)

Nx	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in 1–3 regional lymph nodes
pN2	Metastasis in 4 or more regional lymph nodes

Adopted from the American Joint Committee on Cancer (AJCC) 7th edition colon and rectum cancer staging.

Table 3: Pathological T stage (pT)

Tx	Primary tumor cannot be assessed
pTis	Carcinoma in situ: intraepithelial or invasion of lamina propria.
pT1	Tumor invades submucosa.
pT2	Tumor invades muscularis propria.
pT3	Tumor invades through the muscularis propria into pericolorectal tissues.
pT4	pT4a: Tumor penetrates to the surface of the visceral peritoneum. pT4b: Tumor directly invades or is adherent to other organs or structures.

Adopted from the American Joint Committee on Cancer (AJCC) 7th edition colon and rectum cancer staging.

The percent distribution of the clinical stage as per the SEER summary stage was evidently the highest in the regional and distant stages. Exactly 67 of reported cases were found to be in the distant stage at diagnosis. Another 66 cases reported at a regional clinical stage. This construes into an alarming 38.5% for distant and 38% for regional stage-disease. The remaining stages of localized and un-staged occupied only 18.5% and 5% respectively as stated in table 4.

Table 4: Distribution of cases at diagnosis according to SEER summary stage

SEER	Number of cases	%
Localized	32	18%
Regional	66	38%
Distant	67	39%
Un-staged	9	5%
Total	174	100%

The data assembled revealed a significant geographical distribution across Libya, encompassing 28 cities from all three districts, Tripoli, Fazzan, and Barqa. As noted on table 5, beyond half of the cases presented were from Misurata (25.3%), Tripoli (18.4%), and Khums (9.20%). The remaining cities collectively made up 47.7% of the cases.

Table 5: Geographical distribution of cases across Libya

City	Number Cases	Percentage
Alamamra	1	**0.57**
Aljmail	1	0.57
Ben jawad	3	1.72
Ben walid	5	2.87
Benghaze	5	2.87
Brak shate	1	0.57
Garaboli	4	2.3
Ijdabiya	5	2.87
Jofra	2	1.15
Kaser Khayar	3	1.72
Khums	16	9.2
Merzeq	1	0.57
Mesalata	2	1.15
Misurata	44	25.29
Obari	1	0.57
Rojban	1	0.57
Sabha	9	5.17
Sert	12	6.9
Tarhuna	7	4.02
Tazerbo	1	0.57
Tobrouk	1	0.57
Tripoli	31	17.82
Weddan	1	0.57
Zam Zam	1	0.57
Zawiya Garbiya	2	1.15
Zliten	14	8.05

Eighty nine cases (51.1%) underwent surgical intervention due to curative, palliative, urgent or elective measures. Specimen-histopathology revealed that most cases were pT with 66 cases (74.2%), pT4 was second to follow with 17 (19.1%), followed by pT2 (3.4%), pT1 (2.2%), pTx (1.1%), and pT is (0%). As for the pathological N stage (pN), only 31 patients (34.8%) were lymph node free (pN0) while 33.7% (30 cases) and 27.0 (24 cases) for pN1 and pN2 respectively. Leaving an insignificant 4.5% (4 cases) unknown (pNx).

DISCUSSION:

The highlight of this study is to showcase the prevalence of advanced colorectal cases at diagnosis. The fact that a striking 77% of cases in 2018 were presented at stage III or higher raises much concern.

It's unfortunate to reveal such concordance when exploring a disease of such significant mortality magnitude. Especially considering today's modern advances in healthcare and technology, our statistics should point otherwise. In addition, looking at operated cases, even the patients that were candidates for surgery the majority were lymph node positive, precisely 60.7%, as per pathology reports.

Relation to other publications:

These results fall behind findings in the United States and Canada. There is quite the inverse comparison, recent reports in the US and Canada revealed approximately one-fifth of new cases diagnosed at a distant stage of the disease. While our results showed only one-fifth at a local stage of the disease[2,5], further specific statistics are elaborated on table 6. Outlining that, the vast difference in prevalence of stage at diagnosis is mainly due to rigorous screening programs, yielding improved mortality rates than respective previous statistical reports[2,5].

Table 6: Canadian percent distribution of colorectal cancer cases by stage at diagnosis for 2018 and American percent distribution of colorectal cancer cases by stage at diagnosis for 2017

Colorectal cancer cases	Localized	Regional	Distant	Un staged
Canadian Statistics*	47%	29%	19%	5%
American Statistics**	39%	35%	21%	5%

* Obtained from Canadian cancer society cancer statistics 2018 report[2].

** From the American Cancer Society(7).

Clinical Implications:

An advanced colorectal cancer means lymph node involvement or distant dissemination or both, i.e. stages III and IV. Patients presenting at an advanced stage carry a hopeless prognosis and a minimal survival rate. Hence, promoting earlier detection of colorectal cancer is crucial.

Various studies have demonstrated the efficacy of screening programs in detection of early-stage of the disease, even in a pre-cancerous stage[2]. In Libya currently, no screening program holds a platform in the healthcare

system. Not even in an opportunistic nor organized capacity, as well as those at higher risks are neglected. As a result, this could explain the aggressive presentation of the disease in many of the patients.

Preventive medicine is the foundation of any healthcare system. The above results only reinforce the desperate need for some structure of preventive measure such as a screening program. It's without a doubt that advanced-stage cancer patient are a burden on the health system. They often require multiple hospital admissions, multi-disciplinary care, and long-term surveillance. Again, earlier detection of the cancer allows for better allocation of such resources. Availability of various screening modalities truly facilities the implementation of a screening structure. These methods can meet different socioeconomic status, ranging from colonoscopy to inexpensive fecal occult blood testing. They have all been proven to reduce colorectal cancer stage at diagnosis. Firs et al studied the effect of screening with colonoscopy during the first year of a nation-wide screening program. Revealing that indeed screening lowers the stage of diagnosed colorectal cancer[8]. Another study by Selby et al found that screening through flexible sigmoidoscopy can reduce the mortality from colon and rectum cancers[9]. Also, a nationwide cohort study conducted in Denmark revealed that patients who underwent Fecal Immunochemical Test (FIT) screening led to detection of almost 2-fold more cases of colorectal cancer than the control arm[10].

This current study lends support to the Libyan healthcare system with figures needed to appropriately allocate resources. One limitation of this study is the small sample size which prohibits extrapolation of its results to the population. However, Misurata NCI is in fact the largest cancer-patient intake center in Libya which could reflect an approximation of figures. Also, study lacked analysis of rural versus urban cases[11] nor did it take into consideration the socioeconomic variations in patients.

Future Directions:

Stage at diagnosis prevalence tracking with a more statistically significant sample size. Attention to socioeconomic status could be of value. Most importantly, efforts on a local and a national level to introduce screening at least in an opportunistic fashion. By Examining the changes in cancer stage distribution over time, it can be used to help assess the effectiveness of screening and early detection programs[12]. It can also be used to determine if a new treatment has been used according to guidelines and has improved outcomes.

CONCLUSION:

This study is an effort to call attention to the concerning high prevalence of late-stage colorectal cancer cases during 2018 in Misurata National Cancer Institute. Review of 174

medical case records declared 134 (67.5%) were diagnosed at a late-stage of the disease. This only further stresses the importance of early detection. Implementing a screening program would create a monumental change in the country's healthcare. Stage at diagnosis might not only be influenced by screening program but implementing it is a step in the right direction to optimizing prevalence and survival rate.

REFERENCES:

1- Cancer [Internet]. Who.int. 2019 [cited 27 January 2019]. Available from: https://www.who.int/en/news-room/fact-sheets/detail/cancer

2- Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics 2018. Toronto, ON: Canadian Cancer Society; 2018. Available at: cancer.ca/Canadian-Cancer-Statistics-2018-EN (accessed January 2019).

3- American Cancer Society [Internet]. Survival Rates for Colorectal Cancer, by Stage: American Cancer Society; 2018. Available from: https://www.cancer.org/cancer/colon-rectal-cancer/detection-diagnosis-staging/survival-rates.html (accessed January 2019).

4- Maringe C, Walters S, Rachet B, Butler J, Fields T, Finan P, Maxwell R, Nedrebø B, Påhlman L, Sjövall A, Spigelman A. Stage at diagnosis and colorectal cancer survival in six high-income countries: a population-based study of patients diagnosed during 2000–2007. Acta oncologica. 2013 Jun 1;52(5):919-32.5.

5- Facts and Stats | Fight Colorectal Cancer [Internet]. Fight Colorectal Cancer. 2019 [cited 28 January 2019]. Available from: https://fightcolorectalcancer.org/prevent/about-colorectal-cancer/facts-stats/

6- Summary Staging Manual – 2018 – SEER [Internet]. SEER. 2019 [cited 5 February 2019]. Available from: https://seer.cancer.gov/tools/ssm/?fbclid=IwAR3j0t bdTEJMaBWDLMTY75hS0RRZyd762GifJGdTww WHmLssv470grKVg8Q

7- American Cancer Society. Colorectal cancer facts & figures 2017–2019.

8- Fris TL, Jepsen MH, Madsen MR. Screening Colonoscopy Indeed Lowers the Stage of Diagnosed Colorectal Cancer – A Prospective Registration of the Findings by Screening Colonoscopy during the First Year of a National Screening Programme. Colorec Cancer 2016, 2:2.

9- Selby JV, Friedman GD, Quesenberry Jr CP, Weiss NS. A case–control study of screening sigmoidoscopy and mortality from colorectal cancer. New England Journal of Medicine. 1992 Mar 5;326(10):653-7.

10- Larsen MB, Njor S, Ingeholm P, Andersen B. Effectiveness of colorectal cancer screening in detecting earlier-stage disease—a nationwide cohort study in Denmark. Gastroenterology. 2018 Jul 1;155(1):99-106.

11- Campbell NC, Elliott AM, Sharp L, Ritchie LD, Cassidy J, Little J. Rural and urban differences in stage at diagnosis of colorectal and lung cancers. British Journal of Cancer. 2001 Apr;84(7):910.

12- Schreuders EH, Ruco A, Rabeneck L, Schoen RE, Sung JJ, Young GP, Kuipers EJ. Colorectal cancer screening: a global overview of existing programmes. Gut. 2015 Oct 1;64(10):1637.

Clinical quiz

A forty one years old, recently diagnosed as diabetic patient, C/O poor vision and blaming that his physician is responsible for it. What else you like to know? Visual acuity for far was 6/24 both eyes, improved with pin hole and for near N1 at 40 cm. What is the next step?

His non cycloplegic refraction was +1.5 D. Sph. Both eyes. With correction he gained 6/6 far vision. Is it essential to have cycloplegic refraction in this case, what is the alternative? What is happening in this case?

Answer on page 66.

Development of a FIA method for ascorbic acid determination

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ABSTRACT:

A flow – injection analysis (FIA) method for ascorbic acid was developed in which a commercial oxygen sensor was used as the detector. Copper {Cu(II)} ion in buffered solution was used as a catalyst for the oxidation of ascorbic acid dissolved oxygen. The response of the oxygen to the uptake of oxygen provides the analytical signal was investigated. It was shown that the reagent could be re-cycled at least once after re-oxygenation. There was a linear relationship between the heights of the FIA traces and the concentration of ascorbic acid. The method was applied to the determination of ascorbic acid in fruit juice and vitamin C 50 mg tablets.

INTRODUCTION:

Flow injection analysis may be defined as automated or semi automated analytical process consisting of the insertion of sequential discrete sample solutions into an unsegment, continuously moving liquid stream with subsequent detection of the analyte.

The oxygen sensor is an electrochemical device which is used to measure oxygen concentration usually in aqueous solution. A diagram of an oxygen sensor is shown in figure (3). It has a threated collar on the plunger so that it was possible to vary the effective cell volume. Another aim was therefore to find out how variation in the cell volume affected the FIA traces. Flow injection analysis is relatively recent analytical technique, but because of the advantages created FIA is interfaced with established forms of analytical instrumentation, and because of the ease with which FIA can be automated, it is now a quickly growing field of study.

