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From the Editor



Ahmad Husari (*Chief Editor*)
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In this issue we have a good number of papers from the region with a focus on ophthalmology.

A prospective study was conducted in Royal Medical Services where a total of one hundred and forty patients underwent extracapsular cataract extraction by two different surgeons who were enrolled in the study. All patients had in the bag lens implantation. Stitches were removed six to eight weeks after surgery. Ocular assessment included postoperative refraction one month and four months after surgery. Astigmatism was recorded for each surgeon at the two visits.

Seventy two patients were done by each surgeon. Age range was 32.7 years to 87.3 years. Post operative with the rule astigmatism of more than 1 Diopters occurred in 58 cases for the first surgeon and 41 cases of the second surgeon. The majority of cases were corrected by removal of stitches. The authors concluded that better wound suturing technique minimizes suture related astigmatism. It also prevents residual astigmatism that occurs after removal of stitches. A study at King Hussein Medical Center attempted to report all cases of endophthalmitis that occurred after Intravitreal bevacizumab injection at King Hussein Medical Center and to investigate its etiology. A total number of 1854 patients had Intravitreal bevacizumab injection. Eight cases have endophthalmitis. Six patients had the injection in clinic. Two patients were not given antibiotics after the injection. The authors concluded that injecting Intravitreal bevacizumab in operating theater under sterile condition with the use of antibiotics decreases the risk of endophthalmitis

A case-control study of 50 children attempt to Evaluate the prevalence of H. pylori infection in children with different types of cancer, admitted to Nanakaly hospital for blood disease and malignancy, during the period of 3 months . The prevalence of H. pylori seropositivity accounted for 20% in the patient group versus 44% in control children. No associations were found

between prevalence of H. pylori infection and any factor tested including sex, age, blood group and crowding index, but a significant association between socioeconomic status and H. pylori seropositivity was present. The authors concluded that there was no significant association between H. pylori positive patients and childhood cancer.

A prospective study from Hawler University looked at impaired glucose tolerance test among B thalassemia patients in Hawler province, Iraq. A total of 50 transfusion dependent B thalassemia patients aged 10-15yrs (31 males and 19 females).

The prevalence of impaired glucose tolerance was 26% and there was no diabetes mellitus. The risk factors for abnormal glucose tolerance were: total units of blood transfusion/year($p=0,046$). The authors concluded that frequently transfused patients with under or poor compliance with iron chelation therapy increase the risk of development of complications including impaired glucose tolerance. Early starting of desferrioxamine therapy will prevents such complications.

A strategy for diagnosis and management Entamoeba histolytica was evaluated in Jordan by studying 181 patients aged 2 - 50 years. After doing stool analysis for every patient, Metronidazole 500 mg three times was given to the adult group and 40 mg/kg/day in three divided doses for the pediatric group for 10 days, and septrin 960 mg twice daily for adults and 5 ml twice daily for children for ten days of co-trimaxazole, with follow up stool analysis after one week of treatment. The authors concluded that the efficacy of 10 day of course Metronidazole and co-trimoxazole as (double therapy) is more effective than metronidazole alone as single drug therapy in eradication intestinal amoebiasis for which the causative organism is identified by simple stool examination.

A retrospective observational hospital based study of 400 women at term pregnancy were studied. The objective of the study to obtain an estimated fetal weight from the fetal parameters, and to highlight the predictive value of this procedure, by comparing the estimated fetal weight with the actual birth weight. During the study period, 400 women were studied; 41% of them were primigravidas and 59% were multigravidas. When we compared the results after applying paired t test on ultrasonically calculated weight taken before birth of fetus and actual birth weight we found that it was not significantly different. The authors concluded that the sonographic EFW is highly correlated with birth weight. The use of multiple parameters, gives the most accurate prediction of fetal weight, and Hadlock formulas showed the most stable results in all of the weight groups.

Prediction of birth weight by ultrasound: hospital-based study

ABSTRACT

Objectives: To obtain an estimated fetal weight from the fetal parameters, and to highlight the predictive value of this procedure, by comparing the estimated fetal weight with the actual birth weight.

Methods: This is a retrospective observational hospital based study of 400 women at term pregnancy. This study was conducted between the 1st of April 2010 and the end of May 2011 at Prince Rashid Bin-Al-Hassan Military hospital in the north of Jordan. Prenatal fetal ultrasound database and actual birth weights (BWs) were obtained.

Results: During the study period, 400 women were studied; 41% of them were primigravidas and 59% were multigravidas. The mean age of the women was 27.5 years. The mean of ultrasonic estimated weight calculated was 3167 ± 487 g. When we compared the results after applying paired t test on ultrasonically calculated weight taken before birth of fetus and actual birth weight, we found that it was not significantly different. Also Hadlock's formula showed that 80% were within 10% of the actual birth weight.

Conclusion: The sonographic EFW is highly correlated with birth weight. The use of multiple parameters, gives the most accurate prediction of fetal weight, and Hadlock formulas showed the most stable results in all of the weight groups.

Key words: fetal weight estimation, birth weight, ultrasound.

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Introduction

Monitoring fetal growth is a standard component of antenatal care, and screening and management of abnormal fetal growth, whether it be macrosomia or growth restriction, remains an important objective of prenatal care. Estimation of fetal weight (EFW) can be done by mothers (if they are parous), by clinicians using Leopold maneuvers or by ultrasound.

The two main methods for predicting birth weight in current obstetrics are: (a) clinical techniques based on abdominal palpation of foetal parts and calculations based on fundal height, as Dare et al(1) who used the product of symphysio-fundal height and abdominal girth measurements in centimeters in obtaining fairly predictable fetal weight estimation, and (b) sonographic measures of skeletal foetal parts which are then inserted into regression equations to derive estimated foetal weight. Since the 1970s, the use of ultrasound to estimate fetal weight gained popularity because of the perceived ability to standardize and reproduce measurements(2).

Ultrasound is a basic diagnostic tool in obstetrics and its benefits extend from use in diagnosing localization of early pregnancy to estimation of fetal weight at the time of delivery. An estimate of fetal weight (EFW) in a term pregnancy represents an important variable which in many cases influences the decision-making process in obstetrics(3).

Investigators have developed several equations for estimating fetal weight in the late second and the third trimester. Accurate prenatal estimation of fetal weight (EFW) in late pregnancy and labour is extremely useful in the management of labour and delivery, permitting obstetricians to make decisions about instrumental vaginal delivery, trial of labour after caesarean delivery and elective caesarean section for patients suspected of having a macrosomic fetus(4). Also

fetal weight is an important predictive parameter of neonatal mortality and morbidity.

Ultrasound examination typically involves measurement of multiple biometric parameters that are incorporated into a formula for calculating estimated fetal weight (EFW). Most commonly, a combination of biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL) is used. The two most popular formulas are Warsof's(5) with Shepard's modification(6) and Hadlock's(7). These formulas are included in most ultrasound equipment packages.

So in this study we try to obtain an estimated fetal weight from the fetal parameters, and to highlight the predictive value of this procedure, by comparing the estimated fetal weight with the actual birth weight amongst women attending an outpatient clinic in this hospital in the north of Jordan.

Methods

This is a retrospective observational hospital based study of 400 women at term pregnancy. This study was conducted between the 1st of April 2010 and the end of May 2011 at Prince Rashid Bin-Al-Hassan Military hospital in the north of Jordan. The inclusion criteria included women with full term singleton pregnancy leading to live birth. Patients with malpresentation, gestational diabetes, multiple pregnancy, congenital fetal malformation or advanced labour were excluded. The study was approved by the ethics committee and informed written consent from all participants was obtained.

The fetal weight was estimated within a week prior to the delivery for all women involved in the study. If the delivery did not occur within a week of the estimations, the estimations were repeated. All examinations were performed using a Dynamic Imaging real time ultrasound machine with a 3.5 MHz curvilinear abdominal transducer. Gestational age and fetal weight based on measurements of head circumference (HC), biparietal diameter (BPD), abdominal circumference (AC) and

length of femoral diaphysis (FL) were collected in all cases.

Fetal weight was estimated for each fetus using Hadlocks formula and ultrasound machine calculated the fetal weight. Prenatal fetal ultrasound database was reviewed for fetal weight estimation, gestational age at delivery, and actual birth weights (BWs) were obtained from the hospital's perinatal database, and compared with the ultrasonographic weight estimates.

Results

During the study period (2010-2011) 400 women were studied; 41% of them were primigravidas and 59% were multigravidas. The age range of the women was between 15 - 44 years with a mean of 27.5 years. Sixty four of the women had normal delivery, 15% had instrumental delivery and 21% had cesarean section. The demographic and obstetric characteristics of study population are summarized in Table 1 (opposite page).

In addition, the study revealed that the cases were distributed as per the birth weight of the babies into four groups. 90 (22.5%) neonates weighed less than 2500 g, 120 (30%), between 2501 and 3000g, 140 (35%) between 3001 and 3500g, and 50 (12.5%) weighed more than 3500g.

The mean of ultrasonic estimated weight of 400 fetuses calculated was 3167 ± 487 g. When we compared the results after applying paired t test on ultrasonically calculated weight taken before birth of fetus and actual birth weight, we found that it was not significantly different (Table 2).

Also our study showed that fetal ultrasound using Hadlock's formula has error in estimation of fetal weight by about 280 gm. 80% were within 10% of the actual birth weight, while in 20% of the cases, there is an error of estimation by more than 10% compared to actual weight.

Discussion

Obstetric sonographic assessment for the purpose of obtaining fetal biometric measurements to predict fetal weight has been integrated into the mainstream

of obstetric practice in the past quarter century. From its inception, this method has been presumed to be more accurate than clinical methods for estimating fetal weight. As such, the ultrasonographic technique represents the newest and most technologically sophisticated method of estimating fetal weight(8).

Fetal weight is an important predictive parameter of neonatal mortality and morbidity. Precise estimation of fetal weight is therefore a valuable item for information for further prenatal and obstetric management. Many regression formulae for sonographic fetal weight estimating have been published during the last 30 years, which, unfortunately, generally showed poor rates of accuracy(9).

