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Editorial:

Topical Macrolide Immunomodulators for Therapy of Atopic Dermatitis

Nidhal Abdul-Muhaimen *PhD*,**Ahmad Hachem muhana** *MSc*

Introduction

To date, tacrolimus (FK 506) and the ascomycin derivative pimecrolimus (SDZ ASM 981) are the most studied topical macrolide immunomodulators. Both of these drugs have a high specificity for inhibiting the expression of inflammatory T-cell cytokines and have shown promising results in the treatment of atopic dermatitis (AD) when applied topically [(1)].

Topical calcineurin inhibitors

Tacrolimus is a topical formulation of the immunomodulatory agent FK 506 and is available as a 0.03% and 0.1% ointment. Originally used for atopic dermatitis, tacrolimus modulates immune-cell function by inhibiting calcineurin-dependent dephosphorylation- activation of specific nuclear factors and therefore preventing transcription of proinflammatory cytokines [(2)].

Improved therapy for atopic dermatitis

Once AD has been diagnosed, two therapeutic strategies can be used to address the pathophysiologic abnormalities found in these patients: the first strategy is the traditional mainstay of topical treatment of atopic dermatitis is steroid ointments [(3)].

Potent topical steroids have a high intial success rate in clearing an eczematous rash, but the effects tend to diminish later on, a phenomenon known as tachyphylaxis.

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Long term use of these medications is associated with many potential risks, especially in infants and children, and stronger steroids are more likely to produce adverse local and systemic effects. Skin atrophy, telengectasia, stria, secondary infection, acneiform eruption, hypopigmentation, purpura, poor wound healing can result from long-term application of topical steroids, particularly when used on face, groin, and intertriginous areas of the body [(4)].

Clinically significant suppression of the hypothalamic-pituitary-adrenal axis also can result from the long term treatment of topical steroids, especially in an infant, whose body surface is large compared with his or her weight. When long-term treatment of AD is required, the adverse effects of steroids make them an unsatisfactory treatment. In addition, Colonization and infection with *Staphylococcus aureus* contributes to the severity of AD and reduce corticosteroids sensitivity. These observations suggest a role for antibiotic/corticosteroid combination or topical macrolide immunosuppressive ointment such as tacrolimus ointment in the treatment of AD. Finally, a number of patients with AD may not response appropriately to their topical steroid due to complication by superinfection with S. aureus [(5)].

The new immunomodulators tacrolimus and pimecrolimus represent a safer class of drugs that alter the local immune response in a more targeted fashion than do older steroids

[6]. These drugs suppress cytokine gene transcription by inhibiting calcineurin, resulting in fewer activated T cells in the skin. Both have proven to be safe and effective in adult and pediatric populations. Systemic absorption is generally not significant with either of these agents. Patients experience less burning if eczematous patches are treated initially with a corticosteroid with transition to calcineurin inhibitors after partial clearing. Improvements tend to be steady, with progressively smaller areas requiring treatment [7]. These agents are particularly useful on the eyelids and face, in cases of refractory dermatitis, in areas prone to steroid atrophy (thus they particuraly useful for the treatment of areas such as the face and intertriginous regions).

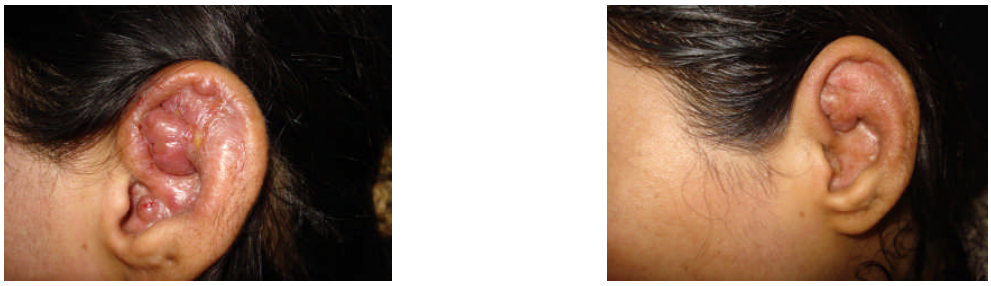

Figure 1: A 29-year-old patient who was insensitive to topical corticosteroid therapy quickly responded to O.l% tacrolimus ointment. (Left) Before treatment with 0.1% tacrolimus;(right) 10days after application of 0.1% tacroJimus. Histology from biopsy taken prior to treatment revealed an eczema; immunohistochemical reactivity,*positive*

IMMUNE MODULATION OR IMMUNE SUPPRESSION?