METHODOLOGY:

The aim of these experiments was to develop a flow-injection analysis (FIA)[1] method for the determination of ascorbic acid in vitamin tablets and possibly in fruit drinks and fruit juices. The catalytic effect of copper(II) Cu(II) on the oxidation of ascorbic acid by molecular was to be used. Since oxygen is absorbed from solution in this process it was decided to use an oxygen sensor as the detector in the FIA system[2]. Also it was decided to investigate the possibility of recycling the reagent to make the FIA more economical. Although FIA is usually economical in reagent use it would obviously be advantageous if the reagent could be re-cycled one or more times. Because the copper(II) ion is a catalyst it will not be consumed in the analysis and therefore it was decided to re-oxygenate the reagent after its first use to see if it could be used second time.

Description of the flow –injection analysis system devised for the present work include five major parts, a propelling system to carry the carrier stream to the detector, an injection system to introduce the sample volume into the carrier stream, a reaction region to allow controlled mixing to take place, a detector and finally a recorder. The flow – injection analysis system[3] used in the present work is shown in figure 1.
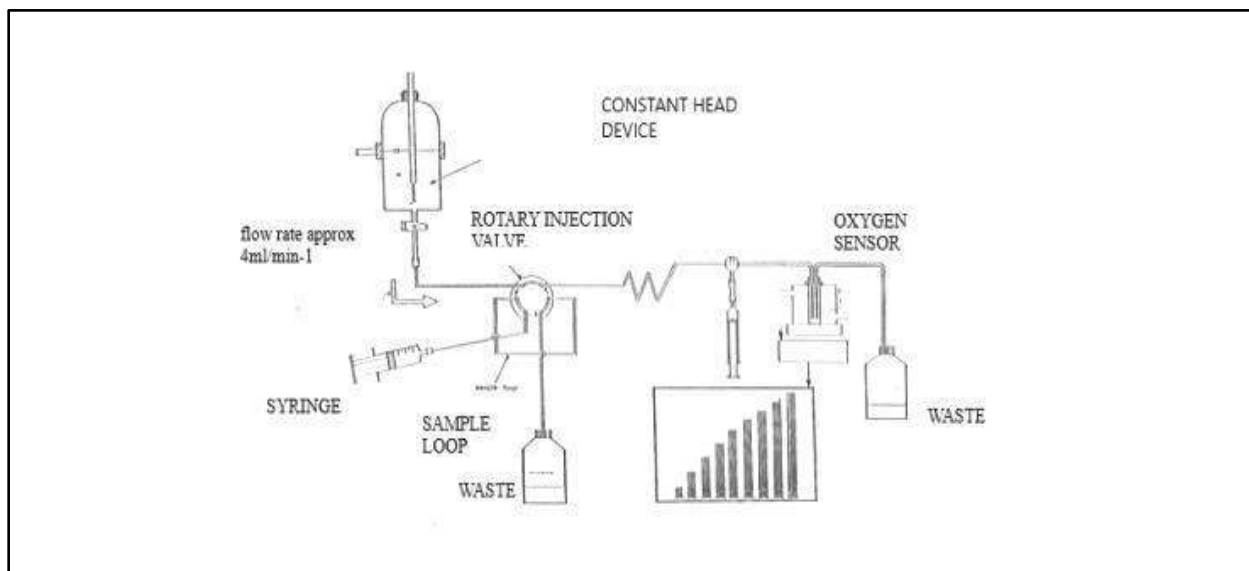

Figure 1: Flow – injection apparatus employing the oxygen sensor as the detector.

THE PROPELLING SYSTEM:

The propelling system used in the present study was a constant head device. This is a pulse free system in which the reagent is gravity fed. The constant head device (figure 2) was based on the Marriote bottle. It had a volume of approximately 1 dm^3 and was made of pyrex glass. The glass air-inlet tube had an air tight seal at the neck. When the Rota – flow valve is opened, the reagent flow through the FIA system to waste. When air begins to bubble slowly from the bottom of the air inlet tube the pressure at this point is equal to that of the atmosphere, regardless of the level of reagent solution in the vessel. Thus, provided that the level of the reagent solution is above the bottom of the air-inlet tube the flow rate remains constant. As a test of the performance of the constant head device, water was run from the device into a weighed beaker on a top loading balance. The weight gain was measured at intervals, increased linearly with time confirming the constancy of flow rate. All the valves including the rotary injection valve were obtained from Omnifit Ltd. The connecting polyethylene (or Teflon) tubing was of 1.0 mm internal diameter and was obtained from Pharmacia Ltd.
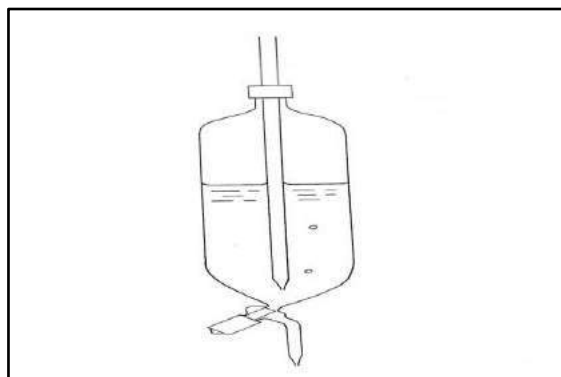
Figure 2: Diagram of the constant head device used in the FIA experiments. The vessel had a volume of approximately 1 dm^3

There are two possible ways to make connection between the flow tubing and the valves. The manufacturer (Omnifit Ltd) supplies a set of rubber "O" rings that tighten on the tubing. The alternative way of connection is to use small Teflon cones that are also supplied by the manufacturer ; this was the preferred method. To make a connection, the Teflon or polyethylene tubing was drawn out to a taper. The screw connection was then slipped over the tubing and tapered end of the tubing was passed through the hole in the cone from the base end drawn through until quite tight. The end of the tube was then cut flush with the tip of the cone with a craft knife. To make tug-resistant connections to the waste bottles, two holes were drilled in the screw caps one of these holes being slightly smaller than diameter of the Teflon or polyethylene tubing so that, after tapering the end of the tubing, it could be drawn through the hole so that it was held firmly and then cut to the required length.

The recorder:

In the present apparatus a Servoscribe potentiometric recorder with an offset control was employed.

The detector:

The detector of the FIA apparatus was an oxygen sensor. The theory of the oxygen has been dealt with in the Introduction. The sensor is made by Rank Brothers Ltd , Cambridge and illustrated in figure 3.
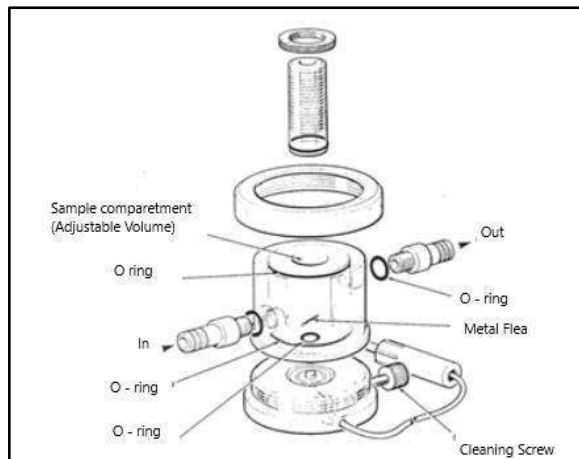

Figure 3: An exploded view of the inverted oxygen sensor used in this work as a detector for FIA and stopped – flow studies. In the design used in the present work the plunger of the cell had two holes, one was the inlet for the reagent or reactants and the other was outlet to waste.

A special plunger for the top of the sensor was ordered. This plunger has two holes unlike the usual design which has only one hole. In the two-hole design one hole is used as the inlet, the other being the outlet.

This allow the sensor to be used in flow systems (including stopped–flow). Thus, the tubing from the; injection valve of the flow-injection analysis system led to the inlet of the oxygen sensor while the outlet led to the waste collection bottle.

Electronic circuitry for the oxygen sensor is very simple. A polarizing circuit is employed to impose a voltage 0.6 V between the platinum cathode and the silver anode. The current, which flow in the circuit when oxygen is present in the experimental solution, is measured as an equivalent voltage across a suitable resistor in the circuit. The circuit shown in figure 4 which was the one employed in the present work, is a more advanced circuit with greater amplification of the signal.

REAGENTS:

Ascorbic acid standard:

Ascorbic acid (1.76g) was dissolved in water and made up to 100cm^3 in a graduated flask. By serial dilution of this standard 0.0010, 0.0020, 0.0040, 0.0060, 0.0080 and 0.010M solutions were prepared.

Acetate buffer 0.2M of pHs:

3.6, 4.0, 4.6, 5.9 and 5.6.

Copper sulphate solution:

Copper sulphate, $CuSO_4.5H_2O$ (24.97g) was dissolved in water and made up to a total volume of 1.0 dm^3 to give a 0.10M solution.
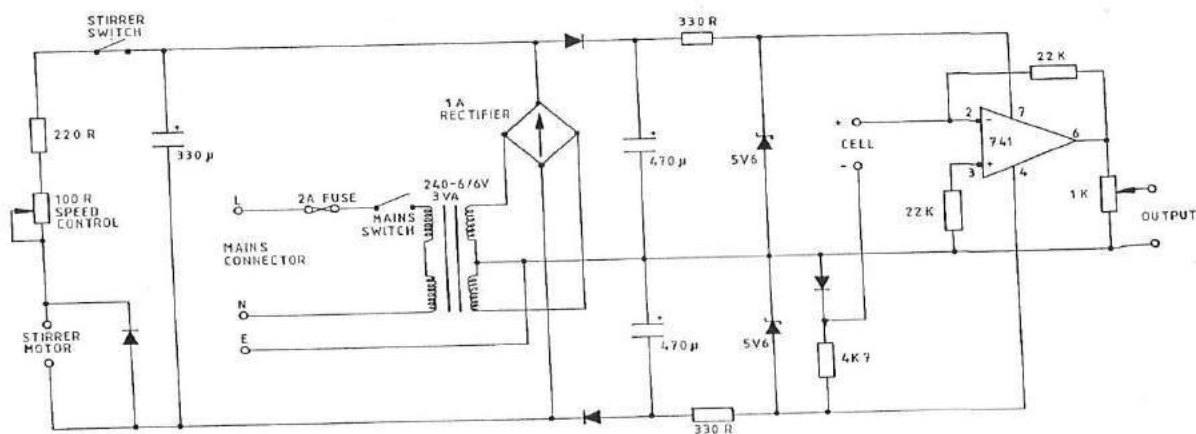
Figure 4: Circuit diagram for the oxygen sensor used in the FIA and stopped – flow experiments

SAMPLES:
a) One vitamin C 50 mg tablet was crushed and dissolved in 50cm^3 of water.
b) orange juice drink.
c) Sun-top juice drink.

PROCEDURE:
Copper sulphate solution buffered with an equal volume of acetate buffer to pH 4.6 was placed in the constant head device and bubbles were removed from the FIA system by injecting water through all the tubing with a 20cm^3 syringe. The reagent solution was allowed to run from the constant head device by unscrewing the Rota-flow valve. While the stirrer was operating and a steady flow reagent was flowing through the oxygen sensor to waste, a steady baseline signal was obtained. Sample of the ascorbic acid solutions were injected into the loop of the rotary injection valve while the valve was in the load position. On switching to the inject position the sample solution was carried towards the oxygen sensor. In the cell of the sensor the Cu(II) catalyzed oxidation of ascorbic acid occurred and a oxygen absorbed peak was obtained on the mV recorder. Each standard and each unknown, was injected three times.

RESULTS:
An example of the FIA recorder traces obtained in this way is shown in figure 5.

Table 1 :Dependence of trace height on the ascorbic acid (AH$_2$) concentration for the flow-injection analysis of ascorbic acid. The reagent was 0.10M Copper(II) sulphate solution in0.20M acetate buffer pH 4.6 and the detector was an oxygen sensor. The sample loop volume was 120μl.

