MMSJ

Misurata Medical Sciences Journal

Published By Misurata University Medical Schools

MMSJ

Misurata Medical Sciences Journal

Contents

THE RELIABILITY AND VALIDATION OF A 2D IMAGE ANALYSIS SYSTEM WHEN APPLIED TO THE MEASUREMENT OF TWIN STUDY MODEL SAMPLES

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ABSTRACT

This study aimed to investigate dental fluctuating asymmetry of tooth dimensions in monozygotic (MZ) co-twins as a measure of how dental development is affected by epigenetic and environmental factors. The mesiodistal (MD), buccolingual (BL) dimensions of the central incisor, lateral incisor, second premolar and first molar in each of the four quadrants, on 20 sets of study models of MZ twin pairs were determined manually and two dimensional (2D) image analysis. The extent of asymmetry was assessed by determining intra-class correlation coefficients (ICCC's) between pairs of antimeric teeth between individuals, then the fluctuating asymmetry (FA) between twin pairs determined. Intra-operator repeatability for 2D measurement was substantial or excellent. Differences were detected between left and right antimeres for all the four measurements, and these differences were not the same for both twins in a pair. 2D image analysis facilitated the additional measurements of surface area and perimeter. Asymmetry between twin pairs for each tooth type followed a pattern fitting with the morphogenetic field theory with the key teeth showing the least asymmetry (upper centrals, upper sixes, lower laterals, lower sixes) and the variable teeth showing the most asymmetry (upper laterals, upper fives and lower sixes). The MD dimension also followed this trend.

KEYWORDS: Twin studies, Genetic, 2D image analysis, Manual measurement, Dental development, Asymmetry.

INTRODUCTION

Twin Models:

Twin studies provide a useful approach to investigating the roles of genetic and environmental factors in tooth development. Such studies allow researchers to determine the heritability of different dental traits. Estimates of heritability are traditionally achieved by comparing the similarities between monozygotic (MZ) twin pairs with those between dizygotic (DZ) twin pairs[(1)]. The MZ co-twin model assumes that MZ twins share the same genotypes, so that phenotypic differences must be due to epigenetic and/or environmental factors. It also assumes that findings from MZ co-twins can be extrapolated to singletons (individual from a group) in the general population. The MZ co-twin model is a valuable approach to apply within a dental setting and it has been used previously in orthodontics in the treatment plan of a twin-pair demonstrated by Pangrazio-Kulbersh V[(2)] and in the study of dental anomalies such supernumerary teeth[(3)].

Asymmetry:

Variation in dental crown size can be measured on contra lateral sides of the dental arch, i.e. on antimeric teeth and has been found to have a major genetic component[(4)]. Failure of antimeres to develop identically suggests underlying instability related to epigenetic and environmental effects[(5-9)]. Therefore, the study of asymmetry is a means of investigating stability of a developmental process and providing a measure of developmental interference with the "genetic blueprint" during ontogeny. There are two types of asymmetry. The first is 'directional' and always favours the same side of the individual. The second, 'fluctuating' is the random or non-directional difference between sides. Previous asymmetry studies involving twins have shown an absence of evidence of gene contribution in fluctuating asymmetry[(10,11)].

Aims:

This study aimed to quantify dental asymmetry using an established manual methodology and 2D image analysis, as a measure of epigenetic and environmental factors affecting dimensions of permanent teeth of MZ co-twins.

Null Hypothesis:

Reliability of the 2D image analysis is poor. MZ phenotypic differences cannot be measured using manual and 2D image analysis. There is no difference in the amount/degree asymmetry within the dentitions between pairs of MZ co-twins.

MATERIALS AND METHODS

Two techniques of measurement were used to record the mesiodistal (MD) and buccolingual (BL) diameters of permanent teeth of MZ co-twins. These techniques were manual measurement, using electronic callipers, and 2D image analysis.

Twenty sets of dental study models of MZ twins from Adelaide, South Australia were selected for

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measurement. Duplicate models were stored in the University of Liverpool. Internal university ethical approval was granted (RETH000063).
The teeth types measured on each model were the central incisor, lateral incisor, second premolar and first molar in each of the four quadrants. The choice of teeth to be measured was based on concepts of variation described in the Morphogenetic Field theory[12].

Manual Measurement:
The methods described by Moorrees et al[13], Hunter and Priest[14] and Lavelle[15], were applied to measure the M-D and B-L distances of the specified teeth of the study models using an electronic calliper (figure 1). Measurements were obtained in a systematic manner under standardised conditions from the upper left quadrant, and then upper right, then lower left, then lower right quadrants as reported by Brook et al.[16]

(Figure 1) Electronic Mitutoyo callipers used for manual measurement

2D Image Analysis:
The 2D image analysis system is a useful means of measuring additional variables such as perimeter and area accurately, allowing an increased discrimination between within-pair differences. It also enables permanent storage of images so that they can be reviewed later for reliability analysis and further measurement[17].
A Kodak DCS Pro SLR digital camera, which was connected to a computer (Dell XP, Pentium 4, Dell UK), was used to capture images of the study models from the labial (only for the UR1) and occlusal views. The M-D and B-L distances from each image were measured using Image Pro Plus software (Version 5, Media Cybernetics) (figure 2).

(Figure 2) Example of an image taken from buccal view. UR1 showing the perimeter from which the area is derived

STATISTICAL ANALYSIS AND VALIDATION

Reliability:
The results were analysed using SPSS 18.0 package. Intra-operator repeatability was determined by re-imaging and measuring the 4 selected teeth in the upper left and right quadrants of 20 study models twice using the manual and 2D image analysis method. In addition, the labial view of the UR central incisor was also taken on each of these 20 upper study models and the M-D, B-L diameters measured to validate the technique from an alternative view. This was then analysed using Fleiss intra-class correlation coefficients (ICCC)[18]. The results were then classified into the Donner and Eliasziw scale (table 1-a)[19].

(Table 1-a) Classification of the Value of R according to Donner and Eliasziw

Value of R	Reliability
0.00-0.20	Slight
0.21-0.40	Fair
0.41-0.60	Moderate
0.61-0.80	Substantial
0.81-1.00	Excellent

Bias calculations were then performed to assess the significance of any bias observed.

RESULTS
(Table 1-b) displays the results for displays the results for the intra-operator repeatability manual measurement. The ICCC results fall into the category of excellent[19].

(Table 1-b) Manual Intra-operator repeatability descriptive statistics for the upper right central, upper right second premolar, upper left lateral and upper left first molar teeth (occlusal views)

Variable	UR1 Occlusal		UR5 Occlusal		UL2 Occlusal		UL6 Occlusal	
	MD	BL	MD	BL	MD	BL	MD	BL
Mean Dif.	-0.02	-0.05	0.00	0.03	-0.01	0.00	0.00	0.00
ICCC	0.98	0.96	0.98	0.88	0.99	0.99	0.99	0.94

(Table 2-a) 2D Intra-operator repeatability descriptive statistics for the upper right central (labial and occlusal views) and second premolar (occlusal view) teeth

Variable	UR1 Labial	UR1 Occlusal		UR5 Occlusal	
	MD	MD	BL	MD	BL
Mean Dif	-0.12	-0.16	0.01	-0.03	0.01
SD of Dif	0.31	0.38	0.25	0.21	0.16
Standard Error	0.07	0.09	0.06	0.05	0.04
ICCC	0.71	0.73	0.9	0.86	0.93
RC	0.61	0.75	0.48	0.42	0.31

Mean Dif= Mean Difference, SD of Dif=Standard deviation of difference, ICCC= Intra class correlation coefficient, RC= Repeatability coefficient

(Table 2-b) 2D Intra-operator repeatability descriptive statistics for the upper left lateral (occlusal view) and upper left first molar (occlusal view) teeth

Variable	UL2 Occlusal		UL6 Occlusal	
	MD	BL	MD	BL
Mean Dif.	0.02	0.01	-0.04	-0.07
SD of Dif	0.4	0.17	0.13	0.15
Standard Error	0.3	0.04	0.03	0.03
ICCC	0.96	0.64	0.98	0.98
RC	0.27	0.33	0.26	0.29

(Table 3) shows the correlation between measurements using the manual and 2D measurement methods. The average was taken from two repeat measurements and comparisons made. The PCC varied between 0.24 and 0.91. The UR1 had the highest overall ICCC values suggesting the least difference between the methods for this particular tooth.

(Table 3) Correlation data for manual and 2D measurement

Variable	UR1 Occlusal		UR5 Occlusal		UL2 Occlusal		UL6 Occlusal	
	MD	BL	MD	BL	MD	BL	MD	BL
Mean Dif.	-0.13	0.30	0.04	-2.13	0.24	0.43	-0.36	0.14
SD of Dif.	0.42	0.30	0.40	1.35	0.96	0.87	1.14	0.57
Standard Error	0.10	0.10	0.10	0.30	0.21	0.20	0.25	0.13
PCC	0.59**	0.91**	0.64**	0.24	0.91	0.15	0.36	0.4

***= Correlation is significant at the 0.01 level (2-tailed)*

DISCUSSION

Intra-operator repeatability for manual and 2D measurement was high. For 2D measurement Fleiss' ICCC reliability results ranged from 0.639- 0.978 (table 2-a) and (table 2-b). These values indicated'substantial/good' or 'excellent' reliability according to the Donner and Eliasziw scale[19] (table 1-a). The descriptive statistics for the intra-operator repeatability measurements excluding one, (tables 1-b, 2-a, 2-b) showed no significant bias.

The reliability data for both methods (1b, 2a and 2b), shows that for 2D measurement technique was higher than those for manual measurement, as has been reported in previously[17]. The correlation data (table 3) showed that the UL6 had the lowest overall PCC value between linear measurements and the UR1 from the occlusal view had the highest. The results showed that overall the MD and BL PCC values between the two methods showed 'fair' correlation, with little difference between the two.

The extent of asymmetry was assessed using intraclass correlation coefficients between antimere pairs. Where the trend of asymmetry between tooth types fits the morphogenetic field theory[12], each variable displays a different degree of asymmetry. Twin pairs showed varied amounts of asymmetry. For manual measurement, the FA ranged from 0.03-0.28 compared with 0.01-0.16 for 2D measurement. The difference between the two methods may be due to 2D image analysis being a more accurate methodology as the measurement error is reduced.

The order of differences in FA for manual measurement showed that MD>BL and for 2D measurement BL>MD. It is important to compare the magnitude of the differences observed between the left and right sides with the differences observed in the intra-operator repeatability study, as the difference observed may be due to measurement error. The size of the asymmetries observed was less in comparison to the size of the typical measurement error in the reliability study.

CONCLUSION

The manual and 2D image analysis measurement approaches proved reliable and the 2D system was validated for use in such studies. The current study was able to quantify dental asymmetry for tooth type and tooth dimensions between twins. The teeth that are the most variable are upper laterals, lower centrals and upper fives, with the upper centrals and lower sixes being the least variable.

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DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETER METHOD FOR THE QUICK ESTIMATION OF OLIVE LEAF EXTRACT (OLE) IN PHARMACEUTICAL FORMULATION

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ABSTRACT

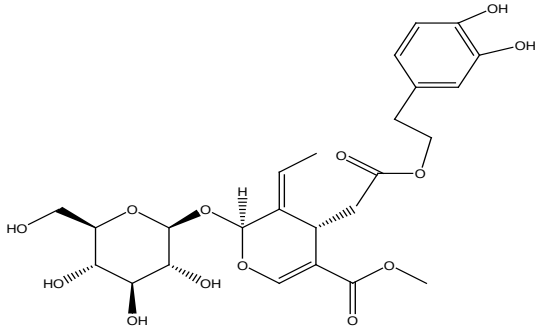
Olive (Olea europaea), a rich source of natural antioxidant is native to the Mediterranean region. The main active constituents of olive include oleic acid, phenolic constituents like hydroxytyrosol and oleuropein and squalene are abundantly found in its leaf. Therefore, the aim of our research is to develop and validate simple, sensitive and specific spectrophotometric method for olive leaf extract (OLE). The developed method was validated with respect to linearity, accuracy, precision and specificity. The adequate drug solubility and maximum sensitivity were found in ethanol. The λ_{max} or the absorption maxima of the drug was found to be 279 nm. The samples were prepared in ethanol and method obeyed Beers law in concentration ranges 5- 50 µg/ml. The content of OLE in herbal pharmaceutical formulation was determined. The results of analysis were validated statistically and confirmed the accuracy of the proposed method. Hence the proposed method can be used for the reliable quantification of olive leaf extract in herbal pharmaceutical formulation.

KEY WORDS: UV spectroscopy, Olive leaf extract, Validation.

INTRODUCTION

Olive tree is native to Asia Minor and Syria, but is cultivated in all Mediterranean countries as well as in Chile, Peru, South Australia and the USA[1,2]. Olive trees have been cultivated for thousands of years, but the immune and circulatory benefits of olive leaf have only recently become fully realized. Olive leaf was first used medicinally in Ancient Egypt and was a symbol of heavenly power. More recent knowledge of the olive leaf's medicinal properties dates back to the early 1800s when pulverised leaves were used in a drink to lower fevers. A few decades later, green olive leaves were used in tea as a treatment for malaria[3]. Numerous scientific studies have been added to investigate the extract's beneficial properties, and olive leaf extracts are suggested as its hypotensive effects[4], antioxidant properties[5], hypoglycemic[6-8], antimicrobial[9], radioprotective[10], antiatherogenic[11,12], anti-inflammatory[13,14], and hepatoprotective[15]. Olive leaves contain around 60~90 mg per gram (dry weight) oleuropein, additionaly significant levels of a glucosidic esterof elenolic acid and hydroxytyrosol (3,4-dihydrophenylethanol) (figure 1).

Literature survey reveals that several high pressure liquid chromatography (HPLC) methods are developed and validated for oleuropein[16-19] but there is no reported UV-visible method for quick estimation of olive leaf extract. Hence, a simple UV spectrophotometer method was developed and validated as per International Conference on Harmonization (ICH) Q2A. As the formulations are available without combinations of any drugs, there is a need for coming up with analytical method which is simple, sensitive, rapid and accurate for estimation of OLE in pharmaceutical preparations. Therefore, the aim of the present work is to develop and validate a method for the analysis by UV-Visible spectrophotometer which is easily adaptable as a routine in quality testing laboratories. This has enabled us to reduce total time of analysis besides taking care of the error caused due to in complete extraction and use of internal standard[20].



(Figure 1) Structure of oleuropein

MATERIALS AND CHEMICALS

Chloroform, acetone and ethanol were purchased from Sigma Aldrich, Germany. Herbal capsules containing olive leaf extract were purchased from Oliver PhytoFlore Les laboratories, Arrazi. Agilent Carry 60, UV- Vis spectrophotometer was used for the analysis. All chemicals and reagents used were of analytical grade.

Preparation of olive leaf extract

The olive leaves were collected from olive orchid of Misurata, Libya. The collected leaves were cleaned and dried under shade (at ambient temperature). The

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dried olive leaves were weighed (2.5 kg) and stored in desiccator. The extraction was done by simple maceration process. The dried leaves were mixed in ethanol, placed for 15 days under room temperature with occasional shaking. The mixture was filtered with muslin cloth, simple filter paper and then finally with Whatmann filter paper to obtain clear liquid extracts. The clear liquid extract was dried in oven at 40 ˚C to obtain green colored crude extract, which was stored in desiccator until further use.

METHOD OPTIMIZATION

Selection and optimization of solvent

It is well known that the solvent does exert a profound influence on the quality and shape of the peak[13]. The choices of solvents for UV method development are: chloroform, acetone, ethanol etc. Different solvents were tried. Out of which ethanol satisfied all the conditions related to peak quality and non-interference at the specified wavelength.

Preparation of standard stock solution of OLE

The stock solution (100 µg/ml) of OLE was prepared by dissolving accurately about 10 mg of drug in sufficient quantity of ethanol and then volume was adjusted to 100 ml with ethanol. Further, a series of dilution was made with ethanol.

Calibration curve of olive leaf extract

A series of calibrated 10 ml volumetric flask was taken and appropriate aliquots of the working stock solution of OLE were withdrawn and diluted up to 10 ml with ethanol. The absorbance was measured at absorption maxima 279 nm against the blank without the OLE. Absorption maxima and Beer's law limits were recorded and data, that prove the linearity and obeys Beer's law limits, were noted. The linear correlation between these concentrations (x-axis) and absorbance (y-axis) were graphically presented. The slope (m), intercept (c) and correlation coefficient (R^2) were calculated for the linear equation ($y=mx\pm c$) by regression.

METHOD VALIDATION

The method was validated for linearity, accuracy, precision, robustness, limit of detection (LOD), limit of quantification (LOQ) and system suitability by the following procedures:

Linearity

Ten different concentrations of OLE were analyzed and their calibration curve was constructed in the specified concentration range (5-50 µg/ml). The calibration plots were generated by replicate analysis (n = 3) at all concentration levels and the linear relationship was evaluated.

Precision

The precision was examined by performing the intraday and interday assays of three replicate injections of the mixture of standard solutions at three concentration levels (15, 35 and 50µg/ml). The intraday assay precision was performed with the interval of 4 h in 1 day, while the inter-day assay precision was performed over 3 days.

Accuracy by recovery

The accuracy of the method was determined by calculating the recoveries of OLE by the method of standard addition. A known amount of standard (50%, 100% and 150%) was added to pre-analyzed sample solution, and the amount of the standard was estimated by measuring the absorbance and by fitting these values to the straight-line equation of calibration curve.

Limit of detection and limit of quantification

The LOD and LOQ of OLE were determined by using standard deviation of the response and slope approach as defined in ICH guidelines. LOD and LOQ values were calculated using the relation:

$LOD=3.3\delta /S$

$LOQ=10\ \delta /S$

Where, δ= standard deviation of residuals from the curve; S= slope of the curve

Ruggedness

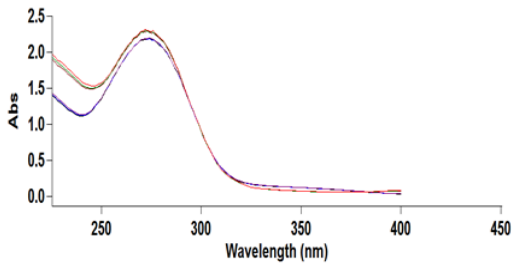
Ruggedness of this method was determined by analyzing the OLE with different equipment on different days and by different analysts.

Determination of OLE in pharmaceutical formulation

A pharmaceutical formulation (soft gelatin capsule) claiming 25 mg of OLE was taken and the drug content was taken out by cutting the shell. The drug content was transferred into 100 ml volumetric flask containing 30 ml of ethanol and made up to the mark using ethanol. An appropriate volume, 0.1 ml of this solution was transferred to 10 ml volumetric flask and the volume was made up to the mark using ethanol to give concentration of 2.5 µg/ml. The resulting solution was scanned on spectrophotometer in the UV range 200 - 400 nm. The concentrations of the drug were calculated using linear regression equations.

RESULT AND DISCUSSION

The development of a simple, rapid, sensitive, and accurate analytical method for the routine quantitative determination of OLE will reduce unnecessary tedious sample preparations, the cost of materials and labor. OLE has a UV-absorbing molecule with specific chromospheres in the structure that absorbs at a particular wavelength and this fact was successfully employed for their quantitative determinations using the UV spectrophotometric method. The absorption spectrum of OLE in ethanol was shown in (figure 2).



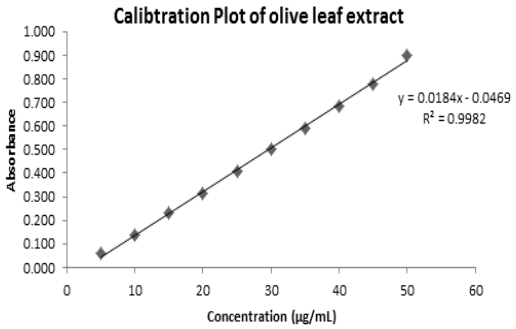
(Figure 2) Absorption spectra of olive leaf extract

A calibration curve was constructed in the range of the concentrations of 5-50 µg/ml, which also obeyed Beer's law as shown in (table 1).

(Table 1) Calibration plot of olive leaf extract

S. No.	Concentration (µg/ml)	Absorbance ± S.D (n=3)	%RSD	S. E	95% confidence interval	
					Lower value	Upper value
1	5	0.062±0.0010	1.613	0.0006	0.060	0.064
2	10	0.137±0.0020	1.460	0.0012	0.132	0.142
3	15	0.231±0.0024	1.088	0.0015	0.225	0.238
4	20	0.315±0.0031	0.971	0.0018	0.307	0.322
5	25	0.406±0.0025	0.620	0.0015	0.399	0.412
6	30	0.501±0.0028	0.503	0.0015	0.494	0.507
7	35	0.589±0.0035	0.597	0.0020	0.580	0.597
8	40	0.686±0.0042	0.607	0.0024	0.676	0.697
9	45	0.777±0.0026	0.341	0.0015	0.770	0.784
10	50	0.901± 0.0055	0.611	0.0032	0.887	0.914

The regression equation was found to be y = 0.0184x - 0.0469. The correlation coefficient (r^2) of the standard curve was found to be greater than 0.998 (figure 3). The OLE was scanned for the entire UV region for λ_{max} and it was found to be 279 nm.



(Figure 3) Calibration plot of olive leaf extract

Precision

The precision of the method was expressed in terms of % relative standard deviation (%RSD). The %RSD values found to be less than 2 for intra-day and interday precision, which indicated that the proposed method is precise for analysis. The results are expressed in (table 2).

(Table 2) Intraday and Interday Precision

S. No.	Concentration (µg/mL)	Interday precision		Intraday precision	
		Absorbance ± SD (n=3)	%RSD	Absorbance ± SD (n=3)	%RSD
1	15	0.231±0.0035	1.522	0.232±0.0040	1.745
2	35	0.588±0.0085	1.446	0.590±0.0080	1.356
3	50	0.895±0.0098	1.100	0.897±0.0134	1.498

Accuracy by recovery

Accuracy of the method was confirmed by recovery study from marketed formulation at three levels of standard addition. % Recovery for OLE was found to be 99.38-102.63%. The recovery studies are reported in (table 3).

(Table 3) Accuracy by recovery

S. No.	Initial Concentration (µg/ml) [A]	Addition of known quantity (µg/ml) [B]	A+B	Absorbance	Concentration recovered (µg)	% Recovery	Average recovery n=3
1	20	10	30	0.506	30.05	100.16	99.38%
2				0.498	29.61	98.71	
3				0.501	29.78	99.26	
4	20	20	40	0.686	39.83	99.58	100.21%
5				0.691	40.10	100.26	
6				0.695	40.32	100.80	
7	20	30	50	0.892	51.03	102.05	102.63%
8				0.898	51.35	102.71	
9				0.902	51.57	103.14	

Limit of detection and limit of quantification

The LOD and LOQ for OLE were found to be 0.988µg/ml and 2.993 µg/ml respectively.

Ruggedness

Absorbance was measured for same concentration solutions, six times. The results are given in (table 4).

Specificity

The specificity was the ability of an analytical procedure to measure accurately an analyte in presence of components that may be expected to present in sample matrix. Standard and sample solution were prepared separately and standard solution was spiked with sample solution and the absorbance was found at 279 nm which showed that the method was

specific and was not affected in presence of any other component in the sample (figure 2).

(Table 4) Ruggedness

S. No.	Concentration (µg/ml)	Analyst I Amount found % ± S. D	Analyst II Amount found % ± S. D
1	30	99.08±0.21	101.55±0.38

Analysis of OLE in pharmaceutical formulation

The concentrations of the drug were calculated from linear regression equations. The % assay was found between 98.34% - 100.77% as shown in (table5).

(Table5) Analysis of olive extract in marketed preparation

Sample	Concentration (µg/ml)	Absorbance n=3	% Assay
Test (marketed preparation)	50	0.893	98.34% 100.77% 99%
		0.906	
		0.895	
Standard (Plant extract)	50	0.908	
		0.899	
		0.904	

CONCLUSION

UV spectrophotometric method has been developed and validated for quick estimation of olive leaf extract in herbal formulations. The proposed methods are accurate and precise as indicated by good recoveries of the drugs and low % RSD values. All the analytical reagents are inexpensive, have excellent shelf life, and are available in any analytical laboratory. The proposed methods could be applied for routine analysis and in quality control laboratories for quantitative determination of the olive leaf extract both in the pure and dosage forms.

ACKNOWLEDGEMENT

The authors are thankful to the College of Pharmacy, Misurata University, for providing all the facilities to carry out this research work.

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LIPID SCREENING IN 100 PEDIATRIC PATIENTS WITH TYPE 1 DM IN TRIPOLI CHILDREN HOSPITAL (2008-2009)

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ABSTRACT

DM is a chronic metabolic disorder characterized by abnormalities in fuel metabolism including glucose, lipids and amino acids. Lipid disorders are common in diabetes mellitus, diabetic dyslipidemia is characterized by hypertriglyceridemia, increased levels of (VLDL), small dense LDL lipoprotein, and decreased levels of high density lipoproteins (HDL). Dyslipidemia will increase risk of cardiovascular disease in patients with diabetes mellitus. The study is designed to screen type1 diabetic patients for lipid abnormality and to know its relation to HbA1c, BMI and duration of DM. Case series study was done on 364 diabetic patients with type 1 DM of both sexes and aged between 1.5-18 yrs with different duration of DM, who attended endocrine clinic at Tripoli children hospital 2008-2009. Those patients were investigated for fasting TC, TG, LDL, HDL, and HbA1C, only 100 patients. (Convenient sample) was included in the study according to complete investigations results which were done at national accredited laboratory, data were analyzed according to weight, height, BMI, HbA1c and duration of diabetes mellitus. Lipid profiles of our patients showed abnormality in TC, TG, LDL, and HDL with significant positive correlation between triglycerides level and HbA1c level. The age of the patients ranged between 1.5 to 18 years, with mean age 10.7±4.2 years. Female: Male ratio 1.4: 1, By using nonparametric chi-square; the difference between observed and expected count was insignificant (p=0.072). The duration of DM among our patients ranged between 1 month and 9.5 years, with mean 2.8±2.5 yrs.; the majority of our patients (92%) had normal weight. 3 % of them were overweight (z score >+2SD units). Only 1% were under weight. HbA1c was between 4.5% and 18.6 %, with mean HbA1c 9.3± 2.6%, so about 52% of the patients had accepted HbA1c and 45% had non accepted HbA1c. Total cholesterol, LDL, TG, and HDL were the parameters determined in this study; the mean value of each of them is within normal range. We found that 5% of the patients have high cholesterol level, and about 9% have high LDL cholesterol and 13% have low HDL cholesterol, 6% had high TG level. So the commonest lipid abnormality is low HDL cholesterol by using T student test for independent samples: HbA1c was significantly greater in patients with high triglyceride levels (mean HbA1c 11.9%) than in those with normal TG level (mean HbA1c 9.2%) P value = 0.024. There is an abnormality in lipid profile among patients with type1DM especially who have poor diabetic control. Further longitudinal study with large sized sample is needed to get more informative results.

KEYWORDS: Lipid profile, DMT, Libyan children, HbA1c, Dyslipidemia.

INTRODUCTION

Diabetes Mellitus is a chronic metabolic disorder characterized by abnormalities in fuel metabolism including glucose, lipids and amino acid, hyperglycemia is the cardinal feature for diabetes mellitus.

The major forms of diabetes are classified according to those caused by deficiency of insulin secretion due to pancreatic B-cell damage, type1DM and those that are a consequence of insulin resistance occurring at the level of skeletal muscle, liver and adipose tissue with various degree of B-cell impairment, type2 DM[1].

Incidence:

Incidence of type1 DM is rapidly increasing in specific regions, type1DM accounts for about 10% of all diabetes, affecting 1.4 million in the united states and about 15 million around the world. It is one of the most common severe chronic childhood diseases.

It is predicted that the overall incidence of type1DM will be about 40% higher in 2010 than in 1997[1].

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There is a little argument that type 2DM in children and adolescents has become an epidemic, reports from throughout the united states show that the percentage of patients with new onset diabetes diagnosed as having type 2DM increased from 2%-4% in 1994 to 20%-50% by 2000[2].

Dyslipidimea in DM:

Lipid disorders are common in diabetes mellitus, diabetic dyslipidemia is characterized by hypertriglyceridemia, increased levels of (VLDL),small dense LDL lipoprotein, and decreased levels of high density lipoproteins(HDL)[3].The major lipid abnormality are seen in patients with type 2DM[4].

Diabetes Mellitus: is a strong risk factor for cardiovascular disease, which constitute the main cause of morbidity and mortality in both type1 and type2 diabetes in adulthood. Type1 diabetes is associated with 10-folds increase in CVD over that of people without diabetes[5]. Risk factors that independently increase cardiovascular risk in people with diabetes include hypertension, dyslipidemia, hyperglycemia and renal dysfunction[6]. A body of evidence now shows that elevated levels of plasma lipids especially low density lipoproteins (LDL-C) are associated with an increased probability of premature cardio-

vascular disease which constitute the main cause of morbidity and mortality in both type 1 and type 2 diabetes in adulthood[7]. Therefore preventive measures should be initiated as early as possible to prevent progression of the disease[8].

American Diabetes Association (ADA) recommended in 2008 that fasting lipid profile in screening program of children and an adolescent with type1 DM. If there is a family history of a hypercholesterolemia or cardiovascular events before age 55 yrs or if family history is unknown, then fasting lipid profile should be performed on children > 2 yrs of age soon after diagnosis (after glucose control has been established). All children diagnosed with DM at or after puberty should have a fasting lipid profile performed soon after diagnosis. For both age groups, if lipids are abnormal annual monitoring is recommended[9].

AIMS OF STUDY

To screen the patients with type 1 DM for lipid abnormality. To know the relations between the lipid levels and HbA1c, BMI and duration of DM.