Our study revealed that there was no significant difference found between the mean weight obtained through ultrasonically calculated weight and actual birth weight. The same finding was obtained in another earlier study(10,11). So the accuracy of ultrasound estimations of fetal weight performed within 7 days of delivery in term singleton pregnancies was at least similar and sometimes better than that reported in other studies(12).

EFW is a useful parameter with which to predict birth weight and outcome when it is calculated a few days before delivery. It has an accuracy similar to that of clinical ultrasound examination for delivery at or beyond 37 weeks' gestation, whereas it is significantly superior to clinical estimates of weight for preterm birth as shown in our study. When EFW is calculated prior to delivery in order to help in decision making, it can be compared to birth-weight reference charts and, in experienced hands, nearly 80% of EFWs are within 10% of the actual birth weight, with most of the remainder being within 20% of actual birth weight, as seen by study of Salmon et al(13).

In our study, we have found that models based on 4 fetal indices are more accurate for EFWs, so to improve the accuracy of fetal weight estimation, sonographic models that are based on 4 fetal biometric indices should be

Maternal age, mean \pm SD, y	27.5 \pm 4.2
Primigravida	41%
Multigravida	59%
Maternal weight, mean \pm SD, kg	75.24\pm3.90
Gestational age at delivery, mean \pm SD, wk	39 \pm 2.8
Normal delivery	64%
Instrumental delivery	15%
Cesarean section	21%
Birth weight, mean \pm SD, g	3140 \pm515 g
Median time from fetal weight estimation to delivery	2(0-4)

Table 1: Demographic and obstetric characteristics of study population

Method of calculation	Mean weight
Actual birth weight	3140 \pm515 g
Ultrasonically estimated weight	3167 \pm487 g

◀ $t = -2.7, p = 0.001$

Table 2: Actual and ultrasonically estimated weight (n=400).

preferred, as shown by the study of Melamed et al(14). Recognizing the accuracy and the tendency for underestimation or overestimation of each of the available models is important for the judicious interpretation of fetal weight estimations, especially at the extremes of fetal weight. But other studies have added thigh circumference measurement when it was combined along with BPD, HC, AC and FL measurements, and clearly indicate that fetal TC measurements add to the accuracy of birth weight estimation in obstetric practice(15).

In this study, the ultrasound estimations of fetal weight were performed within a week prior to delivery. Although some authors studying reliability of ultrasound estimation of fetal weight have included estimations performed up to 14 days prior to delivery(16), others have restricted their data to estimations performed within 7 days(17) or 3 days(18). Hadlock 1 and 2 formulas gave the closest approximation of birth weight in the Turkish population(19); also in our population we see the same findings by using Hadlock's formula.

Conclusion

We can conclude from this study that the sonographic EFW is highly correlated with birth weight. Ultrasound presented good accuracy in the estimation of fetal weight. The use of multiple parameters, gives the most accurate prediction of fetal weight, and Hadlock formulas showed the most stable results in all of the weight groups. Further work to improve the universal validity and accuracy of fetal weight estimation formulae is also required. Also there is a need for routine evaluation of the accuracy of fetal ultrasound of each examiner, and to make suggestions as to what fetal parameter must be measured more precisely.

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Relationship between metronidazole and co-trimoxazole on eradication of *Entamoeba histolytica* in Queen Alia hospital (Jordan)

ABSTRACT

Objective: To compare the efficacy and safety of Metronidazole and co-trimoxazole together as double therapy with metronidazole alone as single drug therapy in the treatment of diarrhea caused by *Entamoeba histolytica*, cyst and trophozoite in patients who presented to the emergency department and emergency pediatric clinic in Queen Alia Hospital (Jordan).

Methods: A strategy for diagnosis *Entamoeba histolytica* was evaluated by studying 181 patients aged 2 - 50 years. Between the 1st of May 2009 and the beginning of May 2010, 181 patients with intestinal amoebiasis were recruited for this study from the Emergency Department and emergency Pediatric Clinic at Queen Alia Military Hospital. After doing stool analysis for every patient, Metronidazole 500 mg was given three times to the adult group and 40 mg/kg/day in three divided doses for the pediatric group for 10 days, and septrin 960 mg twice daily for adults and 5 ml twice daily for children for ten days of co-trimoxazole, with follow up stool analysis after one week of treatment.

We used double therapy because we note that 20% of patients treated with metronidazole still have symptoms after one week while with double therapy the percentage was 0% and the fever subsided in 24-48 hours

Results: Out of 181 patients 81 patients were adult ages 14-50 years and 100 patients were children aged 2-14 years. About 5.5% of the patients showed the amoebic trophozoite in their stool while the remaining showed only the amoebic cysts. Overall metronidazole and co-trimoxazole produced a clinical response rate of 95% in both the adults and children group after a 10 day course of Metronidazole, while metronidazole alone produced an 80% response rate.

Conclusion: Our findings demonstrated that the efficacy of a 10 day course of Metronidazole and co-trimoxazole as (double therapy) is more effective than metronidazole alone as single drug therapy in eradication of intestinal amoebiasis for which the causative organism is identified by simple stool examination.

Key words: *Entamoeba histolytica* cyst, Metronidazole (Dumozol), Septrin (Co-trimoxazole), *Entamoeba histolytica* trophozoite

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Introduction

Enteric protozoan infections are among the most common infections in humans worldwide, and a significant cause of morbidity and mortality.

Symptomatic patients typically present with diarrhea and abdominal symptoms including cramps, pain and bloating. Although a number of protozoa may cause these symptoms, *Giardia intestinalis* and *E. histolytica* are the most commonly reported. Amoebiasis (Amoebic dysentery) is an infectious disease caused by protozoan parasite called *Entamoeba histolytica*. It causes colitis characterized by painful passage of a bloody mucoid stool. (1, 2)

Entamoeba histolytica is protozoan parasite, found worldwide and 12% of the world's population are estimated to be infected. The prevalence of infection varies between 1% in developed countries to 50-80% in tropical countries where transmission of *E. histolytica* cyst from humans by untreated drinking water is common. Ingestion of food and drink, contaminated with *E. histolytica* cyst from human faeces and direct faecal oral contact are the commonest means of infection. (3) Cyst carriers are the main reservoir of infection. Cysts may remain viable for three months but may be destroyed by hyper chlorination or iodination of the drinking water. About 10% of patients infected have clinical symptoms, 80-98% present with amoebic colitis, 2-20% present with extra-intestinal disease (liver abscess). The clinical picture of amoebic colitis is characterized by abdominal pain, cramps, generalized weakness, tenesmus and passage of blood and mucus in the stool. (4)

Chronic abdominal pain and frequent bowel disturbances are common symptoms experienced by more than 15% of apparently healthy people. In areas endemic for *E. histolytica*

infection, these symptoms are often diagnosed as non-dysenteric intestinal amoebiasis and irritable bowel syndrome is not distinct. (5,6)

Metronidazole is the most popular drug of choice in treatment of *E. histolytica* infections which is given either orally or intravenously especially in severe cases. It has a low toxicity and it is effective against both intestinal and extra-intestinal amoebiasis. (7)

Ingestion of the quadrinucleate cyst of *E. histolytica* from fecally contaminated food or water initiates infection. Infection with *E. histolytica* may be asymptomatic or may cause dysentery or extra intestinal disease. (8)

Methods

The study protocol was designed with reference to guidelines was proposed to compare between single drug (metronidazole) and double drug therapy (metronidazole and septrin) in treatment of diarrhea caused by *Entamoeba histolytica*.

This study was done between the 1st of May 2009 and the beginning of May 2010, on 181 patients aged 2-50 years with intestinal amoebiasis who were recruited for this study, from the Emergency department and Pediatric emergency Clinic of Queen Alia Military Hospital. Metronidazole 500 mg three times was given to the adult group and 40 mg/kg/day in three divided doses for the pediatric group for 10 days, and septrin 960 mg twice daily for adults and 5 ml twice daily for

children for ten days of co-trimaxazole. Patients with gastroenteritis due to other causes like Rotavirus, *Giardia*, and *Shigella* were excluded from our study.

80 patients were given metronidazole alone while the remaining patients (101) were given the double therapy mentioned above. Duration of treatment was 10 days for both regimens. After doing stool analysis by inspection and microscopic examination for every patient, in addition to nutritional and fluid support, 20% of children required admission for dehydration and 5% of adults required admission because of constitutional symptoms like fever, hypotension and association with chronic illness like Diabetes mellitus.

Follow up of the study group was done by taking history, physical examination and stool analysis after one week and repeated after 2 weeks of treatment.

Results

Faecal samples of 181 adult patients aged 15-50 years and children aged 2-14 years were screened for identifying the causes of the disease. The samples were analysed by microscopic examination and found that 82.8% have liquid stool and 7.4% have semisolid stool.

The median duration of diarrhea at the time of treatment was 5 days; 86% of the patients reported 5-10 motions per day but the others reported more than 10 motions per day. 80% of the patients reported complaints of abdominal pain cramps and distension.

11.1% showed blood in their stool. 5.5% showed the amoebic trophozoite while the remaining patients showed cysts of *Entamoeba histolytica*. Over all Metronidazole alone produced a response rate of 80% after a 10 day course of Metronidazole. While the response of patients who were on double therapy was 95%, the response appeared due to negative *Entamoeba histolytica* in the stool analysis as follow up.

The duration of diarrhea in adult males and females was 3-5 days in (79.6%, and 76.9% respectively which was less than that of children (85.8% males, 83.3% females); also the duration of diarrhea was more in males than females in both adults and children as seen in the Table (below).