AH$_2$ concentration\M	Trace height\ s.c.u
0.0010	7.5
0.0020	17.2
0.0040	30.6
0.0060	46.5
0.0800	64.3
0.010	86.1

(s.c.u. small chart units)

It was observed that on rotating the rotary injection valve in either direction, spikes were produced on the recorder traces. These spikes were in the direction of an apparent increase in oxygen concentration and probably arise because of slight pressure changes on closing the valve, which momentarily compress the membrane covering the cathode. These spikes did not appear to affect the magnitude of the signals obtained.
The heights of the recorder traces for varying concentrations of ascorbic acid are presented in table 1 and are shown graphically in figure 6.
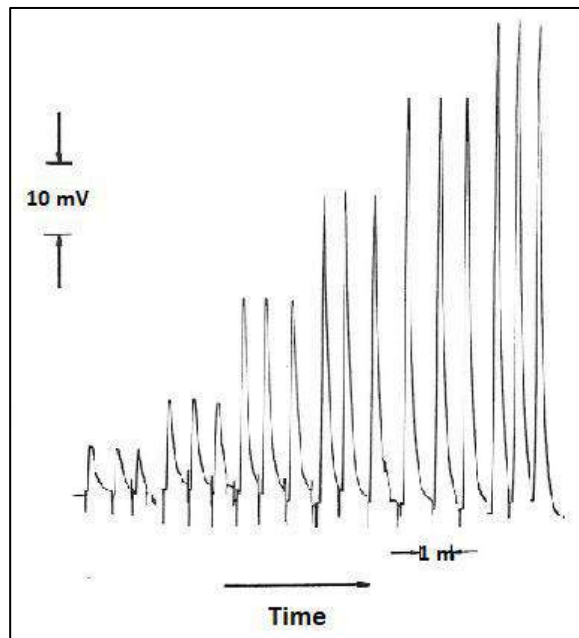
Figure 5: Recorder trace for the FIA of ascorbic acid using Cu(II) –acetate buffer as the reagent and the oxygen sensor as the detector . The peaks (triplicate) correspond to the oxygen consumed on injecting 0.0010M, 0.0020M, 0.0040M, 0.0060M, 0.0080M, and 0.010M of ascorbic acid respectively.
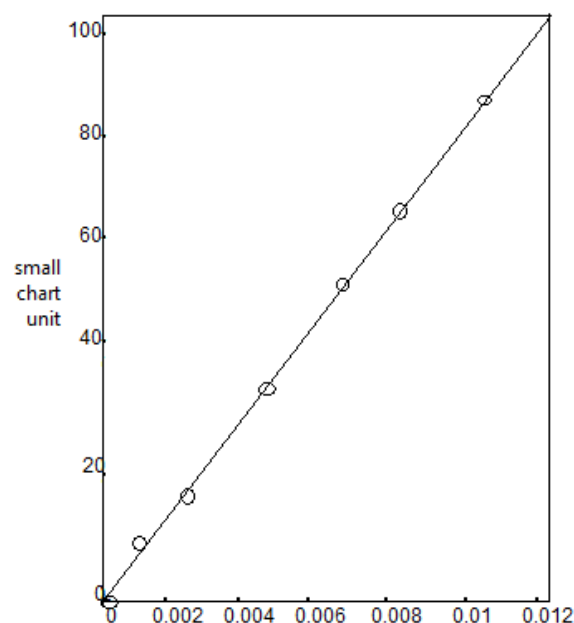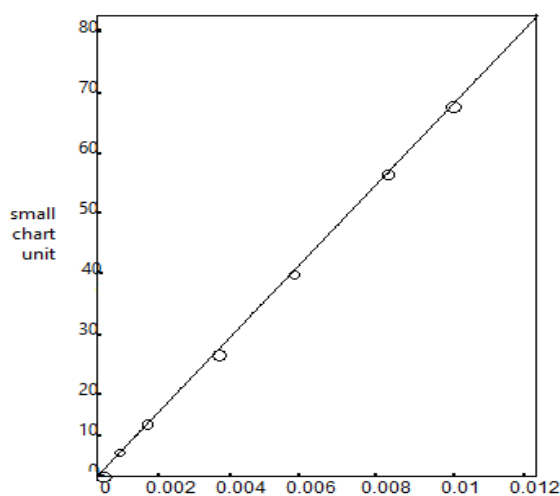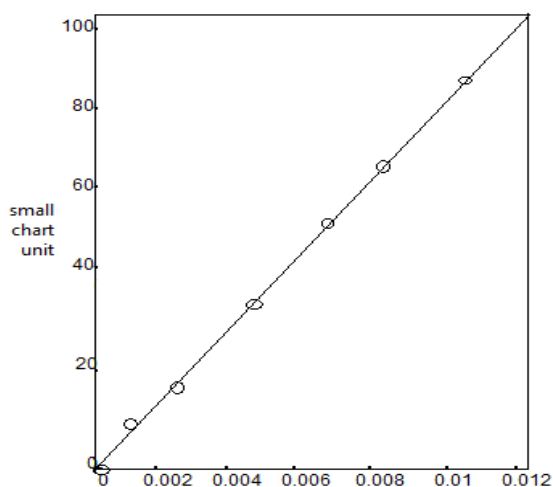
Figure 6: Dependence of peak height on the concentration of ascorbic acid for flow- injection analysis of ascorbic acid using a reagent containing freshly 0.1M CuSO₄ solution buffered at pH 4.6 with acetate buffer. The detector was an oxygen sensor (data from table 1).

Table 2: Dependence of trace height on the concentration ascorbic acid for the flow-injection analysis of ascorbic acid using re-cycled Copper(II) sulphate in 0.20M acetate buffer pH 4.6 as the reagent. The oxygen sensor was used as the detector sample loop volume was 120μl.

Ascorbic acid concentration\M	Height s.c.u
0.001	6
0.002	12
0.004	25
0.006	40
0.008	55
0.01	68
Suntop drink(bizagr Co.Ro.Ltd	37
Orange juice drink	22

The results obtained using re-cycled reagent (ie CuSO₄\ acetate buffer which had used once then deoxygenated and used a second time) are presented in table 2 and shown graphically in figure 7.

In another set of experiments the Copper(II) concentration of the reagent was changed from 0.10M to 0.20M. For both of these Cu(II) concentrations of the injected ascorbic acid standards were kept the same and the same setting were

used for the oxygen sensor amplifier and the mV recorder. The higher concentration of Cu(II) gave greater peak height (table 3) but it was concluded that this increase did not justify the use of the higher concentration of Cu(II) since this would increase the cost of the reagent.

Table 3: Flow-injection analysis of ascorbic acid using an oxygen sensor as the detector showing the recorder trace height for the injection of different concentrations of ascorbic acid into a reagent stream composed of (a) 0.10M copper sulphate in acetate buffer, pH 4.6 and (b) 0.20M copper sulphate in acetate buffer pH 4.6.

Ascorbic acid concentration\M	peak height\ s.c.u	
	(a)	b)
0.0010	5.0	6.5
0.0020	11.0	12.0
0.0040	22.5	27.0
0.0060	37.0	43.0
0.0800	49.0	59.0
0.010	59.0	71.0

Figure 7: Dependence of peak height on the concentration of ascorbic acid for the flow-injection analysis of ascorbic acid. The reagent was re-cycled 0.10M Copper(II) sulphate solution in acetate buffer pH 4.6 and the detector was oxygen sensor (data from table 2).

Further FIA experiments were carried out in which the Cu(II) concentration of the reagent was fixed at 0.10M while the pH of the acetate buffer was varied between 3.6 and 5.6. A fixed concentration of ascorbic acid (0.10M) was injected.

The maximum peak height was obtained for pH 4.6 as shown in table 4 and figure 8. This was the pH which had been chosen arbitrarily in the earlier experiments. This pH was used in all subsequent.

Table 4: Dependence of the peak height (measured in small chart units, s.c.u) on the pH of the buffer for the FIA of ascorbic acid using $CuSO_4$\acetate buffer as the reagent and the oxygen sensor as the detector. The concentration of ascorbic acid was fixed at 0.01M.

pH of buffer	Height\ s.c.u
3.6	44
4.0	50
4.6	76
5.0	58
5.6	62

Figure 8: Dependence of peak height on the concentration of ascorbic acid for flow-injection analysis of ascorbic acid using a reagent containing freshly prepared 0.1M $CuSO_4$ solution buffered at pH 4.6 with acetate buffered. The detector was an oxygen sensor (data from table 1).

In another set of experiments at fixed Cu(II) and ascorbic acid concentration, the cell volume was varied. This was accomplished by raising or lowering the plunger which fits the cell, measuring the height from the base and estimating the cell volume. Table 5 shows that the cell volume has a significant influence on the observed peak height. A volume of 2.5cm^3 was chosen for subsequent work.

Table 5: Effect of the volume of the oxygen sensor cell on the trace height for the FIA of ascorbic acid using a reagent containing Cu(II) sulphate (0.10M and 0.20M acetate buffer pH 4.6 The recorder speed was 120mm\hour and the full scale deflection of the recorder was 100mV.

Volume of vessel\cm^3	peak height\ s.c.u
4.2	32.6
3.5	32.0
2.5	61.3
1.7	36.0

In another series of experiments solutions of ascorbic acid were made up to known concentration. Then samples of the solutions were injected into the FIA system. The concentrations found in this way were compared with the concentrations taken[6]. The results are presented in table 6 and 7 for both fresh and re-cycled regent.

Table 6 : Comparison between the concentration taken and the concentration found for the determination of ascorbic acid using fresh $CuSO_4.5H_2O$ solution in acetate buffer, pH 4.6 as the reagent in a FIA determination.

Concentration taken\ mol dm^3	Concentration found \ mol dm^3
0.0060	0.0057
0.0080	0.0075
0.010	0.0091
0.0080	0.0074
0.0060	0.0054

Table 7 : Comparison between the concentration of ascorbic acid taken and the concentration found using in a FIA determination, re-cycled $CuSO_4.5H_2O$ \ acetate buffer, pH 4.6 as the reagent.

Concentration taken\mol dm^3	Concentration found \ mol dm^3
0.0080	0.0075
0.0060	0.0063
0.010	0.0092
0.010	0.0093
0.0080	0.0074
0.0060	0.0054

Because fruit juice and fruit drinks contain other naturally occurring compounds such as citric acid and amino acids it is important to find our if significant interference with the method occurs if these substances are present. Table 8 shows the influence of different substances on the peak height obtained using FIA with the oxygen sensor as the detector. The reagent was fresh copper sulphate\acetate buffer solution pH 4.6. The concentration of the possible interferents was the same as that of the ascorbic acid i.e 0.005M. It will be seen from table 8 that only in the case of iron (III) was there a significant effect on the peak height. In further experiments the concentration of iron (III) was reduced to 0.0005M. At this concentration the effect on the peak height was less it was still significant (the peak height was reduced by 8% compared with the solution of ascorbic acid containing no added iron (III).

Table 8: Flow injection analysis of ascorbic in the presence of other substances. The reagent was Cu(II) sulphate in pH 4.6 acetate buffer.

Sample and concentration\ M	Peak height\s.c.u
0.005 M ascorbic acid alone	31.5
Ascorbic acid+0.0050M Histidine	31.0
Ascorbic acid+ 0.0050MCitric Acid	31.0
Ascorbic acid+0.0050M Fe(II)	31.5
Ascorbic acid +0.0050M Fe(III)	26.5
Ascorbic acid +0.005M Tyrosine	31.5

In another test of the FIA\oxygen sensor method for ascorbic acid, a Vitamin C tablet (normally 50 mg) was dissolved in water and made up to 50 cm^3. Samples of the solution were injected into the FIA apparatus using 0.10M Cu(II) pH 4.6 acetate buffer as the reagent. From the measured peak height the concentration of ascorbic acid was determinate by reference to a calibration graph prepared on the same day for a series of standard ascorbic acid solutions. From the measured concentration the number of milligram of ascorbic acid in the tablet was calculated. The results are given in table 9.

Table 9: Repeated flow – injection analysis of ascorbic acid in a vitamin C tablet using the oxygen sensor as detector. One vitamin C tablet was dissolved in water And made up to 50 cm^3 with deionized water and samples were analyzed by the FIA method. The concentration of ascorbic acid was read off a calibration curve prepared for a series of standards and the number of mg of ascorbic acid contained in the tablet was calculated.