PATIENTS AND METHODS

Case series study was done on 364 diabetic patients with type 1 DM of both sexes and aged between 1.5-18yrs (younger age group with unknown family history of dyslipidemia were included according to ADA recommendation) with different duration of DM, who attended endocrine clinic at Tripoli children hospital 2008-2009. Those patients were investigated for fasting (means consuming nothing orally after midnight) TC, TG, LDL, HDL, and HbA1C, only 100 patients (Convenient sample) were included in the study according to complete investigations results which were done at national accredited laboratory, data were analyzed according to, HbA1c, diabetes mellitus duration, weight, height, BMI; by using z score (standard deviation classification system) which is widely recognized as the best system for analysis and presentation of anthropometric data; normal weight (-2 to +2SD), under weight (-2SD), over weight (>+2SD) t), statistically by using SPSS program, results considered statistically significant when P. value <0.05.

RESULTS

Age distribution (figure1):- The age of the patients ranged between 1.5 to 18 years, with mean age 10.7±4.2 years.

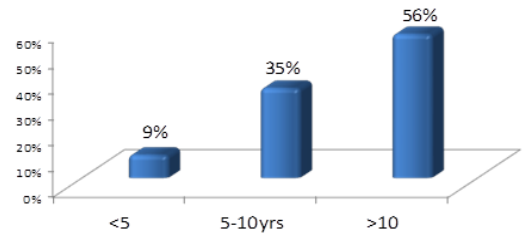

Figure (1) age distribution of children with type I DM (under study) attending endocrine clinic in Tripoli children hospital (2008-2009)

Sex distribution (figure 2):- Female: male ratio= 1.4: 1, by using nonparametric chi-square; the difference between observed and expected count was insignificant (p=0.072).

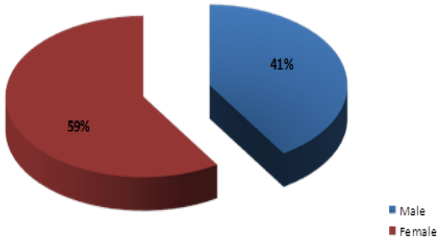

Figure (2) sex distributions of children with type I DM attending endocrine clinic in Tripoli children hospital (2008-2009)

The duration of DM among our patients (time between diagnosis and time of study) ranged between 1month and 9.5 years, with mean 2.8±2.5 years as showed in (figure3).

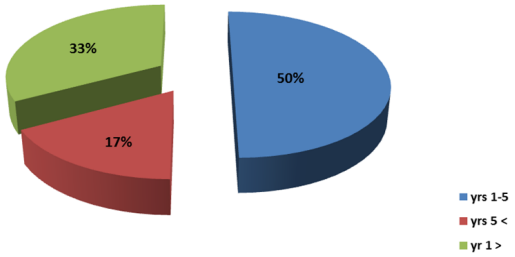

Figure (3) distributions of patients according to duration of DM

Body mass index in (figure 4): the majority of our patients (92%) had normal weight, 3 % of them were overweight (z score >+2SD units) and only 1% were under weight(ZS <-2SD units).

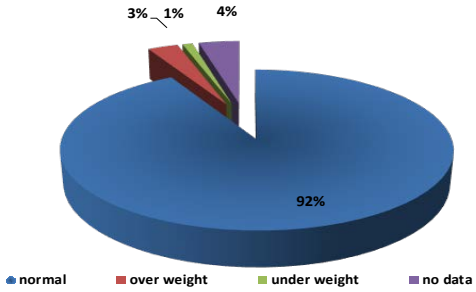

Figure (4) distribution of our patients according to BMI Z-score

HbA1c found to be ranged between 4.5% and 18.6 %, with mean HbA1c = 9.3± 2.6%, so about 52% of our patients had accepted HBA1c and 45% had non accepted HbA1c (figure 5).

Total cholesterol, LDL, TG, and HDL (Lipid profile) were the parameters determined in this study:

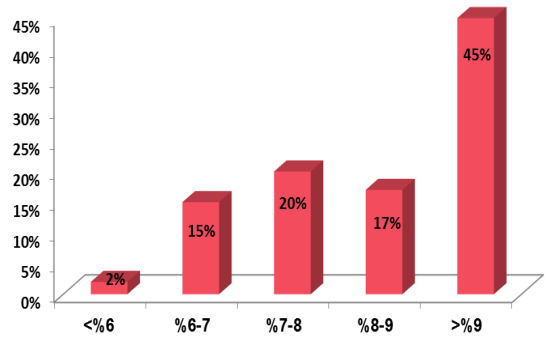

Figure (5) distribution of patients according to the level of HbA1c

We found that 5% of our patients have high cholesterol level, and about 9% have high LDL cholesterol and 13% have low HDL cholesterol, 6% had high TG level. So the commonest lipid abnormality is low HDL cholesterol (figure 6).

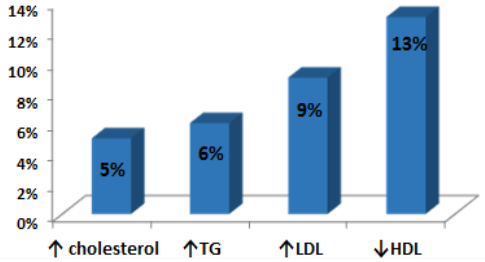

Figure (6) distribution of patients under study by abnormal lipid profile

The relation between lipid profile and HbA1c (table1). By using T student test for independent samples: HbA1c was significantly greater in patients with high triglyceride levels (mean HbA1c=11.9%) than in those with normal TG level (mean HbA1c=9.2%) P value=0.024. However HbA1c did not differ significantly with; LDL level (P value=0.222), HDL level (P value=0.144) nor cholesterol level (P value =0.738).

Table (1) the relation between lipid profile and HbA1c

Lipid profile	Mean HbA1c %	P-value
S cholesterol -High -normal	 8.9 9.3	0.738
S. LDL - High - normal	 10.3 9.2	0.222
TG - high - normal	 11.9 9.2	0.024
HDL - high - normal	 8.1 9.6	0.144

The relation between lipid profile and BMI z-score:- We compared the mean of BMI for normal and abnormal lipid profile. The difference between the means for each parameter is statistically insignificant as showed in (table 2).

Table (2) Relation between BMI and lipid profile

Lipid profile	Mean of BMI z- score	P.value
S.Cholesterol - normal -high	 0.46 1.21	0.114
HDL - normal -high	 0.48 0.81	0.416
LDL - normal - high	 0.462 0.87	0.283
TG - normal - high	 0.49 0.48	0.980

The net table shows the relation between lipid profile and mean duration of DM: T student test for independent samples used to compare the mean duration by years for normal and abnormal lipid profile, as seen in (table 3).

Table (3) relation between lipid profile and duration of DM

Lipid profile	Mean duration of DM (years)	P.value
Cholesterol - normal - high	 2.83 2.4	 0.724
HDL - normal - high	 2.9 3.7	 0.412
LDL - normal - high	 2.9 1.5	 0.112
TG - normal - high	 2.93 0.9	 0.059

The mean duration was inversely related with cholesterol, LDL and TG level (i.e. high lipid level among patients with short duration of DM) but this difference is statistically insignificant except for triglyceride where it is nearly significant (p=0.059).

DISCUSSION

The incidence of type 1 DM is rapidly increasing, in USA annual incidence has risen from approximately 16 cases per 100,000 populations in 1990 to 24.3 per 100,000 populations (2008) and is probably still increasing[10].

The frequency however is highly correlated with increasing age; it is one case in 1430 children at 5yrs of age to one case in 360 children at 16 years [1].

This study showed that the majority of our patient (56%) were between 10yrs and 18yrs, 35% of our patients in age group between 5-10yrs, only 9% aged less than 5yrs; this means that DM increases in frequency with age, also these results achieved by Kadiki et- al (1991– 2000)[11].

Diabets is more common in females:

Our study showed female to male ratio =1.4 : 1 which agree with Kadiki et al (1998) study that shows the total of 73 females and 53 males (F:M=1.37:1) under 15yrs of age were diagnosed DM type1 in the period between 1991 to 1995 on Libyan children in Benghazi[12].

In 1998 national health survey (NHS) in Singapore showed the crude prevalence of diabetes was 8.5% in males and 9.6% in females[13].

In Finland during 1987 – 1989, the incidence of type1DM was higher in boys (38.4/100.000) than in girls (32.2/100.000) with M: F = 1.2:1[14].

Other studies showed males and females are almost equally affected [1].

Body Mass Index:

The majority of our patients (92%) have normal weight, only 3% of them are overweight, it is well known that obesity is common among diabetes type2 patients because insulin resistance is a result of fat mass.

One study was done on African patients (1988 - 1995) comparing BMI between 50 patients with type 2DM and type 1DM, the mean BMI±SE at diagnosis of type 2DM patients was 35±1.1 KG/M^2 in contrast to 20± 0.8 KG/M^2 for type 1DM. 96% of type 2DM and only 24% of type 1DM youths had BMI > 85^{th} percentile[15].

HbA1c:

Measurement of Glycosylated HB (HbAIc) provide a reliable index of long term glycemic control, this measurements reflects the average blood glucose concentration of the preceding four months.

Our goal in the management of our patients to reach normal or near normal glycemic level.

The diabetes control and complication trial (DCCT) established conclusively the association between higher glucose levels and long term micro vascular complications and intensive management produced dramatic reductions of retinopathy, nephropathy and neuropathy by 47 – 76%[16].

Our study showed about 52% of our patients had accepted HbA1c, and 45% had HbA1c > 9% which is not acceptable. These results can be explained by; 31% from patients with high HbA1c were newly diagnosed according to age distribution among the same group; we found 32% of them were under 10yrs old, and 68% were more than 10yrs old, however it is more difficult to obtain a good HbA1c value during puberty since the secretion of growth hormone will raise blood glucose level.

During puberty it is not uncommon to have an increased HbA1C of up to 1% even if the patient is as carful with his diabetes as he was before puberty[17].

Dyslipidemia in diabetes:

Our study showed some abnormality in the levels of TC, TG, LDL, HDL-C. The lipid alterations were expected in type 1DM[18].

Studies on diabetic patients showed most significant lipid finding are high value triglyceride, LDL and total cholesterol, however HDL and total cholesterol were found low, normal or high in the literature. [19]

Results of one longitudinal study was done on 360 patients with type 1DM in Barbara Davis Center for childhood diabetes in Colorado between 1994–2004 showed sustained abnormalities existed for TC (16.9%), decrease HDL (3.3%) and high LDL (3.3%)[20].

Relation between lipid profile and HbA1C:

Those patients with high triglycerides had worse glycemic control (significant positive relation) than those with normal TG level but there is no statistical relation between TC, LDL-C, HDL-C and HbA1c.

In comparing with the results of a study was done in Morocco on 100 patients with type 1DM aged 3-17 years, where they had high HbA1c >8% (poorly diabetic control), showed that the level of triglyceride, LDL-cholesterol were higher ($p<0.01$, $p<0.05$ respectively) than those of the control group, HDL-cholesterol level was significantly lower ($p<0.01$) in these children[21].

In various studies, HbA1C level was noted as showing positive correlation with triglycerides and total cholesterol and LDL cholesterol in diabetic patients[18].

Relation between lipid profile and BMI:

When we compare those patients with high lipid level to those patients who have normal lipid level, we found they were similar in BMI z score, which is the same result achieved by longitudinal study on 360 patients with type 1 DM in Barbara Davis Center for childhood diabetes[20].

Relation between lipid level and duration of DM:

We found those patients with higher TC, TG, LDL level had short duration of DM and this relation is nearly significant for triglyceride and this can be explained by that those patients with high TG were newly diagnosed patients and still need time to stabilized their blood sugar.

CONCLUSION

There is an abnormality in lipid profile among patients with type 1diabetes mellitus.

Those patients with poor diabetic control (high HbA1c) showed high triglycerides level.

RECOMMENDATION

To screen our patients of DM type1 for dyslipidemia at diagnosis (after stabilizing blood sugar) and to be repeated yearly for those patients with poor control.

Further longitudinal study with large sized sample is needed to get more informative results.

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COMPARISON BETWEEN USING LIDOCAINE IN DIFFERENT VOLUMES AND CONCENTRATIONS FOR INTRAVENOUS REGIONAL ANAESTHESIA

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ABSTRACT

Biers block is used to provide regional anaesthesia for more than one hundred years ago worldwide with high degree of safety .This study designed to compare the efficacy of Xylocaine when used in different volumes and concentrations. Prospective randomized study, single blinded, done after taking patient consent and approval from hospital ethical committee done on 28 patients, 30-40 years old, 17 female and 11 male undergoing elective soft tissue surgery on the upper limb as trigger finger, cut tendon, carpel tunnel syndrome and ganglion. 40 ml of (0.5 %) lidocaine given to group A and 20 ml of (1%) lidocaine given two group B. Lidocaine used is preservative free. All injected done by usng 20 ml syringe size and given through 22 gauge cannula in the dorsum of the hand and the injection done over 90 seconds after inflating the proximal tourniquet. The patients classified randomly into two groups Group A receive 40 ml of (0.5%) lidocaine to do biers block and in Group B 20 ml of 1% lidocaine. Intraoperative and postoperative, assessment of the pain, and patient satisfaction in group A and B determine it is nearly similar, VAS ($P<0.05$). by using the T test. 40 ml of lidocaine (0.5%) is equal in efficacy to 20 ml lidocaine at (1%) in performing the intravenous regional anaesthesia of upper limb.

KEY WARDS: Visual analogue scale (VAS), Lidocaine, Intravenous regional anaesthesia (IVRA or Biers block).

INTRODUCTION

IVRA is a technically simple and reliable technique, with success rates between (94%) and (98%)[1,2]. However, the local anesthetic most often used is lidocaine (0.5%) in volume of 40 ml with total dose of 200 mg. Despite vast clinical experience and success with IVRA , the site and mode of action of the local anesthetic agents remains controversial[3]. Some tried to modify it by adding other drugs[4-9] .Others change the site of the tourniquet and decreased the dose[10].

We hypothesize that adequate IVRA can be achieved with the same local anesthetic dose but with (50%) less volume.

Preparation of 40ml (0.5%) lidocaine consumes time as the commercially available concentrations of lidocaine from manufacturer are in concentrations of (1%) and (2%). Theoretically it is beneficial to have volume of 40 ml 0.5% lidocaine to do efficient biers block[11] but adult patients are different in body size this means depending on the volume of the local anaesthetic to do efficient block not rational.

In this study we compare the efficiency of 20 ml of (1%) lidocaine from 40 ml of (0.5%) lidocaine (the same total dose of 200 mg) in performing the IVRA.

PATIENTS AND METHODS

The study was approved by the Misurata Central Hospital scientific committee and written informed consent was obtained from the patient. Twenty eight unpremedicated healthy patient coming for elective minor forearm and hand surgery, ASA physical status I participate in this prospective randomized study (age 30-40 yr; seventeen female and, eleven male), comparing 40 ml of (0.5%) lidocaine preservative free diluted in N/S and 20 ml of (1%) lidocaine commercially prepared. Patients with liver disorders, hypertension, diabetes, obesity, history of allergic reaction to local anaesthetics, those not wishing the IVRA technique, or whom venipuncture was difficult were excluded. Patients were allocated to one of two groups according to a table of random numbers. Patients in one group(A) (n=14) including 8 females and 6 males received 40 ml of (0.5%) lidocaine, Eleven operation were done on the forearms and three on the hands . Whereas those in the other group (B) (n=14) including 9 females and 5 males received 20ml (1%) lidocaine, Ten operation were done on the forearms and four on the hands A 22-gauge catheter was introduced into a vein on the dorsum of the hand to be operated upon and another 20-gauge catheter was inserted into a veins of the arm not requiring surgery for maintenance fluid infusion. The operative arm was exanguinated by elevating it and wrapping it with a rubber Esmarch bandage. The proximal cuff of a double tourniquet was then inflated minimally 100 mm Hg above systolic pressure until the pulse trace disappear on the pulse oximeter and lidocaine was injected over 90 seconds.Then we inflate the second tourniquiet after fifteen minute. Boluses of fentanyl were provided whenever there was a (20%) increase in baseline values of arterial pressure and/or heart rate or when analgesia was graded as poor by the patient. All patients received entonox intraoperatively (N_2O and O_2 mixture 50:50). Patient's vital signs (arterial pressure, ventilatory frequency, ECG, pulse oximeter), analgesic request, and presence of adverse events related to unexpected deflation of the tourniquet were assessed intraoperatively .The surgeon allowed to start five minute after the tourniquet inflation after absence of pin brick sensation. Adequate intraoperative analgesia was determined by the

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need for supplementary medication intraoperatively and by the visual analogue scale taken five minute after the surgeon start, then postoperatively three minute after the tourniquet release the visual analogue scale reported and. Symptoms of dizziness, nystagmus, tinnitus, facial dysaesthesia, convulsions, depression of the central nervous system, bradypnoea (ventilatory frequency ≤ 10 breaths min^{-1}), bradycardia (heart rate ≤ 50 beats min^{-1}), and cardiovascular depression (≤ 25% decrease in baseline arterial pressure) were noted, if present.

RESULTS

Patients characteristics and data of the operation site in both of the study groups are shown in (table 1) There were no statistically significant differences in relation to age, weight, height, gender, duration of operation, and site of surgical procedure.

(Table 1) Demographic features

	Group A	Group B
Number	14	14
Age (Year)	34 (±2,8)	36 (±3.2)
Sex (M / F)	8/6	9/5
Weight (kg)	79 (±4.2)	76 (±6.1)
Height (cm)	165 (±9.7)	162 (±12.3)
Operative site(forearm/arm)	11/3	10/4
Operative duration (min)	27.1 (±4.7min)	25.4 (±6.2min)

The visual analogue scale in group A intraoperatively and postoperatively are shown in (table 2) .The mean of the intraoperative VAS 1.24(±0.52). However, postoperative one 2,66 (±0.93)

(Table 2)

Group A	Intraoperative VAS	Postoperative VAS
1	1.3	2.1
2	0.8	1.3
3	0.9	1.5
4	1.7	3.7
5	2.3	4.3
6	1.2	2.8
7	1.6	3.2
8	0.6	2.1
9	1.3	3.4
10	0.9	2.7
11	2.1	3.5
12	0.9	2.4
13	1.1	2.9
14	0.7	1.3

However, the visual analogue scale in group B intraoperatively and postoperatively are shown in (table 3). The mean of the intraoperative VAS 1.31(+-0.52) and the postoperative one 2.63(+-0.84)

In all patients involved there were no need for supplementary analgesia .postoperatively with regard to adverse event as dizziness, nystagmus, tinnitus, facial dysaesthesia , convulsions, depression of the central nervous system, bradypnoea (ventilatory frequency ≤ 10 breaths min^{-1}), bradycardia (heart rate ≤ 50 beats min^{-1}), and cardiovascular depression (≤ 25% decrease in baseline arterial pressure) on release of the tourniquet which were not present in the study group. Statistical comparison of VAS intraoperatively and postoperatively in groups A and B showed no statistically significance difference ($P < 0.0001$) according to the analysis by using the T test to compare both groups.

(Table 3)

Group B	Intraoperative VAS	Postoperative VAS
1	1.8	2.7
2	0.7	1.2
3	0.9	1.6
4	1.4	2.4
5	0.6	2.2
6	1.4	3.6
7	2.1	3.9
8	1.5	2.8
9	2.3	4.1
10	0.9	2.6
11	1.6	3.1
12	1.2	2.7
13	0.8	2.1
14	1.1	1.8

DISCUSSION

In this study, we demonstrated that, during the period of tourniquet inflation, IVRA with 20 ml 1 % lidocaine provides anesthesia of similar efficacy as IVRA with 40 ml 0.5% lidocaine. Patients intraoperatively do not ask for analgesic drugs this may be because all of them received entonox which have good analgesic affect[12].

The rapid return of normal sensation three minutes after tourniquet release may be the cause behind increasing in VAS postoperatively in our study. This is consistent with the report that, within three minutes of tourniquet release, 58% of a compound similar to lidocaine (0.1 mg of HIDA labeled with 100 mCi of 99 mTc in 40 mL of saline) was eliminated from the arm[13].

Some study have reported complications as seizures promptly related to postdeflation time[14]. However this is rare as lidocaine has to high uptake by the lung[15] and extraction by the liver[16]. In our study there is no reported postoperative complications may be because the total dose of lidocaine 200mg which is equal to 2.6 mg per one kilogram body weight as the average weight of the patients involved in this study was 77.5 Kg indicating the safety of such dose. Postoperative VAS is the similar in both groups without significant difference ($P < 0.05$)

CONCLUSION

This study indicates that 20 ml 1% lidocaine was equal in efficacy to 40 ml 0.5% lidocaine. This indicate the effectiveness is related to total dose not to

the volume of the local anaesthetic Dilution of lidocaine in multiple syringes is time consuming and not necessary. In addition, smaller volumes are easier to inject and simpler to prepare and safer than mixing and dilution.

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INGUINAL HERNIA REPAIR UNDER LOCAL ANAESTHESIA

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ABSTRACT

Tension-free Lichtenstein procedure was performed under local anaesthesia in 113 patients. During 2006-2009 in 7th October Hospital and Aljala Hospital, Benghazi, Libya. After a mean follow-up of one year, the operative outcome (operation time, pain, bleeding, infections) and long-term results (recurrences, chronic pain) were recorded. The rate of wound infection (1.7%) and seromas (4.4%). One recurrences (0.9%) were found at follow-up. Although 10% of the patients reported some groin pain afterwards, over 90% were very satisfied with the operation. Open mesh repair under local anaesthesia is a cost-effective, simple and safe operation.

KEY WORDS: Inguinal hernia, Local anesthesia.

INTRODUCTION

Inguinal hernias occur in about 16% of adult men and herniorraphy is one of the top three surgical procedures in most western countries. Approximately 12,000 inguinal herniorraphies are performed each year in Finland, over 80,000 operations in England and over 800,000 in the US[1–3]. About 20% of groin hernia repairs are undertaken for recurrences and 4% as an emergency[4]. Therefore, the socioeconomical impact of groin hernia surgery is high on health care system. Lichtenstein hernioplasty is a tension-free technique, which uses polypropylene mesh to support the inguinal muscular layers[5]. Its learning curve is even shorter than traditional groin hernioplasties, therefore, the Lichtenstein procedure has rapidly increased as a primary operation for inguinal hernias. Several randomised and retrospective studies have shown that inguinal hernia repair under local anaesthesia results in less postoperative analgesic requirements and side-effects, reduced hospital stay, lower costs and shorter recovery times[6–9].

Recent quality control studies have reported that chronic pain after inguinal hernia operation may occur in 10-30% of patients in a long-term follow-up[10–12]. The etiological factors include irritation or damage of inguinal nerves by sutures or mesh[13], inflammatory reaction against the mesh[14] or simply scar tissue[15–17]. The preliminary reports of the Lichtenstein procedure were very optimistic with nil or a very low rate of chronic pain[18]. First randomized follow-up studies indicated that the use of light-weight meshes may be associated with significantly less pain during exercise and the feeling of a foreign object compared to standard heavy meshes[19–22].

MATERIALS AND METHODS

The study is a prospective analytical study conducted from October 2006 to April 2009 in the general surgery unit of 7th October and Aljala hospital. The study subjects (n = 113) were >18 years old with elective inguinal hernias. Recurred, bilateral, strangulated or incarcerated cases, and patients with allergic history against the anesthetics applied, were excluded from the study. The patient selection for open mesh repair under local anaesthesia was based on the common clinical criteria of ambulatory surgery. The procedure was always performed under local infiltration anaesthesia, using 9 x 13 cm polypropylene mesh. The local anaesthetic mixture consisted of 25ml of 1% lignocain with 1:200,000 adrenaline and 25ml of 0.9% saline . 1 g of intravenous cefotriaxone was administered in the anaesthetic room to all patients. In the anaesthetic room, approximately 20 ml of the local anaesthetic mixture was infiltrated along the line of incision in the subcutaneous plane, around the pubic tubercle and the deep ring.

A skin and external oblique aponeurosis incision was then performed, after which subaponeurotic infiltration of the mixture deep to the external oblique layer was undertaken. Further infiltration was performed into the spermatic cord avoiding the testicular vessels, nerves and the vas deferens. The sac was dissected and excised and Lichtenstein repair was performed, If the hernia sac was large and direct, it was inverted with absorbable 2-0 PDS sutures. The mesh was trimmed and placed between the conjoint tendon, inguinal ligament, pubic bone and internal oblique aponeurosis[5,23]. The ilioinguinal, genitofemoral and iliohypogastric nerves were identified if possible and carefully preserved. Care was taken not to involve the nerves within the sutures. No drain left in the wound . A 0.5-1.0-mg bolus of intravenous alfentanil was administered if the patient felt pain during the operation. Six young patients were anxious and feeling pain converted to general anaesthesia. Diclofenac sodium or paracetamol were prescribed for postoperative pain. 102 (90%) patients discharged on the same day and 11 (10%) stay overnight in the hospital. The immediate outcome was analyzed from the operative reports and patient's records. The patient characteristics, type of hernia, operation time and wound complications were recorded. The long term follow-up was performed by the surgeon team. Time to return to

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normal activities, chronic pain, need of medication, feeling of foreign object and satisfaction of the procedure were recorded at each time interval. Twelve patients of the original groups were dropped because they could not be reached.

RESULTS

The median age of the study group was 36 years (range18–65). The median body mass index (BMI) of the study group was 28 (range 20.2–32.5). Because 12 patients were lost during the follow-up, a final one year analysis left a total of 101 patients .

(Table 1) Characteristics of the patients

Number of patients	113
Male\Female	104\9
Mean age	36
Indirect/direct hernia	92\17
Combined	4
Right\Left sided	67\46
Mean operative time(min)	58
Mean volume of local anesthesia(ml)	50

(Table 2) First week postoperative course of the patients

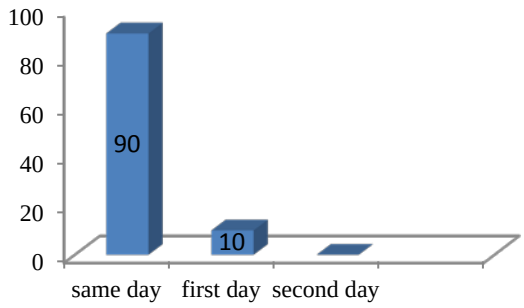
Normal wound healing	106
Wound infection	2
Wound seroma	5
Analgesic use - Daily	29
- Sometimes	67
- Non	17
Painless Walking	75

(Table 3) First Month postoperative course of the patients

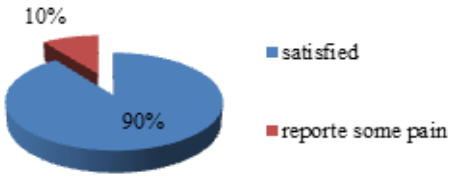
Pain feeling	11
Analgesic use	11
Feeling of foreign body	4
Normal daily activity	98
Missed follow up	4

(Table 4) One year postoperative course of the patients

Pain feeling	4
Analgesic use	4
Feeling of foreign body	3
Normal daily activities	97
recurrences	0.9
Missed follow up	12



(Figure 1) Hospital stay



(Figure 2) patients satisfied with the procedure

DISCUSSION

Inguinal hernias are common in the population that centralization into specific hernia centers in United States has been carried out, recurrences between 0 and 1% and infections between 0 and 5% have been reported[23,24,25]. Lichtenstein hernioplasty under local anesthesia was rapid and an effective surgical technique for inguinal hernia repair. Patients did not have urinary retention postoperatively, which is rather commonly seen after spinal anesthesia of elderly men[26]. The surgical technique was relatively simple and straightforward. Despite receiving widespread acceptance overseas, local anaesthetic inguinal hernia repair is not popular with surgeons in the Libya . Previous studies have reported higher patient satisfaction rates with local anaesthetic inguinal hernia repair[6,27,28]. However, one study[29] has reported a patient dissatisfaction rate of 8% following local anaesthetic inguinal hernia repair, mainly due to intraoperative discomfort or pain and it has been suggested that a large dose ilioinguinal-iliohypogastric block in combination with stepwise infiltration might result in reduced intraoperative discomfort.

It is well known that traditional inguinal hernioplasties (Bassini, Shouldice, McWay etc.) have long-lasting pain due to tension[1]. In tension-free techniques chronic pain has also been reported in 20–30% of patients[30]. The etiological factors may include irritation or damage of inguinal nerves by sutures or mesh[13]. To avoid chronic nerve irritation and the feeling of a foreign object, recent multicenter studies have hypothesized that partially absorbable or lightweight meshes would improve operative outcome[19–22]. The present study indicated that postoperative seromas were not a big problem in Lichtenstein hernioplasty , and also indicated that severe chronic neuralgia was rare when the patients were properly followed up, Only four patients (3.5%) needed analgesics at one year of hernia repair. When postoperative neuralgia occurred, it is usually healed with nonoperative treatment. Laparoscopic techniques may give some short-term advantages in terms of pain and patients' perception of health[31], but the long-term comparative follow-up studies to open techniques are still few and patients should be fit for general anaesthesia[32]. The present study indicated that although 10% of patients reported some pain sensations afterwards in the groin, this was mild in nature since over 90% were very satisfied with the operation. It is cost-effective since 90% of the pa-

tients discharged on the same day and 95% avoid general anesthesia.

CONCLUSION

Open tension free mesh repair (Lichtenstein) under local anaesthesia is cost-effective, simple and a safe operation. The open tension free mesh technique under local anaesthesia is simple enough to be learned well in general surgical training. It can be the primary standard operation for many of the adult inguinal hernias.