Discussion

In this study, our findings demonstrated the efficacy of a 10 day course of Metronidazole in resolving diarrhea for which the causative organism was identified by microscopic examination of stool samples to be *Entamoeba histolytica*; so Metronidazole which is an amoebicidal and bactericidal agent with low toxicity is the drug of choice to treat acute amoebic colitis and it is found that Metronidazole is effective against amoebic liver abscess, (7,12,13) although surgical aspiration may be needed sometimes, but it is demonstrated that use of another agent in addition to Metronidazole that is active against cysts is needed in some cases, like Septrin which has an efficacy rate of more than 90% in eradication of the amoebic cysts. (14) The use of this agent however is limited because of its

		Duration of Diarrhea		Stool Frequency		Microscopic Examination		
Age (years)	Sex (No. of Patients)	3-5 Days	More than 5 days	Liquid Stool	Soft Stool	Occult Blood	Mucus	Pus
Adults (15-50)	Males (55)	79.6%	20.4%	85.5%	14.5%	7%	90%	100%
	Females (26)	76.4%	23.1%	88.5%	11.5%	7.7%	100%	100%
Children (2-14)	Males (64)	85.9%	14.1%	93.7%	6.3%	15.6%	100%	100%
	Females (36)	83.3%	16.7%	97.2%	2.8%	13.9%	100%	100%

Table 1: Age and sex distribution and results of stool examination according to study group

adverse effects (Gastrointestinal and neurological side effects) which were produced in 9% of the patients given the treatment after 14 years experience with the use of Septrin. We used double therapy because we note that 20% of patients treated with metronidazole still have symptoms after one week while with double therapy the percentage was 0% and the fever subsided in 24-48 hours.

The clinical syndrome of non-dysenteric intestinal amoebiasis or chronic amoebiasis has been a controversial entity for some time. Although accepted by WHO, the definitive diagnosis of non-dysenteric intestinal amoebiasis has been thrown into doubt by new methods of investigation. In this study we compared patients who had dysenteric intestinal amoebiasis with a few who had non-dysenteric intestinal amoebiasis (who had soft stool) as seen in the Table, which showed a similar response to the study medication.(9,10)

In the study of Ressignal(2) clinical and parasitological response rates for the nitazoxamide treatment group were similar to those reported for open-label studies of Augmentin with Metronidazole for amoebiasis and giardiasis.(11)

The study emphasizes the importance of a 10 Day course of Metronidazole and septrin in treatment of invasive amoebiasis and considering its use in asymptomatic cyst passers who didn't respond to Metronidazole and become cyst carriers and who needed another luminal agent to eradicate the cysts. Controversy remains over which agent to use, and this will require further comparative trials.

Conclusion and Recommendations

It is illustrated in this study that Metronidazole and septrin together are more effective in treating amoebic colitis and abdominal pain, than giving Metronidazole alone, especially if they are given for a two week period, although we have a few patients, who became cyst carriers.

The authors end by saying that another intra-luminal agent such as Septrin should be given for treating asymptomatic patients who are passing Entamoeba histolytica cysts.

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Trend Of Immunological Markers of Type 1 Diabetes Mellitus in a Sample of Iraqi Children

ABSTRACT

Objectives: to study type 1 diabetic children for trends and presence or absence of auto-immunological markers.

Patients and Method: A cross sectional study on 91 diabetic children, aged 0-14 years, who were screened for type 1 diabetes autoimmune markers ICSA, IAA, IA-2A and GAD-A, in the National Diabetes Center Baghdad, Iraq.

Results: Children with positive results for one or more of the auto-immunological markers were 78 (85.71%) and 13 (14.29%) children did not show positive results, for type 1B diabetes. The ICSA was positive among 40.0% of children within one year from diagnosis. The IAA, IA-2A and GAD-A were 74.35%, 56.41% and 64.10% respectively after different durations from diagnosis.

Conclusions: The immune mediated diabetes was slightly less prevalent among Iraqi diabetic children than Europeans. The highest prevalence of IAA and GAD-A were at 3-4 years from onset of disease; and the autoantibodies continue to be detected in excess of five years.

Key words: Type 1A diabetes mellitus, Type 1B diabetes mellitus, Auto-immunological markers.

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Background

Type 1 Diabetes Mellitus is an immune-mediated disease in over 90% of cases (type 1A DM) and idiopathic in less than 10% (type 1B DM, idiopathic type 1 diabetes). (1) It is recommended to sub classify Type 1 Diabetes Mellitus into type 1A (immune-mediated) and type 1B (other forms of diabetes occur without evidence of any autoimmune disorder, particularly in non-white individuals, with severe insulin deficiency); (2, 3, 4) most of them were of Asian or African origin. (5)

The most important factor differentiating type 1A from type 1B diabetes is the presence of islet autoantibodies. The emerged autoantibodies as the most useful autoimmune markers of type 1 diabetes are Islet cell (cytoplasmic) autoantibodies (ICA), islet cell surface autoantibodies (ICSA), insulin autoantibodies (IAA), glutamic acid decarboxylase autoantibodies (GAD-A) and tyrosine phosphatase IA-2 autoantibodies (IA-2A). (6)

Measurement of diabetes-associated autoantibodies, such as ICAs, GAD-A and IAA, early after diagnosis of type 1 diabetes is valuable in confirming the autoimmune origin of disease because the prevalence of positivity for GAD-A and IAA declines with diabetes duration, and there is conflicting evidence whether diabetes associated autoantibodies may also be related to long-term development of microvascular complications. (7) Although, GAD-A levels are inversely correlated with severe retinopathy in young type 1 diabetic patients, higher GAD-A levels may predict subsequent nerve damage. (7, 8)

Prevalence of type 1 diabetes varies among ethnic groups and geographic regions. (9) The highest incidence of immune-mediated type 1 diabetes mellitus is in Scandinavia and northern Europe; the annual incidence of type 1 diabetes decreases across the rest of Europe. In the United States, the annual incidence of type 1 diabetes was higher in states more densely populated with persons of Scandinavian descent such as Minnesota. Worldwide, the lowest incidence of type 1 diabetes is in China and parts of South America. Evidence and observations showed that type 1 diabetes mellitus is more common in Scandinavian countries and becomes progressively less frequent in countries nearer and nearer to the equator. (5, 10)

Many studies have been done, worldwide and in the Middle East region, for the incidence, prevalence and measuring of the diabetes associated autoantibodies; few have studied the trend and presence or absence of the immunological markers. (6, 11-23) Our aim was to study a sample of Iraqi type 1 diabetic children for the trend and presence or absence of autoimmunological markers.

Patients and Methods

Setting

A two month period (2nd January - 28th February 2012) cross sectional study was conducted on type 1 diabetic children registered in the National Diabetes Center (NDC), Al-Mustansiriyah University, Baghdad, Iraq.

Ethical approval

All patients and their families were informed about the aim and suspected benefits of the study before obtaining their agreement for participation according to the medical research and ethical regulations; thus, a verbal consent was taken from all enrolled participants and their families. All the medical research ethics rules and instructions adopted in National Diabetes Center (NDC) regarding patient's privacy, humanity and security; as well as the medical research, laboratory data and investigation results were strictly considered throughout all the steps of the study.

Patients (inclusion and exclusion criteria)

All children were thoroughly interviewed and examined by a consultant pediatrician and nutritionist according to the standard medical and laboratory work up which is adopted in the NDC; they were checked for any associated diseases, side effects, complications, coexistent treatment, adverse events, hypoglycemic events and examined physically.

Children enrolled in the study were:

- Registered type 1 diabetics, on insulin therapy.
- Accepted glycemic control, HbA1c < 8%.
- Aged 0-14 years.
- Had no any comorbid auto-immunological conditions such as celiac disease, thyroiditis, vitiligo etc.

Laboratory Analysis

Blood samples were taken from all participants during their regular visits; for laboratory analysis and screening for the autoimmune markers of type 1 diabetes: ICSA, IAA, IA-2A and GAD-A.

The EUROIMMUN, Medizinische Labordiagnostika AG, ICSA are detected by indirect immunofluorescence using monkey pancreas as substrate; while the IAA, IA-2A and GAD-A used ELISA test kits to provide a quantitative in vitro assay for determination of human antibodies in serum and/or plasma.

Statistical Analysis

Statistical analysis and reporting of obtained data were carried out by using SPSS for Microsoft Excel - Windows XP professional program.

Results

The 91 registered diabetic children's data was found to be as following: the mean age was 11.3 ± 2.8 years, range 4-14 years, male/female ratio was 1.33 (52 boys and 39 girls), BMI was 19.45 ± 4.16 kg/m², the daily insulin requirement to obtain good control was 0.846 ± 0.295 IU/Kg/day and duration of disease since onset of diabetes was 4.48 ± 3.38 years,

ranging from <1 up to 14 years. (Table 1 - next page)

The autoimmunological tests ICSA, IAA, IA-2A and GAD-A were done for all patients. We found 78 (85.71%) children with positive results for one or more of the four forward autoimmunological tests, in different degrees, forming a group of type 1A diabetes; and the remaining 13 (14.29%) children did not show any positive results for the four autoimmunological tests, forming a group of, idiopathic, type 1B diabetes. (Tables 1 and 2)

The group of type 1A diabetes children showed a positive result for the ICSA (2/5) with 40.0% among children within one year of diagnosis; while the IAA (58/78) 74.35%, the IA-2A (44/78) 56.41% and the GAD-A (50/78) accounted for 64.10% of all patients after different durations of diagnosis. The highest prevalence of positive IAA 100% and GAD-A 81.81% were at 3-4 years from onset of disease; also, the autoantibodies continue to be detected in children with disease duration in excess of five years. (Table 2 - next page)

Discussion

The International Diabetes Federation (IDF) globally estimated the incidence of number of newly-diagnosed type 1 diabetes cases per year at age group 0-14 year, 2010, was 75,800 children per year; and found the prevalence, number of children with type 1 diabetes at age group 0-14 year, 2010, was 479,600 children per year. (13) Furthermore, the prevalence of type 1 diabetes was estimated in the Middle East region in 1999; in Gaza strip, Iraq, Israel, Jordan Lebanon and Syria it was 11, 10, 10, 12, 9 and 12 cases per 100,000 of population at age 0-14 years. (14)

The autoimmune type 1 A diabetes mellitus forms about 90-95% and, idiopathic, type 1B diabetes mellitus forms 5-10% of newly diagnosed diabetics. (1, 24) while in our study type 1A and type 1B groups form 85.61% and 14.29% respectively among the Iraqi diabetic children; this goes along with the Krishnamurthy et al study, in the north Indian population, where they found higher frequency of type 1B

	T1A DM	T1B DM	All T1DM	P value*
Age (years)	11.4±3.5	12.0±2.9	11.8±3.5±	> 0.05
BMI (kg/m ²)	19.26±4.09	20.52±4.55	19.60±4.16	> 0.05
Dose of insulin (IU/kg/day)	0.835±0.282	0.913±0.357	0.846±0.295	> 0.05
Duration since diagnosis (years)	4.26±3.18	5.76±4.36	4.48±3.38	> 0.05