Height\ s.c.u	Concentration\M	Ascorbic acid\mg
50.0	0.00640	54.32
48.5	0.00650	53.68
46.0	0.00650	51.92
48.0	0.00690	53.68
48.0	0.00610	53.68
047.0	0.00600	52.80

Mean= 53.35mg, SD= 0.850

It has been established in the course of this work that within a certain range of concentration there is a linear relationship between the peak height and the ascorbic acid concentration for the FIA\oxygen sensor method. It was decided therefore to try a ratio method for the determination of an "unknown" . In this method an " unknown" solution of ascorbic acid was injected and the peak height was recorded. Immediately afterwards a freshly

prepared standard ascorbic acid solution was injected and the peak height was recorded. The concentration of the "unknown" was then calculated from the simple relationship;

C (unknown) = peak height for unknown X C(standard)
                        Peak height for standard
                              (were C represents concentration)

This method generally gave better agreement between "taken" and "found" concentrations of ascorbic acid as shown in tables 10 and 11[7].

Table 10: Comparison between the concentration taken and the concentration found for the determination of ascorbic acid by FIA using the ratio method with fresh CuSO\ pH 4.6 buffer as reagent.

Concentration taken\M	Concentration found\ M
0.0060	0.0058
0.010	0.0098
0.010	0.0106
0.0020	0.0018
0.0080	0.0072
0.0040	0.0036
0.0060	0.0054
0.0060	0.0063
0.0030	0.0033

DISSECTION:

The work also showed that the Cu(II) acetate buffer reagent required for FIA could be re-cycled at least once and possibly three times with a corresponding saving in running costs. A fresh calibration graph is required for the re-cycled reagent unless the ratio method is used. The reagent appears to be very stable; it is likely that the Cu(II) ion acts as a preventative for the acetate buffer preventing bacterial growth.   In other set of experiments the copper(II) concentration of the reagent was changed from 0.10M   to 0.20M. Although somewhat greater peak height were obtained using the Cu(II) concentration.

Table 11: Comparison between the concentration taken and the concentration found for the determination of ascorbic acid FIA using the ratio method with recycled CuSO$_4$\pH 4.6 buffer solution as reagent.

Concentration taken\M	Concentration found \ M
0.010	0.0098
0.0080	0.0082
0.0040	0.0046
0.0060	0.0064
0.0060	0.0054
0.0060	0.0060
0.0030	0.0031

It was concluded that this increase did not justify the use of the higher concentration of Cu(II) since this would significantly increase the cost of reagent. In another FIA experiment the Cu(II) concentration of the reagent was fixed at 0.10M while the pH of the acetate buffer was varied between 3.6 and 5.6. It was found that the maximum peak height was obtained for pH 4.6 as show in table 4 and figure 9. Copper(II) ion catalysis of the oxidation of ascorbic acid is selective for ascorbic acid (as a component of nature orange juices) when the FIA method was applied in the presence of a number of potential interferants little interference was observed. Thus, the method is suitable for complex systems such as fruit juices and fruit drinks as well as simple system such as Vitamin C tablets.

Flow injection analysis has several important advantages to offer the analyst over other methods of instrumentation including :

- A rapid start up and shutdown time(less than 5 minutes for each)

- A high sample throughput rate (typically 100-300 samples per hour).

- Fast response time (often less than one minute between sample injection and recorder response).

- Low reagent coasts.

Because of these advantages, FIA is finding increased use in clinical and environmental sampling. Except for the injection system, simpler and more flexible equipment. -

REFERENCES:
 1- J. Ruzicka, E. H. Hansen; Flow Injection Analysis, Chemical Analysis V.62 2nd Ed, 1988,
 2- FIA lab Operation Manual
 3- Skoog, Holler, Nieman Principles of Instrumental Analysis, 5th edition, Saunders College Publishing, Fort Worth, TX, Ch. 10. 1997
4- J. Ruzicka and E.H. Hansen, Anal. Chim. Acta 78, 145-157 (1975).
5- J. Ruzicka and G.D. Marshall, Anal. Chim. Acta 237, 329-343 (1990).
 6- C.E. Lenehan, N.W. Barnett, and S.W. Simon, Analyst 127, 997-1020 (2002).
 7- J. Ruzicka, Analyst 125, 1053-1060 (2000).

Answer to clinical quiz

His vision in the last few years both for far and near. If the vision was disturbed for near at witch age and distance (early onset presbyopia). H/O headache and previously recorded visual acuity , indicate hypermetropia. Any blood sample for sugar or fundus examination may indicate biochemical diabetes.

This patient is suffering from poor vision for far and near most likely because of hypermeropia super-added by presbyopia. Refraction is essential before proceeding to any further intervention (pupil dilatation reduces the visual quality, You are going to be blamed). Cycloplegia refraction in is not essential, fogging is alternative. In those cases complete base line ophthalmic examination is recommended.

In cases of high blood sugar the lens cortex level of sugar rises, it is metabolized to sorbitol. The later increases the cortical osmotic pressure, drives water to the cortex more than to the lens nucleus. This increases the difference in the refractive index between the lens cortex and nucleus. So bending of light increases (myopic shift, refractive myopia). After controlling of blood sugar this needs few weeks to retain back to original stat. It is recommended that in any uncontrolled blood sugar cases, not to prescribe glasses until few weeks after blood sugar control. In this case the patient originally is hypermetropic witch was corrected by the myopic shift.

EVALUATION OF THE EFFECT OF ANTIOXIDANT MICRONUTRIENTS FORMULA ON SPERM QUALITY IN THOSE INFERTILE LIBYAN PATIENTS

By

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ABSTRACT:

Male infertility is responsible for about 20% of infertile couples and contributes in 30-40% in infertile couples. Occasionally, there is no clear reason for the abnormal production of sperms. Lifestyle, smoking, nutrition, Diabetes, and hypertension could be the reason behind the infertility. The aim of the present clinical study was to evaluate the effect of a micronutrients included in the preparation were L-carnitine, L-arginine, zinc, vitamin E, selenium, co-enzyme Q10 and folic acid on sperm quality in those infertile Libyan patients, and to in speculate the correlation between the diabetic, hypertensive, and cigarette smoker with the treatment outcomes. Patients received the treatment twice daily for the three months. Sperm parameters (count, motility, and morphology) were taken before and after the treatment. An improvement in count (92.30%), and progressive motility (38.46%)and morphology parameters (96.15%) were detected, while, 40 % showed an improvement in the three parameters together. There is no significant difference in treatment outcomes between diabetics/non-diabetics, hypertensive/non-hypertensive, and smoker's/non-smokers patients (p$>$0.05). Conclusion, the benefits of incorporating combination antioxidants therapy in clinical settings have been the potential impact on infertile patients, and improve sperm quality parameters, even in hypertensive diabetic patients, and smokers.

KEY WORDS: Smoking, Diabetes, Hypertension, infertility.

INTRODUCTION:

At puberty age, a change in both male and female bodies takes place, and they become able to conceive and have baby. So, fertility is the ability to pregnancy, which ends with having a baby[1]. Conception is normally achieved within 12 months in 80-85% of couples using no contraceptive measures; thus an estimated 15% of couples attempting their first pregnancy will have difficulty conceiving. While certain cases of male infertility are due to anatomical abnormalities such as varicoceles, ductal obstructions, or ejaculatory disorders, an estimated 40-90% of cases are due to deficient sperm production of unidentifiable origin[2]. However, infertility is the inability to conceive, or having pregnancy and it can occur because of the woman, the man, or both. Over10-15 % of couples in the world are infertile. Approximately 15% to 30% of couples have no clear reason for their fertility problem. It can be classified as primary and secondary infertility, primary infertility in which couples have never conceived before while in secondary they have difficulty to conceive again after conceiving ended with miscarriage[3]. Sperm is the male reproductive cell, while the ovum (egg) is female reproductive cell. They form the zygote when the genetic materials from both combine in the fertilization process. The conception achieved after sexual intercourse, where the sperm cells travel through the cervix, uterus, until reach the fallopian tube; and meet the ovulated egg. Only one sperm penetrates the egg and fertilization takes place (as represented in figure 1)[4-5].

However, there are a lot of factors (Table 1) that are important in the successful conception process, but these the most important such as production of healthy sperms, production of healthy ova, unblocked fallopian tubes, so sperm will be able to reach the egg, and embryo with good quality[6]. Age, the most influential on woman's fertility. Changes happen when woman getting older, become less fertile because the oocytes reserve declines[3].
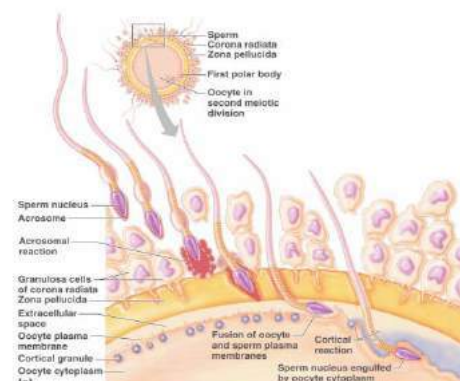

Figure 1: Sperm penetrates the egg and fertilization takes place[5]

Sperm consist of 3 parts (shown in figure 2) head, neck, and tail. Head is the part that contains the nucleus; which contains the half number of human cell chromosomes 23.
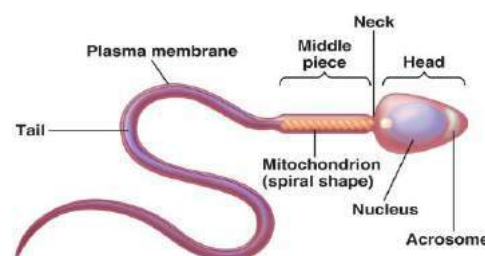

Figure 2: The structure of mature human sperm[8]

Head's function is the penetration of the egg after the binding. Neck it is the part that connect the head with the tail. The later responsible for the movement (mobile part) of sperm in a whipping motion to drive the sperm at the

egg; and contain the middle piece, which is tubular structure in which mitochondria are spirally arranged. It is also called powerhouse of sperm because it gives energy to the sperm to swim in the female genital tract[7].

Sperm production starts by the pituitary and hypothalamus glands both located at the base of the brain. They are responsible for hormones and sperm production. Where the hypothalamus produces GnRH (gonadotrophin-releasing hormone), which stimulate the pituitary to produce and release LH (luteinizing hormone), and FSH (follicle stimulating hormone) in blood stream. These tow messenger hormones rise at puberty stage to help in the development of testes and make them ready to produce sperms; LH and FSH act by stimulation of testes. The former hormone stimulates the leyding cells, which lies between seminiferous tubules in the testes; to make and release testosterone in blood. Testosterone is the male sex hormone, which responsible for the physical changes at puberty stage for the adult man countenance such as facial and body hair, growth, development of penis and testes. Testosterone hand in hand with the FSH act on the seminiferous tubules to stimulate them to produce sperms in the testes [7-9].

At the puberty, spermatogenesis is started (the process of production of sperms). It is a continuous process of production of millions of sperms in daily manner. Producing of complete developed sperm that able to swim and penetrate the ovum needs about 70 days. As a result, sperm exist at different stages of development in the testes.

Male infertility occurs as result of problems in sperm production or sperm transport. A sperm production problem considers the most common cause of infertility. It occurs in about two-thirds of infertile men, including the production of low number of sperms or the production of sperm that not work properly[10].

Table 1: The main causes of infertility in the couple[4].

Sperm problems	30%
Ovulation problems	25%
Non obvious reason	25%
Tubal damage	20%
Endometriosis	5%
Irregular intercourse	5%
Cervical problems	3%
Uterus problems	<1%

Sperm transport problems is the second cause of male infertility caused by obstruction of transporter tubes that transport sperm from testes to penis. It can cause complete absence of sperm in the ejaculate[7]. It occurs in about one in five infertile men including infection, genetic problems as absence of vas deferens, obstruction of epididymis or ejaculatory duct, sexual problems due to premature ejaculation, failure of ejaculation, erectile dysfunction, infrequent intercourse. Also, men who have had a vasectomy; by cutting the vas deferens surgically prevents the transporting of sperms from testes, cause permanent infertility. Furthermore, there are other causes of the male

infertility such as, sexual problems, hormonal problems, and sperm antibodies[10].