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BURNS INJURY IN UNDER 5 YEARS CHILDREN ADMITTED TO BURN AND PLASTIC SURGERY HOSPITAL FROM 2009 TO 2011

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ABSTRACT

Burns are a common cause of preventable injury and most of these injuries are in children under the age of 5 years and have the greatest length of stay for all hospital admission due to injuries. As the Children are not little adults, the symptoms, signs, and management will be completely different. The study was conducted to identify the epidemiological features of burns in children and analysis of the outcome of used management. Retrospective analysis of data of patients files under 5 years old who were admitted to pediatric burn and intensive care unit burn units in Burn and Plastic surgery hospital- Tripoli, in the period between (January 2009 to December 2011). 21% of the total admission were children under 5 years, 85% of those patients were mild to moderate injury and 15% were with severe injury. Male patients represent 61% of the admissions and female patients represent 39% of the admissions. Scald burn represent 69% of cases, fire burn with 14% and the rest because of electrical burn, therefore more cases in winter season. 50% of cases managed surgically with mean duration of stay in hospital 8 days. The study shows 60% of the patients were males, Scald burn injuries are most common, early surgical excision and grafting decline the duration of stay in hospital.

KEYWORDS: Burns, Duration of stay, Early surgical intervention.

INTRODUCTION

Due to their small body weight/surface area ratio and more circulating volume (80 ml/Kg vs 65 ml/kg in adultes), fluid losses in children in burn injury are proportionally greater than adult (more than twice)[(1)]. Because the linear relationship between body weight and surface area does not exist in children, use of weight based formula result in under or over resuscitation[(2)]. Pediatric burned patients should be resuscitated using formula based on body surface area, which can be calculated from height and weight using standard normogram or formula[(3)].

Evaluation of the efficacy of resuscitation is difficult in children because usual signs of hypovolemia are late due to:-

-Large cardiopulmonary reserve
-Require loss of 25% of circulating volume
-Tachycardia often reflex with trivial injury
-Blood pressure commonly low.
-Continued urine production despite hypovole mia[(4)].

So, reflective of volume status is:

-Mental clarity
-Pulse pressure
-Arterial blood gasses
-Distal extremity color
-Capillary refilling.
-Body temperature

Finally the smaller aperture of the pediatric trachea predisposes it to increase in resistance & decrease in cross section area by minimal amount of edema, therefore early intubation is advocate[(5,6)].

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AIM AND OBJECTIVES OF THE STUDY

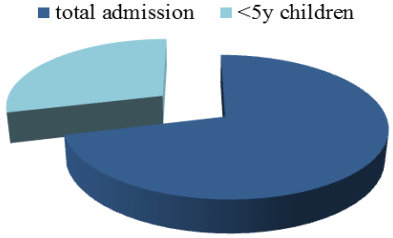
1- Identify epidemiological features of burns in children.
2- Determine the mechanisms of their lesions.
3- Evaluate the outcome of used management.

METHOD & SUBJECTS

Retrospective study of data (patient's files) of patients under 5 years old who were admitted to pediatric burn and ICU burn units in Burn and Plastic Surgery Hospital-Tripoli, ((which is the only specialized hospital in Libya for treating burn injury victims, There is only one burn unit in trauma hospital (Aljala hospital) in eastern side of Libya. Also there is no private hospital dealings with such cases)) In the period between (January 2009 to December 2011), the data includes gender, causes of burn, burn surface, management and duration of hospital stay.

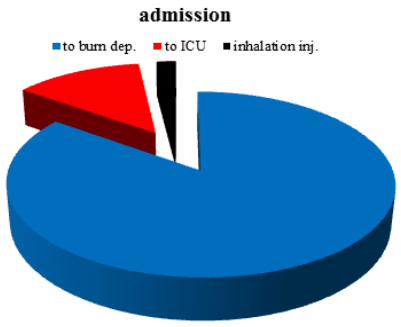
RESULT

Total number of admission to the burn department and ICU burn was 2087 patients, 440 patients were children under 5 years old that represent 21% of the total admission (figure 1).



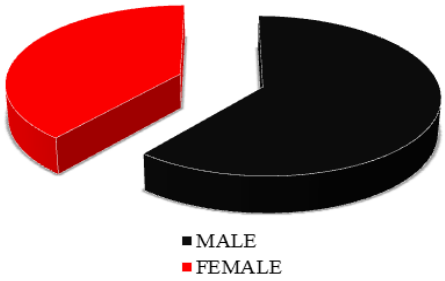
(Figure 1) Percentage of admitted patients who are under 5y old

374 patients out of 440 patients admitted to pediatric burn department, 85% mild to moderate injury (burn surface area less than 25% TBSA), where 66 patients admitted to ICU burn,15% severe injury (burn surface area more than 25%TBSA), 9 of them sustained inhalation injury (2% inhalation injury) and 2 patients with inhalation injury have been expired (0.5% expired) (figure2).



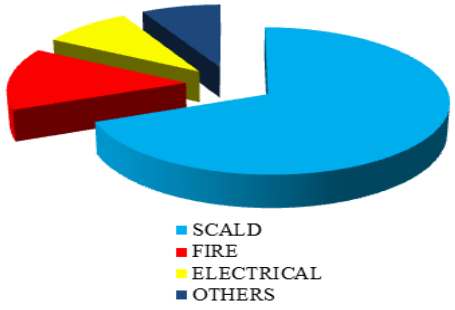
(Figure 2) Distribution of admission in different burn departments

Male patients represent 61% of the admitted patients and Female patients represent 39% (figure 3).



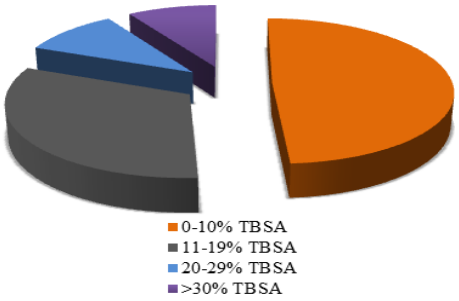
(Figure 3) Male to female ratio of admitted patients

We observed highest percentage 65% (286 case) of admission during winter season.
The cause of burn was as follow: Scald burn represent 69% of admitted cases, Fire burn represent 14% Electrical burn represent 9% and Other causes represent 8% of them (i.e chemical burn, thermo mechanical burn, contact burn) (figure 4).



(Figure 4) Burn causes among admitted patients

The distribution of patients according to the burn surface was as following:
In 49% of the patients the burn was less than 10% of body surface. 32% of them the burn were involving 10-19% of body surface. 10% of cases the burn were involving 20-29% of body surface. 9% of cases the burn were involving >30 of body surface (figure 5).



(Figure 5) Severity of burn injury in admitted patients

Total number of patients treated surgically with auto skin graft or debridement was 221 patients out of 440 patients that represent 50% (table 1).

(Table1) Surgical management

operations	NO. of patients	%
debridement	39 patients	18%
skin graft	182 patients	82%

Duration of stay in hospital: we observed that among the patients who admitted to pediatric Burn department, surgically managed patients group, stay in the hospital less than non-surgically managed patients (table 2).

(Table 2) Duration of stay in hospital

Patients groups	Mean of duration of stay in hospital
Surgically managed Patients (188)	8 days
conservatively managed Patients (186)	13 days

DISCUSSION AND CONCLUSION

-Under 5 years burned patients, represent about 20% of total burn admission to the burn & plastic surgery centre, Tripoli.
- Male patients had been injured in more than 60% of cases (male to female ratio 1.5:1). decreasing the possibility of child abuse in our society, similar results were obtained in Benghazi in 1981and in U.K in 1999[7,8].
-Burn injury occurs more frequently during cold weather because of usage of hot water and heater.
-Scald burn injuries are most common. Due to house hold accidents, these may include spilling hot tea, soup or hot water which can be avoided, similar results were obtained in India 2000[9].
-Burn surface area was below 20% in more than 80% of patients.

-In 50% of patients the burn was 2nd degree (superficial) that managed conservatively.
-Early surgical excision and grafting lowering the duration of stay in hospital, similar results were obtained in researching papers from Nigeria 2010, India 2001, U.K 1999 and Saudi Arabia 2006[10,11,12,13].
-Mortality rate was 0.5% among those children, due to major burn injury and inhalation injury.
-Child abuse is an important issue concerning burns, but could not be included in such research due to lack of the activation of social workers in our community, child abuse was reported in a study conducted in India in 2001[11].

RECOMMENDED PREVENTION PROGRAM

1- Educational cessations for all the community in the media about burn injury.
2-We recommend early surgical intervention in doubtful deep burn
3- Enclosing cooking area to prevent scald burn which is more prevalent.
4- Electrification to reduce dependency on kerosene.
5- Safe stove design.
6- Installation of detectors.
7- Reduce temperature level of the water heater.

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EXAMINATION UNDER ANAESTHESIA IN OPHTHALMIC PRACTICE

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ABSTRACT

Ocular examination is a sophisticated procedure. The patient has to be exceptionally cooperative and relaxed. If those are not achieved, not only the examination is not reliable but it may be dangerous also. This study is aimed to determine the ophthalmic indications and the final diagnosis in children were examined under general anaesthesia (EUA) in Albasar Ophthalmic clinic, Masuria- Libya over a period of six years (2008-2013). All examined children underwent cycloplegic refraction and dilated fundoscopy. Other recordings like corneal diameter, axial length and intra ocular pressure measurements were done when needed. 265 cases were included. The commonest ophthalmic indication for EUA among children was strabismus in 235 cases (89%). In 30 cases (11%) the indications for EUA were nystagmus, corneal haziness, white pupil, trauma, fundus examination and ptosis. Ocular pathology was found in two cases only (less than 1%) in strabismus group, while it was found in 19 cases (63.3%) in the other group. A complete precise ocular examination is mandatory procedure in all ophthalmic patients who are unable to tolerate a complete examination within the ophthalmic clinic setting. The higher the rate of performing this relatively safe and effective technique is an indicative of improvement of ophthalmic survives.

KEY WORDS: General anaesthesia, Refraction, fundoscopy, Axial length, Nystagmus.

INTRODUCTION

Ocular examination is a sophisticated procedure. Examination under anaesthesia (EUA) has to be resorted for ophthalmic patients who are unable to tolerate a detailed examination within the outpatient clinic[1]. Paediatric patients form the bulk of such patients due to the lack of cooperation because of their age. They therefore have to be examined under short period of general anaesthesia in the operating room. The use of ketamine anaesthesia is safe and effective[2].

Ocular morbidities and blindness in children constitute serious public health challenges[3,4] for a number of reasons. Firstly, treatable causes of blindness in children, if left uncorrected, may leave them permanently blind. Secondly, a blind child poses great challenge to education and emotional development[5]. Many amblyopic children will suffer irreversible vision loss that could have been prevented. The consequences of not identifying and treating strabismus and amblyopia early include permanent visual impairment, adverse effects on school performance, poor fine motor skills, social interactions and self-image[6].

MATERIALS AND METHODS

The files of 265 children examined under general anaesthesia using ketamine in Albasar Ophthalmic clinic, Misurata-Libya over a period of six years (2008-2013) were analysed retrospectively. Age, sex, presenting complain, indication of examination, refraction results (spherical error, cylindrical error and its axis), fundoscopic finding and other clinical findings when found were collected from the files. The name age of each child were recorded by the receptionist, the decision for the examination under anaesthesia (EUA) was taken by the consultant eye specialist on duty. In all cases a strong cycloplegic mydriatic drug (atropine 1% eye drops) was applied twice daily in both eyes three days prior to examination. Each child was kept fasting for 4- 5 hours prior to anaesthesia, in all cases short general intravenous ketamine anaesthesia in the operating room was given. Retinoscopic refraction by streak Nitez retinoscope, plane mirror effect technique with 0.5 D step power of trial spherical lenses in two meridian and the cylinder axis was approximated to the nearest 30 degrees.. The refractive error up to two dioptres of hypermetropia in the first twelve months of life and one dioptre of hypermetropia in the age group above twelve to twenty four months of age were regarded as normal. Any spherical error above the age of 24 months was regarded as abnormal. Isolated astigmatic error of half dioptre or less at any age was regarded as normal also.

The fundi were examined by Keeler direct and indirect ophthalmoscope. Special attention to the media clarity, optic disc and retina were considered. Intraocular pressure, corneal diameter and axial length were recorded when indicated by the use of Schiotz tonometer, squint calliper and A-scan ultrasonography respectively.

RESULTS

A total of 265 children whose age and sex distribution is as illustrated in (table 1) had examined under general anaesthesia (EUA) between 2008 and 2013. 108 cases (41%) were males and 157 cases (59%) were females. More than 40% of the children were presented before age of one year.

Strabismus (latent, manifest or history of deviation of one or both eyes from the fixation point) was the indication for examination under anaesthesia (EUA) in 235 cases (89%) while the other indications include nystagmus, corneal haziness, white pupil,

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trauma, fundus examination and ptosis constitute for 30 cases (11%).

(Table 1) Age and Sex distribution

Age	No. of cases	%	Males	Females
>6 months	42	(15.9%)	24	18
6->12 months	73	(27.5%)	31	42
12->18 months	52	(19.6%)	15	37
18->24 months	56	(21.1%)	25	31
24 months and more	42	(15.9%)	13	29
Total	265	(100%)	108 (41%)	157 (59%)

(Table 2) gives a breakdown of the indications and results for EUA in the study population.

(Table 2) Distribution of the indications and results of the EUA.

Strabismus indication				Other indications			
Ametropia	Emmetropia	Ocular pathology	Total	Ocular pathology	Normal	Refractive error	Total
204 (87%)	29 (12%)	2 (1%)	235	19 (63.3%)	10 (33.3%)	1 (3.3%)	30

In the strabismus indication group, 204 cases (87%) were suffering from refractive errors, where only two cases (less than 1%) were found to have ocular pathology. In the other indications group, ocular pathology was found in 19 cases (63.3%).

Two patients found to have refractive error in one eye only. So 408 eyes (77%) found to have refractive error in the examined children. Astigmatism is found in 278 eyes in the examined children who suffer a refractive error (68%). Ocular pathology were found in 21 cases (8%) of all the studied population. (Table 3) gives the distribution of ocular pathology in the study group.

In general, examination was positive in 226 cases (85%) of the examined children, out of them 21 cases (8%) were found to have ocular pathology.

(Table 3) Distribution of ocular pathology

Ocular pathology	No. of cases
Retinopathy of prematurity	4
Optic atrophy	3
Congenital glaucoma	4
Microphthalmia	2
Congenital cataract	3
Commotio retinae	3
Retinoblastoma	1
Keratitis	1

DISCUSSION AND CONCLUSION

Most of the children needed examination under anaesthesia (EUA) in this study were below age of two years, 223 children (84%), as older children are likely to understand spoken instructions and co-operate better with some of the different diagnostic procedures without anaesthesia. Female to male ratio was 1.45 which is coincides with the general population in the city of the study.

In the study the indications for examination under general anaesthesia and clinical findings were studied. The examination was positive in 226 (85%) of the examined children, out of them 8% (21 cases) were found to have ocular pathology, while the others were found to have refractive errors. Both causes are significant. Some ocular diseases are not only vision threatening like retinopathy of prematurity, congenital glaucoma and congenital cataract but also dangerous for life like retinoblastoma.

Strabismus (latent, manifest or suspicion of strabismus) was the major indication of examination (89%) under anaesthesia in this study while in a similar study done in Nigeria strabismus indication was only in 5.1% of the cases[(1)]. This difference may be explained by the large difference in the study population (265 versus 39 children). Global estimates indicate that more than 2.3 billion people in the world suffer from poor vision due to refractive error, of which 670 million people ate considered visually impaired because they do not have access to corrective treatment[(7)]. In this study 205 cases (77%) were found to have refractive error, these refractive errors if uncorrected, results in an impaired quality of life.

In conclusion if the child forced to receive the ophthalmic examination, it is difficult to deliver accurate diagnosis and treatment which may cause negative influence up on physical and mental health. Ketamine anaesthesia is safe and effective and should be considered in any child to do complete and comfortable examination.

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THE TOP TEN CAUSES OF DEATH AMONG GHERIAN POPULATION (2005)

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ABSTRACT

Data on mortality by age, sex, and cause are primary inputs for assessing population health status, and a good evidence for the effectiveness of health policy in combination with other epidemiology and socioeconomic indicators. The aim of this study is to illustrate the top ten causes of deaths in one region of Libya, in order to known the size of problems in our community and to enlighten the policy maker about the serious public health problems which can to put strategy to reduce the magnitude of preventive death. This study was conducted at Gherian teaching hospital (2005), it is a retrospective descriptive study. The data were collected from statistic health department from death certificates. The sample size was 220 death certificates. The total admissions in the hospital were 9978 patients in 2005. The causes are as the following: cardiac diseases, cerebral stroke, road traffic accidents, cancer, chest infection, renal failure, head trauma, birth asphyxia, liver cirrhosis and bronchial asthma. The unknown disease represents 8.6% and other disease are (14.1%). In comparison the results of this study with others study in the world, we observed differences in the rank of causes of death due to genetic, life style, environment, health situation, socioeconomic status…etc.

KEY WORDS:

Top causes of death, cardiac disease, Death certificate, Unknown causes, Limitation in diagnostic.

INTRODUCTION

Data on mortality by age, sex, and cause are primary inputs for assessing population health status, and a good evidence for the effectiveness of health policy in combination with other epidemiology and socioeconomic indicators[(1)].

Measuring how many people die each year and why they died is one of the most important task of the health authority in all over the world for assessing the effectiveness of a country health system[(2)].

Ischemic heart diseases, stroke, lower respiratory and chronic obstructive lung diseases have remained the top major killers during the past decades in the world[(3)].

In Libya, the five risk factors that accounts for the most diseases burden are dietary risks, high blood pressure, high body mass index, high fasting plasma glucose and low physical inactivity[(4)].

In 2012, an estimated 56 million people died worldwide. Non communicable diseases were responsible for 68% of all deaths globally in 2012, up from 60%in 2000[(5)].

About 6.6 million children died before reaching their fifth day in 2012; almost all (99%) of these deaths occurred in low and middle income countries. The major killers of children aged less than 5 years were prematurity, pneumonia, birth asphyxia and birth trauma and diarrheal diseases. Malaria was still a major killer in sub-Saharan Africa, causing about 15% of under 5 deaths in the region[(5)].

About 44% of deaths in children younger than 5 years in 2012 occurred within 28 days of birth (the neonatal period). The most important cause of death was prematurity which was responsible for 35% of all deaths during this period[(5)].

The major causes of death and its burden have not been appropriately identified in Libya. Thus, the aim of this study is to highlight the major causes of death among Gherian population to help policy-makers to draw strategy to reduce the preventable common causes of deaths in our community.

Subject and method

This study was conducted at Gherian teaching hospital (2005) and it is the only teaching hospital in the area. It serves more than 250000 persons with a capacity of 450 beds. It was rebuilt in 1973.

The study is a descriptive study and was done retrospectively. The data were collected from statistic health department from death certificates. All documented deaths in the department in 2005 were included in the sample. The nomenclature of death causes was taken as found in death certificates.

All death certificates were reviewed, arranged, summarized and analyzed by age, sex, causes of death, place of death. etc. All data was analyzed by using Excel 2007.

Data was presented as frequency, percentage, mean, SD and illustrated in form of tables and figures.

RESULTS

(Table 1), shows the distribution of deaths according to sex. Total of 220 deaths were registered in 2005,137 males (63.3%) and 83 females (37.7%). The total admission in the hospital were 9978 patients in 2005[(6)]. The crude death rate was 0.76 per 1000 in this study. The percent of death among the admission was 2.2% in 2005.

The percent of death in this study represent 1.3% from total death in Libya in 2005.

The mean age of death was 56.7 years (SD ± 23.2). Illustrates the top ten causes of death among Gherian

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population. It represented 77.2% from the total deaths. The top ten causes of death as seen in (table 1), were cardiac diseases, cerebral stroke, road traffic accident, cancer, chest infection, renal failure, head trauma, birth asphyxia- liver cirrhosis and bronchial asthma respectively.
However, the other causes of death formed 14.1 % of total deaths and the cause reported as unknown in 8.6 % of deaths (table 1).

(Table 1) The top ten causes of death among Gherian population by gender

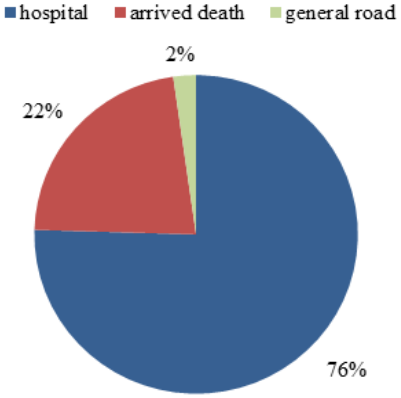
Causes	Male	%	Female	%	Total	Total %
Cardiac diseases	49	22.3	28	12.7	77	35
Cerebral stroke	20	9.1	18	8.2	38	17.3
Road trafic	11	5	2	0.9	13	5.9
Cancer	8	3.6	2	0.9	10	4.5
Chest infection	6	2.7	2	0.9	8	3.6
Renal failure	3	1.4	5	2.3	8	3.6
Head trauma	4	1.8	1	0.45	5	2.3
Birth asphyixa	4	1.8	-	-	4	1.8
Liver cirrhosis	2	0.91	2	0.9	4	1.8
Bronchial asthma	1	0.45	2	0.9	3	1.4
Unknown	14	6.4	5	2.3	19	8.6
Other causes	15	6.8	16	7.3	31	14.1
Total	137	63.3	83	37.7	220	100

The age of deaths ranged from 0 to older than 86 years, deaths was classified and grouped, (table 2), indicates the distribution of death according to age.

(Table 2) Distribution of deaths among Gherian population according to age group

Age in years	Numbers	%
0-<6	14	6.3
6-<11	7	3.2
11-<16	3	1.4
16-<21	8	3.6
21-<26	4	1.8
26-<31	14	6.3
31-<36	5	2.3
36-<41	3	1.4
41-<46	7	3.2
46-<51	7	3.2
51-<56	8	3.6
56-<61	10	4.5
61-<66	14	6.4
66-<71	29	13.2
71-<76	20	9.1
76-<81	27	12.3
81-<86	22	10.0
86+	18	8.2
Total	220	100

It clear from the table that the high frequency of death occurred between 66-70 years (mode =29). This age group represented 13.2 % of the total death and the percentage of death among preschool children was 6.3% as seen in (table 2).
(Figure 1), presented the places of death. As it can be seen in the table that 75.6 % of death were occurred at hospital and 2.3% of death occurred at the general road.



(Figure 1) Distribution the places of death among Gherian population

DISCUSSION

Studies on major causes of death in Libya are very rare. There are many reasons for the variation in causes of death among the countries due to dissimilarity among risk factors of death in different countries.
Measuring how many people die each year and why they died is one of the most important along with gauging how diseases and injuries are affecting people and for assessing the effectiveness of a country health system[(1)].
This study identified the top ten causes of death in one region of Libya to enlighten the policy maker about the serious public health problems in the community and to put strategy to reduce the causes of preventive death among population.
The present study showed that cardiac diseases is the top causes of death in Libya.
The results of this study showed that the top ten causes represented 77.2% from the total death, other causes formed 14.1% and unknown causes represent 8.6%. However, those patient died with undetermined causes in this study reflects certain diagnostic limitations.
The crude death rate was 0.76 per thousand in the studied area. However, the percent of death among admission patient was 2.2%. The total admission patients in 2005 were 9978 patients[(5)].
In comparison the result of this study with other studies, regarding the causes of death we observed the differences between the ranking of the causes of deaths between the countries due to socioeconomic, environment, genetic, life style, health situation, risk factors …. etc.
In Egypt, the top causes of deaths were ischemic heart disease with 13.7% from the total death followed by stroke as the second cause of death with 10.5%[(6)], in this study the first causes of deaths were cardiac diseases with 35% from the total causes, followed by cerebral stroke with 17.3%.
Other studies in Tunisia recorded that ischemic heart disease is the first cause of death with 16.3%

from the total deaths[7]. The percent of deaths in Tunisia is half of the first cause of death in this study.

In Kuwait, the leading causes of death among male were ischemic heart diseases, traffic accidents and cancer. Meanwhile cancer, ischemic heart diseases and hypertension were more common in female[1].

In Jordan, the three leading causes of death were diseases of circulatory system, malignancies and accidents[8].

In Turkey, the first leading causes of death were ischemic heart diseases among male with 20.7% and female with 22.9%. The second leading cause was cerebrovascular disease with 14.5% in male and 15.7% in females[9].

The cerebral stroke as a cause of death was ranked as the second cause of death in this study and in Turkey. However the percentage in present study was lower than in Turkey (in male with 9.1%, female 8.2%).

In the national level (Libya), the top ten causes of death were: coronary heart diseases, stroke, road traffic accidents, diabetes mellitus, hypertension, influenza and pneumonia, lung diseases, lung cancer, kidney diseases and prostate cancer[7].

In Iranian population, it seems that cardiovascular diseases, motor vehicle accidents, cancers, intentional and unintentional injuries are the major causes of death[10].

In Sudan, the first cause of death was lower respiratory infection with percentage of 10.4%, followed by diarrheal disease with 8.8%[7].

In Saudi Arabia, the first cause of death was coronary heart disease with 24.34%, followed by stroke as second cause of death with 17.96%[7].

It is clear from the most studied in the world regarding the top causes of death that the cardiac diseases rank as the first cause of death in the world. The finding in this study regarding the first cause of death is similar to other studies mainly in rich country.

The conflicts between counties regarding the top causes of death are depended mainly on the genetic factors, environment, quality of health services, social economic status, risk factors and life style. The top 10 leading causes of death in the US were: heart disease, cancer, chronic lower respiratory disease, accident, stroke, Alzheimer disease, diabetes, influenza and pneumonia, kidney disease and suicide[11].

The crude death rate as found in this study was 0.76 per 1000 in the studied area while the crude death rate in the national level was 4.08 per thousand in 2012[12].

The percent of death in this study represented 1.3% from the total death in Libya in 2005. However, the data in this study were collected from death certification from statistical department in Gherian teaching hospital and there is limitation in writing procedure of death certification.

Death certification, in Libya should be up dated according to the international standard and training programs for the physicians about the writing protocol of death certificates.

CONCLUSION

In conclusion, this study shows, the top ten causes of death, among Gherian population. The common causes of death were cardiac diseases, cerebral stroke, road traffic accidents, cancer, and chest infection.

Unknown causes of death in this study represented 8.6%, this leads to limitation in diagnostic side. Other causes of death in the present study were 14.1%.

RECOMMENDATION

1-The physician should be given training courses in writing death certification according to international standard (WHO) with coding system.

2-We noted in this study that certain death certificate recorded mode of deaths instead the cause of death. These issues should be handled.

ACKNOWLEDGMENT

The author would like to thanks intern doctors for their help in this study, also thanks to directors of Gherian teaching hospital and heath statistic staff for their kind help in this study.

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THE USE OF MISOPROSTOL AS ALTERNATIVE TO CURETTAGE POST ABORTION

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ABSTRACT

Termination of abortion is performed nowadays medically rather than surgically in most cases by means of misoprostol, in order to minimize the hospitalization and it`s costs. This study is aimed to evaluate the effectiveness of misoprostol used buccally in cases of incomplete abortion to avoid uterine curettage. The study was conducted in the department of Obstetrics and Gynecology in Misurata central hospital, Misurata, Libya. The study performed during the period from January 1st 2013 to June 30th 2014. 300 patient were involved in the study. They were aborted either spontaneously or induced by misoprostol, they were all hemodynamically stable with sonography proved diagnosis of incomplete abortion. They were given misoprostol 400 mcg buccally two times a day for a period of five days under cover of antibiotics. Pelvic sonography was performed on day 5, day 10 and day 15 to confirm the complete expulsion of the retained tissue. Complete evacuation rates with medical treatment using misoprostol were 84.3%. 80% of cases of age group within 20 - 40 years and nearly 70% had history of abortion, nearly 48.2 % of the aborted group (84.3%) were less than 8 weeks gestation which indicates that the efficacy is more in early gestational ages. The spasmodic pain is the most obvious side effect to misoprostol which is relieved by brufen tablets 400mg used whenever needed while the duration and amount of bleeding were reduced and in more than 50% of cases stopped by the fifth day. Medical treatment using misoprostol 800 mcg daily for incomplete abortion is effective and acceptable in hemodynamically stable patients.

KEYWORDS: Misoprostol, Medical termination of pregnancy, Retained products of conception.

INTRODUCTION

Misoprostol is a synthetic analogue of prostaglandin E1 (PGE1). It was approved by the US FDA for the prevention of nonsteroidal anti-inflammatory drug (NSAID)-induced gastric ulcers. The action of misoprostol on the pregnant uterus was first described by Rabe et al in 1987. They discovered that it binds to the EP-2/EP-3 prostanoid receptors inducing effective uterine contraction[1].

Although misoprostol is licensed for oral administration, it is now often used vaginally and sublingually and also rectally in some instances to treat incomplete or missed abortion. Misoprostol as a thermostable prostaglandin E1 analogue has been previously tested in the management of incomplete miscarriage in different regimens and settings[2]. Following oral administration, the plasma concentration increased rapidly with a peak of 30 min, declined rapidly by 120 min, and remained low thereafter. In contrast, after vaginal administration, the plasma concentration gradually increased, reaching maximum levels after 70–80 min and slowly declined with detectable levels present even after 6 hrs. Vaginal misoprostol was present in the circulation longer than oral misoprostol and hence its duration of stimulation of the uterus exceeds that of oral misoprostol**.** vaginal application of misoprostol results in slower increase and lower plasma concentrations of misoprostol acid than does oral administration, but overall exposure to drug is increased[3,4].

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Approximately 11–15% of pregnancies end in spontaneous first-trimester miscarriage[5].