* T-test, P value at 0.05 level of significance

Table 1: Descriptive criteria of study groups

Duration of diabetes (years)		ICSA		IAA		IA-2A		GAD-A	
(years)	(n)	n	(%)	n	(%)	n	(%)	n	(%)
(< 1)	(5)	2	(40%)	2	(40%)	3	(60%)	3	(60%)
(1-2)	(17)	1	(9.09%)	15	(88.23%)	11	(64.7%)	11	(64.7%)
(2-3)	(20)			15	(75%)	13	(65%)	9	(45%)
(3-4)	(11)			11	(100%)	6	(54.54%)	9	(81.81%)
(4-5)	(13)			8	(61.53%)	4	(23.07%)	10	(76.92%)
(> 5)	(12)			7	(63.63%)	7	(63.63%)	8	(72.72%)
Total	(78)	3	(3.84%)	58	(74.35%)	44	(56.41%)	50	(64.1%)

Table 2: Autoantibodies of type 1a diabetes according to duration of disease

diabetes, about 45%;(25) other studies claim the increase in the frequency of diabetes and particularly of type 1B diabetes to the racial, genetic and environmental differences which are higher near the equator and in Asian, African, Indo-Asian and Jewish (Semitic) races.(5, 10, 18, 20, 24, 25)

We studied the frequency and clinical characteristics of type 1A and type 1B diabetes; we found that there was

no statistically significant differences between both groups of diabetes regarding their age, BMI, insulin requirement and duration of disease, t-test, P > 0.05. Krishnamurthy and Damanhouri also proved resemblance of clinical features of type 1A and type 1B diabetics. (18, 25)

The autoimmune antibodies IAA and GAD-A, detected in the type 1A diabetes group, showed highly positive rates between 3-4 years from onset of diabetes;

and for the IAA, IA-2A and GAD-A, they continue to be detected even after more than 5 years from onset of diabetes. While, Odugbesan and Kelly found that after one month of onset of diabetes the antibody positivity declined with increasing disease duration, as reported among Euripides, Indo-Aryan and Indian origin populations. (20, 21)

In the current study, like the study of Kelly et al, the frequency of antibodies to insulin, IAA, were significantly increased

with increasing duration, suggesting the possibility of a predominant consequence of insulin therapy rather than an autoimmune response to endogenous insulin. (21)

The Autoantibodies of type 1A diabetes children in our study, ICSA, IAA, IA-2A and GAD-A, were equivalent to the results of a Saudi Arabian study; 56% of the newly diagnosed diabetic children were reported to be positive for islet cell antibodies(22) and another Saudi study for MSc degree (24) which showed that the frequency of ICA, GAD and IAA autoantibody were 33%, 60% and 70% respectively; and were less than what El-Khateeb et al found in their study about the prevalence of antibodies to GAD in newly diagnosed Syrian, and Jordanian cases 88.8%,(16) but are similar to Kelly et al results of ICA, GAD and IAA 35.4%, 56.3% and 85.4% respectively and for IA2A 16.7%.(23)

Conclusion

We concluded that the immune mediated, type 1A, diabetes was slightly less prevalent among Iraqi diabetic children than Europeans.

The IAA and GAD-A markers showed highly positive rates among diabetics between 3-4 years from onset of diabetes; and the IAA, IA-2A and GAD-A markers continue to be detected in excess of 5 years from the onset of diabetes.

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Impaired glucose tolerance test among B thalassemia patients in Hawler province, Iraq

ABSTRACT

Background: Thalassemia is one of the commonest hemolytic anemias and serious complications due to iron overload still occur in the thalassemia patients. Endocrinal complications are among the complications of hemosiderosis especially the development of diabetes. The aim of the study is to focus on the prevalence and risk factors of impaired glucose tolerance in transfusion dependent B thalassemia patients.

Material and Methods: Prospective study of a total of 50 transfusion dependent B thalassemia patients aged 10-15 years (31 male and 19 females). Full history and examination and full laboratory investigations, serum ferritin, hepatitis B and C markers, and oral glucose tolerance test were recorded from the 1st of January to the 31st of April 2010.

Result: The prevalence of impaired glucose tolerance was 26% and there was no diabetes mellitus. The risk factors for abnormal glucose tolerance were: total units of blood transfusion/year ($p=0,046$).

Conclusion: Frequently transfused patients with under or poor compliance with iron chelation therapy increase the risk of development of complications including impaired glucose tolerance. Early starting of desferrioxamine therapy will prevent such complications.

Key words: thalassemia, impaired glucose tolerance, diabetes mellitus

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Introduction

Thalassemias are genetic disorders in globin chain production. The homozygous state, thalassemia major, results in a severe anemia and often death before puberty. The heterozygous state, thalassemia minor is less severe and may be asymptomatic with little or no anemia (1,2). Iraq is one of the countries in which 6-10% of the population have hemoglobinopathy of which thalassemia is a major part (1,3). Depending on the mutation and the degree of fetal hemoglobin production, transfusions in patients with thalassemia major are necessary in the 2nd months of life or the 2nd years of life, but rarely later (4). A decision to initiate regular transfusions in patients with β -thalassemia may be difficult and should be based on the presence and severity of the symptoms and signs of anemia, including failure of growth and development. But, transfusion results in a second disease due to iron overload (5,6). Most clinical manifestations of iron loading do not appear until the second decade of life in patients with inadequate chelation. Endocrine abnormalities are among the common complications of thalassaemia. (5,7,8)

Hypogonadotropic hypogonadism, diabetes mellitus, and hypothyroidism represent the most common endocrinopathies in thalassaemic patients (8-9). Impaired glucose tolerance (IGT) is suggested as a replacement for terms such as asymptomatic diabetes, chemical diabetes, subclinical diabetes, borderline diabetes, and latent diabetes (1). IGT may precede type 2 diabetes mellitus by many years (10).

The pathogenetic mechanisms leading from siderosis to the development of diabetes are still poorly understood (11).

Impaired glucose tolerance and diabetes mellitus may be the consequence of pancreatic β -cell destruction secondary to iron overload, chronic liver disease, viral infection and/or genetic factors (7,11)

Three mechanisms are involved :

- 1) insulin deficiency,
- 2) insulin resistance, and
- 3) hepatic dysfunction (12,13).

Risk factors for diabetes in patients with β -thalassemia major have been suggested to include age, increased amount of blood transfusion, serum ferritin level, compliance with iron-chelation therapy, family history of diabetes, hepatitis viruses, and pubertal status (14-16).

Aim of the study

To study impaired glucose tolerance among patients with b- thalassemia major and risk factors for impaired glucose tolerance among patients with b- thalassemia major and to evaluate the compliance of the patients with the chelation therapy.

Patients and Methods

A prospective study was conducted at January 2010 to the end of April 2010 on 50 thalassemic patients in the thalassemia center in Hawler governorate. The diagnosis of thalassemia was based on clinical

features and hematological criteria (peripheral blood evaluation and hemoglobin electrophoresis of the patients). Those eligible for study were between 10-15 years and were receiving frequent transfusions (10-15 ml packed erythrocytes per kg body weight or whole blood 20 ml/kg given every 2-4 weeks. Cases with family history of diabetes were excluded from the study. Information regarding Name, age, sex, height, body weight, age at the first blood transfusion, frequency of blood transfusion per year, age at the start of iron-chelation therapy, compliance with iron-chelation therapy, history of splenectomy, were taken. The compliance with defesrioxamine chelation therapy was assessed as good (≥ 5 desferrioxamine infusions per week) and poor (≤ 4 infusions per week) (14).

Physical examination was done: the height, weight, liver span and spleen size in non splenectomized patients were recorded. Serum ferritin was measured by Automated Architect

Machine (Abbott Company) in the Media Center.

- Tests for HBs Ag and HCV-Ab were detected by using ELISA technique.

Plasma glucose level was assessed by performing oral glucose tolerance test with estimation of fasting and post prandial glucose (2 hr) plasma glucose (by Trinder’s glucose oxidase told to be fasting or called by telephone).

Oral glucose tolerance test : was estimated using World Health Organization’s definition of impaired glucose tolerance and diabetes, an oral glucose tolerance test (OGTT) was performed in the morning after an overnight fast. A (base line) blood sample was drawn; Glucose was ingested in a dose of 1.75 g/kg up to a maximum of 75 g, and plasma glucose was estimated 2 hours later. Impaired fasting glucose (IFG) was diagnosed if fasting plasma glucose was ≥ 110 mg/dL and less than 126 mg/dL (6.1-7.0 mmol/L). Impaired glucose tolerance test was diagnosed if the 2 hour post glucose plasma glucose was ≥ 140 mg/dL and less than 200 mg/dL (7.8- 11.1 mmol/L) and fasting plasma glucose was <126 mg/dl (7.0 mmol/L). Diabetes was diagnosed if the fasting plasma glucose

Patient characteristics	Mean	Range
Age(years)	12.3 \pm 1.5	(10-15)
Height(cm)	131.8 \pm 8.12	(110-150)
Weight(kg)	30 \pm 5.4	(17-42)
Age at first blood transfusion (months)	10.5 \pm 5	(3-22)
Age at starting Desferrioxamine (years)	5.7 \pm 2.1	(3-11)
Units of blood transfusion/year	14.2 \pm 1.9	(12-20)
S.Ferritin(ng/ml)	6127 \pm 2.4	(992-10679)
Splenic size(cm) below costal margin In 24 cases	4.7 \pm 2.8	(1-12)
Liver span(cm)	11.3 \pm 2.6	(7-20)
Fasting plasma glucose	99 \pm 12.3	(75-124)
2 hours post prandial plasma glucose	122 \pm 27	(71-184)

Table 1: Demographic characteristics of 50 thalassemic patients with mean and range of each item

Patient characteristics	NO.	%
Gender		
Male	31	62%
Female	19	38%
Hepatitis C infection	34	68%
Hepatitis B infection	0	0%
Splenectomy	26	52%

Table 2: Demographic characteristics of 50 thalassemic patients in No. and % of each character

Patient characteristics	Normal GT	Impaired GT	P-value
No. of patients	37 (74%)	13 (26%)	
Age(years)	12±1.5	13±1.5	0.055
Gender			
Male	22 (59.5%)	9 (69%)	0.532
Female	15 (40.5%)	4 (31%)	
Weight(kg)	29.32±5.3	31.85±5	0.148
Height(cm)	131.7±8.2	132.38±8.1	0.798
Mean age at first blood transfusion(months)	10.5±4.8	10.3±5.8	0.876
Mean age at starting Desferrioxamine (years)	5.3±1.8	6.7±2.6	0.046*
Units of blood transfusion/year	13.7±1.7	15.5±2.1	0.004**
S. Ferritin(ng/ml)	5810±2.3	7030±2.6	0.117
Hepatitis C infection	24 (64.9%)	10 (77%)	0.423
Splenectomy	17 (45.9%)	9 (69%)	0.148

P-Value (significant), ** P-Value (highly significant) This Table shows Correlation of patients characteristics with Impaired glucose tolerance and Normal glucose tolerance and p-value of each characters.