Varicocele affects approximately three of twenty men. It lowers sperm production and movement, and increases the production of abnormal sperms. However, Some men with varicoceles have normal sperm count and can have children[7,11].

Number of medicines and drugs used for treatment of some cancers, kidney disorders, inflammatory bowel diseases, ulcerative colitis, Crohn's and rheumatoid arthritis can cause permanent infertility if given for long period because of their effect on sperm production. In addition, using the testosterone either for treatment of testosterone deficiency, or taken just for body building and sporting purposes, leads to reduction in the size of the testes and lower or stop sperm production due to the negative feedback of the pituitary hormones (FSH and LH) production[7]. Damaging of the testicular tissue by intra-testicular hematoma or testis rupture that caused by trauma to the scrotum lead to anti-sperm antibody production.[9] However, when all tests results are normal, and there is no clear reason for the abnormal production of sperms. Life style, environment, obesity, smoking, nutrition, alcohol intake, could be the reason behind the idiopathic infertility[7, 12].

The semen quality, however, is affected by several factors:
-Diabetes
It is s a chronic disease characterized with metabolic and endocrine disorder[13]. Both types consider a risk factor for sexual and reproductive problems (impotence, erectile dysfunction, retrograde ejaculation, and reduced libido). Due to the metabolic disorder, many problems can occur that will alter and affects sperm parameters such as endocrine disorder, neuropathy and increasing in the oxidative stress (which leads to damaging in sperm and mitochondria DNA). In addition the histologic damage of the epididymis, that lead to problem in sperm transport[14]. The fragmentation in the DNA of diabetic patient leads to infertility because the sperm loses its full genetic material and codes when fuses with oocyte and fails to be an embryo with the egg. The elevated insulin which accompanying type 2 called hyperinsulinemia affects and reduces the spermatogenesis also affects the sex hormone binding globulin (SHBG) and decreases it synthesis leading to rising in the free estrogen, and conversion of the free testosterone to estrogen, and the final result is abnormal and reduction in testosterone level[12].

-Oxidative stress (OS)
In all living aerobic cells the oxygen is important to continue the cell's life[15]. but increasing in the amount of some of its metabolites; called the reactive oxygen species (ROS) such as superoxide anion, hydroxyl radical and hydrogen peroxide to extent that creates imbalance between the ROS and the protection mechanisms in the semen results in the oxidative stress. This imbalance occurs as a result of the environmental pollution, obesity, poor nutrition, infection, and alcohol intake[16-20]. The ROS affects male fertility by affecting the spermatozoa membrane, (figure 3 represents the mechanism of DNA damage caused by ROS) which contains high amount of polyunsaturated fatty acid (PUFAS), which enhance its flexibility and induce the acrosome reaction and fusing the sperm membrane with the oocyte. Because of this the

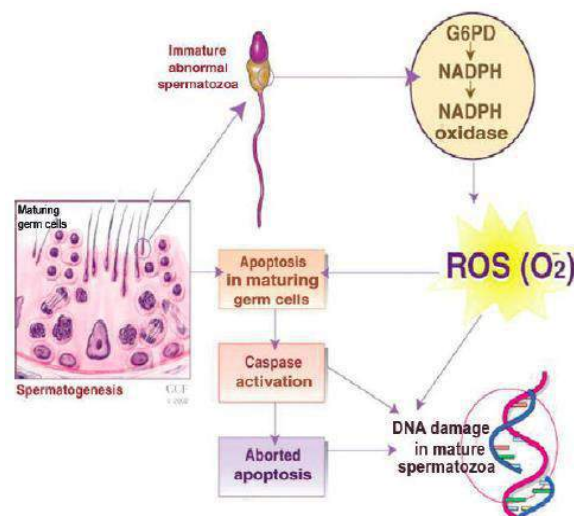spermatozoa membrane is highly susceptible to the ROS attack.

Figure 3: Mechanism of DNA damage caused by ROS[20]

The attack reduces the PUFAS and the docosahexaenoic acid (DHA); which plays an important role as an antioxidant due to its high content of double bond leading to less antioxidant capacity and oxidative stress[16]. When the OS affects the spermatozoa changes occur on the phospholipid membrane making it less flexible with reduced integrity and fluidity, and that reduces sperm motility and causes DNA damage and fragmentation.(as shown in figure 4). As a result, ROS should be inactivated continuously by the antioxidant to a level, which is important for normal sperm function[15] .The limited concentration of ROS increases sperm ability to move and fertilizing by stimulating sperm capacitation and acrosome reaction[17-20].
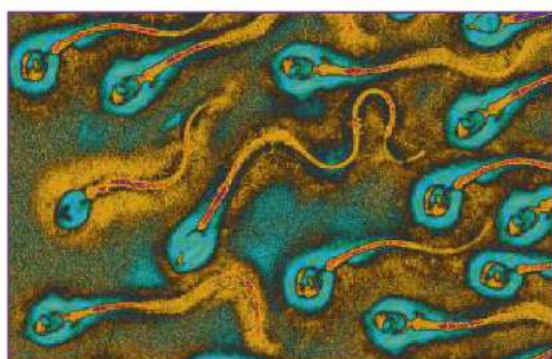
Figure 4: Reactive oxygen species, including oxygen ions, free radicals and peroxides, can damage the sperm membrane and DNA, leading to male subfertility[20].

-Cigarette Smoking
It has been associated with decreased sperm count, alterations immobility, and an overall increase in the number of abnormal sperm. A study designed to evaluate seminal zinc levels in smokers and non-smokers found that although smokers did not have significantly lower zinc levels than non-smokers, seminal cadmium levels were significantly increased, especially in those smoking more than one pack per day. There is an increasing body of

evidence that shows that life style factors can impact on reproductive performance. Multivariate logistic regression reveals that smoking habits are significant major contributors for infertility in DM men[20].

AIM AND OBJECTIVES
The aim of the present clinical study was to evaluate the effect of a nutraceutical containing seven micronutrients on sperm quality (sperm count, motility, and morphology) in male's with/without Hypertension, Diabetes, and Smoking. Micronutrients included in the preparation were L-carnitine, L-arginine, zinc, vitamin E, selenium, co-enzyme Q10 (CoQ10) and folic acid. The treatment time of three months was selected according to the period of 90 days (3 months) for spermatogenesis   and the common interval between first and usual follow-up semen analysis

METHODS
The present case series study was performed from January 2017 to March 2017 at the outpatient Fertility Centre Alsafwa, Libya, Misurata.
Men (26 patients) with at least one year of Infertility and at least one prior and one recent abnormal semen analysis were invited to participate and take two daily supplement of the proposed nutraceutical for three months, after which a follow-up semen analysis was performed.
Exclusion criteria were, aspermia, varicocele and recent urogenital infections. Participants in the active treatment group were requested to give signed consent after   being informed of the study, its aims and methodology.
Preparation (Nutraceutical) product:
Each supplement of the active ingredient, Include the following (table 2).

Table 2: Nutraceutical product.

L-carnitine	**(440 mg)**
L-arginine	(500 mg)
Zinc	(2,25 mg)
Vitamin E	(15 mg)
Selenium	(30 μg)
CoQ10	15 mg)
Folic acid	(400 μg)

Semen Analysis Assessment:

A semen analysis was performed at baseline and after three months in the active treatment group. These data were compared with each other[1] (Before and after) and had two semen analyses three months apart (baseline and confirmatory). *Baseline*, it means before starting treatment. *Confirmatory*, it means after finishing treatment, 3 months' period.
Statistical Analysis:
Statistical analysis was performed using SPSS® software   package   (Version   21   for   Windows,   SPSS Inc., Chicago, Illinois, US).   Data are quantal and presented as frequencies and percentages. The significance of differences between groups is tested by Chi square analysis where ($P < 0.05$).
Limitations:
The limitation of the study was that we could not perform the complimentary semen tests such as immunologic and genetic tests (antisperm antibodies, karyotype, Y chromosome micro-deletion test, motile sperm organelle

morphology examination). In some cases, infertility might be associated to these factors and suppose the antioxidant properties can correct the resulting abnormalities.

Effect of micronutrients antioxidant formula on sperm parameters (count, motility, and/or morphology) in Libyan infertile patients:

About 30-40% of all infertile males have no obvious or clear reason for their infertility (idiopathic infertility). They have no history of diseases or endocrine problems that may affects their fertility, but the semen analysis detects a reduction in number of spermatozoa (oligozoospermia, spermatozoa < 15 million/mL), or in sperm motility (asthenozoospermia, < 32% motile spermatozoa), or increment in the abnormally shaped sperm (teratozoospermia, < 4% normal sperm forms)[21-25]. Usually the three problems occur together and the case called oligo-asthenoteratozoospermia (OAT) syndrome. According to the WHO, the normal ranges for each parameter, a normal semen sample should have a volume of 1.5-5.0 ml. A normal sperm has an oval head about 5-6 micrometres long and 2.5-3.5 micrometres wide, and a single long tail, and must be a symmetrical to pass through the egg's protein coat[26-30].

In this clinical study, the patients were received active supplement containing seven micronutrients including L-carnitine, L-arginine, zinc, vitamin E, selenium, co-enzyme Q10 (CoQ10) and folic acid of 2 sachet/ twice a day for 3 months. The age distribution of the total number of patients (26 therapeutic group) is shown in figure 5, in which most of the patients are aged from 40-49 (10 patients) and 20-29 (9 patients)[38-43].
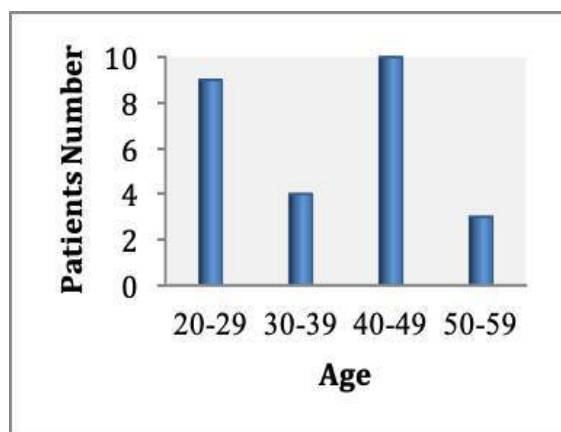

Figure 5: Distribution of age in therapeutic groups.

All the patients were requested to perform a semen analysis to detect the changes of sperm parameters after 3 months of treatment. Table.3 shows sperm parameter for 26 infertile men before and after the treatment. Sperm count, motility, and morphology has been improved for 24,10, and 25 of the total 26 patients, respectively. For three months, the sperm count; motility, and morphology have been increased by 92.30%, 38.46%, 96.15% compared to the baseline groups, respectively. Furthermore, results showed that by the end of three months course of treatment, there was 10 patients increase in the progressive motility compared to the not improved patients (Table 3).

Table 3: Effect of micronutrients antioxidant formula on sperm parameters (count, motility, and/or morphology); the changes after 3 months of treatment.

Parameter	Number	Range before treatment	Range after treatment	%
Count	24	3 – 91 Million	18 – 400 Million	92.30%
Motility	10	20 – 49 %	35 – 50 %	38.46%
Morphology	25	1 – 28 %	6 – 40 %	96.15%
Motility - Morphology	0			0%
Morphology - Count	14			53.84%
Motility – Morphology – Count	10			38.46%

These results are in conformity with Lenzi et al, Garolla and Balercia et al evaluated the effect of LC and LAC or combined LC and LAC on the semen motion kinetics and total oxygen radical scavenging capacity (TOSC)[31-33]. A meta-analysis showed that supplementing infertile men with CoQ10 does not increase live birth or pregnancy rates, but there is a global improvement in sperm parameters such as sperm concentration and motility and CoQ10 concentration in semen. On another hand, Ebisco and colleagues revealed that patients who received 5 mg of folic acid and 66 mg of zinc for 26 weeks reported improving sperm concentration[31-37].

Oxidative stress affects the testicular function by disrupting germinal cell epithelia division, differentiation and also induces germ cell apoptosis and subsequently decrease spermatogenesis, sperm count, mobility, viability and morphology . In several times, overwhelm of ROS generation exceeds endogenous antioxidants defences capacities, thus recourse to antioxidants supplementation is highly recommended. It is presumable that the free radical scavenging effect of the antioxidants used in the treatment of infertility decreased the oxidative stress, prevents DNA damage and restored the spermatogenesis and spermiogenesis[44-47].