Vaginal surgical evacuation of retained products of conception (RPOC) was the main stay of treatment for a long time to reduce complications such as infection and unscheduled hemorrhage. However, surgical management may be complicated with infection, uterine perforation or bowel damage[6], this paved way to more recourses to medical and expectant management which are practical and feasible, although it may increase anxiety associated with the impending abortion[7,8].

The available Cochrane systematic review evidence suggests that expectant care as well as medical treatment with misoprostol are acceptable alternatives to routine vaginal surgical evacuation. Neilson et. al 2010[9].

Some other studies used the sublingual route instead of the oral or vaginal route for uterine evacuation after early pregnancy failure[10-13].

AIM OF THE STUDY

The aim of this study is to assess the effectiveness and acceptability of using buccal misoprostol for management of first trimester incomplete abortion as an alternative to direct vaginal surgical evacuation.

MATERIAL AND METHODS

This is a prospective observational study which included 300 patients who have been diagnosed as first trimester incomplete abortion requesting or agreed for medical management. The study was carried out over a period of one and half year in the department of Obstetrics & Gynecology in Misurata central hospital, Misurata, Libya. from January 1st 2013 to June 30th 2014. The patients involved in the study were aborted either spontaneously or by the

use of misoprostol and were hemodynamically stable.

The criteria used for the diagnosis of incomplete abortion depends of patient symptoms and signs versus laboratory test (β HCG drop) and sonographic findings and the duration of follow up (RPOC eventually resorbed or are passed), women who opted for medical termination using pills were further counseled regarding the procedure and written valid consent was taken. All patients were explained about the complications of the procedure and the need for surgical uterine evacuation in case of failure.

They all were given a dose of misoprostol 400 mcg every 12hrs buccally for five days under cover of broad spectrum antibiotics. Pelvic ultrasonography was performed for all patients before starting misoprostol to confirm the diagnosis then repeated on day 5 and day 10 and day 15 to confirm the complete expulsion of the retained tissue. Pain, a predominant symptom is relieved by brufen tablets 400mg used whenever needed. Exclusion criteria were patients who are hemodynamically unstable, with septic abortion, fever, bronchial asthma, severe anemia, suspected ectopic pregnancy, known case of coagulopathy or were on anticoagulant therapy, cardiovascular diseases such as uncontrolled hypertension, angina, valvular disease, and arrhythmia, severe renal, liver, or respiratory disease, uncontrolled seizure disorder, inherited porphyria, and allergic to misoprostol. Anti-D injections were administered if the pregnant women had Rh- negative blood group.

RESULTS

The youngest patient was aged 18 while the oldest was 44 years old with a mean age of 32.3 ± 9.3 years. The majority of patients were aged between 31 – 40 (table 1).

(Table 1) Patient distribution according to age groups

Age group	No of pts	percentage of pts
<20	32	10.7%
20 – 30	110	36.7%
31 – 40	130	43.3%
>41	28	9.3%

The highest incidence of abortion were in parous women while it is too low in first pregnancy (12%), as shown in the (table 2).

(Table 2) Patient distribution according to parity

Parity	No of pts	percentage of pts
Primi-parous	38	12.6%
P1 – P4	158	52.7%
≥P5	104	34.7%

Around 69% of the cases had history of one abortion or more with 30% of them had aborted once (table 3).

(Table 3) Patient distribution according to H/O of abortions

Abortions	No of pts	percentage of pts
0	93	31%
1	97	32.3%
2	69	23%
≥ 3	41	13.7%

The gestational age before abortion was less than 12 weeks gestation with a percentage of about 42% of them less than 8 weeks gestation (table 4).

(Table 4) Patient distribution according to gestational age before abortion

Gest. Age	No of pts	percentage of pts
< 8 wks	126	42 %
8-10 wks	97	32.3 %
10-12 wks	77	25.7 %

Complete abortion by misoprostol was achieved in around 84% of the cases while around 15% had underwent a surgical intervention (table 5).

(Table 5) Patient distribution according to response to misoprostol

	No of pts	percentage of pts
Complete abortion	253	84.3%
Completed in 5 days	109	36.3%
Completed in 10 days	82	27.3%
Completed in 15 days	62	20.7%
Incomplete abortion	47	15.7%
Curettage	43	14.3%
Sepsis + curettage	4	1.3%

Out of the 15% of the cases(47) Whom had underwent a curettage, about 59% (8%) had the procedure done within the first five days post abortion due to their poor response to the drug (table 6).

(Table 6) Patient distribution according to curettage timing post abortion

Days post abortion	No of pts (47)	percentage of pts (15%)
< 5 days	28	59.6 %
5-10 days	12	25.6 %
10-15 days	6	12.7 %
> 16 days	1	2.1

Most of the cases are less than 8 weeks gestation which assures the efficacy of the medicine in the earlier gestational age (table 7).

(Table 7) Patient distribution according to gestational age post abortion

Gest. Age	No of pts (253)	percentage of pts
< 8 wks	122	48.2 %
8-10 wks	87	34.4 %
10-12 wks	44	17.4 %

The most obvious side effect was the spasmodic pain due to the strong uterine contraction that induced by the drug, followed by prolonged bleeding in some cases and gastro-intestinal side effects (table 8).

(Table 8) Patient distribution according to side effects to misoprostol

Complications	No of pts	percentage of pts
Pain	112	37.3 %
Bleeding	58	19.3 %
Nausea &vomiting	44	14.6 %
Mouth ulceration	15	5 %
Fever & Rigor & Chills	6	2 %
No complications	65	21.7

Bleeding was ceased within the first 10 days post abortion in most of the cases while it may persist longer in about 12% 0f them (table 9).

(Table 9) Patient distribution according to duration of bleeding after misoprostol

Duration of bleeding	No of pts	percentage of pts
2 – 5 days	168	56%
6 – 10 days	94	31.3%
>10 days	38	12.6%

The vast majority are satisfied with the medicine according to a questionnaire delivered to them after the end of the procedure while others were not because of the side effects or the need to do curettage (table 10).

(Table 10) Patient distribution according to their drug satisfaction

Satisfaction	No of pts	percentage of pts
Completely satisfied	248	82.7%
Unsatisfied	42	14 %
No comment	10	3.3%

DISCUSSION

Medical abortion offers a great potential for improving abortion access and safety as it requires less extensive infrastructure than surgical abortion and there is no need for operation theater facilities and maintains patient's need for privacy. The disadvantages would be that the women requires at least three visits to the hospital, longer duration of bleeding and resulting unpredictable outcome in few patients. The factors that may affect the woman`s decision about the medical method of termination of pregnancy is the abdominal cramps and heavy bleeding, longer duration of bleeding (average 7–10 days), and the need to follow-up after 2 weeks for clinical examination and sonography.

in this study, we assess the effectiveness of buccal misoprostol 400 mcg (Cytotec) every 12 hours for five days of spontaneous or induced first trimester incomplete abortion .

Most of the patients would start cramps and increased bleeding within 6 hours of misoprostol tablets administration, The overall satisfaction was high as concluded from written questionnaire and they promise to recommend the method to friends. No serious side effects or complications were reported except of secondary infection in four cases which were treated by antibiotics and curettage thereafter.

The use of misoprostol to facilitate complete uterine expulsion of products of conception was mentioned repeatedly in literature either to ripen the cervix facilitating manual vacuum aspiration or to help complete expulsion of the retained intrauterine conception products[14-19]. Trans-vaginal ultrasound was carried out to evaluate the condition, the need for medical or surgical therapy according to the thickness of the endometrial echogenicity[20].

Home self-administration of a daily dose of 800 mcg buccally was feasible and acceptable for medical post abortion evacuation[21].

The high efficacy, safety, and acceptability of the daily 800-mcg buccal misoprostol indicate that can be an alternative to surgery for incomplete abortion, Hence, misoprostol might improve post-abortion care when surgical treatment is unavailable[22,23].

The side effects reported in our study were transient and tolerable which agrees with the findings of other studies. It was reported that cramping usually starts within the first few hours after misoprostol administration[24]. Our results are also in agreement with the results of Neilson et. al 2010[9], who reported that the administration of misoprostol to women with incomplete abortion appears to be safe and can avoid vaginal surgical evacuation in 80% of cases while in our study the percentage is 84.3%.

It was also considered as an acceptable choice by some women. However, women should be given a proper analgesia and advise them about possible occurrence of more than average bleeding and given the availability of health service resources to support all expectant medical and surgical side effects.

CONCLUSION AND RECOMMENDATIONS

Although vaginal surgical evacuation of the uterus is more effective than misoprostol in solving the problem but still the medical treatment is effective and acceptable in cases of missed and incomplete abortion especially when surgical management is not attainable or risky or patients prefers to avoid surgical management. About 80% of patients are satisfied with the procedure while the others had some side effects. Misoprostol buccally in a dose of 400 mcg daily two divided doses per day for five days is effective medical evacuation of RPOC in a 84.3% of the case, hence it`s recommended for termination of unhealthy pregnancy.

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24- Obstetrics and Gynecology 672 Indian Journal of Clinical Practice, Vol. 24, No. 7, December 2013.

CLINICOPATHOLOGICAL CHARACTERISTICS OF COLON CANCER IN LIBYA

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ABSTRACT

The study describes demographic and clincopathological features of colorectal cancer in the middle region of Libya. The study was conducted on 229 patients with colon cancer, admitted to the Misurata Cancer Centre, during the years 2010-2014. The clincopathological features were collected from pathology reports and hospital files of the patients. The mean age of colon cancer patients in Libya was 56.06 years, which in men is much higher than in women (p=0.02). The histological types of the colon cancer in Libyan populations showed that the adenocarcinoma was the predominant type followed by mucinous carcinoma. Among Libyan patients the systemic and LN involvement, higher stage tumors, and more tumor extension were strongly associated with poor survival. Although, the men patients had shorter life span than women did, this survival difference was not statistically significant. The histological types and other histopathological risk features show similar importance in respect to survival as the data from European colon cancer. In Libya, the colon cancer is slightly more common in female than in male. Libyan mucinous colon cancer is dominantly seen in younger adult and displays unfavorable features such as high histological grade and stage, large size, and frequent systemic involvement.

KEY WORDS: Colorectal cancer, Libya, North Africa, Europe, Demography, Duke's, Histopathology, Survival, clinicopathological features .

INTRODUCTION

Colorectal cancer is one of the most common pathological problems in the world particularly in the western countries. More than 1 million new cases worldwide. Colorectal cancer (CRC) is contributing to 13% of all cancers[1,2,3].It is well known that the colon cancer more frequently in male than female patients, and its prevalence increases with age in both gender.Over thirty percent of patients with CRC are over the age of 70 years in the Western world[1,4,5,6]. In several countries, colon cancer mortality is figured of nearly half of new cases and accounts for 10-13% of all cancer deaths. It is the second leading cause of female cancer death and the third common cause of male cancer mortality[3,7]. It is well known that, in countries where rates were initially very high, gradual falls in mortality have been noted with time[1]. because in developed countries the colorectal cancer screen is well established which might diagnosed CRCs in their early, more curable stages by using faecal occult blood test (FOBT) and colonoscopy, no such screening test exist in developing countries[8]. Majority of colon tumor patients' complain of polypoid lesions that may cause intestinal obstruction and bleeding per rectum[1,2]. Globally, the incidence of CRC varies 10-fold, with the highest incidence rates in North America, Australia, and northern and western Europe. Some recently developed countries particularly Malaysia, Korea and developing countries of Africa and Asia have lower rates[2,9]. These geographic differences appear to be attributable to differences in dietary and environmental exposures that are imposed upon a background of genetically determined susceptibility[3].

In general, Colon cancer incidence is increasing worldwide in the recent 3 decades, but it varies from areas to areas[6]. For example, in the USA, the incidence has been increasing steadily by about 20% during the period from 1973 through 1987 and remained relatively constant[2,8]. Contrast with Japan and Korea the incidence is rising rapidly[2,9].

In the African and Arabic countries, the studies are not fully covering. In North Africa, colon cancer incidence is about 16.0 new patients per 100.000 persons[3,10]. The background of Arabic colon cancer incidences may be more related to other African colon cancer incidences than to European colon cancer incidences.

Most colorectal carcinomas are located in the sigmoid colon and rectum, but there is evidence of changing distribution in recent years, with an increasing proportion of more proximal carcinomas[11] which tend to grow as exophytic masses and are usually circumscribed with about 20% are mucinous[12]. Proximal colon cancers tend to have high levels of microsatellite instability (MSI-H) or ras proto-oncogene mutations[12,13,14]. In this study, we would like to characterize some demographic and clincopathological features that associated with colon cancer in Libya. To the best of our knowledge, such results on Libyan database have not been published previously.

MATERIALS AND METHODS

Patients and Methods: A retrospective pathological study was conducted on 229 patients (table 2). All

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were treated at the Misurata Cancer Center, Libya during the years 2010-2014.The pathological features were collected from pathology reports and patients hospital files. The estimated clinical or pathological characteristics included sex, age, body mass index, presenting complain, clinical stage; TNM staging system including (location and extension of tumor, LN status, systemic metastasis), Duke's stage, histological grade, histological type, and follow-up of the patient. Patients were followed-up until they died or to the end of the observation period in the end of 2014. Some patients were lost during follow-up prior to 2014. For these patients, the last date of contact was defined as the date for the end of follow-up. The follow-up period ranged from 1 to 60 months with an average of 13.0 months. The patients' files show that the number of readmissions during the study period varied between patients, Many patients seem to have entered the hospital for a preliminary diagnosis, after which they negotiated with their families and decided about the treatment. Many patients stayed until the histopathological diagnosis, usually after the primary surgery was carried out, and decided about further action thereafter;46 patients were completely lost of follow up post to the surgery. Some patients started therapy at the Misurata Cancer Center, but interrupted it and were also lost from the follow up. Finally, around half of the patients were diagnosed, treated, followed up, and subjected to further therapy at the center. The lost patients were generally treated elsewhere (other Libyan hospitals, or abroad).

Statistical analysis:

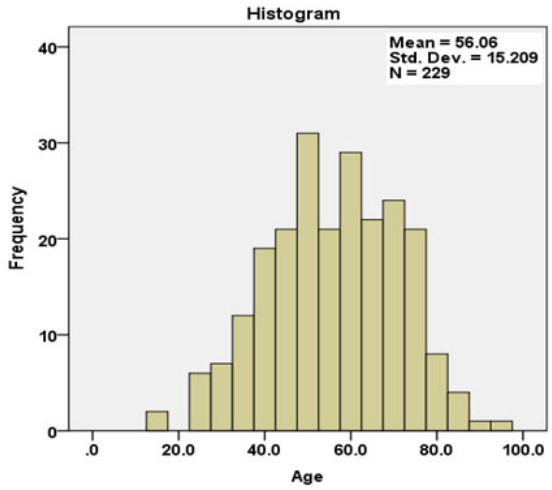
The variables of the Libyan patients were grouped and descriptive statistics calculated for the continuous variables by using SPSS software packages for Windows, versions 21.0 (SPSS, Inc., Chicago, USA). For survival analysis, Kaplan- Meier curves were plotted, and differences between the curves analyzed using the log-rank test. Pearson and Spearman's correlation tests were used for comparison between two variables. P-values below 0.05 were regarded as significant. Comparison of numerical data was done by the chi-square test. Student t-tests and ANOVA were also used to test differences between the groups. Microsoft Excel 2007 was used to draw graphs and to evaluate relationships between variables.

RESULTS

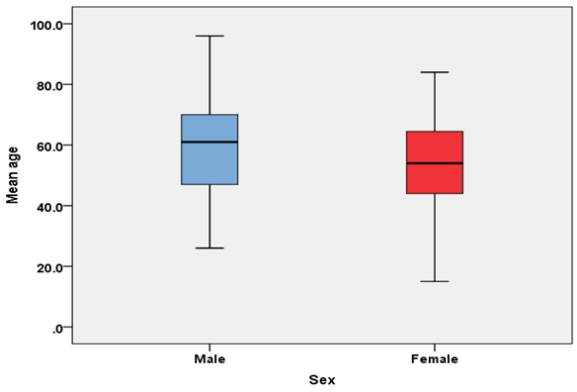
Age, sex and body mass index at presentation:

The study shows 116 females of mean age 53.78±14.65 years (range 15-84 years) and 113 males of mean age 58.39±15.47 years (range 26-96 years) who had colon cancers (figure 1).

Mucinous carcinoma had lower mean age than ordinary adenocarcinoma cancers (table 1). Male patients usually have higher age than female (figure 2). The difference between the mean ages of men and women patients is statistically significant (p value = 0.02).The mean weight of our patients is 68.6kg; 23% of them have body mass index (BMI) >27 kg/m².



(Figure 1) Age distribution at diagnosis of histologically verified colon cancer patients in the middle region of Libya in 2010-2014. The graph is based on 229 patients.



(Figure 2) Shows Mean patients age ±2SD in histological section of colorectal cancer of Libyan patients in male and female patients. Clearly, the mean age is increased with the male gender (P (T-test) = 0.021)

(Table 1) Pathological type of colon carcinoma, along with their clincopathological characteristics and their relative 5-year survival.

Describes pathological features in colon cancers

Histological type:

The histological type's distribution in Libya are shown in (table1) with relation to clinicopathological features.

Histological grade:

In this study 56% of Libyan colorectal cancer patients have high grade while 44% have low grade.

Tumour extension:

The majority of colon cancer in both female and male Libyan patients are extended to muscle layer; only 6 patients (2.6%) had tumour localized to mucosa and submucosal tissues with size of 2cm or less (table 1). Present study shows the average tumor

extension of high grade carcinoma was deeper than the average of low grade carcinoma.

(Table 1) Pathological type of colon carcinoma

Histological Type	Frequency (%)	Mean age (year)	Tumor extension to muscle layer (%)	Nodal involvement (%)	Systemic disease (%)	5 years survival (%)
Adenocarcinoma	95.2	56.5	97.2	63.3	8.7	65.1
Mucinous carcinoma	4.4	43.9	100.0	60.0	10.0	57.1
Adenosquemous carcinoma	0.4	70.0	100.0	0.0	0.0	100.0

(Table 2) The frequency of different stages among 229 colorectal cancer cases listed based on the TNM classification of 2006. The majority of Libyan colorectal cancer patients belong to stages B and C (combined 79.1% of all patients).

(Table 2) The frequency of different stages among 229 colorectal cancer cases listed based on the TNM classification of 2006

Clinical Stage	Duck's stage	Corresponding TNM categories	Frequency	%
0	0	Tis N0M0	0	0
1	A	T1N0M0	5	2.2
	B1	T2N0M0	18	10.0
2	B2	T3N0M0	57	24.8
		T4N0M0	5	2.2
3	C1	T(1/2)N(1/2)M0	45	19.7
	C2	T(3/4)N(1/2)M0	79	34.5
4	D	T(0-4)N(0-2)M1	20	8.7
Total			229	100.0

Lymph node status and distant metastases. proximately 63% of Libyan colon cancer patients had regional lymph node involvement at the time of surgery (table 2). Distant metastases (to one or multiorgan including bone, lung and liver) were present in 8.7% of our patients. In current study, systemic metastases were significantly more common in mucinous than in Adenocarcinoma (table 1).

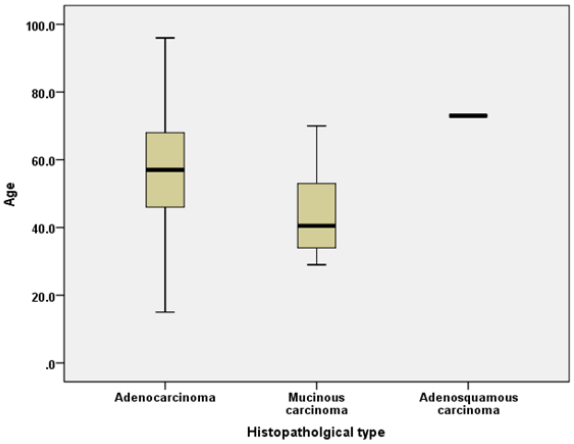
Stage: More than 60% of Libyan patients were seen in stage 3 and 4. While 85 colon cancer patients had early stage at the time of surgery (23 stage 1 and 62 stage 2).

Location site:

The most frequent colorectal cancer sites were the left side has (80.7%) particularly, rectosigmoidal region. The right side colon involved by (19.3%).

Survival analysis:

By the end of follow-up, 41 patients were known to have died, Mean survival for the whole series of 229 patients was 13 months (range 1-60 months).



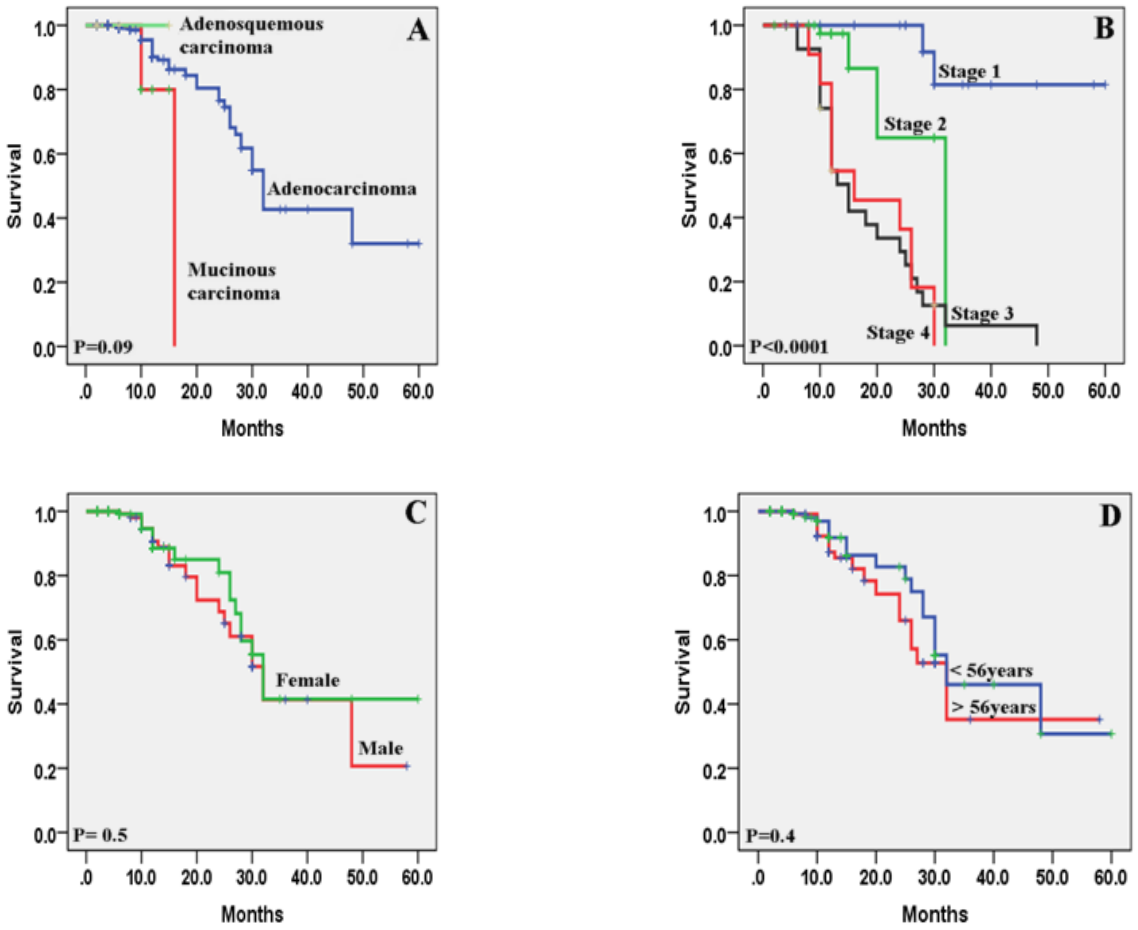
(Figure 3) Mean patients age of different histological types of colorectal cancer in Libyan patients. Clearly there are significant difference among different histological types (P (ANOVA-test) = 0.01)

Clincopathological features:

Among Libyan patients the gender, tumour grade and age of patient did not seem to influence survival. However, systemic involvement, advanced stage of tumor were strongly associated with shortened survival rate. The group of patients with stage 1 had the best 5-year survival ($p < 0.0001$), (figure 4-B). The mucinous histological type of tumor also associated with shortened survival rate but with only trend to be significance (Kaplan-Meier and log rank ($p = 0.09$), (figure 4-A).

DISCUSSION

Age at presentation: The occurrence of colon cancer in Libyan population is age related with nearly 65.0% of cases arising in-patient who are 50 years or older. With contrast to European countries; colon cancer is a rare diagnosis before the age of 40, with 90 % of cases occurring after age 50 years[15,16]. Recent reports show that, in the USA, it was the most frequent form of cancer among persons aged 75 years and older[6,8]. In New Zealand the incidence of colorectal cancer has continued to rise in older age group of population, but has fallen in age group below 50 years[17]. In this study, 61.0% of male colon cancers aged more than 50 years. On contrast with female colon cancer, we found that in females aged older than 50 years there is about 54.0% of female colon cancers (figure 2). In low-risk (developing) areas and new developed countries such as Korean the colon cancer was the most common cancer in middle-aged females, whereas, in industrial countries such as Italy, colon cancer is usually presents in the seventh decade[6,8]. Currently study, shows statistical difference in the mean age at diagnosis between female and male patients (43.6 and 56.2 respectively) with p-value = 0.024. The younger age female have more risk for colon cancer, this might partly be related to estrogen factor.



(Figure 4) Overall survivals of patients according to the histopathological type of colon cancer, patients with mucinous carcinoma type have trend to be more worse survival than other type (p = 0.09). B. Survival curves of Libyan colon cancer patients in different clinical stages. The group of patients with stage 1 had the best 5-year survival (p < 0.0001).
C and D. Survival curves associated with patients' sex and age are not show any significant

Gender:

In Libya, nearly 50.7% of colon cancer patients were women, which left 49.3% for men patients. Although, it is well known that the male gender has colorectal cancer incidence slightly greater than in the female. Unlike rectal cancer the colon cancer is more common in women with age of 55 and below but thereafter becomes slightly more common in men[16]. In Europe and United States colon cancer, the men are affected about 20% more common than female[3,17]. In Japan colon cancers reveals about 40% more frequent in males than females, affect (39.5 / 100.000) of male population and (24.6 / 100.000) of female population with ratio nearly 2:1[3], the cause of this decreased incidence of colon cancer in Japanese women still is unclear. However, in Central American, the colon cancer incidence in males is almost equal that is seen in females. The latter is true especially in Mexico where the incidence in Mexican male and female population was 10.8 and 10.4 per 100,000, respectively[8].

Obesity status and hyperlipidemia roles:

The fraction of obese patient is rare in current study. However, approximately 50% of Americans between 20 and 75 years of age are overweight with BMI >27 kg/m². It was clearly that Libyan patients had lower obesity; about 20% lower in respect to the developed countries population who had a higher average weight in related to same age group as well as higher animal fat consumption[18,19]. Which might be an additional factor that has resulted in an decreasing of obesity in Libyan patients decrease the mutagenic effect of lipid related factors. That may responsible for the low incidence of colon cancer in Libyan patients.

Tumour extension:

Libyan colon cancer patients like other North African had higher tumor size extension than developed countries patients. this data from developed countries suggests the efficiency of more sophisticated and advanced diagnostic facilities in detect smaller lesions in that population[2]. This suggests that the start of fecal occult blood test (FOBT) as stool screening test associated with advanced endoscopic diagnostic facilities should be considered in Libya.
Present study shows the average tumor extension of high grade carcinoma was deeper than the average of low grade carcinoma.

Lymph node status and distant metastases:
The significant increasing of systemic and regional lymph nodes metastases in Libyan patients may suggest a delay in diagnosis in developing countries, and lack or inefficacy of advanced diagnostic facilities. However, the aggressiveness of biological features in African colon cancer should also be considered.

Histological grade:
Colorectal adenocarcinoma can be graded according the degree of differentiation to well differentiated (grade I), moderately-differentiated (grade II) and poorly differentiated (grade III) carcinomas, or into low-grade (encompassing well and moderately differentiated adenocarcinoma) and high-grade (including poorly differentiated adenocarcinoma and undifferentiated carcinomas). Poorly differentiated adenocarcinoma should have at least some mucin and gland like formation; tubules are typically irregularly folded, deformed, and distorted. When a carcinoma has variability in differentiation, grading should be based on the least differentiated component, not including the border of invasion. Small foci of apparent poor differentiation are common found at the advancing edges of tumours, but this feature is inadequate to classify the tumour as poorly differentiated[20]. In general, the percentage of the tumour showing formation of gland-like structures can be used to define the grade. Well differentiated (grade 1) lesions exhibit glandular structures in > 95% of the tumour; moderately differentiated (grade 2) adenocarcinoma has 50-95% glands; poorly differentiated (grade 3) adenocarcinoma has 5-50%; and undifferentiated (grade 4) carcinoma has < 5%. Mucinous adenocarcinoma and signet-ring cell carcinoma are considered poorly differentiated (grade 3). Medullary carcinoma with MSI-H appears undifferentiated. Additional studies of the biological behavior of MSI-H cancers are needed to relate the morphological grade and molecular subtypes of mucinous, signet ring cell and medullary carcinoma to outcome since MSI-H carcinomas have an improved stage-specific survival[21,22].In this study more than 50% of Libyan colorectal cancer patients have high grade. Libyan patients had more aggressive colorectal cancer than European patients, however, their age is lower than in European cancer patients (figure 3). African results are in line with the results on African American patients[1,2,3,8,23]. One explanation for grade differences may just because the younger patients group in African population have more active proliferation tumours.