Table 3: Patients’ characteristics and plasma glucose

was ≥ 126 mg/dL (7.0 mmol/L) and 2 hour post glucose plasma glucose ≥ 200 mg/dL (11.1 mmol/L) (17)

Data Analysis:

Data were entered into Statistical Package for Social Science (SPSS) program for Windows version 16 to generate the

general characteristics of the study. Quantitative variables were summarized by finding mean \pm SD. Statistical analysis: Differences between patients with and without abnormal glucose tolerance were tested with the independent t-test, x2 test and C-test to identify the potential risk factors. A two-tailed P-value of 0.05 was considered to be statistically significant.

Age group	Normal GT	Impaired GT	Total
10-11.9	18 (85.7%)	3 (14.3%)	21 (100%)
12-13.9	14 (73.3%)	5 (26.3%)	19 (100%)
14-15	5 (50%)	5 (50%)	10 (100%)
Total	37 (74%)	13 (26%)	50 (100%)

◀ P-value= 0.106 which is not significant.

Table 4: Relation of age group with GT

Table 4 shows the Distribution of Impaired glucose tolerance and Normal glucose tolerance in thalassemic patients with age group.

Age at starting desferrioxamine	Normal GT	Impaired GT	Total
Below 5 years	14 (87.5%)	2 (12.5%)	16 (100%)
5-10 years	23 (72%)	9 (28%)	32 (100%)
over 10 years	0 (0%)	2 (100%)	2 (100%)
Total	37 (74%)	13 (26%)	50 (100%)

◀ P.value < 0.026 which is significant difference

Table 5: Relation of the age at starting desferrioxamine therapy with Impaired GT and Normal GT in thalassemia patients

The age at starting desferrioxamine therapy with plasma glucose where it is shows that 87.5% of normal glucose tolerance patients start desferrioxamine therapy below 5 years but it was 12.5% among impaired glucose tolerance patients.

Serum Ferritin	Normal GT	Impaired GT	Total
<5000	15 (78.9%)	4 (21.1%)	19 (100%)
5000-10000	22 (75.9%)	7 (24.1%)	29 (100%)
>10000	0 (0%)	2 (100%)	2 (100%)
Total	37 (74%)	13 (26%)	50 (100%)

◀ P-value= 0.05 which is not significant.

Table 6: Relation of Serum Ferritin With Impaired GT and Normal GT for patients with thalassemia

This table shows that 21.1% of patients had IGT at S.Ferritin < 5000 while 100% of them had IGT at S.Ferritin above 1000. This mean the risk of development IGT increase with increasing S.Ferritin, but serum ferritin was not risk factor, p-value not significant.

Units of blood transfusion/year	Normal GT	Impaired GT	Total
≤12	14 (93.3%)	1 (6.7%)	15 (100%)
13-15	19 (76%)	6 (24%)	25 (100%)
16-18	4 (44.4%)	5 (55.6%)	9 (100%)
≥19	0 (0%)	1 (100%)	1 (100%)
Total	37 (74%)	13 (26%)	100 (100%)

Table 7: Relation of Units of blood transfusion/year with Impaired GT and Normal GT for patients with thalassemia

Table 7 show 6.7% of patients with IGT received < 12 units of blood/year,55.6% of them received 16-18 units of blood/year, while 100% of them received > 19 units of blood/year, but it was not risk factor.

Age group	<3 rd Centile NO. %	>3 rd -<50 Centile NO. %	>50-<97 Centile NO. %	Total NO. %
10-11.9	9 (43%)	11 (52%)	1 (5%)	21 (100%)
12-13.9	10 (53%)	9 (47%)	0 (%)	19 (100%)
14-15	7 (70%)	3 (30%)	0 (%)	10 (100%)
Total	26 (52%)	23 (46%)	1 (2%)	50 (100%)

P-Value = 0.019 which is significant
Table 8: Relation of weight with age group

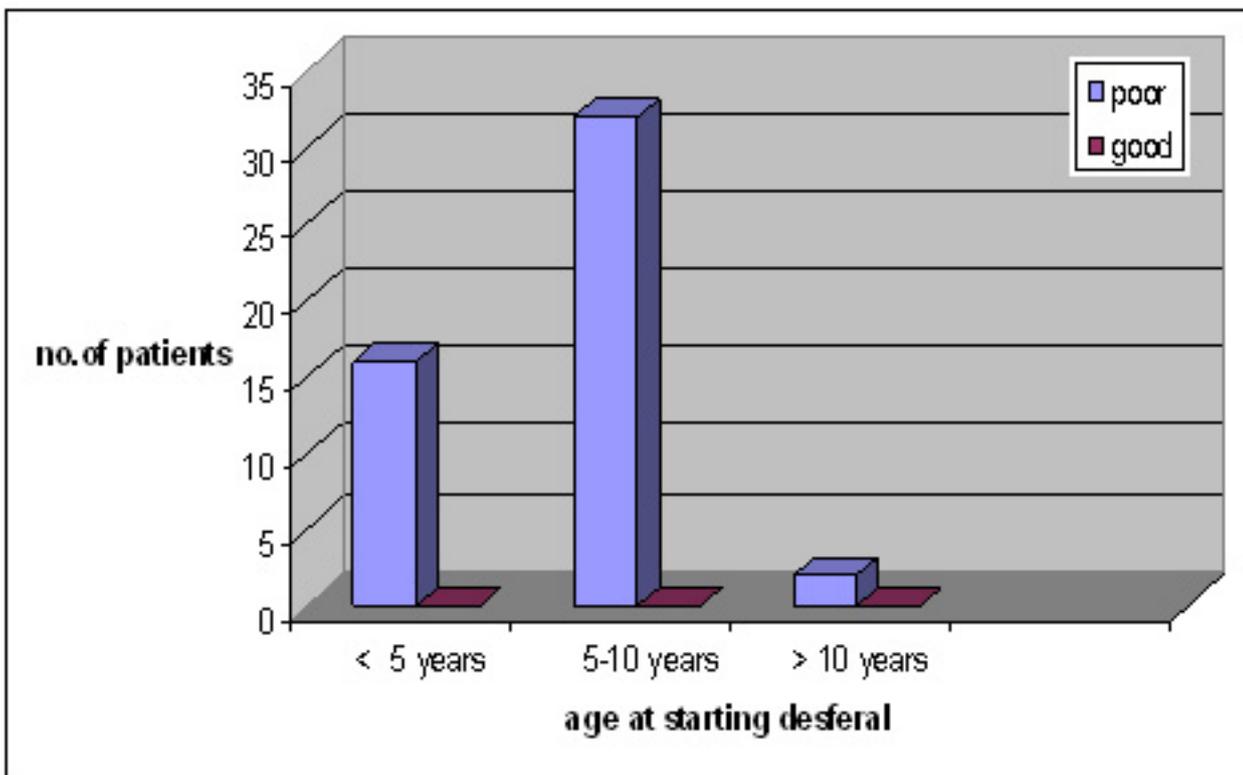


Figure 1: Compliance of patients with desferrioxamine therapy

Discussion

In this study prevalence of IGT was 26% which is nearly similar to a study done by Hafez et al, in which prevalence was 24.1%, (18).

while the mean age of patients who had IGT was 13 years and with increasing age the possibility of development of impaired glucose tolerance increase (Table 4-), but in our study age was not a risk factor for IGT which disagrees with the results of Najafipour (8) in which the mean age of those who had IGT was 18.5 years and age was a risk factor. This may be due to the fact that our range of age is limited to <15year males (62%) who were more than females (38%), similar to the result obtained by Torres et al (16, 19), Najafipour (8) and a study done by Suvarna et al (20) in which male percentages were 60%, 64% and 60% and females were 40%, 36% and 40% respectively.

The mean age of first blood transfusion of patients with thalassemia was 10.5 months, which was much lower than the mean age in a study done by Jimmy et al (14) 12 (15.1 months) and Shamshirsaz et al (21, 17) in which the mean age was 15.4 months. It appears that earlier presentation of the disease may reflect the severity of the disease in our country.

Patients' mean requirement for blood transfusions was 14.2 transfusion/year. This is nearly similar to the result obtained by Hamdoon (22). Those who required frequent blood transfusions (mean of 15.5 transfusions/year) were impaired in glucose tolerance in comparison to those who required less frequent blood transfusions (mean of 13.7 transfusions/year) in whom the glucose tolerance was normal. This is in agreement with the result obtained by of Najafipour in which the number of blood transfusions was the risk factor (Table 7) (8).

Splenectomy was done in 52% (26 cases) of the patients and this is higher than the result obtained by Jimmy et al (14, 12) in which only 20.2% of cases were splenectomized. This may be due to irregular blood transfusions

and increased extramedullary activity. in those who had impaired glucose tolerance in 69.2% of cases splenectomy was done for them and this is higher than the result obtained by Leetanaporn et al (23) in which those with IGT, for 50% of cases splenectomy was done for them and this may be due to the older age group and bad follow up of our patients.

In this study mean age of starting desferal was 5.7 years and this is in agreement with a study done by Shamshirsaz et l (21) in which the mean age was 5.1.