Thereby, vitamin E enhance the activity of a range of antioxidants enzymes involved in scavenging free radicals and improve motility and fertilization or pregnancy rates in infertile men with high ROS by influencing the expression of genes involved in the intracellular redox pathways Zinc (Zn) is a trace element essential to maintain optimal functional levels of antioxidant enzymes, cell proliferation and differentiation, immune function, DNA replication and transcription as well as for reproduction due to its fundamental role in germ cell development and expression of steroid receptors for spermatogenesis. Selenium (Se) is a micronutrient plays an

important antioxidant role against oxidative sperm DNA damage and is necessary for testicular development, spermatogenesis, sperm motility and for the biosynthesis of testosterone. L carnitine protects cell membranes and DNA from damage caused by free oxygen radicals. It is also crucial to transport fatty acids into mitochondria matrix within spermatozoa for utilization in metabolism and energy production through β-oxidation and subsequently contributes directly to sperm metabolism, nutrition, maturation, count and motility[31-37].

Looking to our results, it is seems that treatment in this population of infertile men can restores partially or completely all altered sperm parameters (sperm count, motility, morphology) to the normal range and subsequently improves semen quality and pregnancy rates. These beneficial roles may be due to the ability and synergic effects of their multivitamins and micronutrients antioxidants components in scavenging free radicals, promoting sperm enzymatic and or non-enzymatic antioxidants define and thereby prevent DNA damage and membrane peroxidation that will reduce its fusogenic capacity, rendering fertilization less probable. So, because our study is preliminary to test the efficacy of combination micronutrients as therapy in men subfertility[38].

Effect of diabetes/hypertension on micronutrients treatment outcomes in infertile patients

According to the World Health Organization (WHO), in 2000 DM affected 177 millions of people all over the world. However, this number will have probably arrived at the three hundred million since 2025. This increase will be owed to ageing, obesity and population growth. Almost 90% of patients with noninsulin-dependent diabetes mellitus or type 2 DM are diagnosed before they reach the third decade of their life. Thereafter, diabetes will affect even more reproductive males. Consequences of DM may include effects on ejaculation and penile erection, lack of efficient endocrine control of spermatogenesis or even on spermatogenesis itself. Despite spermatogenesis being a function of only the mature testis, environmental injury during maternal, perinatal and prepubertal phases can indirectly influence eventual sperm production in the adult male. It is believed that exposure during these phases of the developing testis leads to irreversible effects on spermatogenesis, while the accompanying effects of adulthood exposure are in all probability reversible[2]. Figure 6 illustrates that either diabetic nor hypertensive have low sperm count compared to non-diabetic or non-hypertensive patients. According to Padron's and Garcia-Diez's studies, DM intensely affects male reproductive performance. A decrease in all semen parameters (semen volume, sperm count, motility and morphology) has been observed in two studies of IDDM people. [2] Also, men with Type 2 diabetes mellitus have a higher prevalence of low testosterone levels than age-matched controls. In numerous cross-sectional studies, levels of testosterone in men have been inversely associated with several recognized risk factors for the development of Type 2 diabetes, such as obesity, central adiposity, and an elevated fasting plasma concentration of insulin and glucose. Several prospective studies found that low levels of testosterone and sex hormone–binding globulin predict the subsequent development of Type 2 diabetes among aging men. Low plasma testosterone concentration is associated with other correlates of diabetes, such as cardiovascular disease and hypertension. The researchers concluded that diabetes is

associated with increased sperm nuclear and mtDNA damage that may impair the reproductive capability of diabetic men[2].

Figure 6 and 7 illustrate sperm count and morphology for infertile men before and after the treatment. Sperm count has been improved for most patients either diabetic/non-diabetic or hypertensive/non-hypertensive. For three months, the sperm count and morphology have been increased and there was significant effect on count or morphology. No difference (p > 0.05) was noted between both diabetic/non-diabetic and hypertensive/non-hypertensive in terms of semen variables. Combination treatment resulted in significantly improved sperm parameter rates. These results are in line with Bener et al. (2009) who showed that a lifestyle modification program that includes exercise and improved dietary habits need to be established to lose weight improve fitness and improve reproductive functioning. In addition to count and morphology.
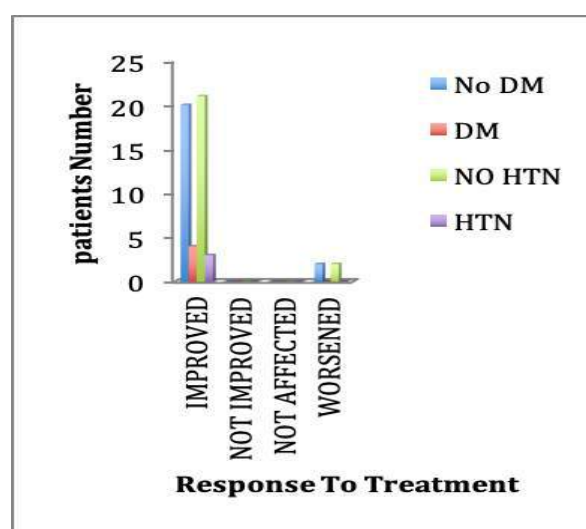
Figure 6: Effect of micronutrients antioxidant formula on sperm count (diabetic/non-diabetic or hypertensive/Non-hypertensive); the changes after 3 months of treatment. (P > 0.05).
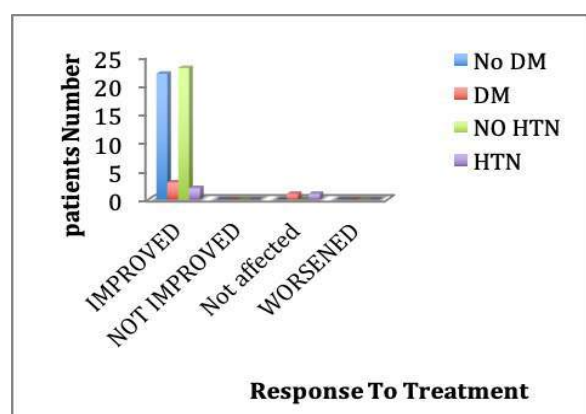
Figure.7: Effect of micronutrients antioxidant formula on sperm morphology (diabetic/non-diabetic or hypertensive/Non- hypertensive); the changes after 3 months of treatment (P > 0.05).

Figure 8 shows sperm motility for infertile men, which has been improved for 9 cases of both non-diabetic and non-

hypertensive. On other hand, Sperm motility has not been ameliorated for diabetic//hypertensive patients (p > 0.05); (3 and 2 respectively). These results are consistent with (Delfino et al, 2007) who showed that DM affects the quality of sperm and the ejaculation mechanism, as well[2].
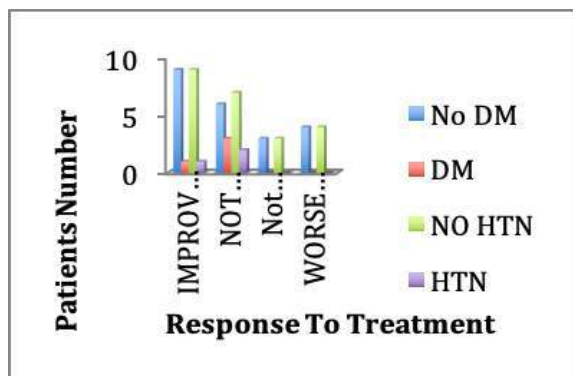

Figure 8: Effect of micronutrients antioxidant formula on sperm motility (diabetic/non-diabetic or hypertensive/ Non- hypertensive); the changes after 3 months of treatment. (p> 0.05).

Effect of cigarette smoking on micronutrients treatment outcomes in infertile patients: According to the literature, infertility is no longer just a result of health problems but choices of people's lifestyle nowadays, as well. As it is evidenced by recent studies, Environmental, socio-economic factors, and smoking increase the risk of infertility of a couple[39]. Figures 9 and 10 show sperm count and morphology for infertile men before and after the treatment. Sperm count has been improved for most cases either (13, smokers) or (12, non-smokers), out of 26 patients. For three months, the sperm count and morphology have been increased (p > 0.05). In addition to count and morphology, Figure 11 shows sperm motility for infertile men before and after the treatment. Sperm motility has been improved for non-smokers (4 out of 10 patients). On other hand, Sperm motility has been ameliorated for smokers (6 out of 13 patients); (p > 0.05).
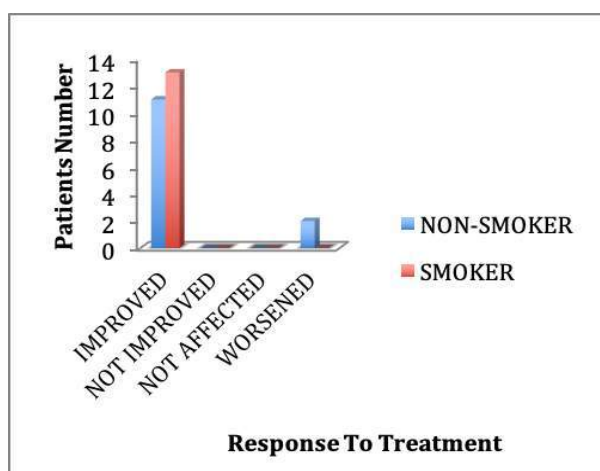

Figure 9: Effect of micronutrients antioxidant formula on sperm count (Smokers/Non-smokers); the changes after 3 months of treatment, (P > 0.05).

There is strong evidence of the adverse effects of smoking on fertility. In men, smoking negatively affects sperm

production, motility, and morphology, and is associated with an increased risk of DNA damage. Experimental evidence suggests nicotine can alter the function of the hypothalamic-pituitary axis, affecting growth hormone, cortisol, vasopressin, and oxytocin release, which then inhibits the release of luteinizing hormone (LH) and prolactin.
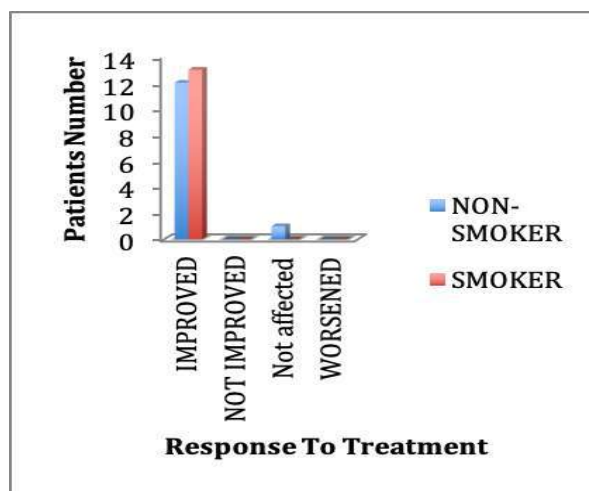

Figure. 10: Effect of micronutrients antioxidant formula on sperm morphology (Smokers/Nonsmokers); the changes after 3 months of treatment, (P > 0.05).

Cigarette smokers were also shown to have higher levels of circulating estradiol and decreased levels of LH, follicle stimulating hormone (FSH), and prolactin than non-smokers, all of which potentially impact spermatogenesis. Smokers with low prolactin levels also demonstrated defects in sperm motility. However, these improved changes attributed to combination treatment; also, could be due to life style modification (smoking cessation, and exercise)[39].
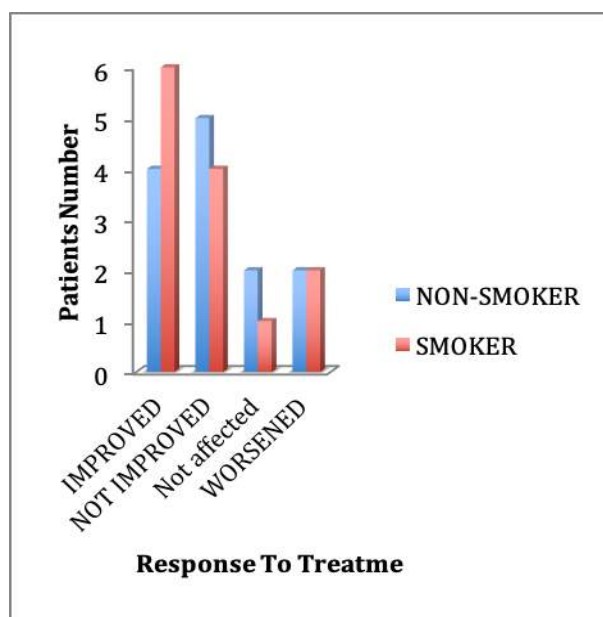

Figure 11: Effect of micronutrients antioxidant formula on sperm motility (Smokers/Non-smokers); the changes after 3 months of treatment (P > 0.05).