Stage: The staging system currently in use for colon cancer is based on the extension of primary tumour, degree of spread to lymph nodes and presence of systemic metastasis. The Libyan colon cancer staging in our study is based on the TNM classification of 2006[24]. The large fraction of patients in advanced stages (table 2) Because early-stage CRC may be asymptomatic or produce vague, nonspecific symptoms, many cases are diagnosed at later stages, when regional nodal or systemic metastasis is more likely[25]. However, it may reflects delayed presentation and late diagnosis, which was also obvious in the study of Ermiah et al 2012 on Libyan material[26]. On other hand, screening through colonoscopy and other facilities (such as CT virtual colonoscopy) has been quit not practiced in Libya[27].

Location site:
The most frequent Libyan colorectal cancer located at rectosigmoidal region. This is in line with other previous studies which show about 40% of all large bowel cancers occur in the rectum and rectosigmoid area. The sigmoid colon accounts for a further 25%. Of the remaining bowel, the ascending colon is a site of predilection and it would appear that the incidence of cancer in the right colon is increasing[2,27], especially in high-risk areas for colorectal cancer. However, this could be in part an age-related phenomenon compounded by the greater use of flexible endoscopy in elderly subjects. Most cancers of the colon and rectum are ulcerating tumours with raised everted edges.

The relation of histological type to clincopathological features:
The frequencies for each of histological types of colon cancer were found in the present study is in line with other studies. Adenocarcinoma is the most common colon cancers worldwide. In the current study, adenocarcinoma was the predominant type (95.2%) among both men and women, These figures in line with international fraction range which are (95-98%)[19]. Mucinous carcinoma is common in our populations (4.4%) , however, it still lower than in West of Europe (10%) which might be related to younger age patient's presentation[2,28,29]. Mucinous adenocarcinoma occurs with increased frequency in HNPCC but is more obviously over-represented and likely to be poorly differentiated amongst sporadic MSI-H cancers[30,31].

Prognostic value of clinicohistopathological features in Libyan colon cancer:
The Libyan and other North African colon cancer patients have slight worse prognosis than that recognized by studies in European patients. However, in respect to progressive pathological indicators, the North African colon cancer behaves as the European colon cancer as shown by current study (figure 4). For example, early clinical stage associated with very significant better survival rate while patients have high stage with LN involvement, systemic involvement and tumor extended to muscle layer were strongly associated with shortened survival rate (Kaplan-Meier and log rank ($p < 0.0001$). However, the Adenosquemous carcinoma and well differentiated adenocarcinoma show only tendency to significant better survival (Kaplan-Meier and log rank (p =

0.09). This online with other studies that stated the patients with larger size tumors (T3 or more), lymph node involvement and distant stage tumors were associated with local recurrence, and poorer survival among both men and women. The presence of lymph node metastases is greatly worsens prognosis. More than 83.0% of patients without lymph node metastases disease (i.e. Dukes A and B cases) survive 5 years but the figures markedly drop to 32.0% for lymph node-positive patients (higher stages)[32]. It well known that approximately 30% of colorectal cancers will die with blood-borne metastases. The current study and other studies found that the liver is by far the most frequently involved organ (>60%), followed by the lungs, bones and brain in respectively of order of frequency[33]. Some authors have found that grading system associated with colon cancer has significant independent prognostic influence, particularly if staging is performed suboptimally[34,35]. However, several studies stated that the microacinar morphology and mucinous differentiation are associated with a poor prognosis but does not appear to be an independent prognosticators[20,36]. One cause for the above discrepancies may be associated with studies methodological variability in the use of different other prognosticators. Several authors provide that WDTC particularly adenocarcinoma stage 2 or below is the most common colon cancer that can be treated by only surgical intervention, and usually associated with an excellent prognosis with overall survival more than 90 %[2,16]. On other hand, among Libyan patients the histological type, gender, and age of patient did not seem to considerably influence patients' survival. These results are in line with the results of other studies[16].

CONCLUSION

Libyan colon cancer is affect women like men and is dominantly seen in older age group , it displays unfavorable features such as high histological grade and stage, deeper extension and frequent lymph node involvement, and systemic metastases were strongly associated with poor outcome. The adenocarcinoma was the most common type of colon cancer followed by mucinous carcinoma then other rare types. Finally, in our hospital setting, the results of this study could be used as a baseline data for further research studies. Furthermore, to increase the health education and raising awareness about cancers and widespread implementation of screening programme which can lead to early detection and significantly improve the outcome.

Author's Contributions:

This work was carried out in collaboration between all authors. Author ABF participate in the design and preparation of the manuscript and performed the statistical analysis. Author RM, AF and AR provided the clinical data, and participated in the organizing the clinical data. Author AW conceived of the study, and participated in the organizing the pathological data. Author BMJ participate in the design and coordinate the research and drafted the manuscript. All authors read and approved the final manuscript.

Consent: The proposed study has been examined and approved by the Research Council of Misurata Cancer Center

ACKNOWLEDGEMENTS

The authors grateful to the Misurata Cancer Center for it support of this study, in providing the research facilities and help in the publication of this work.

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RESULTS OF RENAL BIOPSY IN CHILDREN WITH NEPHROTIC SYNDROME AT TRIPOLI CHILDREN HOSPITAL

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ABSTRACT

Nephrotic syndrome is an important renal disorder in children. The role of renal biopsy in children with nephrotic syndrome is controversial, especially in children with frequent relapses or steroid-dependent nephrotic syndrome. The aims of this study are to verify indications of renal biopsy in children with nephrotic syndrome, to identify patterns of glomerular disease and its corresponding outcomes. This is a descriptive study reviewed retrospectively a 25 renal biopsies from children with nephrotic syndrome who followed up in nephrology unit at Tripoli Children Hospital from Jun. 1995 to Jan. 2006. Children with either steroid resistant or steroid dependent who underwent renal biopsy were included. Twenty five of children (14 male and 11 female) with nephrotic syndrome were included. The mean age 5.2±4.6years (range was from 1-14 years). 14(56%) children were steroid resistant and 11(44%) children were steroid dependent. Minimal-change disease (MCD) accounted for 12(48%) children, focal and segmental sclerosis (FSGS) was accounted for 10(40%) children and 3**(**12%) children accounted for other histopathological types. 7(87.5%) of children with FSGS had progressed to end stage renal disease. Steroid resistant was the main indication for renal biopsy in children with nephrotic syndrome. There was increased frequency of FSGS nephrotic syndrome among children with steroid resistant type with poor outcomes.

KEY WORDS: Nephrotic syndrome, Renal biopsy, Minimal change disease, Focal segmental glomerulosclerosis.

INTRODUCTION

Minimal change disease (MCD) is the most frequent lesion associated with idiopathic nephrotic syndrome in children[(1)]. In 1970, the International Study of Kidney Disease in Children (ISKDC) reported an increased frequency of MCD than focal segmental glomerulosclerosis (FSGS) and other renal pathology. On the basis of data from the ISKDC conducted in 1978, it has been accepted that MCD is by far the most frequent lesion associated with idiopathic nephrotic syndrome in children and adolescents, accounted for 77% of cases in all biopsies performed in children while FSGS represented nearly 8-10%[(2)]. However, recently several reports have been noted that there is an increase trend of FSGS in both children and adults who were biopsed for their nephrotic syndrome to rates as high as 50%[(3,4)]. The role of the renal biopsy in children with nephrotic syndrome is controversial, especially in patients with frequent relapses or steroid dependent nephrotic syndrome[(5)]. Steroid resistant still remain the main indication for renal biopsy in children with nephrotic syndrome[(6)]. Certain clinical features are consider to be atypical in steroid sensitive nephrotic syndrome these include, extreme of age (less than 1 years, or greater than 12 years), persistent hypertension, persistent renal impairment, gross hematuria and low plasma complement concentration[(7)]. It is well recognized that FSGS in children with idiopathic nephrotic syndrome carries poor prognosis. Although initially considered a resistant lesion but the data suggest that more aggressive therapies can induce a response in more than 50% of patients[(8,9,10,11)]. Our objectives are to verify the indications of renal biopsy in children with nephrotic syndrome, identifying patterns of glomerular disease frequency as well as their outcomes.

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PATIENTS AND METHODS

A retrospective review was conducted of children with idiopathic nephrotic syndrome who underwent percutaneous renal biopsy from Jun, 1995 to Jan, 2006. The study include children with steroid resistant nephrotic syndrome and children with steroid dependent who presented with atypical presentation which include Age (less than 2 years and more than 10 years), persistent hypertension, renal function impairment persistent hematuria and decrease serum complement.

At presentation, they were evaluated for hypertension, hematuria, renal function status and serum complement. After discussion with parents, kidney biopsy was performed in all patients. The procedure done in Tunisia or Jordan. The specimens had examined by light microscopy, Immunoflourenscnce stained and electron microscopy. Minimal change disease was diagnosed by normal glomeruli on light microscope, lack of immuno deposit on Immunoflourenscnce and foot process effacement by electron microscope.

In idiopathic FSGS, the glomeruli show mesangeal proliferation and segmental scaring on light microscope, Immunoflourenscnce show IgM and C3 staining in area of segmental sclerosis. By electron microscope show segmental scaring of glomerular tuft with obliteration of glomerular capillary lumen. FSGS was diagnosed when at least one glomerulus demonstrate segmental sclerosis on light microscope.

A diagnosis of steroid resistant was made if there is no response to 4-week course of prednisone at a dose of 60 mg/m2/day. Steroid dependent was defined as development of 2 consecutive relapses during steroid therapy or within 2 wk of its cessation. Hypertension was defined as a blood pressure consistently above 95th centile for height, age and sex. Hematuria and proteinuria are assessed by dipstick urine analysis.

STATISTICS ANALYSIS

After data collected they were coded and transferred into the Statistical Package for the Social Sciences (SPSS), version 12. Results are expressed as either means ± SD or percentage. The statistical tools used like frequencies, ratio, and chi-square test. The level of significance was set at P value < 0.05 in all cases.

RESULTS

This study provided the histopathological classification of nephrotic syndrome in children followed up in Tripoli Children Hospital over a period of 10 years (1995-2006) on a total 25 renal biopsies, 14(56%) were males and 11(44%) were females. The mean age 5.2 ± 4.6years (range was from 1-14 years). The mean period before biopsy was 15.8 mo (range 1-84 mo) and mean follow up duration (6.5 ± 3.1) years range (2-11) years.

The indications of renal biopsy were as following 14(56%) were steroid resistant and 11(44%) were steroid dependent as shown in (table 1).

(Table 1) Indications of renal biopsies

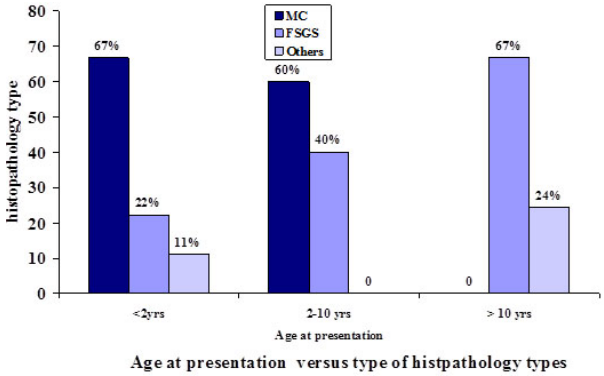
Type	MCD (%)	FSGS (%)	Other pathology	Total (%)
Steroid resistant	4(28.6)	8(57.1)	2(14.3)	14(56)
Steroid dependent	8(72.1)	2(18.2)	1(9.1)	11(44)
Total	12(48)	10(40)	3(12)	25(100)

MCD minimal change disease, FSGS focal segmental glomerulo-sclerosis SR steroid resistant, SD steroid dependent.

Other histopathology accounted for 3(12%) which include lupus nephritis in one case, IgA nephropathy in one child and mesangio proliferative glomerulosclerosis (MPGN) in one child.

At presentation 12(48%) of these children had presented with typical presentation and 13(52%) had presented with atypical presentation. The atypical presentation include extreme of age, hypertension, hematuria, renal impairment, low serum complement.

When compare age at presentation versus histopathology types of nephrotic syndrome 9(36%) children were less than 2 years of age, 10(40%) children are between 2-10 years of age and 6(24%) are more than 10 years of age as shown in (figure 1).



(Figure 1) age at presentation n versus Type of histopathology types

When compare MCD with FSGS and other histopathology types, children MCD were younger at diagnosis than FSGS and other pathology (2.9yeares versus 7 and 8.7 years), boys were more likely to be MCD than FSGS (64.3% versus 28.6%) and steroid resistant children were more likely to be FSGS than MCD while steroid dependent were more likely to be MCD than FSGS as shown in (table 2).

(Table 2) MCD versus FSGS and other histopathology types

Characteristic	MCD	FSGS	Other pathology
No. of children	12	10	3
Mean age at presentation	2.9 ± 2.5 yrs	7 ± 4.8 yrs	8.7± 6.9 yrs
Male: female ratio	3	0.66	0.5
Steroid resistant	23%	61.50%	15.50%
Steroid dependent	75%	16.70%	8.30%

MC minimal change disease, FSGS: focal segmental glomerulonephrosis

Regarding the clinical outcomes of these children a chi-square was done between histopathology types and development of end stage renal failure, no children with MCD advanced to end stage renal failure however 7(87.5%) of children with FSGS progressed to end stage renal failure as shown in (table 3).

(Table 3) Long term follow up

Type	No RF (%)	RF (%)	Total (%)	P value
MCD	12(48)	0(0)	12(48)	0.002
FSGS	3(17.6)	7(87.5)	10(40)	0.001
Others	2(8)	1(4)	3(12)	0.001
Total	17(68)	8(32)	25(100)	

MCD minimal change disease, FSGS: focal segmental glomerulonephrosis, RF: renal failure

DISCUSSIONS

Idiopathic nephrotic syndrome in children has conventionally been associated with minimal change disease. White et al reported that MCNS in up to 90% among all children with idiopathic nephrotic syndrome, FSGS has generally been considered a

relatively infrequent cause[1]. In first ISKDC report (1970) 127 children, MCD was diagnosed in 77%, FSGS in 9% and MPGN in 5% of children who were biopsy prior to treatment[2]. In second ISKDC report (1978) 521 children, FSGS account only for 7%[3]. In recent studies there were increased trends in FSGS as high as 50%[4,12,13]. In this study, there was an increasing trend for FSGS which accounted for 10(40%) in these children who under went renal biopsy while MCD was found in 12(48%). This figure was different from ISKDC previous reports. The increase in frequency of FSGS case is mainly due to highly selectiveness of cases and renal biopsies are not usually preformed in children with idiopathic nephrotic syndrome and being recommended for the small proportion of atypical cases. 57% of children with steroid resistant were FSGS while 72.1% of children with steroid dependent were MCD. Steroid resistant still the most common important indication for biopsy in children with nephrotic syndrome[8] it accounted for 14(56%) in this study. The second indication for renal biopsy was steroid dependent nephrotic syndrome it accounted for 11(44%).

The incidence of MCD has been found to be higher in younger children presented with idiopathic nephrotic syndrome. However FSGS and other renal pathology found to be more in older children. Girls were more likely than boys to develop FSGS and other pathology than MCD these finding was similar to Olivia B et al[10].

Churg et al reported that children with FSGS at time of diagnosis of nephrotic syndrome showed a clinical pattern of rapidly developed steroid resistant and commonly progressed to end stage renal disease (ESRD)[1]. The South west paediatric nephrology study group reported that 21% of children who biopsed for steroid resistant had development of ESRD[1]. In this study there were a high percentage of children who diagnosed as FSGS by renal biopsy progressed to ESRF (87.5%) this high rate may be related to late presentation of these children and late performing a renal biopsy. In many studies including this study MCD had excellent prognosis, the current recommendations of kidney biopsy in childhood idiopathic nephrotic syndrome were put forward to minimize unnecessary kidney biopsies in children with idiopathic nephrotic syndrome.

CONCLUSION

MCD remains the most common histopathological subtype in children with steroid dependent nephrotic syndrome while FSGS is the most histopathological subtype in children with steroid resistant nephrotic syndrome. Most children with steroid resistant due to FSGS progressed to end stage renal disease at the same time no children with MCD progressed to end stage renal disease. Based on these observations, we recommended minimizing renal biopsy in children with steroid dependent nephrotic syndrome. FSGS children were more likely to be girls, older age at presentation and steroid resistant. Children with MCD were more likely to be boys, younger age at presentation and steroid dependent. Renal biopsy should be done as early as possible in children with steroid resistant nephrotic syndrome and more aggressive therapeutic modalities for children with FSGS pathology.

ACKNOWLEDGMENT

Thanks are due to Dr. Omar abosnena community medicine at Tripoli University for his guidance, advice and kindness.

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THE DIAGNOSTIC YIELD OF CORE NEEDLE US-GUIDED TRANSTHORACIC LUNG BIOPSY IN THE DIAGNOSIS OF PERIPHERAL LUNG LESIONS COMPARED TO FLEXIBLE BRONCHOSCOPY A SINGLE CENTER STUDY FROM TRIPOLI-LIBYA

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ABSTRACT

Safe and effective diagnostic modalities are needed for the assessment of peripheral lung lesions. Ultrasound (US) guidance for trans thoracic lung biopsy (TTLB) is safer, quicker, and less expensive than guidance by CT or fluoroscopy, and unlike flexible bronchoscopy (FB); TTLB allows the operator to biopsy the lesions without relying on central airway anatomy to reach the target. This is a descriptive prospective study to evaluate the diagnostic yield of core needle US-guided TTLB in the diagnosis of peripheral lung lesions compared to FB.

Patients with peripheral lung lesions referred to the respiratory clinic at Tripoli Central Hospital during the period from July 2005 to December 2014 were evaluated. They were subjected to history taking, clinical and radiological examination. Flexible bronchoscopic (FB) examination was performed with or without transbronchial biopsy (TBB). When the FB was negative or the biopsy was inconclusive or needed to be confirmed, core needle US-guided transthoracic lung biopsy (TTLB) was performed. 8 patients were considered clinically fit for FB and directly underwent TTLB. None of these patients had INR >1.5, platelets < 100,000/ml, forced expiratory volume (FEV1) <35% of predicted, pulmonary hypertension, severe respiratory failure, sever, emphysema, or previous pneumectomy. Samples taken from suspicious sites were sent for histopathological examination.

The 91 consecutive patients were involved in the study, 76 (83.5%) were males and (15%) were females, their mean age was 63.8 ±17.9 (SD) (range 16-91 years). In 83 patients FB was performed, out of them 65 had transbronchial biopsy (TBB). TBB histopathology results gave a clear diagnosis in 28/83 patients (33.7%). The 91 patients underwent TTLB and a tissue diagnosis was obtained in 81 (89%) patients. 64/91 patients (69.2%) had malignant lesions and 17 patients (18.7%) had benign ones. In the remaining 10 (1.1%) patients the result was inadequate or inconclusive. The diagnostic yield of TTLB in the 38 patients who had normal FB findings was 92.1%; 22/38 had malignant and 13/38 had benign lesions. Malignant lung lesions were significantly associated with older age. Squamous cell lung cancer was detected in 17/91 patients (18.7%), adenocarcinoma in 15/91(16.5%) and small cell carcinoma 14/91 (15.4%) patients. No serious complication was reported except for a pneumothorax that necessitated chest tube insertion in one patient (1.2%). The diagnostic yield of TBB in this study was low (33.7%). The yield of US-guided TTLB was high (89%) and was higher (92.1%) in the patients with negative FB findings. Overall 69.2% of the studied patients had malignant lung lesions that were significantly associated with older age, and squamous cell cancer was the most frequent diagnosis.

KEY WORDS: Peripheral lung lesions, Ultrasound-guided transthoracic lung biopsy, Core needle biopsy.

INTRODUCTION

In the evaluation of a patient with suspected lung lesions, it is important to decide on the optimal site and modality for the tissue biopsy[(1)]. Lung samples may be obtained by transbronchial lung biopsy (TBLB), computed tomography (CT)-guided, video-assisted thoracoscopic, or surgical biopsy[(2)]. For patients with symptoms suggestive of airways involvement such as, increasing cough or hemoptysis with or without radiographic finding of central lesions; flexible bronchoscopy (FB) is preferred diagnostic procedure[(3)]. The principal advantages of FB include an extensive view of the tracheobronchial tree, no requirement for general anesthesia and low complication rate[(4-6)]. The overall diagnostic yield of FB varies depending on the size, location and extent of the lung lesion. In addition to the nature of underlying lung disease, the results of TBLB also depend on the experience and technical skills of the bronchoscopic operator[(7)]. Patients with negative bronchoscopy require more concerted effort to achieve a timely diagnosis and treatment[(8,9)].

US-guided TTLB is a well-established technique capable of providing sufficient tissue for histopathologic diagnosis of lung lesions. It is safe, quick, and less expensive[(10,11)] and according to the BET Guidelines 2003[(2)]; it should be used when possible. Like TBLB, the results of TTLB depend on the experience and technical skills of the physicians performing the procedure who should have excellent knowledge of pleural and thoracic anatomy and good judgment in interpreting the ultrasound images. The biopsy can be taken by either fine needle aspiration (FNAB) for cytological examination or core needle biopsy (CNB) for histological examination. The diagnostic yield of both FNAB and CNB are

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reported to be high, though, CNB is superior in benign lesions[12,13]. According to the BET Guidelines 2003; the decision on the type of needle used depends on the operator experience, available cytological support, and the position of the lesion**.**

The aim of this study is to evaluate the diagnostic yield of TTLB performed at the respiratory clinic in Tripoli Central Hospital and to compare it with the FB yield.

MATERIALS AND METHODS

Prior chest imaging (when available) was reviewed and CT scan chest was performed to evaluate and localize the pathology site. Patients with any of the following were excluded; INR > 1.5, PTT > 40, Platelets < 100,000/ml, Forced expiratory volume (FEV_1) <35% of predicted, pulmonary hypertension, severe respiratory failure, or sever emphysema. FB was performed in 83 patients, out of them 65 had transbronchial biopsy (TBB). The TTLB was performed jointly by a senior consultant physician with outstanding experience in US and a senior respiratory physician using an Aloka US unit (Tokyo, Japan) model SSD 4000 with Doppler and 3.5- MHz small-sector convex probe. A dedicated cytopathologist was not available, so CNB was chosen using True-cut needle (18G - 20G). Samples obtained were placed in formalin and sent for histopathologic examination. At the end of the procedure, the patient was examined by auscultation for the presence of pneumothorax and an erect chest X-ray was performed 1 hour after the biopsy. Most of the biopsies were performed on inpatients.

Data analysis:

It was performed using the SPSS software (Statistical Package for the Social Sciences, version 16.0 (SPSS Inc, Chicago, Ill, USA). Continuous variables are demonstrated as means (±SD), and categorical variables as numbers and percentages. Categorical variables were analyzed by chi-square test and student's t-test for continuous variables. P values less than 0.05 were considered significant.

RESULTS

As shown in (table 1); the study included 91 consecutive patients, 76 of them (83.5%) were males and (15%) were females, their mean age was 63.8 ±17.9 (SD) (range 16-91 years). The radiological diagnosis was cavitating lesions in 10 patients, opacities in 43 and mass lesions in 36 patients. FB was performed in 83 patients and showed; visible endobronchial growth in 35 patients (42.2%), endobronchial narrowing in 12 patients (14.4%), and normal findings in 38 patients (45.8%) patients. In 65 out of the 83 patients TBLB samples were taken. The TBLB histopathology results gave a clear diagnosis in only 28/83 patients (33.7%); 24 patients (28.9%) had malignant lesions and 4 (4.8%) patients had benign ones. All of the studied patients underwent TTLB and a tissue diagnosis was obtained in 81 (89%); malignant lesions in 64/91 patients (69.2%) and benign lesions in 17 patients (18.7%). In the other 10(%) patients the result was inadequate or inconclusive.

(Table 1) Summary of radiologic, FB, TBB, and TTLB findings of the 91 studied patients

Parameter	Percentage or mean
Age	63.8±17.9, (range 16-91 years
Gender (males)	76/91 (83.5%)
Radiological diagnosis	
Cavitating lesion	10/ 91(11%)
Opacity	43/ 91(47.2%)
Mass	36/ 91(39.6%)
FB	83/91(91.2%)
Visible endo-bronchial growth	35/83 (42.2%)
Narrowing	12/83(14.4%),
Normal FB visual yield	38/83 (45.8%) 47/83 (56.6%)
Transbronchial biopsy(TBLB)	
Tissue diagnosis	28/83 (33.7%)
negative or inconclusive	37/83 (44.6%)
not performed **Total FB diagnosis yield**	18/83 (21.7%) 28/83 (33.7%)
Transthoracic lung biopsy (TTLB)	91/91 (100%)
Tissue diagnosis	81/91 (89%)
Malignant lesions Benign lesions Inconclusive **TTLB diagnostic yield**	64/91(69.2%) 17/91 (18.7%) 10/91(11%) 81/91(89%)

Percentage or mean ±SD

(Table 2) shows the TTLB results of the 38 patients who had normal FB findings; 22/38 (57.9%) had malignant lesions, and 13 (34.2%) had benign lesion with a total diagnostic yield of 35/38 (92.1%).

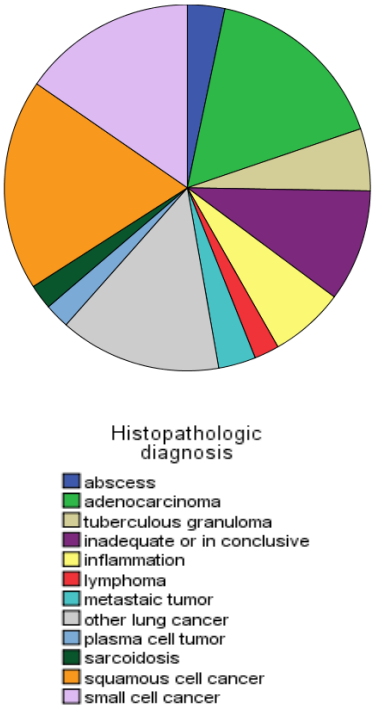
(Table 2) Histopathology results of TTLB in the 38 patients with normal FB

Diagnosis	percentage
Malignant lesion	22/38 (57.9%)
Benign lesion	13/38 (34.2%)
Non-conclusive	3/38 (8%)
Diagnostic yield of TTLB	35/38 (92.1%)

(Table 3) and (figure 1) show the histopathologic results of the TTLB samples; squamous cell lung cancer was the most frequently reported malignancy 17/91(18.7%), followed by adenocarcinoma and small cell lung cancer 15/91(16.5%) and 14/91(15.4%) respectively.

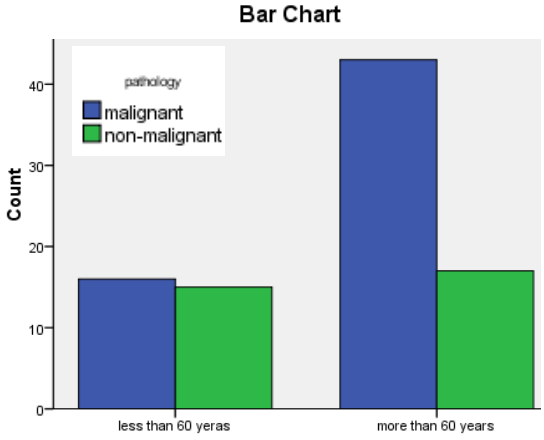
(Table 3) Histopathology results of the TTLB performed in the 91 studied patients

Diagnosis	Percentage
Adenocarcinoma	15 /91(16.5%)
Squamous cell carcinoma	17/91(18.7%)
Small cell carcinoma	14/91(15.4%)
Other lung cancer	12/91(13.2%)
Metastatic tumor	3/91(3.3%)
Lymphoma	2/91(2.2%)
Plasma cell tumor	2/91(2.2%)
Sarcoidosis	2/91(2.2%)
Tuberculosis granuloma	5/91(5.5%)
Abscess	3/91(3.3%)
Inflammation	6/91(6.6%)
Inadequate or inconclusive	10/91(10.1%)



(Figure 1) Distribution of the studied patients by the histopathologic diagnosis

The mean age of the patients with malignant lesions was 68.1 ± 15 years compared with 53.4 ± 20.2 for patients with benign lesions (P <.000) (figure 2), and 52 of them were males (P .370).



(Figure 2) Age and pathologic diagnosis

DISCUSSION

According to the result of a comparative systematic search performed by Rivera et al[3]; the diagnostic yield of bronchoscopy for peripheral lung lesions more than 2 cm in diameter was (63%) compared with (34%) yield for lesions less than 2 cm (34%). The (33.7%) diagnostic yield of FB in this study was comparable. According to Rivera et al findings; the pooled diagnostic yield of TTNA for the diagnosis of lung cancer was 90%. The results of this study were comparable too with (89%) diagnostic yield for TTLB.

Previous studies by Milam et al[14] and Levine et al[15] showed (73.8%) and (43%) diagnostic yield of TTLB following negative FB. In this study, following negative FB findings in 38 patients, the diagnostic yield of TTLB was higher (92.1%).

In 10 out of the 91 patients (10.1%), the result of TTLB was inadequate or inconclusive, which could have been due to inadequate needle adjustments, or extensive central necrosis[16]. A repeat biopsy would have been recommended but the patients were lost for follow up.

Pneumothorax is the most frequently encountered complication of TTLB, with reported incidence of (21% – 43%)[17], in this study, one patient developed pneumothorax that needed chest catheter insertion (1.2%). No other complication reported.

Like other solid tumors, lung cancer is predominantly a disease of the elderly[18]. 83.5% of this study patients were males with a mean age of 63.8 ±17.9 and based on the TTLB results; 64 out of the 91 studied patients (69.2%) had malignant lesions .The malignancy was statistically associated with older age (P <.000), but not with male gender (P .370). The most frequently detected lung malignancy was squamous cell cancer in 18.7%, followed by adenocarcinoma in 16.5% and small cell carcinoma in 15.4% of the patients.