Patients who started desferrioxamine therapy earlier at a mean age of 5.3 years had better glucose tolerance than those who started later at a mean age of 6.7 years, and for those who started desferrioxamine at > 10 years of age, 100% of them had IGT (Table 5) and this means iron over load is a risk factor for IGT and DM. This is similar to a study done by Jimmy et al (14).

Hepatitis C virus was positive in 68%, which is nearly similar to the result of a study done by Maria et al (24) in which 57% of their cases were sero positive for hepatitis C, and in our study all cases were sero negative for hepatitis B. This may be due to the national vaccination program.

But there is no clear association between IGT and Hepatitis C in our study which is similar to a study done by Perifanis et al (25, 21) and Mowla et al (26).

In our study the mean of liver span was 11.3cm and splenic size was 4.7cm below costal margin (24 cases) which agrees with a study by Suvarna et al (16)done in India in which mean liver span was 12cm but it disagrees with him in splenic size in which splenic size was 7cm below costal margin. This is probably because most of our cases were splenectomized. The weight of 52% of patients in this study was below the 3rd centile. This result is higher than that found in a study done by Gomber and Dewan (27)in which only 31% of their cases were below the 3rd centile.

The height of 76% of cases were below the 3rd centile and this disagrees with study done by Yesilipek et al (28)in which (32.4%) were below the third centile for height. This difference may be due to irregular visits and unavailability of blood, chelation therapy, infusion pump, supportive therapy of complications of thalassemia such as Calcium, thyroxin, growth hormone, estrogen and testosterone and poor compliance with treatment.

Patient's compliance regarding acceptance of desferrioxamine therapy, was found to be poor in 100% of our cases while only 51% had poor compliance in a study done by De Santics et al. (29) This is may be due to poor education of the families and the patients about the importance of iron chelation therapy and unavailability of centers with good facilities and equipment.

Serum Ferritin level in our study was high (mean value=6127ng/ml) which is nearly similar to the result of a study done by Suvarna et al (19, 23) (mean value = 7627ng/ml) and mean value of serum ferritin in cases with IGT was 7030 ng/ml, and this is nearly similar to study done by Leetanaporn (23) in which mean value of serum ferritin in cases with IGT was 8679 ng/ml. But in our study serum ferritin was not a risk factor which is similar to a study done by Najafipour in which serum ferritin was not a risk factor also (Table 6).

In our study the mean values of plasma glucose were 99mg/dl for fasting plasma glucose and 122mg/dl for 2 hours post prandial plasma glucose which is nearly similar to the results of Suvarna et al (19, 23) in which the values of plasma glucose were 91mg/dl for fasting and 127mg/dl for 2hours post prandial plasma glucose.

Conclusion

Patients who started desferal therapy earlier are less liable to develop impaired glucose tolerance. Most of the patients were hepatitis C positive, with poor compliance with iron chelating therapy.

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H.pylori infection among children with cancer in Nanakaly hospital for blood diseases in Erbil

ABSTRACT

Background: Helicobacter pylori (H. pylori) are spiral-shaped gram negative bacteria, associated closely with a gastric and duodenal ulcer in adults and children.

Objective: Evaluate the prevalence of H. pylori infection in children with different types of cancer, admitted to Nanakaly hospital for blood disease and malignancy, during a period of 3 months.

Study design: A case-control study of 50 children (31 male, 19 female) with different types of cancer (30 ALL, 2 AML, 1 CML, 9 HL, 4 NHL, 2 NB, 1 WT, 1 RMS). The age ranged from 3-14 years, and those who received corticosteroids, cytotoxic drugs or both were enrolled into the study. In addition 50 age-and-sex matched children served as a control group. All children were subjected to history taking, clinical examination and serum ELISA for the detection of IgG antibodies specific for H.pylori antigens.

Results: The prevalence of H. pylori seropositivity accounted for 20% in the patient group versus 44% in control children. No associations were found between prevalence of H. pylori infection and any factor tested including sex, age, blood group, and crowding index, but a significant association was found between socioeconomic status and H. pylori seropositivity being present.

Conclusion: There was no significant association between H. pylori positive patients and childhood cancer.

Key words: H pylori bacteria, children, cancer

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Introduction

The pattern of infection is an early childhood acquisition of H. pylori. This has been attributed to poor socioeconomic status and overcrowded conditions.[1,2] H.pylori infection and extra gastrointestinal diseases have been increasing, especially in immuno-compromised subjects. [3] There are two types of diagnostic tests used to detect H. pylori infection; non-invasive and invasive. Non-invasive tests include the urea breath test, stool test, and serological tests antibodies (IgG, IgM and IgA) in serum. Tests of serum IgA or IgM antibodies are unreliable in detecting gastric colonization and, therefore, only IgG antibodies against H. pylori denote active infection which continues throughout life unless a course of eradication therapy is instituted.[4] Infection is more frequent and acquired at an earlier age in developing countries.[5] Factors such as density of housing, overcrowding, number of siblings, sharing a bed, and lack of running water have all been linked to a higher acquisition of H. pylori infection.[6-7] Person-to-person transmission of H. pylori through either fecal/oral or oral/oral exposure seems most likely.[8] Many investigators from different parts of the world have observed an association between H. pylori and recurrent abdominal pain. [9-10]

The aim of the study was to identify the frequency of H. pylori among patients with cancer with correlation between H.pylori and age, sex, blood group, crowding index and socioeconomic status in both groups.

Patients and Method

A case-control study of 50 children (31 male and 19 female) with different types of cancers (acute and chronic leukemia, ALL, AML, CML, and Solid tumours) who were admitted for treatment, from 1st of March 2011 to 29th of May 2011 in the Nanakaly hospital for malignancy and blood diseases in Erbil city Iraq, to receive chemotherapy or steroid or both (just two patients were newly diagnosed; blood sample tested before using chemotherapy or steroid); their age ranged from 3-14 years. Another 50 children matched for age-and-sex (26 male and 24 female) acted as the control group. Information regarding age, sex, residence, Clinical symptoms and signs (abdominal pain, dysphagia, vomiting, hematemesis, melena etc.) was taken.

Types of cancer (ALL, AML, CML, and solid tumors) and Family history of peptic ulcer, and crowding index was calculated as the total persons in the household divided by the number of rooms. Low, <1; medium, 1-2; high, >2}. [11-12] A special scoring system of socio-economic status was developed, which is modified from Darwish et al [13] Toukan et al [14] and Shabu [15]. The socio-economic status of the family was divided arbitrarily into three main categories: low status (≤ 9 points), medium status (10-18 points) and high status (>18 points). The socio-economic status of the family was determined according to educational

level of parents, occupation of parents, crowding index, type of housing (owned or rented), possession of car (no car or \geq one car) and number of electrical appliances like TV, refrigerator, air conditioner etc.

Enzyme immunoassay serology was used to detect anti-H. pylori immunoglobulin-G (IgG) antibodies using the AccubindTMH. pylori IgG kit (Monobind, Inc., United States). According to the manufacturer, this kit presents 98.7% sensitivity and 97.0% specificity.

Cut-off was defined with positive and negative control sera that were included in each assay, according to the manufacturer's instructions. Samples were considered positive if the value was > 20 u/ml and the value <12.5 u/ml was considered negative and the values between (12.5-20u/ml) considered equivocal and were excluded from the study. A statistical analysis program (SPSS version 18; SPSS, Inc), and Graph PadInStat (version 3) were used to analyze the data. The data were expressed and comparisons were performed using chi square and t-test; p-value of less than 0.05 was considered as statistically significant.

Results

The majority of the subjects were male with male:female ratio equal to 1.6:1, while in the control group male:female ratio was equal to 1.08:1, with a p value >0.05 .

The mean of age (in years) in the patient group was ($X=8.58\pm 3.21$) and in the control group was ($X=8.75\pm 2.78$).

		Age		P value
		≤ 6 yr	>6 yr	
Patient	IgG -ve	15(30%)	25(50%)	0.29
	IgG +ve	2(4%)	8(16%)	
Control	IgG -ve	10(20%)	18(36%)	0.32
	IgG +ve	5(10%)	17(34%)	

Table 1: Distribution of age in patient and control groups according to H.pylori-IgG

Table 1 shows that there is no significant association between age (in both patient and control groups) and H.pylori, as p-value >0.05 .

	Patient (n=50)	Control (n=50)	p value
H. Pylori-IgG +ve	10(20%)	22(44%)	0.017
H. Pylori-IgG -ve	40(80%)	28(56%)	

Table 2: Results of H. pylori antibody testing among patients and controls

Table 2 shows that the seroprevalence of anti-H. pylori antibodies was 20% in patients with cancers versus 44% in control children.

There is a statistically significant higher percentage of patients with negative anti H.pylori IgG compared to the control group as p value < 0.05 .

There is no significant association between crowding index and H.pylori as p-value is more than 0.05 in both patient and control groups.

Cancer Type	Number	H. Pylori-IgG -ve	H. Pylori-IgG +ve
ALL	30(60%)	24(48%)	6(12%)
HL	9(18%)	8(16%)	1(2%)
NHL	4(8%)	2(4%)	2(4%)
CML	1(2%)	1(2%)	0(0%)
AML	2(4%)	1(2%)	1(2%)
RMS	1(2%)	1(2%)	0(0%)
NB	2(4%)	2(4%)	0(0%)
WT	1(2%)	1(2%)	0(0%)

ALL acute lymphocytic leukemia; AML acute myeloid leukemia; HL Hodgkin lymphoma; NHL non Hodgkin lymphoma; CML chronic myeloid leukemia; RMS rhabdomyosarcoma; NB neuroblastoma; WT Wilms tumor.

Table 3: Anti- H. pylori IgG status with different types of malignancies in patient group

	Crowding index	H.pylori-IgG +ve	H.pylori-IgG -ve	p-value
Patient	low	0(0%)	2(4%)	0.7
	moderate	3(6%)	14(28%)	
	high	7(14%)	24(48%)	
Control	low	0(0%)	3(6%)	0.64
	moderate	6(12%)	13(26%)	
	high	16(32%)	12(24%)	

Table 4: Relation between crowding index and H.pylori-IgG in patients and controls

	symptomatic	asymptomatic	Total	p-value
H. pylori-IgG +ve	7(70%)	3(30%)	10(100%)	0.04
H. pylori-IgG -ve	9(18%)	31(82%)	40(100%)	

Table 5: Symptoms and H.pylori among patient group

Table 5 shows that there is a significant association between symptoms and H.pylori as p-value is less than 0.05.