Conclusion.

Presently, multi-antioxidant supplementations are considered as an effective therapy for men infertility. The synergetic effect of multi antioxidants made them noteworthy for researchers. This study carried out to determine the effect of oral anti-oxidant treatment upon the sperm parameters in those with/without diabetes, hypertension, and smoking, during a period of 3 months. Results showed that an improvement in count, motility, and morphology parameters was observed. There is non-significant association between the diabetic, hypertension or smoking state and the micronutrient formula efficacy in those patients. Findings of this study suggest that antioxidant treatment improves sperm quality not only in terms of key seminal parameters, but also helps even those hypertensive diabetic patients, and smokers. Therefore, administration of antioxidants can help in new medical treatments.

RECOMMENDATIONS:

Long term of treatment could have a better effect on sperm motility; future study to better establish optimum daily dose of dietary supplements and period of treatment time is necessary.

We also suggest further investigations on the effect of this combination in azoospermic patients with large sample sizes and genetic tests.

Continuous research effort to better understands infertility conditions and its correlation with the hyperglycemia, as a potential risk factor among men and women is required.

REFERENCES:

1- Care4ba.com. 2017 [cited 7 November 2017]. Available from : http://www.care4ba.com/uploads/Age_and_Fertility_ASRM.pdf

2-Sinclair S. Male infertility: nutritional and environmental considerations. Alternative medicine review: a journal of clinical therapeutic. 2000 Feb;5(1):28-38.

3- Eniola OW, Adetola AA, Abayomi BT. A review of Female Infertility; important etiological factors and management. Journal of Microbiology and Biotechnology Research. 2017 Mar 31;2(3):379-85.

4- Health.gov.ie. 2017 [cited 7 November 2017]. Available from: http://health.gov.ie/wpcontent/uploads/2014/03/infertBiomedEvid_Full.pdf

5- Elmussareh M, Mahrous A, Kayes O. Antioxidant therapy for male subfertility: myth or evidence-based?. Trends in Urology & Men's Health. 2015 Jan 1;6(1):35-9.

6- Weiss RV, Clapauch R. Female infertility of endocrine origin. ArquivosBrasileiros de Endocrinologia & Metabologia. 2014 Mar;58(2):144-52.

7- Andrologyaustralia.org. 2017 [cited 7 November 2017]. Available from: https://www.andrologyaustralia.org/wp-content/uploads/Male-Infertility-Guide-WEB.pdf

8-What is the structure of a mature human sperm cell? - Lifeeasy Biology: Questions and Answers [Internet]. Biology.lifeeasy.org. 2017 [cited 26 October 2017]. Available from: http://www.biology.lifeeasy.org/95/what-is-the-structure-of-a-mature-human-sperm-cell.

9- Raheem AA, Ralph D. Male infertility: causes and investigations. Trends in Urology & Men's Health. 2011 Sep 1;2(5):8-11.

10- Andrologyaustralia.org. 2017 [cited 7 November 2017]. Available from: https://www.andrologyaustralia.org/wp-content/uploads/Factsheet_MaleInfertility.pdf

11- Comhaire FH, Decleer W. The Benefit of Nutraceutical Food Supplementation and Antioxidants for the Treatment of the Infertile Couple and in Assisted Reproduction. Reproductive Sys Sexual Disord S. 2012;1:2.

12- Aboua G, Oguntibeju OO, du Plessis SS. Can lifestyle factors of diabetes mellitus patients affect their fertility?.InDiabetes Mellitus-Insights and Perspectives 2013.InTech.

13- George GS, Opuene E, Onuoha EA. MALE HYPERGLYCEMIC-INDUCED INFERTILITY: AN INTEGRATION OF SOME BIOCHEMICAL FACTORS. European Journal of Biology and Medical Science Research. 2014 Dec;2(4):78-84.

14- EDIZ C, ALTINTAS R. The Metabolic Syndrome and Male Infertility: A Review of the Literature. J Diabetes MetabSyndrDisord. 2014;1(002).

15- Agarwal A, Saleh RA. Role of oxidants in male infertility: rationale, significance, and treatment.

16- Ahmadi S, Bashiri R, Ghadiri-Anari A, Nadjarzadeh A. Antioxidant supplements and semen parameters: An evidence based review. International Journal of Reproductive BioMedicine. 2016 Dec;14(12):729.

17- Agarwal A. Role of oxidative stress in male infertility and antioxidant supplementation. US Kidney and Urological Disease. 2005;122.

18-Adewoyin M, Ibrahim M, Roszaman R, Isa ML, Alewi NA, Rafa AA, Anuar MN. Male Infertility: The Effect of Natural Antioxidants and Phytocompounds on Seminal Oxidative Stress. Diseases. 2017 Mar 1;5(1):9.

19- Comhaire FH, Decleer W. Beneficial effect of food supplementation with the nutriceutical Improve® for the treatment of infertile couple. Asian Pacific Journal of Reproduction. 2012 Sep 1;1(3):169-76.

20- Agarwal A, Makker K, Sharma R. Clinical relevance of oxidative stress in male factor infertility: an update. American journal of reproductive immunology. 2008 Jan 1;59(1):2-11.

21- Sinclair S. Male infertility: nutritional and environmental considerations. Alternative medicine review: a journal of clinical therapeutic. 2000 Feb;5(1):28-38.

22- Cheah Y, Yang W. Functions of essential nutrition for high quality spermatogenesis. Advances in Bioscience and Biotechnology. 2011 Aug 16;2(04):182.

23- Elmussareh M, Mahrous A, Kayes O. Antioxidant therapy for male subfertility: myth or evidence-based?.Trends in Urology & Men's Health. 2015 Jan 1;6(1):35-9.

24- Rengaraj D, Hong YH. Effects of dietary vitamin E on fertility functions in poultry species.International journal of molecular sciences. 2015 Apr 30;16(5):9910-21.

25- Jungwirth A, Diemer T, Dohle GR, Giwercman A, Kopa Z, Krausz C, Tournaye H. Guidelines on.

26- Purvis K, Christiansen E. Male infertility:current concepts. Ann Med1992;24:258-272.

27- Griffin E. Wilson D. Disorders of the Testes. In: Isselbacher K, Braunwald E, Wilson J, Martin B, et.al, eds. Harrison's Principles of InternalMedicine. 13th ed. New York, McGrawHill;1994: 2006-2017.

28- Check JH, Nowroozi K, Lee M, et al. Evaluation and treatment of a male factor component to unexplained infertility. Arch Androl 1990;25:199-211.

29- Purvis K, Christiansen E. Infection in the male

reproductive tract. Impact, diagnosis and treatment in relation to male infertility.Int J Androl 1993;16:1-13.

30- Elmahaishi LM, Abbas AA, Elmahaishi MS. Journal of Gynecology & Reproductive Medicine.

31- Menchini-Fabris GF, Canale D, Izzo PL, et al. Free L-carnitine in human semen: its variability in different andrologic pathologies. FertilSteril 1984;42:263-267.

32- Costa M, Canale D, Filicori M, et al. Lcarnitine in idiopathic astheno-zoospermia: a multicenter study. Italian Study Group on Carnitine and Male Infertility. Andrologia 1994;26:155-159.

33- Vitali G, Parente R, Melotti C. Carnitine supplementation in human idiopathic asthenospermia: clinical results. Drugs ExpClin Res 1995;21:157-159.

34- Scibona M, Meschini P, Capparelli S, et al. Larginine and male infertility. Minerva UrolNefrol 1994; 46:251-253.

35- Favier A. Current aspects about the role of zinc in nutrition. Rev Prat 1993;43:146-151. [Article in French].

36- Kessopoulou E, Powers HJ, Sharma KK, et al. A double-blind randomized placebo cross-over controlled trial using the antioxidant vitamin E to treat reactive oxygen species associated with male infertility. FertilSteril 1995;64:825-831.

37- Vezina D, Mauffette F, Roberts KD, Bleau G. Selenium-vitamin E supplementation in infertile men. Effects on semen parameters and micronutrient levels and distribution.Biol Trace Elem Res 1996;53:65-83.

38-L. Rachid M, Lamia K. Male Subfertility and Efficacy of FertimaxÃ¢Â„Â¢ Therapy. Andrology-Open Access. 2015;04(02).

39- Kulikauskas V, Blaustein D, Ablin RJ. Cigarette smoking and its possible effects on sperm. Fertil Steril 1985;44:526-528.

40- Oldereid NB, Thomassen Y, Purvis K. Seminal plasma lead, cadmium and zinc in relation to tobacco consumption. Int J Androl 1994;17:24- 28.

41- Weisberg E. Smoking and reproductive health. Clin Reprod Fertil 1985;3:175-186.

42- Ochedalski T, Lachowicz-Ochedalska A, Dec W, Czechowski B. Examining the effects of tobacco smoking on levels of certain hormones in serum of young men. Ginekol Pol 1994;65:87-93.

43- Salma U, Gill HK, Keith LG, Tilmon S, Jones CA, Sobti A, Patel A. Male subfertility and the role of micronutrient supplementation: clinical and economic issues. Journal of experimental & clinical assisted reproduction. 2011;8.

44- Menchini-Fabris GF, Canale D, Izzo PL, et al. Free L-carnitine in human semen: its variability in different andrologic pathologies. Fertil Steril 1984;42:263-267.

45- Costa M, Canale D, Filicori M, et al. Lcarnitine in idiopathic astheno-zoospermia: a multicenter study. Italian Study Group on Carnitine and Male Infertility. Andrologia 1994;26:155-159.

46- Vitali G, Parente R, Melotti C. Carnitine supplementation in human idiopathic asthenospermia: clinical results. Drugs Exp Clin Res 1995;21:157-159.

47- Scibona M, Meschini P, Capparelli S, et al. Larginine and male infertility. Minerva Urol Nefrol 1994; 46:251-253.

EARLY VERSUS DELAYED LAPAROSCOPIC CHOLECYSTECTOMY IN ACUTE CHOLECYSTITIS PATIENTS BENEFITS AND COMPLICATIONS

By
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ABSTRACT:
The timing of laparoscopic cholecystectomy for acute cholecystitis remains an issue for debate amongst general surgeons. some prefer to perform early cholecystectomy (within the first 72 hours), while others chose to start conservative treatment until the inflammation subside and delayed cholecystectomy can be performed (within 6-8 weeks). The aim of this study was to compare clinical outcomes between early and delayed cholecystectomy for acute cholecystitis. The primary outcome measures included mortality rates, complication rates, hospital stay and conversion rates to open procedures. This retrospective cross sectional study was performed at Misurata Medical Center, by collecting the data of all patients admitted to surgical departments as diagnosed cases symptomatic gall bladder stones during the period from the 1st of Jan 2018 until the 1st of Jan 2019. Total number of cases with symptomatic gall bladder stones was 234 patients, 59 of them were diagnosed as cases of calculus cholecystitis by clinical, radiological, and blood tests. 42 patients were managed by early laparoscopic cholecystectomy within 72 hours from admission, while 17 patients received conservative treatment with antibiotic and analgesia and delayed cholecystectomy was done to them within six to eight weeks from their hospital discharge date. From all the 42 patients who had early cholecystectomy 4 (9.5%) had conversion of surgery from laparoscopic to open cholecystectomy mainly due to the presence of complications in the gall bladder (gangrenous, perforated, empyema), 1 patient (2.3%) has post-operative complication of biliary injury, and their average post-operative in hospital stay was 2-4 days, there was no mortality among this group. From all the 17 patients who had delayed cholecystectomy there was no conversion from laparoscopic to open technique, 1 patient (5.9%) has post-operative complication of bile tract injury, and their average post-operative in hospital stay was also 2-4 days, and neither this group has no mortality among them. As result of the previous calculations, the outcomes of either early and delayed laparoscopic cholecystectomy regarding the post-operative complications, mortality rate, and post-operative in hospital stay are fairly similar, the only difference is slightly increase in the rate of conversion to open technique in early cholecystectomy comparing to delayed surgery. As a conclusion there is no much of a difference between the postoperative outcome of either early and delayed laparoscopic cholecystectomy, but the early surgery has the benefit of reducing the cost of treatment and pre-operative hospital stay that delayed conservative management consume.