CONCLUSION

In this study the diagnostic yield of TBB in the suspected peripheral lung lesions was low (33.7%) compared with 89% diagnostic yield for US-guided TTLB. Following negative FB findings, the diagnostic yield of TTLB was higher (92.1%). US-guided TTLB was safe with 1.2% complication rate. Malignant lung lesions were detected in 69.2% of all cases study, and squamous cell cancer was the most frequent diagnosis.

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THE INCIDENCE OF POST TONSILLECTOMY BLEEDING IN CHILDREN AND ADULTS

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ABSTRACT

This retrospective study was conducted in Ear, Nose and Throat (ENT) department at Misurata Central Hospital, during the period from January 2006 to December 2007. The aim is to evaluate the incidence of post tonsillectomy haemorrhage in relation to the age, gender and post operative period. The files of 253 patients were reviewed. 153 patients were younger than 15 years and 100 patients aged 15 years and older. All patients underwent tonsillectomy with or with out adenoidectomy. Six patients (2.4%) experienced bleeding within 8 days postoperatively, 4 (1.6%) out them developed the bleeding in the first 24 hours. The bleeding was more in the adult group than the paediatric group (4% vs 1.5%). Compared with other studies, the result was almost the same.

KEY WORDS: It is worth noting that awareness of this factor should help in improving the outcome.

INTRODUCTION

Post tonsillectomy bleeding is the most significant complication of tonsillectomy. The haemorrhage is classified as reactionary (primary) or secondary. The reactionary bleeding occurs up to 24hrs, but the vast majority occurs within the first 8 hrs. However, the secondary bleeding occurs after 24hrs, and classically occurs at the 10th day[(1)].

In fact, reactionary bleeding is dangerous in 2 ways: first, in the phase during which the patient is recovering from anaesthesia, before cough reflex is fully established, blood in the airway can result in laryngeal spasm or asphyxiate the patient by mechanically occluding the air way. Second, severe bleeding, may leads to circulatory failure and death. Furthermore, it may be needed to retake the patient to the OT to stop the bleeding. The second anaesthesia, of course, is hazardous and carries risk of mortality because the patient has already exposed to anaesthesia, has blood in the airway, is hypovolaemic from blood loss and also my has a stomach full of blood[(1)].

In regards to secondary haemorrhage, it is not as common as reactionary bleeding, and usually less severe than reactionary bleeding. But it must be taken seriously as it does has mortality rate.

THE AIM OF THE STUDY

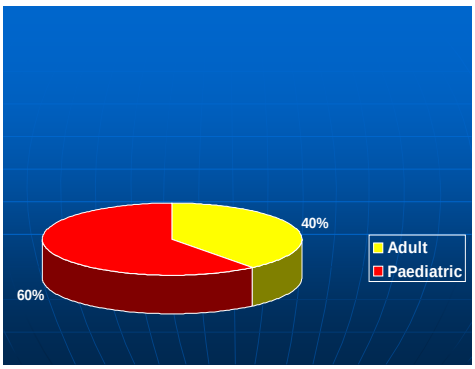
The aim of this study to establish the incidence of post tonsillectomy bleeding in children and adults in relation to age, gender and operative period .

PATIENTS AND METHODS

Over two years (2006 and 2007), the files of 253 patients who underwent tonsillectomy with and without adenoidectomy at Misurata Central Hospital were studied .The indications of surgery were recurrent tonsillitis, previous attack of quinsy and upper respiratory tract obstruction. Patient who had risk of haemorrhage was excluded from the study. The age of patients was ranged from 2,5 - 44 years. The patients are divided into paediatric group (less than 15 years old) and adult group (aged 15 or more). This classification is based on the opinion of many paediatric society as they use 15 years old as borderline for the adulthood. The surgery was done under G A by dissection technique. The haemostasis was achieved mainly by cautry or by ligature. The patients refrained from drinking for 4 hours and from eating for 24 hours postoperatively, and discharged next day. The haemorrhage is classified according to its severity into: mild (controlled without surgical intervention), moderate (with surgical intervention), and severe (surgical intervention and blood transfusion), and all of them were included in our study.

RESULTS

The files of 253 patients who underwent tonsillectomy at Misurata Central Hospital were studied respectively. The pediatric group was 153 patients (60%), while the adult group was 100 patients (40%) (figure 1). Males to females ratio in paediatric group was 1 : 1.3, while in the adult group it was 1 : 2.1. Out of the paediatric group, only 2 patients (1.5%) experienced bleeding (one male & one female) postoperatively, compared with 4 patients (4%) (one male & 3 females) out of the adult group (figure 1).



(Figure 1) Age distribution

Among the children, the bleeding was only secondary in both genders at 1.5% in the male group and

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1% in the female group. However, among the adult patients, the haemorrhage was only primary in both groups, (3.2%) in males and (4%) in the females. In two female patients the bleeding was not controlled conservatively, exploration and control of the bleeding was achieved under general anaesthesia. The bleeding was arterial in one case and was ligated, in the other case the bleeding was due to diffuse oozing from the tonsillar bed, this was controlled by packing, and she received two units of blood.

Regarding the total percentage of the post operative bleeding, it was 2.4%, with the children accounted for 0.7% and the adults 1.7%. Similarly, the percentage of the primary and secondary bleeding was at 1.7% and 0.7 respectively. Male to female ratio followed the same pattern at 1.7 for the females and 0.7 for the males (table 1).

(Table 1) Percentages and type of bleeding, including male to female ratio, among the paediatric and adult groups.

Age	No. of pts	M:F	% of Hge	% of 1^{ry} Hge	% of 2^{ry} Hge
< 15	153 (60%)	1:1.3	1.5%	0%	100%
≥ 15	100 (40%)	1:2.1	4%	100%	0%

DISCUSSION

Although the post tonsillectomy haemorrhage is uncommon, it may lead to serious complications. Therefore, every consideration should be taken to prevent it. Once it happens it should be managed urgently. In general, post tonsillectomy haemorrhage occurs in fewer than 10% of cases[11], The reported incidence of haemorrahnge ranges from 0.38 to 6%[5,7,10].

In this study, the total rate of bleeding was 2.4%, it is comparable with that at Yamanda Red Cross Hospital in Japan (2.7%)[2], and with that at St Lukes Hospital in Matla (3.2%)[3]. Indication of surgery appears to be associated with age, adenotonsillectomy are being performed to treat upper air way obstruction caused by adenotonsillar hyperplasia, but in adult the primary indication is infection[10,11]. According to result of this study, chronic or recurrent infection likely to play a role in incidence of post operative bleeding, this is based on the facts that there was a significantly higher incidence of post tonsillectomy haemorrhage in adult as compared to children (4% vs 1.5%). This finding is in agreement with study of Robert et al[9] and Myssiorek et al[8]. It is noted that the rate of bleeding in adults (4%) and children (1.5%) was obviously different. The percentage was close to that conducted in Germany at Anna Lukes Hospital at 3.9% and 1.6%[6]. During post operative period of tonsillectomy several complications may occur and the haemorrhage is the most severe one[8]. Cause of haemorrhage is lack of visualization of vessels[4] which is not ligated or improper ligation, injuries to tonsillar bed during tonsillectomy[10]and improper check for bleeding lead to more bleeding during intraoperative period.

Most of the studies reported that primary haemorrhage is more common than secondary haemorrhage ,generally acknowledged to poor surgical and inadequate intraoperative haemostasis, is a risk factor for post tonsillectomy haemorrhage[8]. It is also observed in this study that primary haemorrhage (1.7%) is more common than secondary haemorrhage (7%) .

CONCLUSION AND RECOMMENDATION

To sum up, it is apparent from the study that incidence of post-operative bleeding following tonsillectomy increase with age .

Adults with chronic tonsillitis and poor surgical technique were most risk factor for post tonsillectomy haemorrhage. An awareness of these factors can help identify patients with potential bleeding post operatively and tonsillectomy can be safely carried out in a protocol technique. We recommended giving more attention to adult patients in terms of the experience of the surgeon.

ACKNOWLEDGEMENT

We express our sincere appreciation to Dr Mohamed Hussain and Dr Ali DugDug for helping us in conducting this study.

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MALIGNANT SKIN TUMOURS IN MISURATA CANCER CENTRE DURING 2011 - 2014

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ABSTRACT

Skin cancer is a common malignancy worldwide. Non-melanoma skin cancer (NMSC) is the most common cancer affecting white individuals and Caucasian populations. Melanoma represents 4% of all new cancers whereas incidence of non-melanoma skin cancer (NMSC) is nearly equal to that of all non-cutaneous cancers in United States of America. The development of NMSC, including both squamous and basal cell carcinomas is related to ultraviolet light (UV). Alternatively, etiology of melanoma is either due to genetic defects (familial melanoma) or interactions of low-penetrance genes and UV (sporadic melanoma). Malignant tumor able to invade the surrounding tissues and/or metastasize to other parts of the body. Light skin, hair and eye colors, family and personal history of skin cancer, certain types and a large number of moles and people with history of sunburn early in life (as in case of malignant melanoma) are at high risk of skin cancer. This study is aimed to identify epidemiological features of skin cancer in Misurata Cancer Center during 2011- 2014. Total number of cases were 195, out of them 44 (22.5%) cases with malignant skin tumour, basal cell carcinoma 17 (38.6%) cases, squamous cell carcinoma 20 (45.5%) cases, malignant melanoma 3 (6.8%) cases, dermatofibrosarcoma 4 (9%) cases and one (2.3%) case with metastatic skin cancer from a primary in the breast. Early diagnosis and accurate and up-to-date records on skin tumors are necessary for quantification of changes in its incidence to allow for research and planning of services.

KEYWORDS: Malignant skin tumour, Patient age and gender, Site of tumour.

INTRODUCTION

Skin cancer is a common malignancy worldwide. Non-melanoma skin cancer (NMSC) is the most common cancer affecting white individuals and Caucasian populations , and incidence rates are increasing . Melanoma represents 4% of all new cancers whereas incidence of non-melanoma skin cancer (NMSC) is nearly equal to that of all non-cutaneous cancers in United States of America. Three main types of skin cancer are basal cell carcinoma (BCC) which is the commonest skin cancer, locally invasive carcinoma of the basal layer of the epidermis, 30% multiple, metastatic rate is 0.0028%, M:F approximately 2:1, Common sites are in the region above a line drawn between the corner of the mouth and the lobe of the ear (75% occur in the head and neck)[1,2].

Squamous cell carcinoma (SCC) is a malignant tumour of the epidermis in which the cells ((if differentiated)) show keratin formation. 5% of SCCs metastasise, in men the common sites are ears and scalp and in women more in the lower limbs, but in both sexes involving back of hands and face.

Malignant melanoma (M.M) is a malignant tumour of epidermal melanocytes , Spread occurs via superficial lymphatics to give satellite lesions, to regional lymph nodes via deep lymphatics, and via haematogenous spread[3,4].

Malignant melanomas undergo two growth phases radial and vertical which is a poor prognostic sign M.M May be found when a pre-existing mole shows a new black area, texture changes, itching, oozing, or bleeding .

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AIM AND OBJECTIVES OF THE STUDY

This study aims to identify the epidemiological features of skin cancer.

METHODS AND SUBJECTS

A retrospective study of patients following the Plastic and Dermatology out-patient department (with skin lesions who admitted and managed in Plastic surgery department) in Misurata Cancer Center was conducted.

All histopathologically proven cases of skin cancer reported during the years 2011 through 2014 were retrieved and reviewed. Information regarding tumour type, age, gender, and anatomical location were collected and results had been compared with other similar studies.

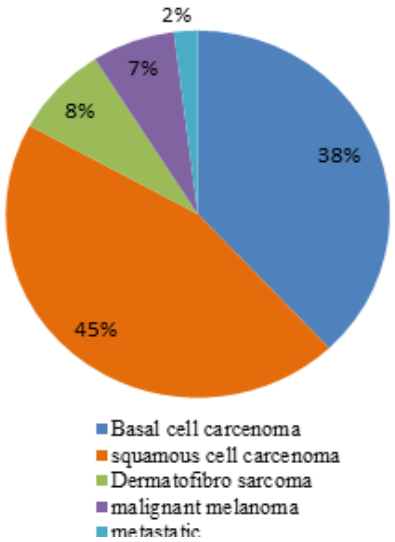
RESULTS

Total number of cases was 195, 44 out of them with malignant skin tumours, basal cell carcinoma 17 cases, squamous cell carcinoma 20 cases, malignant melanoma 3 cases, dermatofibrosarcoma 3 cases and one case with metastatic skin cancer from a primary in breast (figures 1 and 2).

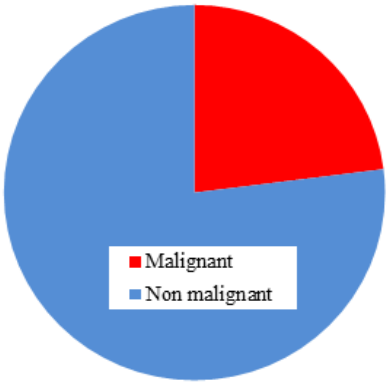
Basal cell carcinoma:

Number of cases with basal cell carcinoma are 17. Ten cases were males (59%) and 7 cases females (41%), the mean of patient age 70 years . The most common sites are nose (45%), scalp (30%), cheek (25%), respectively. Histopathology reports showed free resection lines for all. See (figures 3,4) and (photos 1,2 and 3).

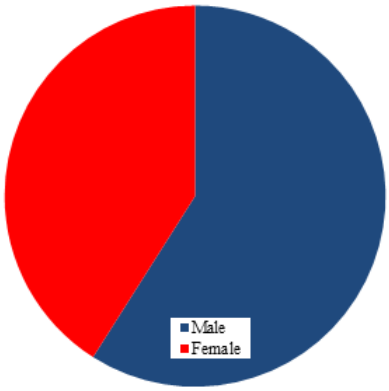
Squamous cell carcinoma (scc):
20 cases was showing scc, 14 cases males (70%) and 6 cases females (30%). The mean age is 60 years. The most common sites are: scalp, ears and limbs respectively. Histopathology reports of six cases revealed that the resection margins were involved, (figures 5,6) and (photos 4,5).



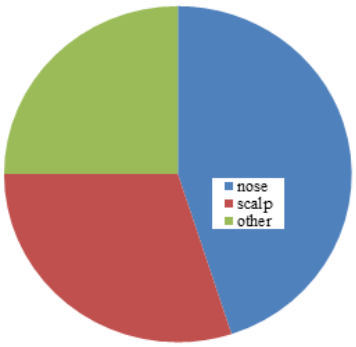
(Figure 1) Distribution of malignant skin tumours



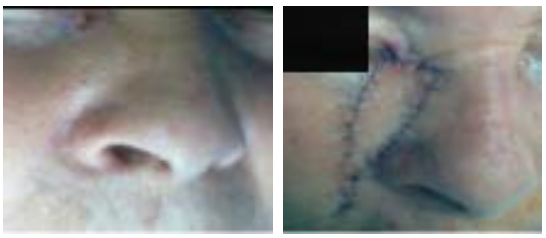
(Figure 2) Distribution of malignant to non-malignant cases



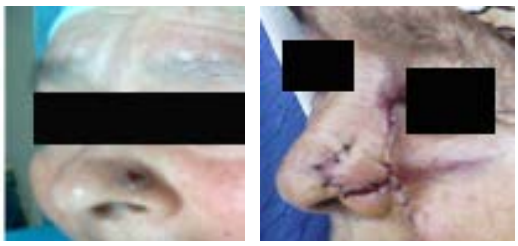
(Figure 3) Sex distribution of BCC cases



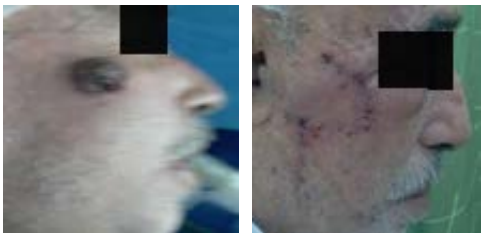
(Figure 4) Site distribution of BCC cases



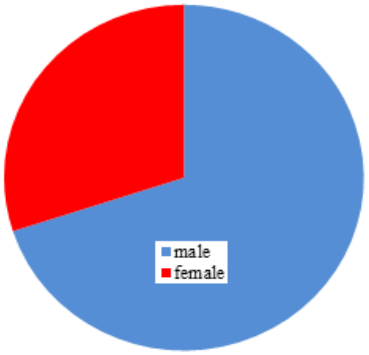
(Photo 1) BCC right inner canthus pre & post-operative



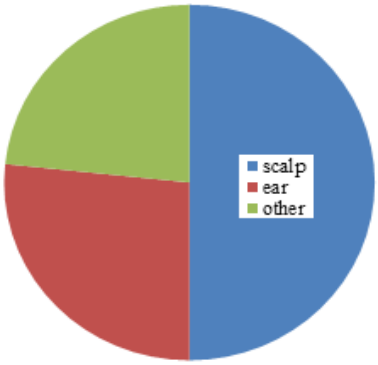
(photo 2) BCC left ala nasi pre & post-operative



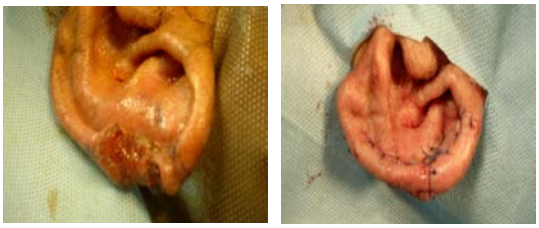
(Photo 3) BCC right zygomatic area pre & post-operative



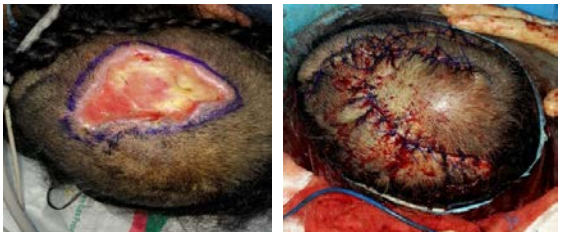
(Figure 5) Sex distribution of SCC cases



(Figure 6) Site distribution of SCC



(Photo 4) SCC right ear pinna pre & post-operative

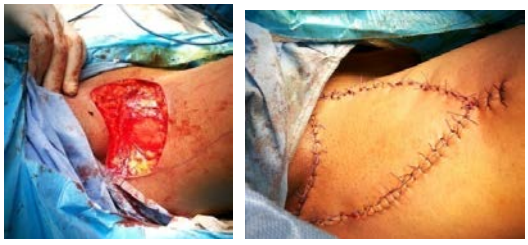


(Photo 5) SCC scalp pre & post-operative

Metastatic skin lesion:
One case is female patient 30- year old shows metastatic skin nodule because of advanced breast cancer.

Malignant melanoma:
3 cases, female- gender with mean age 45 years, diagnosed as malignant melanoma . 2 cases in lower limbs and one in anal margin, two of them re-excised , because of not enough excisional margin.

Dermatofibrosarcoma:
4 cases, 2 females and 2 males , the mean age was 35 years . All of them presented with mass in the thigh and diagnosed as dermatofibrosarcoma 2 cases were recurrent), one case was re-operated because of involved resection margin . (photo 6).



(Photo 6) Dermatofibrosarcoma right thigh

DISCUSSION AND CONCLUSION

About 23% of total cases with skin lesions managed in MCC were malignant , mainly SCC and BCC.
Male gender affected more with SCC & BCC while M.M is more in females, and the same incidence in both gender with dermatofibrosarcoma.
The SCC and BCC were more common in old age group of patients (60 to 80 years) and the M.M and dermatofibrosarcoma were involving more younger age of cases (between 30-50 years).
Nose, scalp and ears are the sites of BCC and SCC, while the limbs are the sites of M.M and dermatofibrosarcoma.
High number of cases re-operated because of involved resection line (because of lack of Mohs surgery in our centre).
In contrast to studies performed in other countries gender and age distribution and anatomical sites involved are similar but SCC cases (45.45%) exceeding the number of BCC (38.63%) in our study and that is may be related mainly to the awareness of referral doctor regarding site of involvement and clinical presentation suggestive of SCC; then dermatofibrosarcoma protuberance (9.09%) and M.M (6.8%), while in Tunisia BCC was the most frequent type (57.5%) followed by SCC (32.6%) then the M.M (4%)[5]. Also, in Southwestern Saudi Arabia, in northern Jordan and in Hyatabad (Peshawar) the most common skin cancers seen are BCC (41%), (52.9%), (32%) and SCC (29%), (26.4%), (18%) respectively followed by Kaposi's sarcoma (18%) then melanoma (4.1%) in Saudi Arabia and Melanoma (11.39%) in Jordan and Melanoma (10%). Mycosis Fungoides (9%) and then Actinic keratosis, Kaposi's sarcoma, Bowen's disease, Dermatofibroma, Atypical fibroxanthoma constituted the remaining in Hyatabad (Peshawar) study[6,7,8].
In Bahrin study: The histological types of skin cancer in the Bahraini group were as follows (50%) patients with BCC, (31.3%) with SCC, (5%) with dermatofibrosarcoma, (4.2%) with melanomas, (4%) with lymphomas, and (5.5%) with other tumours[9].
In Singhabour, the commonest skin cancer was BCC (36.5%), followed by SCC (24.4%), Bowen's disease (16.7%), and mycosis fungoides (9.0%). Malignant melanomas were rare (2.7%).[10] In other hand malignant melanoma was the most common dermatological malignancy in north-western Tanzania (67.5%) which were acral and referred as chronic ulcers followed by Kaposi's sarcoma (10.4%), Squamous cell carcinoma (8.4%) and Basal cell carcinoma (7.8%) . The lower limbs were the most frequent site involved accounting for 55.8% of cases[11].
In Germany similar to other European countries superficial spreading melanoma was the most frequent clinical type (39.1%). The tumours were predominantly located on the trunk in men (46.8%) in contrast to leg and hip in women (39.5%). For NMSC,

More than 80% of all cases were basal cell carcinomas[12].

In our country, sun-related skin cancers have relatively high frequency and a rather stable pattern, compared with other areas with similar climate and skin phenotypes therefore increased awareness by dermatologists, general practitioners and the population can influence the detection of tumors that would have passed unnoticed before. Public health campaigns can also contribute.

RECOMENDATIONS

Early diagnosis and accurate and up-to-date records on skin tumors are necessary for quantification of changes in its incidence to allow for research and planning of services.

Increased awareness of population to avoid outdoor activities during the middle of the day and to seek shade and to protect the skin as possible as they can.

We are in great need of better documentation of cancer cases in Libya and the national tumor registry should be established.

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POSITIVE FECAL OCCULT BLOOD TEST IN CORRELATION WITH INTESTINAL PARASITIC INFECTIONS

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ABSTRACT

700 Stool samples were examined for intestinal parasitic infection and for fecal occult blood among those attending the outpatient department of Ibn-Sina hospital in Sirte-Libya. This work aims to determine the intestinal parasitic infections associated with positive fecal occult blood. Our results showed that 532 samples (76%) were detected positive for parasitic infections (P< 0.0001), *Entamoeba histolytica* was the commonest parasitic infection detected (36.3%). The positive FOB test was observed in 166 samples (23.7%) of the total examined samples, 140 samples (84.3%) of the positive FOB test samples were correlated with the intestinal parasitic infection (P<0.0001), 120 samples of them (72.3%) were correlated with *Entamoeba histolytica* infections (P<0.0001). The present study demonstrated that positive FOB test during routine analysis was correlated with the intestinal parasitic infections, especially with *E. histolytica* rather than any other causes.

KEY WORDS: Parasitic infection, Occult blood, Stool samples.

INTRODUCTION

Infections due to intestinal parasites caused by helminths and protozoa still constitute one of the major causes of public health problems in the world, particularly in developing countries[1,2]. The main intestinal parasites that infect man are Entamoeba histolytica, Balantidium coli, Giardia lamblia, Isospora belli, Cryptosporidium species, Taenia saginata, Taenia solium, Hymenolepsis nana, Dipyllidium caninum, Diphylobothrium latum, Fasciolapsis buski, Metagonimus yokogawai, Heterophyses spp, Ascaris lumbricoides, Trichuris trichiura, Entrobius vermicularis, Hook worms, Strongyloides stercoralis and Schistosoma mansoni[3].

Fecal occult blood (FOB) refers to a nonvisible blood in the stool[4,5]. Several parasitic intestinal infections are correlated with positive FOB including Trichuris trichiura, Hookworm, Schistosoma spp. And Entamoeba histolytica[6,7,8].

This work aims to determine the intestinal parasitic infections correlated with positive fecal occult blood among those attending the outpatient department of Ibn-Sina hospital in Sirte-Libya.

MATERIALS AND METHODS

1- Parasitologic Examination

A-Collection of stool samples:

Stool specimens were collected in a clean, wide mouthed containers with a tightly fitted lid and the time of collection was recorded on the container, which was properly labeled.

B-Direct fecal smear:

Each sample was processed and examined immediately after collection using direct fecal smears (Normal saline, Iodine, Eosin)[9]. Soon after direct smear, the samples were microscopically examined.

C-Centrifugal saline sedimentation technique:

The samples were concentrated as described by Baroody B. J. And Most, H.[10].

2- Fecal occult blood technique

A Commercial kit (guaiac-based test) for detection of occult blood in faeces (Sentinel CH. Milan – Italy) was used. Each kit contains 25 slides and 25 plastic tubes, which contain the reagent.

Procedure: The provided plastic stick was plunged in the stool specimen and removed (usually about 2-3 mg of stool sticks on the plastic stick), then the stick was dipped in the provided reagent in the tube and stirred to mix the attached stool with the reagent. 3-4 drops of the mixture were put on the provided occult blood slide and the result was read after 3 minutes. Appearance of two red lines on the slide indicates a positive test.

3- Statistical analysis

The results for positive samples were expressed as percentages, and statistical analysis was carried out by using Paired t test. A probability p-value of $\leq$ 0.05 was considered as significant whenever appropriate.

RESULTS

The total number of samples included in this study was 700 samples; 532 samples of them (76%) were detected positive for parasitic infections with macro examination and micro-examination (P<0.0001) (table 1).

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(Table 1) The results obtained by direct wet mount method and centrifugal sedimentation method.

	Direct wet mount method	Centrifugal sedimentation method	P value
+ samples	332 (47.4%)	532 (76%)	< 0.0001
- samples	368 (52.6%)	166 (24 %)	

The types of detected parasitic infections are shown in details in (table 2).

(Table 2) Details of parasitic infections obtained by the direct wet mount method and the centrifugal sedimentation method.

	Direct Wet mount method	Centrifugal Sedimentation Method
Total no. Of parasites	407	890
Entamoeba histolytica	199	323
Giardia lamblia	34	64
Entamoeba hartmanni	29	82
Endolimax nana	21	61
Entamoeba coli	6	42
Blastocystis hominis	105	263
Trichomonas hominis	13	52
Enterobius vermicularis egg.	0	3
Adult female: Enterobius vermicularis	4 cases by macroexamination	

Entamoeba histolytica was the commonest parasitic infection detected (36.3%), followed by *Blastocystis hominis* (29.5%).

The positive FOB test was observed in 166 samples (23.7%) of 700 examined samples (table 3 and table 4), 140 samples (84.3%) of the positive FOB test samples were correlated with the intestinal parasitic infection (P<0.0001).

(Table3) Fecal occult blood positivity in parasitic infected and non-infected samples.

	Negative Parasitic infection (n=168)	Positive Parasitic infection (n=532)	
Positive FOB	26 (15.47%)	140 (26.32%)	P-value<0.0001
Negative FOB	142 (84.53%)	392 (73.68%)	

FOB test was positive in 120 sample (72.3%) of Endameba histolytica infection (P<0.0001) and only in 8 samples (4.8%) of Giardia lambilia infections (table 4).

(Table 4) Positive fecal occult blood in relation to parasitic infections.

Total No. of positive FOB samples	No. of positive FOB in parasitic negative samples	No. of positive FOB in parasitic positive samples		
166 (23.7%)	26 (15.7%)	140 (84.3%)		
		E. histolytica	G. lamblia	Others*
		120 (72.3%)	8 (4.8%)	12 (7.2%)

**Blastocystis hominis, Entamoeba coli, Entamoeba hartmanni and Trichomonas hominis.*

DISCUSSION

Intestinal parasitic infection was found in 532 specimens (76%) of the whole 700 samples examined (P<0.0001). The number of protozoal infections largely exceeds the number of helminthic infections. High rates of parasitic infections were also reported in a number of developing countries such as Brazil, Tanzania, Nigeria and Iraq[11-14]. Low rates of infection has been reported in the developed countries such as USA[15]. However, the most common intestinal parasite identified in present study was E. histolytica.

Even though the FOB test was developed to specifically screen for colon cancer[4,5], but indeed there are various causes of positive FOB including infection with some intestinal parasites[6,8], In this study 166 (23.7%) stool samples showed positive FOB test. Of total positive FOB test 140, (84.3%) stool samples showed parasitic infection. Our results demonstrated that positive FOB test during routine analysis was correlated with the intestinal parasitic infection (P<0.0001).

In the present study several pathogenic and nonpathogenic intestinal protozoan parasites were detected and investigated for correlation to FOB positivity. There was a significant difference in FOB positivity between infected and non-infected samples (P<0.0001) (table 3).

Our results shown that E. histolytica was the most caused of positive FOB within the detected intestinal protozoan parasites (P<0.0001), this parasite is the most known as a caused of dysentery or blood loss[8]. A previous study reported four asymptomatic cases with positive FOB test and amebic colitis due to E. histolytica[16].

CONCLUSION

The present study demonstrated that positive FOB test during routine analysis was correlated with the intestinal parasitic infections, especially with *E. histolytica* rather than any other causes.