	Socio economic status	Anti-H. pylori IgG +ve	Anti-H. pylori-IgG -ve	p-value
Control	low	20(40%)	17(34%)	0.04
	medium	1(2%)	8(16%)	
	high	1(2%)	3(6%)	
Patient	low	8(16%)	36(72%)	0.52
	medium	1(2%)	3(6%)	
	high	1(2%)	1(2%)	

Table 6: Relation of H. pylori according to socioeconomic status in control and patient groups

Table 6 shows that the majority of children in the control group have low socioeconomic status (74%) and 40% have anti-H. pylori antibody so there is a statistically significant association between seroprevalence of H. pylori and socioeconomic status. In the patient group there is no statistically significant relationship between socioeconomic status and prevalence of H.pylori infection.

Discussion

In this study, the seroprevalence of anti-H.pylori antibodies was significantly higher in control subjects (44%) than in patients with cancer (20%) (p value < 0.05). It means there is no statistically significant association between H. pylori and the type of cancer. A study was done in adults by Matsukawa Y, Itoh T, Nishinarita S, et al. which showed low seroprevalence of H. pylori in patients with leukemia.[16] Seroprevalence of H.pylori is low in patients receiving organ transplants, possibly due to the use of antibiotics[17-18], suggesting that systemic administration of antibiotics eradicates H.pylori, and most of the patients in Nanakaly Hospital had received antibiotics in their course of treatment as well so the false negatives occur in immunocompromised patients.[19] Nonetheless, the sensitivity of serological assays is poor in children. The strains in Asia are different from those that are circulating in the rest of the world. [20]The mean antibody levels in young children are significantly lower than in older children and adults and these age-related standard values have not been established for children. [21]

The seroprevalence of anti-H.pylori antibodies done by Amal M Abd El-Latif, Adel SA Ali, et al. [22], was 60% (36/60) in patients with secondary immunodeficiency; the remaining cases with malignancies account for 72.2% (26/45) having anti-H. pylori antibodies, so this study reported a significant association between H.pylori seroprevalence and types of cancer.

There is no significant relationship of age with H. pylori seroprevalence, similar to that obtained by Amal SM Sayed et al. in Egypt, Mansour -Ghanaei, et al. in Iran, and Amal M abd El-Latif et al. in Egypt 2010. [23-24] Nguyen BV, et al. in Vietnam, and the study of Vitor Camilo Cavalcante Dattoli et al showed that age more than 8 years was positively associated with prevalence of anti-H. pylori antibody [25-26]

This supports the hypothesis that in developing countries the acquisition of H. pylori infection can occur in early childhood. [27] H. pylori infection was also not found to be related to gender

in agreement with Nguyen et al. in Vietnam 2006, and in a similar study done by Mohammed A Mohammed et al. in Egypt, [25,28] Taiwan, Korea, and Mexico,[29-31] while Mehmet Kanbay et al. in Turkey[32] reported a significant relation between H. pylori and female gender, while another study done by Marilyn L. et al. in California reported a significant association between H. pylori and male gender.[33]

Regarding the symptoms in our study, most patients with H. pylori were symptomatic, similar to a study done by Luigi Satacroce[34], with no significant association between rate of H. pylori infection and crowding index. Similar results were obtained by Hoda M. Malaty et al. in South Korea. [35]Milman N et al.[36] and also A.H.M. Alizadeh, et al.[37], and McCallion WA et al showed positive associations between H. pylori infection and the following household variables; number of children in the household, household density, sharing a bedroom, and sharing a bed with a parent.[38]Low socioeconomic status in the control group is a risk factor for the acquisition of H. pylori bacterium during childhood. This result is similar to that obtained by Hoda M. Malaty et al. and also by Stephen C. Fiedorek, MD et al.[36] Regarding the patient group our study showed that there is no statistically significant association between H. pylori seroprevalence and socioeconomic status, and this result may be influenced by low seroprevalence of H. pylori in children with malignancies in spite of the majority of cases being of low socioeconomic status.

Conclusion

A significant association between H. pylori positive patients and symptomatic patients was present, as well as between socioeconomic status and H. pylori seropositivity in the control group, in contrast to the patient group but no significant association between H. pylori positive patients and childhood cancer, and age, sex, blood group, and crowding index in both groups.

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Endophthalmitis after Intravitreal Bevacizumab Injection

ABSTRACT

Objectives: The aim of the study is to report all cases of endophthalmitis that occurred after Intravitreal bevacizumab injection at King Hussein Medical Center and to investigate its etiology.

Patients and methods: This study was conducted at King Hussein Medical Center. All cases of endophthalmitis that occurred during a one year period were reported. Cases were investigated regarding the causative factor for the occurrence of endophthalmitis. Data collected included the severity of endophthalmitis, the causative organism, the place where injection was given whether operating theater, outpatient ward or clinic, method of sterilization and the use of antibiotic eye drops.

Results: A total number of 1854 patients had Intravitreal bevacizumab injection. Eight cases have endophthalmitis. Six patients had the injection in clinic. Two patients were not given antibiotics after the injection.

Conclusion: Injecting Intravitreal bevacizumab in operating theater under sterile condition with the use of antibiotics decreases the risk of endophthalmitis.

Key words: endophthalmitis, bevacizumab injection

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Introduction

Intravitreal injection of anti-vascular endothelial growth factor has become the standard of care for the treatment of a number of retinal diseases, including exudative macular degeneration; retinal vein occlusions; diabetic macular edema; proliferative diabetic retinopathy; and neovascular glaucoma. (1-4) Intravitreal bevacizumab is widely used in King Hussein Medical Center for various reasons with diabetic retinopathy being the most common indication.

The aim of the study is to report all cases of endophthalmitis that occurred after Intravitreal bevacizumab injection at King Hussein Medical Center and to investigate its etiology and to see whether it is related to method of sterilization.

Patients and Methods

This study was conducted at King Hussein Medical Center. All cases of endophthalmitis that occurred during a one year period (2011) were reported. Cases were investigated regarding the causative factor for the occurrence of endophthalmitis. Data collected included the severity and onset of endophthalmitis (mild, moderate or severe), the causative organism, the place where injection was given whether operating theater, outpatient ward or clinic, method of sterilization (for patient and physician), and the use of antibiotic eye drops. P-value was used to determine statistical significance and was considered significant when $p < 0.05$.

Results

A total number of 1854 patients had Intravitreal bevacizumab injection. Eight cases have endophthalmitis (0.4%). Endophthalmitis was severe in four of them and lead to loss of vision. Four patients were treatable. Six patients had the injection in clinic and two in outpatient ward. Two patients were not given antibiotics after the injection. Staphylococcus was seen in 6 patients and streptococcus in 2 (Table 1 - opposite page).

Discussion

The risk of endophthalmitis in our study was low (0.4%). In literature, the rate is reported to range from 0.01% to 2%. (5-7) Severity of endophthalmitis was assessed by examining visual acuity, degree of pain, redness and photophobia and presence of hypopyon. (8) Endophthalmitis was severe in four of them. They had visual acuity of light perception at presentation. Those patients did not respond to aggressive

Factor	Number of patients	P-value
Severity		
Mild	3	P > 0.05
Moderate	1	
Severe	4	
Place		
Clinic	6	P < 0.05
Theater	-	
Outpatient ward	2	
Sterility		
Doctor alone	-	P < 0.05
Patient alone	2	
Patient and doctor	-	
None	6	
The use of antibiotics		
Used	2	P < 0.05
Not used	6	

Table 1: Distribution of cases of endophthalmitis

treatment and lost their vision. The other four patients had mild and moderate endophthalmitis and were treated with no sequelae.

Six patients had the injection in clinic and two in outpatient ward. Four of the patients with in clinic injection had severe endophthalmitis. This was statistically significant. Regarding sterility of the procedure, neither the doctor nor the patient was scrubbed in six of patients with endophthalmitis. In the remaining two patients, the patient was scrubbed but the doctor did not scrub and wear gloves. When topical antibiotics were prescribed post injection, two cases of endophthalmitis were encountered in comparison with six cases encountered when antibiotics were not prescribed ($p < 0.05$).

Staphylococcus was seen in 6 patients; four of them were aureus species and two were epidermidis. Streptococcus viridians and pneumonia were seen in 2 cases.

In literature, some studies had failed to show direct relation between the use of topical antibiotics and endophthalmitis. (9-10) Others had shown that use of

topical preoperative drops combined with topical povidone 5% reduced the risk of endophthalmitis. (11-12) Our recommendation is to use both topical antibiotic and an aseptic agent like povidone iodine. The type of bacteria we found supports that the infection occurred due to lack of sterility as the majority of these organisms are present in skin and considered as patient flora.

In conclusion, we recommend injecting Intravitreal bevacizumab in the operating theater under sterile conditions with the use of antibiotics to decrease the risk of endophthalmitis.

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Astigmatism after Extracapsular Cataract Extraction

ABSTRACT

Objectives: The aim of the study is to assess suture related astigmatism in extracapsular cataract extraction.

Patients and Methods: This prospective study was conducted in Royal Medical Services during the period between January and December 2012. One hundred and forty patients underwent extracapsular cataract extraction by two different surgeons enrolled in the study. Exclusion criteria included any refractive error prior to surgery and any surgical complication. All patients had in the bag lens implantation. Stitches were removed six to eight weeks after surgery. Ocular assessment included postoperative refraction one month and four months after surgery. Astigmatism was recorded for each surgeon at the two visits.

Results: A total number of 144 patients were included. Seventy two patients were done by each surgeon. Age range was 32.7 years to 87.3 years. Male to female ratio was 1.2:1. Post operative with the rule astigmatism of more than 1 Diopters occurred in 58 cases for the first surgeon and 41 cases of the second surgeon. The majority of cases were corrected by removal of stitches.

Conclusions: Better wound suturing technique minimizes suture related astigmatism. It also prevents residual astigmatism that occurs after removal of stitches.