KEY WORDS: Acute cholecystitis, laparoscopic cholecystectomy, complications, early versus delayed.

INTRODUCTION:
Definition
Acute cholecystitis (AC) is an acute inflammation of the gallbladder. Gallstones are present in over 90% of cases, and cause persistent obstruction of the gallbladder outlet because of impaction in the neck of the gallbladder, Hartmann's pouch, or cystic duct[1,2]. In the remaining 5% to 10% of cases, gallstones are not identified, so-called ''acalculous cholecystitis''[3].

Acute calculus cholecystitis seems to be caused by obstruction of the cystic duct by a gallstone, or local mucosal erosion and inflammation caused by a stone, but cystic duct ligation alone does not produce acute cholecystitis in animal studies. The role of bacteria in the pathogenesis of acute cholecystitis is not clear; positive cultures of bile or gallbladder wall are found in 50% to 75% of cases. The cause of acute acalculous cholecystitis is uncertain and may be multifactorial, including increased susceptibility to bacterial colonization of static gallbladder bile[4].

Incidence/ Prevalence:
The incidence of acute cholecystitis among people with gallstones is unknown. The incidence of acute cholecystitis is about 20% among people with biliary colic. Biliary colic occurs in 1% to 4% of people with gallstones. Of people admitted to hospital for biliary tract disease, 20% have acute cholecystitis. The number of cholecystectomies carried out for acute cholecystitis increased from the mid-80s to the early 90s, especially in older people. The number of cholecystectomies for acute cholecystitis has been decreasing as the rate of elective cholecystectomy has increased. Acute calculus cholecystitis is three times more common in women than in men up to the age of 50 years, and is about one and a half times more common in women than in men thereafter[4].

DIAGNOSIS:
Symptoms of Acute Cholecystitis are typically unremitting right upper quadrant or epigastric pain that persists beyond 6

h. It starts as a visceral-type pain that usually changes from dull and poorly localized to somatic-type pain that is sharp and localized to the right upper quadrant, radiating to the back, right scapula, or right clavicular area. Associated fever, chills, nausea, vomiting, and anorexia are common[5]. However, if untreated, AC can lead to perforations, abscess formation, or fistulae [4]. In most cases, the diagnosis of acute cholecystitis can be initially confirmed with an abdominal ultrasound[6].

INTERVENTION:

Aims of intervention are to reduce mortality and morbidity associated with acute cholecystitis, with minimal adverse effects of treatment[4]. Since its introduction in the 1980s, laparoscopic cholecystectomy is now the standard of care due to its advantages of reduced cost and hospital length of stay, and increased patient satisfaction[2-7]. However, the timing of cholecystectomy has been an area of controversy and continuous debate[8]. An early cholecystectomy is an operation performed within 72 hours since the appearance of the symptoms. In recent studies, the so-called immediate laparoscopic cholecystectomy is being mentioned, defined as cholecystectomy carried out within 24 hours since the patient's admission to the hospital[9]. On the other hand, a delayed cholecystectomy is an operation performed at least 6–8 weeks after the subsidence of the symptoms of acute cholecystitis[10]. During which an initial conservative treatment is considered whereby antibiotics are utilized until there has been complete resolution of the inflammation. Percutaneous cholecystectomy and novel endoscopic gallbladder drainage interventions may be used as a temporizing measure or as definitive therapy in those who are too sick to undergo surgery[6].

METHODS:

This study was formed using cross sectional retrospective structure, all data were collected from the files of patients admitted to surgery department in MMC as cases of symptomatic Gall bladder stones during the period from 1st of Jan. 2018 until 1st of Jan 2019.

All cases files included in this study, had full clinical assessment, blood tests (CBC, liver function test), and radiological investigation (ultrasonography). The included cases files also had sufficient data about the pre-operative condition, inter-operative findings, and post-operative developments occurred until the date of their discharged from the hospital. Any file which lack the previous data was excluded from the study.

Ultrasonography performed for the patients by radiological doctors who has good experience, also all surgical procedures were performed by skilled and expert doctors at MMC.

RESULTS:

Total number of 234 patients with symptomatic gall bladder stone were admitted to surgical department, 59 cases of acute calculus cholecystitis confirmed by clinical, blood tests, and radiological investigations.

From the 59 patients who were confirmed cases of acute calculus cholecystitis, a group of 42 patients had immediate laparoscopic cholecystectomy within the 1st 72 hours from admission, while the other group of 17 patient (as shown in the figure below) received conservative management in the surgical department for 7 to 10 days' period, then discharged and readmitted after 7 to 8 weeks for delayed laparoscopic cholecystectomy.

For both groups of patients there was no mortality among them, and their post-operative average stay in hospital was 2-4 days for each group.
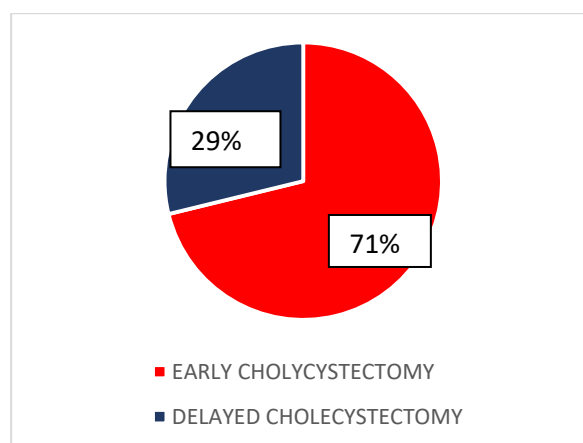
For the 1st group who had immediate surgery, 4 patients (9.5%) had incidence of conversion of their surgeries from laparoscopic to open technique, mainly due to difficulty in identifying the biliary anatomy using laparoscopic technique or the unexpected finding of complications in gall bladder 2ndry to calculus cholecystitis (empyema gall bladder, gangrenous gall bladder, perforated gall bladder). In the other hand patients of the 2nd group with delayed surgeries had no incidence of conversion to open technique, as shown in the table below.

Mortality	Hospital stay	Post. Op. complications	Conversion to open	Time of surgery
None	2-4 days	1 patient (2.3%)	4 patients (9.5%)	Early cholecystectomy
None	2-4 days	1 patient (5.9%)	None	Delayed cholecystectomy

The presence of post-operative complication was similar in each group, only one patient had complication of biliary duct injury during surgery (2.3%) from the 1st group, also one patient from 2nd group had biliary duct injury during surgery (5.9%).

DISCUSSION:

In this retrospective cross-sectional study, the outcome of early laparoscopic intervention for acute cholecystitis was compared to the outcome of late laparoscopic intervention of the disease which showed no significant outcome differences.

To this day, this topic remains controversial as previous studies were inconclusive and various studies supporting different interventions. The Ataturk training and research hospital in 2014 applied a similar study that revealed similar outcomes of either intervention [11]. Moreover, another retrospective study done by department of surgery and gastroenterology, Yodogawa Christian hospital, Osaka, Japan also was in support of similar same results [12].

On the other hand, Gutt et al. in their RCT ACDC study in 2013, showed that immediate cholecystectomy was superior to conservative treatment followed by delayed surgery from a postoperative complications aspect [13]. In 2016, another RCT carried out in Switzerland enrolling 86 cases found that early laparoscopic cholecystectomy is safer and was associated with reduced overall morbidity, shorter total hospital stay, and duration of antibiotic therapy, as well as reduced cost compared with delayed cholecystectomy [14].

The clinical implications served through this study are significant as they provide evidence-based practice for acute cholecystitis. In Libya to this day, the timing of intervention remains solely based on clinical experience and consultant's medical judgment. Therefore, this study would be resourceful in providing evidence for the management of acute cholecystitis.

This cross sectional study bears limitations from a design aspect, cross-sectional methods fall weak in comparison to stronger methods such as interventional designs. However, interventional studies require funding which is challenging to garner. Also, this study requires follow up in seek of late complications in which case is challenging in our hospital. Another limitation is the lack of adequate documentation; many cases are not fully documented making it difficult to obtain reliable data.

CONCLUSION:

Laparoscopic cholecystectomy is still the golden standard for treating acute cholecystitis, the outcome of either early or delayed surgeries are almost the same, despite the increased rate of conversion to open technique in early laparoscopic cholecystectomy, it provides a safe solution with economic benefits as the preoperative hospital stay and medication required for treatment are less than the ones used in delayed surgery.

REFERENCES:

1-Indar A. A. (2002). Acute cholecystitis , Bmj, 325(7365), 639-643

2-Lillemoe, K.D. (2000). Surgical treatment of biliary tract infections. The American surgeon, 66(2), 138-44.

3-Shapiro, M.J., Luchtefeld, W.B., Kurzweil, S., Kaminski, D.L., Durham, R.M., & Mazuski, J.E. (1994). Acute acalculous cholecystitis in the critically ill. The American surgeon, 60(5), 335-9.

4-Halpin V. (2014). Acute cholecystitis. BMJ clinical evidence, 2014, 0411.

5-Halachmi, S., DiCastro, N., Matter, I., Cohen, A., Sabo, E., Mogilner, J.G., ... & Eldar, S. (2000). Laparoscopic cholecystectomy for acute cholecystitis: how do fever and leukocytosis relate to conversion and complications. The European journal of surgery = Acta chirurgica, 166(2), 136-40.

6- Bagla, P., Sarria, J.C., & Riall, T.S. (2016). Management of acute cholecystitis. Current opinion in infectious diseases, 29(5), 508-13.

7-Calland, J.F., Tanaka, K., Foley, E., Bovbjerg, V.E., Markey, D.W., Blome, S., ... & Adams, R.B. (2001). Outpatient laparoscopic cholecystectomy: patient outcomes after implementation of a clinical pathway. Annals of surgery, 233(5), 704-15.

5- Frič, P., & Ryska, M. (1996). Digestivní endoskopie a laparoskopická chirurgie. Praha Publishing.

8-Hadad, S.M., Vaidya, J.S., Baker, L., Koh, H.C., Heron, T.P., Hussain, K., & Thompson, A.M. (2007). Delay from symptom onset increases the conversion rate in laparoscopic cholecystectomy for acute cholecystitis. World journal of surgery, 31(6), 1298-01; discussion 1302-3.

9- Hartwig, W., & Büchler, M. (2013). Akute Cholezystitis. Der Chirurg, 84(3), 177-178.

10- Fric P. and Ryska M. (1996) Digisivni endoskopie a laparoskopicka chirurgie. Praha Publishing

11-Alpir Bilal Ozkards , Mehmet Tokac, Ersen Gurkan Dumlu, Birkan Bozkhurt early versus delayed laparoscopic cholecystectomy for acute cholecystitis, a prospective randomized study. Dep. General surgery, Ataturk Training Hospital. Int. Surg 2014;99:56-1 , DOI 10.9738/INTSURG-D-130068.1

12-Shink G. Noda, T. Hatano, H. Shimizu, J. Hirota. feasibility and safety of urgent laparoscopic cholecystectomy for acute cholecystitis after 4 days from symptoms onset. J Gastrointestinal Surg. DOI 10.1007/s11605-015-2878-0

13-Gutt CN, Eucke J., Koninger J., Harnoss JC., Weigand K. early versus delayed cholecystectomy, a multicenteric randomized trial (ACDC Study, NCT00447304) Annals of Surgery Volume 258, Number 3, September 2013

14-Roulin D., Saadi A., Di Mare L., Demartines N., Halkic N. Early Versus Delayed Cholecystectomy for Acute Cholecystitis, Are the 72 hours Still the Rule? A Randomized Trial. (Ann Surg 2016;264:717–722)