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BISPECIFIC ANTIBODIES: PRODUCTION AND USE

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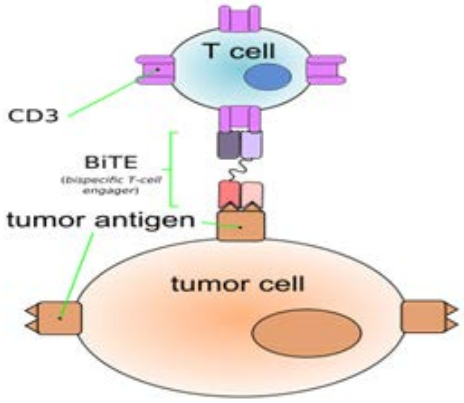
INTRODUCTION

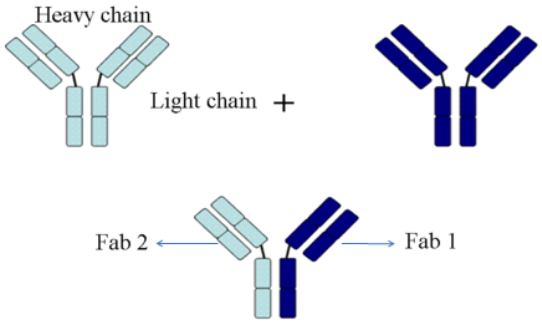
Bispecific antibodies are specific type of monoclonal antibodies, which can bind to two different types of antigens. These monoclonal antibodies do not occur naturally but can be produced by genetic engineering or by cell fusion. However, one exceptional case of natural bispecific antibody was recently obtained from allergic patients receiving therapeutic injections with 2 different allergens during specific immunotherapy[1]. The main advantage of these types of antibodies is that they can recognize more than one protein on the surface of different cells. Bispecific antibodies are mostly designed to recruit cytotoxic effector cells (cytotoxic T-lymphocytes or NK cells) of the immune system effectively against pathogenic target cells thus improving effector cell cytotoxicity[2]. Bispecific T-cell engagers (BiTEs) is one of the typical example of bispecific monoclonal antibody which direct a host's T cells cytotoxic activity against diseased cells like cancer cell (figure 1).



(Figure 1) Bi-specific T-cell engagers (BiTEs) is atypical example of bispecific monoclonal antibody.
Photo taken from wikipedia

Bispecific Antibodies structure:

Bispecific antibodies also represent as a "Y" shaped molecule, and has two different arms, each arm can bind two different types of molecules. Each Y-shaped unit contains 4 polypeptides, 2 identical copies of a polypeptide known as the heavy chain and 2 identical copies of a polypeptide called the light chain. Bispecific antibody, as its name indicates, usually consists of 2 distinct Fab (antigen binding fragment) arms, by which it is capable of simultaneously binding two different antigens, while normal antibody has two identical Fab arms. The third fragment, which forms the base of the Y, is called Fc fragment. This special characteristic of BsAbs confers bispecific antibody huge potential for a wide range of clinical applications as targeting agents for immunodiagnostic and therapeutic. It was specified that the antibody with bispecificity belonged to the IgG4 subclass. In bispecific antibodies one Fab arms by swap with a heavy chain and attached light chain (half-molecule) with another heavy-light chain pair from another molecule bispecific antibodies[1,3] (figure2).



(Figure 2) Bispecific antibody(BsAb) with 2 different Fab regions from 2 different antibodies

Production of Bispecific antibodies:

Bispecific antibodies are mainly produced by two methods: 1st by fusion of two hybridoma cell lines producing and 2nd chemically links two antibody molecules together.

1- Fusion of Hybridoma cells:

As a result of allelic exclusion, plasma cells produce only one set of light and heavy chain of Immunoglobulin (antibody) (figure3).
Specific Mabs producing Hybridoma cells are modified in such a way that they are sensitive to hypoxanthine-aminopterin and thymidine (HAT) containing medium using the drug 8-azaguanine and resistance to neomycin (neo). As a results of this hybridoma cell line (neo /s HAT) is only capable of growing in neomycin but not in HAT-containing medium. The second hybridoma cell line for producing Bispecific antibody will be HAT resistant / neomycin sensitive, is then selected on neo / HAT selection. After fusion of the two these two different hybridoma, the resulting quadroma cell line can be selected by culturing and cloning in HAT- and neomycin-containing medium[4]. Producing Bispecific antibodies by hybridoma is easier and resulting Bispecific antibody is naturally assembled. The drawback of this technology is that Bispecific antibodies produced by somatic fusion of two different hybridoma cell lines expressing monoclonal antibod-

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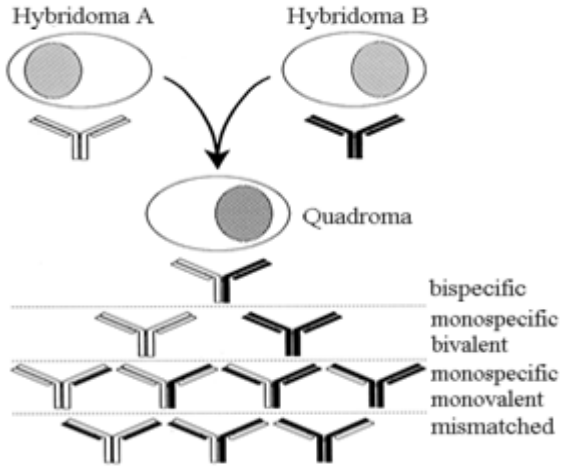
ies with the desired specificities of the bispecific antibody random pairing of two different immunoglobulin heavy and light chains within the resulting hybrid–hybridoma (or quadroma) cell line, up to ten different immunogloblin species are generated of which only one is the functional Bispecific antibody. Another disadvantage of this technology is in stability of the resulting cell lines, low yields, difficulty in purification of the Bispecific antibodies.

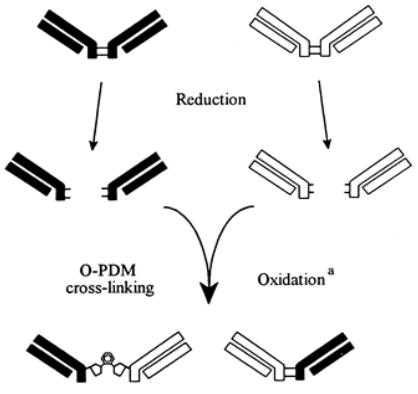


(Figure 3) Bispecific antibodies production by Hybridoma technology: Representation of 10 different bispecific antibodies secreted by a hydrid hybridoma cell as a result of different random association of light and heavy chain from parental hybridoma

2- Chemical method of producing Bispecific Antibodies:

This technique was established by Nisonoff & Rivers in 1961. This technique does not require any cell fusion as the name indicates. The advantage of this technique is that, it is more quick to produce Bispecific antibody and antibody molecule is easy to purify compare to hybridoma technique[5].

Chemical combination can be achieved in two different ways: 1st is direct coupling of the whole antibody molecules or their derivatives, and 2nd is dissociation and reassociation of heterologous immunoglobulin (figure 4).



(Figure 4) Chemical method of producing Bi specific Antibodies

2nd method of producing Bispecific antibodies by chemical method initially requires chemical manipulation to detach immunoglobulins into half molecules and to keep the antigen binding sites intact, then in second step reform the disulphide bonds linking the heavy chains without allowing any interfering side reactions such as the formation of intrachain or mismatch disulphide bonds.

In this straightforward method coupling of two parental antibodies was performed by heterobifunctional cross linker. As a result of this bispecific antibodies production method, there is a significant molecular heterogeneity because reaction of the cross linker with the parental antibodies. To obtain more homogeneous preparations of Bispecific antibodies two different Fab fragments have been chemically cross linked at their hinge cysteine residues in a site directed manner[6].

Various challenging methods have been applied to make immune protective Bispecific antibodies.

A novel Bispecific antibody has been produced by fusion of DNA encoding a single chain antibody (ScFv) after C terminus (CH3-ScFv) or after the hinge (Hinge-ScFv) with antibody of different specificity. Transfection method has been applied to express this fusion protein. Transfected cells secrete a homogenous population of the recombinant antibody with 2 different specificity, one with N terminus (antidextran) and other with C terminus (antidansyl). The CH3-ScFv antibody, maintains the constant region of human IgG3, has some of the associated effector functions such as long half-life and Fc receptor binding[7].

Use of Bispecific Antibodies:

Bispecific antibodies have been used for various medical purposes till now and these are found to be very effective tool for medical purpose specially in human diseases.

1- Molecular Advances in Pre-targeting Radioimunotherapy with Bispecific Antibodies[8]:

For the targeted delivery of radionuclides to treat tumour, Antibodies were used for the first time before 20 years and promising results were achieved using this radiolabled antibodies especially on hematopoietic malignancies. Pretargeted delivery of radiolabeled antibodies has seen to be very effective where this pre-targeted delivery significantly increase the radioactive uptake in tumour cells compare to normal cells and thus enhances the usefulness of both detection and therapy of tumour and cancer. Separations of the radionuclide from the tumor targeting antibody permits slow and effective process of specific antibody localization into tumour cells. Peptide macromolecules are used in pretargetting. These macromolecules are capable of binding with a high affinity to a radioactive agent of low molecular weight and selectively target the tumour antigen. As a treatment of tumour/cancer these mac-

romolecules are administered first into the patient, and the radioactive agent ("the effector") is then given at a later stage, when the concentration of the macromolecule in the tumour is greater than in other tissues. Also the variation in radioactivity between tumour and normal tissue is easily reachable. So this is two steps procedure where the success is based on the clearance of macromolecule sufficiently from the blood and normal tissues, otherwise radioactive effector molecule will remain wherever the macromolecule is allocated. In this study they have produced two bispecificdia bodies (BS1.5 and BS1.5H) for pretargeted delivery of radiolabeledbivalent haptens to tumors expressing CEA. BS1.5 (Mr 54,000) consists of two heterologous polypeptidechains associated noncovalently to form one binding site for CEA from the variable domains of hMN14 (a humanizedanti-CEA antibody from Immunomedics, Inc., Morris Plains,NJ) and one binding site for HSG from the variable domains of 679 (a murine monoclonal antibody specific for HSG).

2- Recombinant Bispecific antibodies for cancer therapy:

Bispecific antibodies have been used for variety of biological applications with potential use in cancer therapy. Most commonly used applications are retargeting of effector molecules (produrg-converting enzymes, radio-isotopes, complement components, effector cells (CTLs. NK cells) and adenoviral vectors. Various approaches have been used to treat cancer using bi-specific antibodies. One study showed that intracellular expressed Bispecific antibodies were used to induce a functional knock out of two cell surface receptors. In another study a bispecific tandem ScFv with cell-penetrating abilities was applied to restore p53 wild type function by intracellular binding to p53. Most application for cancer therapy involves the retargeting of effector cells of the immune system to tumour cells. Wide range of work has been done on the retargeting of cytotoxic T lymphocytes (CTLs) through binding to the T cell co-receptor.

In a recent study, Bispecific antibodies were used as a molecule for immunotherapy against pathogen that infect the heart and it was utilized to cross linking between bacteria and polymorphonuclear (PMN), as these PMN neutrophillic leukocytes are the first line of immune resistance in the body against intramammary infections[(9)].

3- Use of Bispecific antibodies in HIV1[(10)]:

During the HIV-1 infection, HIV virus infects monocytes and T lymphocytes. Viral gp120 binds to CD4 cell surface protein. It has been found that some specific antibodies bind to CD4. This also led to think of making recombinant CD4 to block CD4 binding site on HIV-1 gp120. Monocytes express 3 types of Fc receptor for these antibodies. Bispecific antibodies have been used to target HIV-1 to either Type I, II or III FcγR on these cells. Bispecific antibodies specific for soluble CD4 and Fc region of IgG, on phagocytic cells have been made which potentially link to HIV-1 to the Fc receptor for IgG on phagocyte cells. The disadvantage of this antibody that, antibodies have difficulty in affinity for different strains of HIV-1. An alternative approach involves the use of anti-FcγRIcontaining Bispecific antibodie to target HIV-1 and HIV-1 infected cells for removal by FcγRI-expressing myeloid effector cells. Using these types of antibodies could be useful in target specific removal of HIV infection and to boost immune system of the infected HIV individual.

4- Bispecific antibodies in Hodgkin's Disease[(11)]:

This research explained that refractory Hodgkin's disease was treated with an anti-CD16/CD30 bispecific antibody during the Phase I/II trials. These Bispecific antibodies (HRS-3/A9) were generated against the Fc (gamma)-receptor III (CD16 antigen) and the Hodgkin's-associated CD30 antigen. Promising results were seen when median counts of NK cells and of all lymphocyte subsets were considerably decreased in the patients before therapy. These Bispecific antibodies administered everyday starting with 1mg/m2. As expected there was no clear-cut dose-side effect or dose-response correlation. These promising results obviously prove the effectiveness of necessity of these antibodies and further clinical trials would also require getting it for daily therapeutic role.

5- Bispecific antibodies for malaria[(12)]:

Attempts have been made to treat malaria using Bispecific antibodies. Antibodies have been synthesized against plasmodium antigen and could be used for therapeutic purposes. These antibodies designed in such a way that these could be act like a drug and kill parasites directly or same strategy could be used for vaccine development using these antibodies. Vaccination with these antibodies could protect individual from infection.

Based on the recent research, it has been seen that Bispecific antibodies are very good and advance tool in the therapeutics use. It would be an effective tool in near future to treat various type of tumour or cancer and other challenging diseases to man. Bispecific antibodies are also used in treating HIV infection. There are various other challenging diseases which cause a huge number of death tolls every year, including MTB infection, hepatitis infection, human pappiloma (HPV) virus infection, herpes simplex virus (HSV). Using the recombinant DNA technology Bispeicific antibodies could be used in all these disease and successful clinical trials could be achieved and this way we can lower down the death toll per year due to these diseases. Attempted has already made successfully for High risk HPV infection. To treat these malignant diseases, monoclonal antibodies needs to be routinely modified to get the

better response against these diseases. Extensive work is still going on in the construction, evaluation, and in vivo and in vitro testing of BsAb that target tumor-associated antigens and other disease pathogen and effector cells.

It is not hidden that, lots of poor countries are suffering from various threatening diseases and there is poor disease control management. There is a serious need of production and development of Bispecific antibody based treatment in these poor countries. Cheap antibody based therapy would be a very good alternative to treat these disease where poor people could easily approach these therapy.

All in all Bispecific antibodies production and their use is an important process in novel clinical therapy as it will develop new tools in immune disease diagnosis.

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THE ROLE OF INFLAMMATORY MEDIATORS IN ALZHEIMER'S DISEASE AND THE POTENTIAL FOR TARGETING THE IMMUNE SYSTEM FOR DISEASE TREATMENT

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Alzheimer's disease is the most common age related neurodegenerative disorder the main clinical feature is gradual loss of memory[1]. Synaptic degradation, loss of neurons, neurofibrillary tangles and senile plagues are the neuropathological hallmarks of Alzheimer's disease. Senile plagues are formed of amyloid-β neurotoxic protein (Aβ), which derived from amyloid precursor protein (APP), Accumulation and deposition of amyloid-β protein in the brain is seen as the primary factor in the pathogenesis of Alzheimer's disease[2]. Amyloid-β protein deposits extracellular in senile plaques while paired helical filaments (PHFs) and hyper-phosphorylated tau protein accumulate abnormally in neurofibrillary tangles, neuropil threads and dystrophic neuritis[1,3]. Also formations of neurofibrillary tangles by hyper-phosphorylated tau constitute the primary neuropathological features of Alzheimer disease[4].

Amyloid β is a normal soluble metabolite protein of around 4-kDa produced by processing a large transmembrane glycoprotein, APP, by β- and γ-secretase[5]. Platelets are also considered as main source of amyloid-β in the circulatory system[6]. The main component of Aβ plaques is continuously producing in brains of normal people and patients with AD. Normally, Aβ-associated proteins have been involved in the Aβ amyloidogenic process regulation. However, in Alzheimer's disease brains there seem to be an imbalance between those Aβ-associated proteins that stimulate fibril formation and deposition and those Aβ-associated proteins that prevent it[7].

Aβ plaques are formed from the accumulation and precipitation of secreted Aβ in extracellular space. This perspective suggests that Aβ deposition is a result of production higher than clearance mechanisms by a small amount, and the excess becomes converted to a more stable form that deposits and builds up in a time-dependent manner[8]. This review will discuss the role of inflammatory components in Alzheimer's disease with reference to microglia, astrocytes, complement proteins, and cytokines. Then, it will illustrate the possibilities of targeting the immune system for the disease treatment.

The role of inflammatory mediators in Alzheimer's disease

Microglia and astrocytes, the complement system, cytokines and chemokines are inflammatory components related to AD neuroinflammation[9]. In addition, aggregation of activated microglia and complement factors, leukocytes and astrocytes are increased in brain affected areas which strongly suggests the presence of an ongoing inflammatory process[10]. Microglia represents the first line immune cells against invading pathogens or other types of brain tissue injury. They compose about 10% of the cells in the nervous system[11]. Pathological conditions, like traumatic injury, neurodegenerative disease or tumour, have affected on microglia to become activated, migrated, and surround damaged or dead cells[12]. Amyloid-β plaques and tangles enhance inflammatory reaction to clear this debris[13]. These plaques compose of reactive astrocytes, dystrophic neuritis and activated microglia[14,15]. Long-term activated microglia secrete inflammatory mediators such as Cytokines and chemokines, TNF-α, IL-6 and Complement proteins and amyloid fibrils[16,17]. Moreover, activated microglia can destroy surrounding normal neurons by releasing highly toxic products such as nitric oxide (NO), proteolytic enzymes, reactive oxygen intermediates, complementary factors or excitatory amino acids[18]. However, in some situation the function of microglia has established to be beneficial. Activated microglia can minimize amyloid β aggregation by increasing its phagocytosis, degradation, and clearance[19, 20].

Amyloid β also induce astrocytes to activate and secrete different pro-inflammatory mediators such as leukotrienes, prostaglandins, complement factors, chemokines, ROS and NOS-mRNA that may result in neuronal damage[21,22]. Another study showed that high levels of nitrous oxide synthase (NOS)-positive astrocytes in the AD brains compared to controls which suggest increased production of nitrous oxide in the AD brain[23]. The astrocytes tendency to produce pro-inflammatory molecules is thought to enhance and accelerate the progression of AD[24].

Astrocytes can express all the complements of classical pathway and alternative pathway like C1-C9, many complement receptors such as C1qR, C3aR and C3aR and regulatory factors B, D, H, I[25,26]. The classical pathway activation can be achieved by interaction between C1q and serum amyloid protein[27,28]. Complement system activation causes inflammation, and cell degradation and damage[29].

Inflammatory mediators may stimulate amyloid precursor protein processes and lead to establish a vicious cycle that could be essential in the pathological progression of AD[30]. APP synthesis and Aβ

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production in vitro can be regulated by interleukin-1 with other cytokines[31]. In vivo Il-1 induced production may initiate a vicious circle whereby Aβ deposition stimulates microglia activation to produce further cytokine[32].

Possibilities for targeting the immune system for the disease treatment

The immune system appears to participate in AD pathogenesis. Down-regulation of immune system associated with aging may blunt the immune response to Aβ[33]. Long-term exposure of humans and mouse models immune system to Aβ might lead to hypo responsiveness in terms of cellular and humoral immune responses to Aβ itself, which could contribute to the disease process[34].

Moir and his colleagues have measured the titer of anti-Aβ 42 antibodies in serum from individuals with and without late onset AD by using an ELISA[35]. They illustrated that IgG titer of anti-Aβ 42 peptide antibodies was considerably higher in serum from elderly controls than from AD patients. However, the low titer of anti-Aβ 42 antibodies in AD patients does not reflect the well-established, age-associated defect in the antibody response to most protein antigens. The lower titer of serum anti-Aβ 42 peptide antibodies in AD patients may reflect specific impairment of helper T-cell activity for B cells that produce anti-Aβ 42 peptide antibodies[36]. Also a study of by Du and his colleagues, states that the plasma level of anti- Aβ antibodies that bind to accumulated Aβ were extensively lower in AD patients than in healthy controls, while there was no difference in anti-Aβ antibodies binding to Aβ monomers[37]. Therefore, natural antibodies to aggregated Aβ may have great importance against AD pathology[37].

The conception of immunological treatment of AD becomes a therapeutic approach to enhance brain Aβ plaques clearance[38]. Different active and passive immunizations are providing significant therapeutic benefits in transgenic mouse models of AD by targeting beta-amyloid plaques[38].

Active immunization approaches

Schenk and his colleagues have shown that the transgenic mice over-expressing mutant human amyloid precursor protein V717F (PDAPP mice)[39]. Gradually develop several neuropathological sings of Alzheimer's disease in time dependent manner. The transgenic mice were treated with full-length Aβ1-42, either before the onset of AD or at an older age[39]. They reported that immunization of transgenic mice leads to produce high serum antibody titers against Aβ 42 which inhibit amyloid plaques formation and markedly reduce the extent and progression of these AD-like neuropathologies[40]. Weiner and hiss flowers (2000) have found that PDAPP mice who treated with nasal mucosal administration of human Aβ 1-40 peptide results in reduced Aβ aggregation and deposition in the brain by a 52% and consequently decrease astrocytosis, microgliosis and neuritc dystrophy. This action was specifically related with an anti-Aβ antibody response and with expression of IL-4, IL-10, TGFβ[40]. Transgenic mice that carrying the human amyloid precursor protein, familial AD (hAPPFAD) were immunized with antigen based on Aβ 1-15. The result shows high serum level of anti-Aβ titers, specifically isotypes (IgG1 and IgG2b). These isotypes markedly decreased Aβ plaque and reduced Aβ level. Moreover, compared with mice controls the memory of immunized hAPPFAD mice was improved[40].

Passive immunization approaches

Passive immunization requires administrating anti-Aβ antibodies frequently in order to keep steady state levels of the antibody[40]. They act either directly within the CNS or periphery to provide a therapeutic benefit[41]. Such antibodies have a limit amount access to the brain, since only 0.1% of an intravenous antibody dose can pass through the blood-brain barrier into the brain[41]. In old mice the peripherally administrated antibodies were able to induce clearance of pre-existing amyloid and change plaques shape, whereas in young mice the passive route antibodies prevent plaque formation[42]. Passive immunization of antibodies against Aβ peptide decreased the extent of amyloid burden in the brain of PDAPP Tg mice[43]. These experiments illustrate that although monoclonal antibodies have limited access to the CNS, they may be considered not only for the treatment of Alzheimer disease, but possibly for other CNS disorders as well[44].

In conclusion, Alzheimer's disease is the most neurodegenerative disorder causing dementia and loss of neurons. Amyloid-β protein accumulates abnormally and form plagues which are the main feature of AD. Microglia and astrocytes represent the defence line in the brain. Under certain pathological situations such as Alzheimer's disease these cells become active and release different inflammatory mediators. Inflammatory mediators like complement proteins and cytokines stimulate cell damage and consequently accelerate the AD progression. Increasing evidence has supported that Immune system participates in AD pathogenesis. Therefore, targeting the immune system is the main approach for the disease treatment. Active immunization leads to the production of serum antibodies against amyloid proteins. Passive immunization with anti-Aβ antibodies is another alternative therapeutic goal to decorate plagues and induce clearance of pre existing amyloid.

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ACUTE INFANTILE HAEMORRHAGIC EDEMA

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INTRODUCTION

AIHE is a rare disorder, it´s manifestations are almost exclusively cutaneous. There is often a history of recent upper respiratory and /or treatment with Antibiotics. Clinical features include ecchymoses of the head and extremities. Aetiology of AIHE include infections, drugs and vaccination. Infections are usually respiratory or urinary, e.g Streptococcal , Staphylococal, Esherichia coli, Cytomegalovirus, Adenovirus, Coxsakievirus, or rota virus infections[1].

AIHE may be triggered by infectious agents, although no definitive associations have been made[2].

AIHE represents a hypersensitivity or leukocytoclastic vasculitis, characterized by inflammation of the small dermal vessels with fibrinoid necrosis and extravasation of red blood cells. Although the presentation of AIHE is terrifying for parents, It is self-limiting disease[3].

Case study

We present 9 months old Libyan male infant with acute infantile hemorrhagic edema (AIHE), which is rare transient benign self-limiting skin disorder, who was admitted to Paediatric Department, Zliten Teaching Hospital because of fever and vomiting for 5 days duration and appearance of hemorrhagic skin rash for 4 days before admission. On admission to the hospital, he had upper respiratory tract infection, fever 38.5°C and dehydrated with sunken eyes. His skin rash has appeared on cheeks, ears and upper extremities as non- itchy different sized from 0.4 cm to 3.5 cm in diameter edematous purpuric red annular and medallion-like plaques. Laboratory investigations showed Leukocytosis, thrombocytosis with high ESR and elevated C-reactive protein. During admission child was given I.V fluids and paracetamol syrup, general condition has rapidly improved with resolving of fever and stopping of vomiting. On the other hand the appearance of new skin lesions have continued on lower extremities after one week of onset of skin rash on the face. Within 5 day, the child was discharged in good general condition on short course of systemic Steroids and prophylactic oral Antibiotics.

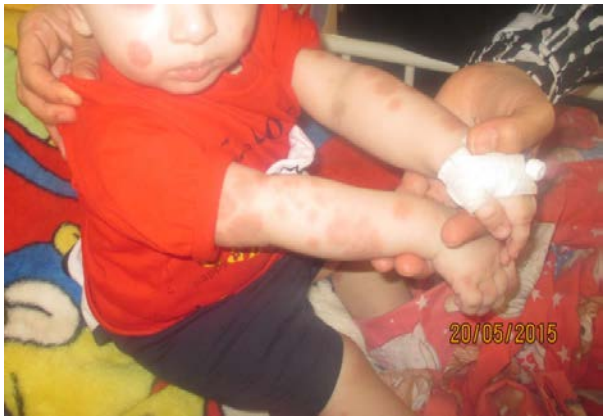
DISCUSSION

AIHE is classified as leukocytoclastic vasculitis of small vessels of skin similar to Henoch-schoenlein purpura (HSP). Our patient had upper airway infection as trigger factor at admission.

Many of the authors consider the disease as an immunological reaction after an antigenic trigger. Infections, drug intake and immunization are the main etiologic factors as in 75% of the cases[4,5,6].

There are no diagnostic criteria for the disease[4,7,8]. So our diagnosis was clinical. The child was non-toxic in good general condition, this was found also in study of 7 cases in Turkey[9].

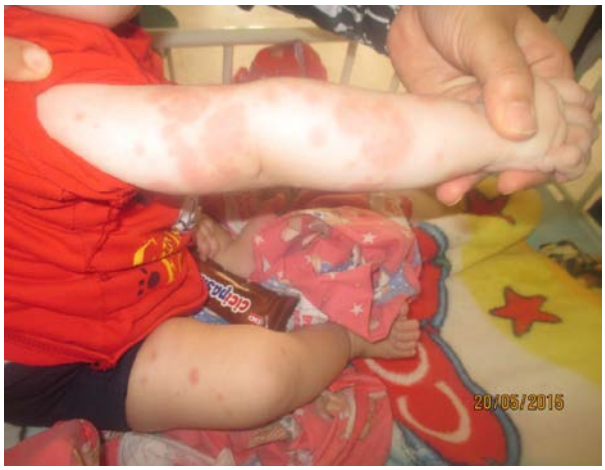
Our patient had multiple different sized red ecchymotic plaques on face and all surfaces of extremities which have appeared, one day after history of fever, on face and upper extremities (figure 1).



(Figure 1) Ecchymotic plaques on face and upper extremities

In the second and third days of appearance of skin lesions more new lesions on arms and lower extremities have appeared (figure 2).

Laboratory findings were similar to laboratory finding of seven cases of Hayrullah Alp, et al[9].



(Figure 2) Ecchymotic plaques on lower extremities

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In our patient urine analysis was normal, the most important differential diagnosis was meningococcemia and septicaemia which was excluded by finding of no involvement of internal organs. No specific treatment is available for AIHE[9].

The prognosis is generally good with complete spontaneous resolution occur within 2-3 weeks[3].

As treatment for AIHE our patient was given Xilone (prednisolone) 5mg/5ml, 2.5ml twice daily for 5 days.

In clinical perspective of Hayrullah Alp, et al Antihistamine (Hydroxyzine HCL or diphenhydramine were given to 4 patients, whose their lesions disappeared earlier in the antihistamine group (mean 4 days) than in other group who has not taken Antihistamine[9].

As topical treatment for our patient Hydrocortisone 1% cream was prescribed.

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SUBTALAR JOINT DISLOCATION

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ABSTRACT

Subtalar dislocations are 'rare' injuries. Although many of these dislocations result from a high-energy injury such as a fall from a height or road traffic accident, a significant number occurs as a result of athletic injuries. Both these cases had medial subtalar dislocations, one of them associated with fracture of the posterior process of the talus. Although this injury pattern is uncommon, but it may be misdiagnosed as "ankle sprains" because of poor visualization on routine ankle radiographs, it is important to recognize the associated fracture as it involves the weight bearing articular surfaces.

INTRODUCTION

Subtalar dislocation (perhaps more appropriately called peritalar dislocation) is the simultaneous dislocation of the distal articulations of the talus at both the talocalcaneal and talonavicular joints Subtalar dislocations are 'rare' injuries[1]. With this injury the tibiotalar joint is undisturbed[2], but it may be misdiagnosed as "ankle sprains" because of poor visualization on routine ankle radiographs[3,4,5]. Subtalar dislocation can occur in any direction and always produces significant deformity it is important to recognize the associated fracture as it involves the weight bearing articular surfaces[6]. Most commonly the foot is displaced medially with the calcaneus lying medially, the head of the talus prominent dorsolaterally and the navicular medial and sometimes dorsal to the talar head and neck[7,8]. Less commonly lateral dislocation occurs.