Key words: astigmatism, suturing techniques

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Introduction

Extracapsular cataract extraction was the procedure of choice for cataract surgery before the evolution of phacoemulsification. (1-2) It is still widely used in developing countries. In this procedure, a wound is created either in the sclera, cornea or limbus in order to extract the natural lens and to introduce the artificial lens. (3-4) At the end of the procedure the wound is usually closed with sutures. Nylon 10/0 is widely used worldwide to close corneal and limbal wounds. (5) Some surgeons use vicryl and virgin silk to close the wound. (6) The type of suture could be continuous or interrupted depending on surgeon preference. In case of interrupted sutures, the number of sutures varies depending on length of the wound and surgeon preference. (7)

Sutures could be tight or loose depending on surgeon technique and experience. Tight sutures may cause with the rule astigmatism, that is corrected with plus cylinder at 90 degrees, while loose sutures can lead to wound gap, iris prolapse and against the rule astigmatism. (8-9) Sutures are usually removed 6 to 8 weeks after surgery. (10)

In our study, we selected patients not having any refractive errors prior to surgery to see the impact of surgery itself on causing astigmatism. The surgeries were done by two different surgeons in order to compare different surgical techniques of wound closure.

Patients and Methods

This prospective study was conducted in Royal Medical Services during the period between January and December 2012. One hundred and forty patients underwent extracapsular cataract extraction by two different surgeons enrolled in the study. Exclusion criteria included any refractive error prior to surgery and any surgical complication. All patients had in the bag lens implantation. Patients with decentered intraocular lens or in sulcus

implantation were not included in order not to count astigmatism from causes other than sutures. Stitches were removed six to eight weeks after surgery. Ocular assessment included postoperative refraction one month and four months after surgery. Astigmatism was recorded for each surgeon at the two visits.

Results

A total number of 144 patients were included in the study. Seventy two patients were done by each surgeon (group 1 for first surgeon and group 2 for second surgeon). Age range was 32.7 years to 87.3 years. Male to female ratio was 1.2:1. Post operative with the rule astigmatism of more than 1 Diopters occurred in 58 cases of group 1 (80.6%) and 41 cases of group 2 (56.9%). With the rule astigmatism of more than 3 Diopters was seen in 7 cases of group 1 and 2 cases of group 2. Against the rule astigmatism occurred in 4 and 11 patients of the two groups respectively. The majority of cases were corrected by removal of stitches (Table 1).

Discussion

We compared the results of two different surgeons in our study. All cases of preoperative refractive errors were excluded from the study to ensure that the cause of astigmatism is related to surgery. Other surgical causes that cause postoperative astigmatism such as intraocular lens decentration, in sulcus lens implantation and vitreous loss were also excluded. (11-12) This leaves the sutures as the only cause of postoperative astigmatism. The wounds in all patients were closed by interrupted 10/0 nylon sutures. All wounds were limbal.

80.6% of group 1 patients had with the rule astigmatism when measured one month after surgery with stitches being not removed compared to 56.9% of group 2 (Table 1). With the rule astigmatism occurs with steeper cornea and is usually corrected by plus cylinder at axes of 90 degrees. (13-14) It is produced by tight stitches. These figures give us an indication that the first surgeon made tighter stitches than the

second surgeon. More than 3 Diopters of with the rule astigmatism, which is considered disabling, occurred in 9.7% and 2.8% of the two groups respectively. On the other hand, against the rule astigmatism occurred in 15.3% of group 2 and 5.6% of group 1. This also means that second surgeon made more loose stitches than the first surgeon.

All stitches were removed 6 to 8 weeks post surgery. Final refraction was done 4 months after surgery. Residual astigmatism occurred in 26.4% of group 1 patients with tighter stitches compared to 18.1% of group 2 patients. This means that more than three quarters of patients showed no residual astigmatism after stitch removal.

In conclusion, better wound suturing techniques minimize suture related astigmatism. It also prevents residual astigmatism that occurs after removal of stitches.

Astigmatism	Group 1		Group 2	
	Number	Percentage	Number	Percentage
With the rule astigmatism				
> 1 Diopters	58	80.6%	41	56.9%
> 3 Diopters	7	9.7%	2	2.8%
Against the rule astigmatism				
> 1 Diopters	4	5.6%	11	15.3%
> 3 Diopters	-	-	-	-
No astigmatism	10	13.9%	20	27.8%
Residual astigmatism				
With the rule	16	22.2%	9	12.5%
Against the rule	3	4.2%	4	5.6%
Total	19	26.4%	13	18.1%

Table 1: Astigmatism obtained by two different surgeons before and after stitch removal

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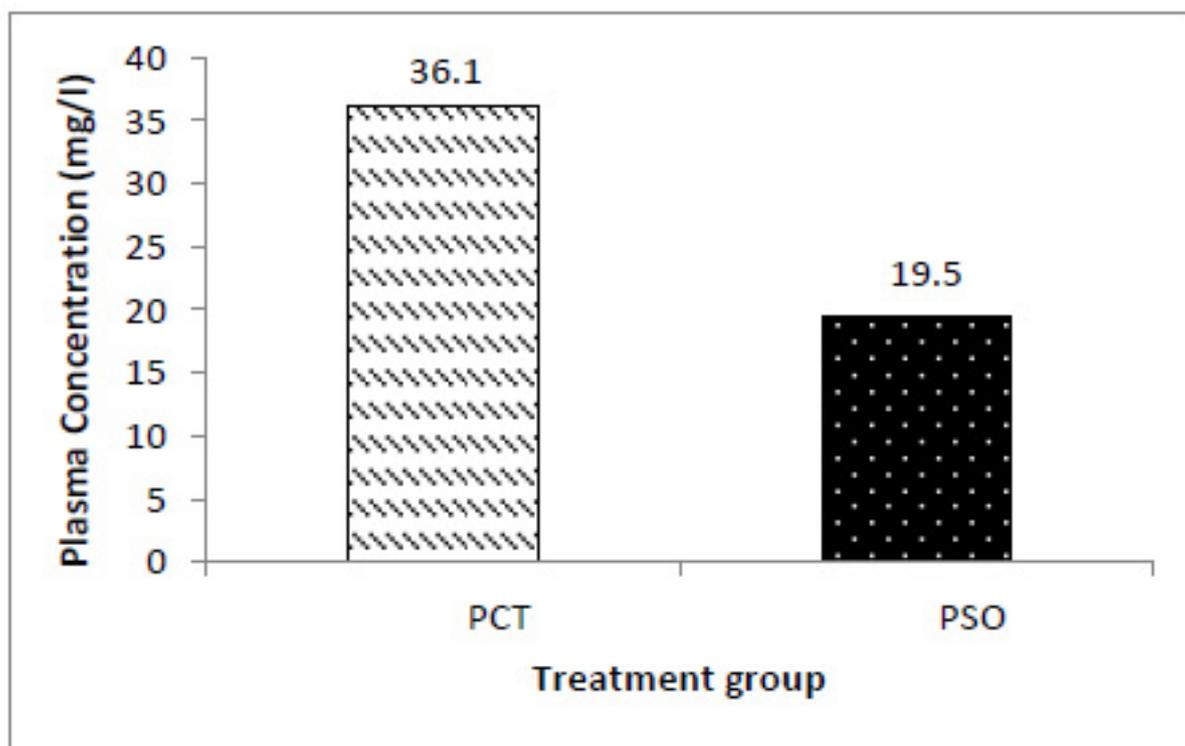


Figure 4: The mean (\pm SEM, n=6) plasma concentration (mg/l) of paracetamol in paracetamol-treated group (PCT) and in pomegranate seed oil treated group (PSO).

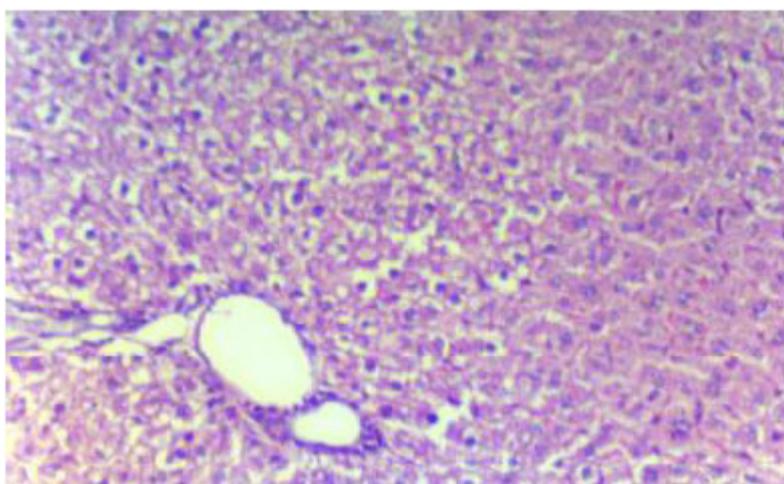


Figure 5: Histopathology of liver sections of control group showing normal hepatic tissue (H & E, 250X)

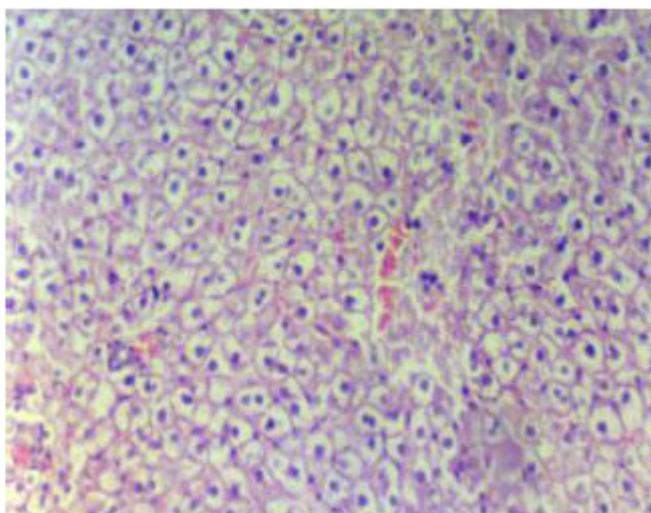


Figure 6: Histopathology of liver sections of paracetamol-treated group showing severe hepatocytes necrosis (H & E, 250X).