Mechanism of Injury

Inversion injury of the foot results in a medial subtalar dislocation, while eversion produces a lateral subtalar dislocation. The strong calcaneonavicular ligament resists disruption, and the inversion or eversion force is dissipated through the weaker talonavicular and talocalcaneal ligaments, disrupting these two joints and allowing displacement of the calcaneus, navicular, and all distal bones of the foot as a unit, either medially or laterally. With a medial subtalar dislocation the sustentaculum tali acts as a falcrum about which the foot rotates to lever apart the talus and calcaneus.

Frequently associated fractures occur in the ankle and foot. Shearing osteochondral fracture from the dislocated articular surfaces of the talonavicular or talocalcaneal joint occur in up to 45% of patients and difficult to identify on routine x-ray even after the reduction of the dislocation. Other bones that are commonly fractured are both malleoli, the base of the 5th metatarsal, the cuboid, and the navicular tuberosity.

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Signs and Symptoms

Significant deformities are present in all cases of subtalar dislocation. Because of the significant amount of displacement of the foot on the talus, and particularly with high energy injuries, between 10%-40% of these injuries are open and in all closed dislocations there is significant distortion of the soft tissues and tenting of the skin over the prominent talar head. Significant swelling occurs soon after the injury and this swelling may mask the bony deformity.

In cases of chronic subluxations patients can walk almost normally but they can no longer perform jumps. Their major complaint is that ‘something is wrong with their foot, sometimes along with reported soreness & increasing pain in their Achilles tendons[9].

Clinical Examination

In the acute phase, palpation of the talonavicular, anterior fibulotalar and tibiotalar ligaments is painful, as is palpation and mobilization of the midtarsal (Chopart's) joint.

Mobilization of the ankle joint in flexion/extension and varus/valgus causes pain. A slight and painful limitation of the ankle extension is noticeable. Subtalar hypo mobility is clearly observed in comparison with the contralateral side. After a few hours, tenderness & swelling appear at the talonavicular joint and at the posterior part of the ankle.

In cases of chronic subluxation, the patient's symptoms and clinical examination are dominated by an acute Achilles tendonitis, which often obscures underlying subtalar joint derangement[9].

Radiologic Assessment

A clear view with standard AP, lateral and oblique x-rays of the foot is difficult to obtain because of the distortion of the foot and frequently inadequate x-rays are taken leading to a delay/error in diagnosis. AP view shows talonavicular dislocation. In the lateral projection close inspection usually reveals the head of the talus lying superior to the acicular or cuboids in the medial subtalar dislocation and the taller head appear to be displaced inferiorly in a lateral dislocation. Associated fractures are not uncommon.

Treatment

The keystone of treatment for all subtalar dislocations is prompt and gentle reduction under general or spinal anesthesia. Subtalar dislocations without fractures should be reduced closely whenever possible. Closed reduction is usually accompanied by a satisfying snap or clunk as the joints reduce and on clinical examination the adequacy of reduction is demonstrated by the normal alignment of the foot and normal, stable range of motion (ROM) of the subtalar and midtarsal joints. After closed reduction and the dislocation is stable, it should be immobilized initially in a short leg posterior plaster splint for 4weeks to allow healing of soft tissues. This should be followed by progressive weight bearing and active ROM exercises for both the ankle and subtalar joints to restore motion, particularly subtalar motion. If an anatomical reduction cannot be achieved by closed means, then a prompt surgical reduction should be undertaken through a dorsal approach, usually over the prominent talar head. Small fracture fragments should be debrided from the joints while large fragments should be anatomically reduced and rigidly fixed. Once the block to reduction is removed the reduction is usually stable; prolonged periods of immobilization should be avoided to prevent persistent joint stiffness.

CONCLUSION

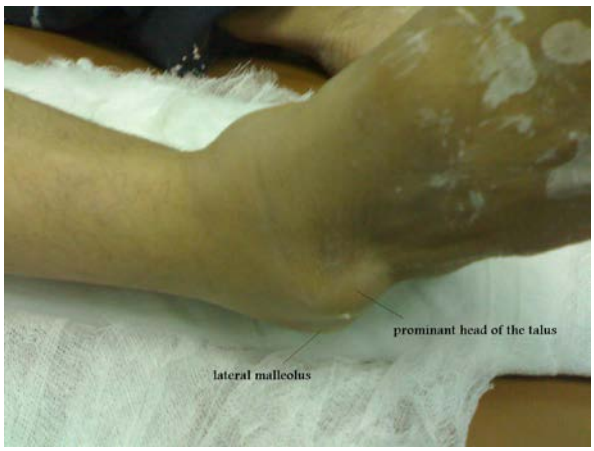
Subtalar dislocations, although not common, have been increasing in frequency over the last decade. The high frequency of medial displacement is explained by the fact that the subtalar joint is only unstable in inversion. The lateral displacement is rare. The prognosis is good in pure dislocation[1]. The majority of patients will suffer minimal disability, with subtalar joint stiffness as the primary complaint[10]. The mechanism of injury is an important factor in predicting long term results. The results are worse with the more violent mechanisms.

Simple inversion rarely produces a dislocation with long term morbidity while more violent injuries e.g. those incurred in motor-vehicle accidents or during a fall from a height are more likely associated with persistent symptoms. These violent injuries are more likely to produce associated fractures and more severe soft tissue injury, both of which decrease the chances of a good long term result.

Case 1

A 53 years old civil teacher by profession with history of fall down from height (2 meters). He sustained an inversion type injury of the right foot, presented to us in the casualty department after about 2 hours complaining of right foot severe pain and deformity.

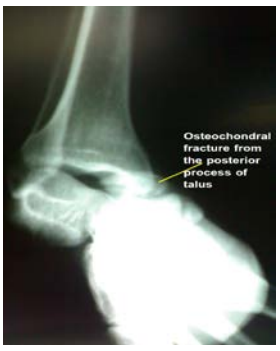
On examination (O/E) there was significant distortion of the soft tissues and tenting of the skin over the prominent talar head. The pain was localized to the midtarsal area. On palpation a sharp pain was felt at the midtarsal and posterolateral joints. Subtalar joint motions were clearly reduced significantly compared with the contralateral side. Ankle extension was limited and painful. Clinically there was no neurological or vascular deficit.

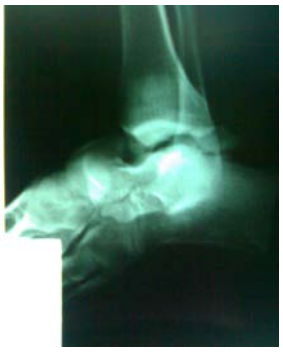


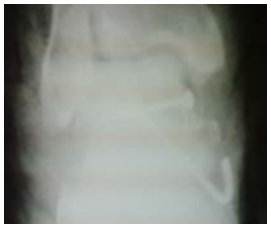
X-ray reveals medial subtalar dislocation with Osteochondral fracture of posteromedial margin of the talus which is entrapped between talus and the medial Malleolus.

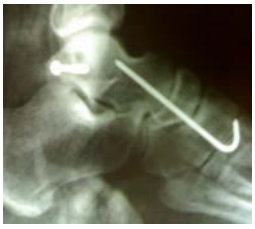
Under general anesthesia, aseptic technique and through medial approach of the ankle, fixation of a large piece of osteochondral fracture from the posteromedial aspect of the talar doom was done with maleoller screw (30mm length), reduction for the subtalar joint was done, but it was unstable, so, retrograde K-wire inserted through the navicular bone to the talus.

The K-wire was removed after 4 weeks & the patient allowed starting weight bearing after another 8 weeks.







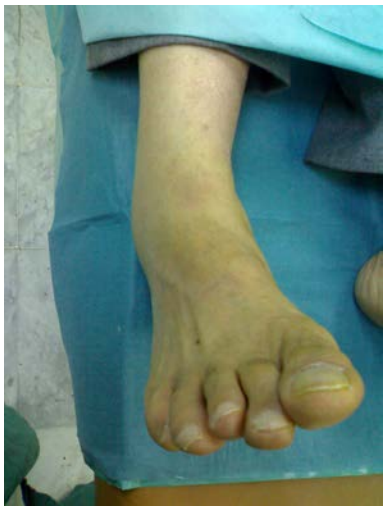


Pre-operative Post-operative

Case 2

A 56 years old man with history of road traffic accident (pedestrian), had a run over type of injury, pre-

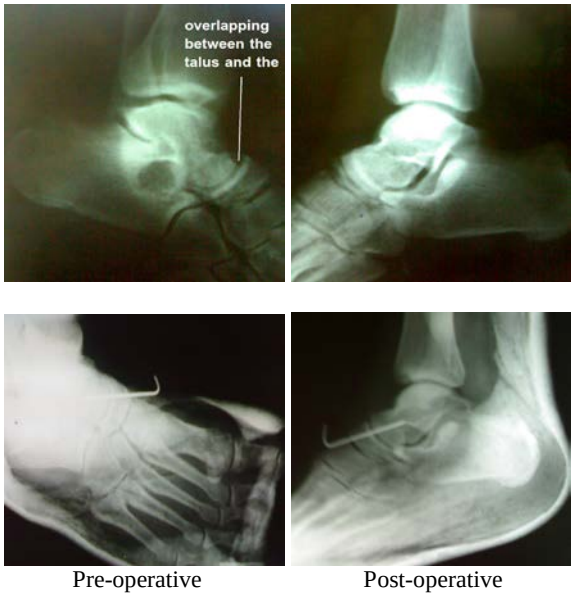
sented to us in the casualty department with right foot pain & deformity.



O/E there was swelling in the lateral malleolar and midtarsal area more towards the lateral aspect. Movements were reduced considerably at the subtalar joint. No neurological or vascular deficit was elicited clinically.

X-rays reveals medial type subtalar joint dislocation.

Under general anesthesia closed reduction done, but the joint was unstable, so it fixed with retrograde K-wire through the navicular bone to the talus, short posterior leg slab applied, the K-wire and the slab was removed after 4 weeks and the patient allowed to start weight bearing after another 4 weeks.



Pre-operative Post-operative

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MULTIPLE PRIMARY CEREBRAL HYDATID DISEASE IN ADULT; CT AND MRI DIAGNOSIS; CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT

The article was a presented case report of multiple primary cerebral hydatid cyst in adult man with review of relevant literature. Role of computed tomography (CT) scan and magnetic resonance imaging (MRI) in the diagnosis of the disease. Case presentation: 50 years old man presented with symptoms of raised intracranial tension. CT scan and MRI showed non-enhanced cerebral cystic lesions, with mild mass effect. Spiral CT scanner and MRI imager 1.5 T were the modalities of choice for diagnosis. Multiple primary cerebral hydatid cysts are very rare. CT scan and MRI were central to diagnose the disease, and revealed typical features of hydatid cysts. Complete cystic remove after craniotomy. The presented case is an adult man and with multiple primary cerebral hydatid cysts located in right temporoparietal lobe, which was rare case in the population. CT and MRI are accurate modalities and they are the easiest method for diagnosis of the disease. Multiple primary intracranial hydatid cysts in adult were rare and should be considered in epidemic area.

KEYWORDS: Intracerebral hydatid cyst, Primary, multiple, Adult, CT Scanner, MRI imager.

INTRODUCTION

Hydatid disease is a parasitic infestation. It is endemic in many parts of the world particularly in Mediterranean Countries including Turkey and Egypt, Middle East, Australia and South America. It is hyper endemic in North Africa including Libya, in Jordon, Iraq and Iran[1-7].

Intracerebral hydatid cyst is very rare. About 1-2 % of patients with hydatid disease have intracranial hydatid cyst. Majority of cases are in the pediatric population and young adult 70% to 80% of patients are children[1-5,7-10].

The disease is caused by larval stage of the taenia echinococcus. The hosts are various carnivores, the commonest being the dog, and all mammals like sheep, cattle, goats and swine are intermediate hosts. Humans are infected through faeco-oral route by the ingestion of food and milk which contaminated by dog faeces containing ova of the parasite or direct contact with dogs. Eggs lose their envelop in stomach, and embryos are released which then pass through gut wall to the portal system and are carried to the liver where most of the larvae are entrapped and encysted. Some may reach the lungs and very rarely some may pass through the capillary filter of liver and lungs and enter into systemic circulation. There may even reach the brain[10-14]. Intracerebral hydatid cysts are usually located in supratentorial region. The parietal lobe is the most frequent site for primary cerebral hydatid cyst[1,8,15,16].

Intracerebral cystic disease may be asymptomatic and discovered accidentally e.g. when X-ray or CT scan brain performed for cases of trauma[17]. Cysts grow slowly subsequently symptomatic and clinical manifestations are caused by the involved organ.

Good diagnostic method to diagnose the disease are CT scan and MRI. CT determines the location, size and wall calcification of hydatid cysts in the brain. MRI becomes more widely used as it can show exact localization, number and other details that are not be seen on CT scan[1,10,18-22].

Here a rare case of multiple primary cerebral hydatid cysts was reported and also reviewed the relevant literature with role of CT scanner and MRI imager in the diagnosis and providing definitive results.

Case presentation:

50 years old Libyan man was referred to Misurata Central Hospital with history of intermittent generalized headache, left side numbness and paraesthesia of the toes and later he developed vomiting.

He had been well until 6 months earlier. No history of fever, visual disturbance or any other symptoms. The central nervous system examination and routine laboratory analysis were within normal limits as well as normal ultrasound abdomen and normal CT chest and abdomen. No evidences of diseases in liver, lungs, spleen or in any extracranial cystic lesions. Echocardiogram roles out any congenital cardiac disease.

Scanning of the brain was performed with contrast material on CT scanner: GE-Hi-speed. MRI examination was performed without contrast on MRI imager: Siemens 1.5T.

In the presented case CT Scan demonstrated multiple, spherical, thin well-defined outlines cysts, with non-calcified walls, non-enhanced with contrast material and homogeneous density similar to CSF. Daughter cyst was seen inside of one mother cyst (figure 1).

MRI imaging showed round, smooth, well defined, thin-walled three multiseparated cystic lesions and

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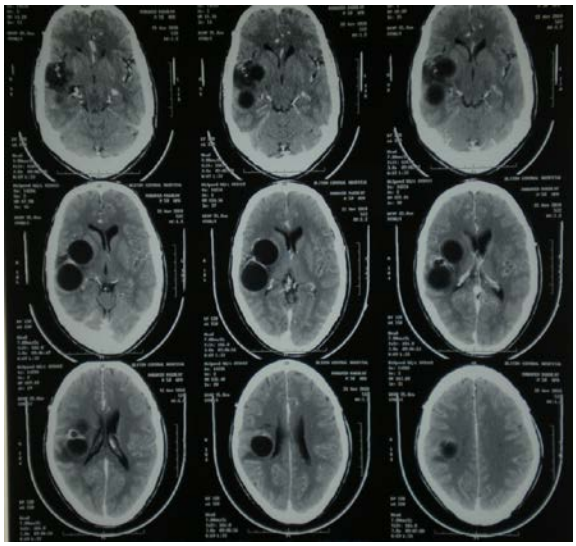
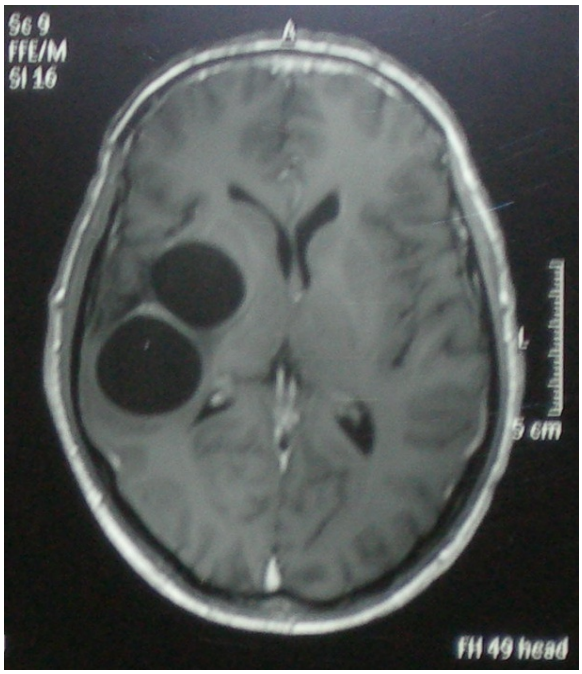
MRI signal intensity similar to CSF, and the cysts located in the right temporoparietal region of the brain.

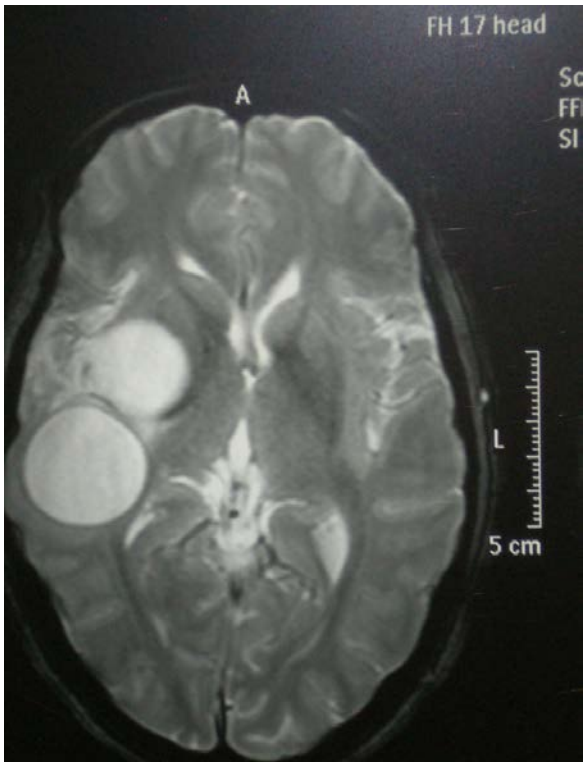


(Figure 1) CT scan with contrast showing multiple spherical cystic lesions with low density similar to CSF with smooth well defined wall and with daughter cyst inside of one mother cyst. No detectable calcification.

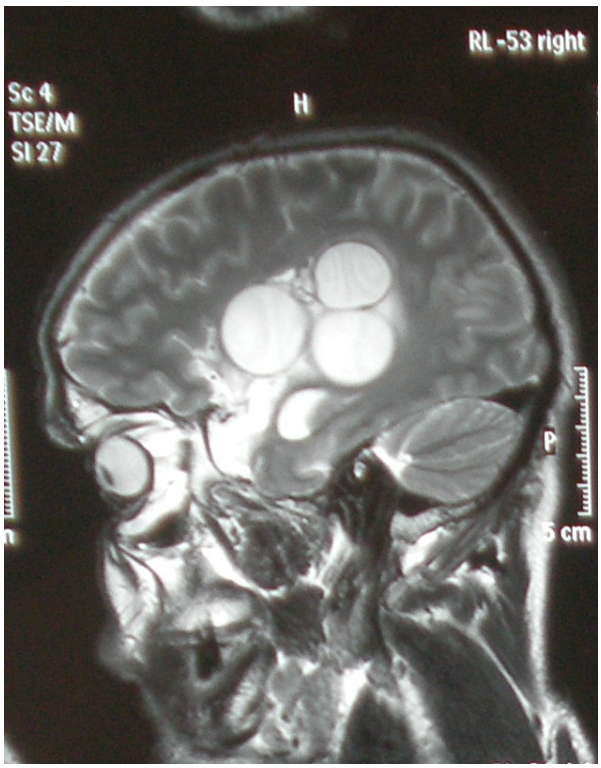
The three cysts were surrounded with brain parenchyma were shown at Sagital T@ MRI. The measurements of cysts were about 3.5, 3.8 and 4.0 cm in dimensions. Mild mass effects on the right temporoparietal region and causes compression on the ipsilateral lateral ventricle. It subsequently causes mild midline shifts toward contralateral side. None of the cysts had collapsed membranes inside (figure 2). Post-surgical operation the specimen was obtained by neurosurgeon and sent to department of histopathology, finally confirmed the diagnosis.



(Figure *2-a)* *MRI axial T1WI*



(Figure 2-b) *MRI axial T2WI*



(Figure 2-c) *MRI sagital T2WI*

(Figure 2-a, b and c) the images showed 3 intracerebral cystic lesions with homogeneous high signal intensity on T2WI and low signal intensity on T1WI similar to CSF and smooth well defined outlines located at the right temporoparietal region.

DISCUSSION

Hydatid disease is endemic in Libya. Human gets infected through the faeco-oral route by ingestion of food, water or milk contaminated by eggs of the parasite or by direct contacts with dogs. The eggs lose their enveloping layer in the stomach releasing the embryos. The embryos pass through the wall of the gut into the portal system and are carried to the liver where most of the larvae get entrapped and encysted. Direct infestation of the larvae in the brain after crossing the gastrointestinal tract, liver, lung and right side of the heart without affecting them[10,12].

Intracranial hydatid cysts may be classified as primary or secondary. Primary intracerebral hydatid disease in adults is more less than in children. Primary hydatid cysts are usually solitary and secondary cysts are usually multiple. 90% of primary hydatid cysts are solitary[4,7,23]. Primary hydatid cysts are formed as a result of direct infestation of brain without evidence of involvement of other organs. Rupture of primary cyst usually results in recurrence. Secondary cyst results from traumatic, spontaneous and seen in extra-axial sites.

Intracranial hydatid cysts are slow growing and become symptomatic when become large. Usually the patients with large intracranial hydatid cysts present with focal neurological deficits and features of raised intracranial pressure may be due to interference with pathway of cerebrospinal fluid flow.

The patient came with history of headache, numbness and vomiting and no history of fever, no neurological deficits.

The patient had no history of contact with dogs. Ultrasound showed normal abdomen and no detectable pathological changes at liver, spleen and other abdominal organs, with normal CT scan chest and abdomen.

The definite diagnosis was provided by CT scanner and MRI imager.

CT scan brain and MRI brain obtained upon admission of our case and revealed typical features of multiple (three) hydatid cysts showed extra axial non-enhanced, spherical, smooth well defined outlines cystic lesions, located in the right temporoparietal region of the brain. CT scan density and MRI signal intensity on T1WI equal to CSF with no rim enhancement. Mild midline shift and mass effect. Daughter cyst was detected at anterior of the largest one of the cysts (figures 1 and 2).

Intracerebral hydatid cyst is rare[6,10,16], about 1-2 % of all patients (children and young adults) with hydatid disease have intracranial hydatid cyst. Most of cases are in the pediatric population (70% to 80% of patients were children, and about 20% to 30% of patients were adults). About 0.3 to 0.7 % of adult patients with hydatid cysts have intracranial cysts.

The patient was an adult man with three cysts in cerebrum caused mild compression on the ipsilateral ventricle and mildly shifted the midline to the contralateral side. The presented case was with history of vomiting and numbness and he had no history of contact with dogs and other animals. Ultrasound and CT scan of abdomen and chest excluded extracranial hydatid cysts. CT and MRI brain showed typical multiseparated primary intracerebral hydatid cysts located at right temporoparietal region. In literature primary intracerebral hydatid cyst is a disease of pediatric and young adults groups and more less than in children. Most cases occurring in the first or second decade. Multiple primary intracerebral hydatid cysts are more less than solitary. The cysts are usually located at supratentorial and frequently located at parietal lobe of the brain. In this case the cystic lesions were removed by the right parietal craniotomy without intraoperative rupture. The specimens obtained by neurosurgeon and sent to histopathology, finally confirmed. Checkup CT scanning was performed for the patient after one year for follow up showed no lesion recurrence.

CT and MRI provided the characteristic features of the disease; size, shape, number, internal structures, contour and location of the lesions.

CT scan demonstrated spherical and smooth well defined thin walled homogeneous cystic lesions containing fluid with a density similar to CSF and calcification could be detected (figure 1). Calcification in cerebral hydatid disease is rare[9], CT scan is better in detection of hydatid cystic calcification[4,5]. MRI is becoming more widely used as a diagnostic tool. MRI is superior to CT scan in detecting multiplicity and delineation of relationship of the cysts with adjacent cerebral parenchyma and demonstrating cyst capsule (figures 2).

In atypical CT findings in cerebral hydatid cysts may cause difficulty in CT scan interpretation and may confused with other diagnosis such as brain tumor or abscess. In these situation MRI including spectroscopy and diffusion sequences becomes the tool of choice for diagnosis of atypical or complicated intracerebral hydatid cysts[9].

CT and MRI imaging are the modalities of choice and central to diagnose the intracranial hydatid cysts [1,10,20]. CT scan and MRI are non-invasive, fast, accurate, easily applied. Both are good for detection and localization of the lesion in the brain. CT and MRI not only increased diagnostic specificity but also allowed us to visualize the size, outermost outline, localization and multiplicity of the cyst are very important for the neuro-

surgeon, thus helping him to plan the cortical excision and approach the lesion accurately[7].

CONCLUSION

Multiple primary intracerebral hydatid cysts in adult man is rare and hydatid cysts in the brain should be considered in patients living in endemic hydatid disease as one of the differential diagnosis in intracranial space occupying lesion. CT scan and MRI imaging are the modalities of choice for diagnosis of intracerebral hydatid cysts.

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OBJECTIVE STRUCTURED CLINICAL EXAMINATION (OSCE)

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Students' assessments are considered an integral part of the educational process. They are intended to result in the graduation of competent, safe doctors capable of professional practice. Assessments are usually used to decide whether the curriculum objectives and intended learning outcomes (ILOs) have been achieved, to identify who should succeed and who should not (summative assessment) and to highlight weaknesses in students' performance levels and give feedback to remedy students' problems (formative assessment).

The Objective (same test) Structured (well-planned, structured mark scheme) Clinical Examination (performance test) (OSCE) was first developed by Harden and Gleeson in 1979. This method of assessment was originally formulated in order to address the unreliability and lack of generalizability of traditional forms of clinical assessment such as the long case[1]. The OSCE is used as both a formative and summative assessment of the clinical competence of medical students. It is defined as "an approach to the assessment of clinical competence in which the components of competence are assessed in a well-planned or structured way with attention being paid to objectivity"[2]. Arguably, the OSCE is not an examination method; rather it is an examination format or framework into which many different types of test methods can be incorporated[3].

The OSCE became widespread in the field of undergraduate and post-graduate medical education from its formulation, mainly because of the improved reliability of this assessment format. It offers a fairer test of candidates' clinical abilities as all candidates are presented with the same test[4].

OSCE process:

In the OSCE, each clinical competence is broken down into various components. Each component is assessed in turn and is the objective of one or more of the stations in the examination. All students complete the same assessment by rotating round 20 or more stations, spending a specific amount of time at each station (5,10,20 min). The time allocated per station should be as uniform as possible to facilitate the smooth movement of examinees from station to station and the duration is decided according to the type and level of assessment (for example, medical students, residents, experienced doctors). In the OSCE, a series of standardized problems is presented to each examinee, often involving simulated patients (SP), who are trained to play roles. A predetermined objective scheme such as a checklist or global evaluation scale is used by the examiners in the rating process. This form of assessment of competence emphasizes: standardization, validity, objectivity and reliability[5].

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VALIDITY OF ASSESSMENT

Refers to the extent to which it measures what it is supposed to measure: a valid test should sample broadly and measure elements from history, giving consideration to applied clinical knowledge, patient management and patient education.

TYPES OF VALIDITY

Face validity involves assessing the different components of skills from history relating to applied clinical knowledge, patient management and patient education.

Construct validity is used to ensure that what is intended to be measured (i.e. construct) is actually measured. Subject experts can examine items and decide what specific items are intended to measure.

RELIABILITY OF ASSESSMENT

Reliability is the degree to which an assessment tool produces stable and consistent results.

TYPES OF RELIABILITY

Test–retest reliability is a measure of reliability obtained by administering the same test twice over a period of time to a group of individuals. The scores from Time 1 and Time 2 can then be correlated in order to evaluate the test for stability over time.

Inter-rater reliability is a measure of reliability used to assess the degree to which different judges or raters agree in their assessment decisions.

The following features help in making the OSCE a reliable tool for assessment of clinical competence: the use of multiple patients or stations, standard checklists for marking student performance, prior examiner training for reduction of examiner bias, and standard and uniform settings at stations for all candidates[6].

ADVANTAGES OF OSCE

- Provides an opportunity to test a student's ability to integrate knowledge, clinical skills and communication with patients. Wide spectrums of clinical tests can be incorporated into the OSCE. Such tests include written multiple choice questions, use of models, and examination of simulated or real patients and reviews of radiographs.
- Can provide valuable information relating to whether course objectives are being accomplished.

Thus, appropriate changes in the curriculum can be made to better address the needs of students.
- Provides the faculty with an assessment tool that is custom-fit to the goals of a specific education program. The examiners can use a wide spectrum of available data.
- Offers an additional parameter by which to evaluate student performance, anda student's core clerkship evaluations for post-graduate training. It is important to have multiple data points from which to determine a student's final grade for several reasons.
- High validity as a result of high level of station content and pre-agreed marking format (checklists) with evidence sourced to the literature or other best practices.
- High reliability as a result of high uniformity of assessment is the benchmark[(5)].

DISADVANTAGES OF OSCE

- Assesses case-specific skills, knowledge and attitudes. Assessments are often specific to a certain clinical problem rather than to a skill able to be generalized across clinical problems.
- Repeated examinations require an adequate pool of stations. This might be limited owing to financial constraints or other logistical difficulties.
- The OSCE format leads to assessment in a compartmentalized fashion. There is no opportunity to observe examinees carrying out complete evaluations of patients.
- It is costly and expensive to setup and requires a large number of personnel for its implementation. High levels of expense are involved in obtaining examination sites, as well as the use of models and simulated patients.
- Compared with other traditional methods of evaluation, the OSCE requires more preparation time and considerable clerical support.
- The time of the examiners can often be intimidating for those considering using an OSCE format for evaluating undergraduate and post-graduate students.

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