The difference between immune modulation and immune suppression is subtle. In AD there is an immune pathology in which skin lesions have infiltrates of inflammatory immune cells (i.e., T cells, macrophages, basophils, eosinophils). In this instance, application of a drug that blocks the activation of these cells at the site of the lesion reverses the immune pathology and thus can be considered to modify the local immune response. On the other hand, systemic immune suppression with such drugs as tacrolimus (Prograf®) and cyclosporin (Neoral®) was developed to suppress a normal immune response to the nonself antigens of an allograft. In doing so, it also suppresses normal immune responses to infectious agents and decreases immune surveillance in the protection against cancer.

Tacrolimus ointment and pimecrolimus cream are considered to be immune modulators because they target a specific immune pathology and because their action seems to be limited to the site of the immune pathology [8].

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Comparison between VDD and DDD Pacing in Symptomatic Second degree and Complete Heart Block

Abbas F. Al-Hashimi *MSc.*

Abstract

Background: VDD pacing provides the physiological benefits of atrioventricular synchronous pacing with the convenience of a single lead system, but is hampered by uncertainty regarding long term atrial sensing and development of sinus node disease.

Objective: To evaluate the efficacy and sensitivity of two different types of dual chamber pacemakers: (VDD and DDD pacemakers) by various electrophysiological and operative parameters in an attempt to determine whether VDD pacemakers are a viable alternative to DDD pacemakers in treatment of patients with 2nd and 3rd degree heart block with normal sinus node function.

Method: The study was conducted during the period between April 2006 to September 2007 on 48 patients with symptomatic 2nd degree and complete heart block, attending the Cardiac Care Unit in Al-Kadhimia Teaching Hospital. Those patients divided into two groups: VDD group and DDD group; each consisted of 24 patients. The VDD and DDD pacemakers were implanted in the patients and the tests of efficacy and sensitivity were done at implantation and in the follow up periods (2nd day of implantation, 10 days, 1 month, and 3 months after implantation) for both groups. These tests were: Atrial sensitivity, atrial lead impedance, P-wave amplitude, event histogram (% of atrio-ventricular synchronous pacing), duration of implantation, and duration of fluoroscopy. The outcomes of these tests were compared in both groups.

Results: Forty eight patients were implanted; half of them received DDD pacemakers, and the other 24 received VDD pacemakers. At the time of implantation and during the 3 moths of follow up, the DDD group showed significant higher efficacy and sensitivity than the VDD group. After implantation; the mean P-wave amplitude, atrial sensing threshold, atrial lead impedance, and % of AV synchrony were 3.42±1.1 mV; 3.46±1.3mV; 568±103.42Ω; 95%±7% respectively in DDD group, while they were 2.91±1.3 mV; 2.46±1.18mV; 624.2±136.26Ω; 90%±8% respectively in VDD group. Implant time was significantly reduced in VDD patients (61.82±14.6 min.) compared with DDD group (72.62±10.4 min.) ($p<0.05$). The exposure to radiation (fluoroscopy time) was significantly reduced in VDD patients (6.53±2.9 min.) in comparison with DDD patients (10.37±3.4 min.) ($p<0.05$).

Conclusion: the dual lead DDD pacing is superior to single lead VDD pacing for long term maintenance of AV synchronous pacing in symptomatic 2nd degree and complete heart block with preserved SA node function. The lower cost, high reliability, and abbreviated implantation time suggest that a VDD pacing is a viable alternative to DDD pacing.

Keywords: DDD pacemaker, VDD pacemaker, AV blocks, AV synchrony and atrial sensitivity threshold.

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Introduction

Most clinicians consider use of dual chamber DDD pacing for symptomatic AV block in order to maintain AV synchrony [7, 8, 12, 15].

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VDD pacing utilizing a single pass lead with far field atrial sensing bipoles is a potentially simpler approach to provide the physiological benefits of atrioventricular synchronous pacing block with a single lead system [3, 4, 7]. Despite this, VDD pacing is utilized in only one percent of patients receiving pacemakers in some countries like North America, though it is more widely used in other countries like Europe [5, 10, 11, 14]. This

may be related to concern regarding stability of atrial sensing or development of sinus node disease. However, a single lead system has the potential to reduce procedure time and complications, and reduce pacing cost compared to dual chamber pacing [1-4]. The comparison of implant and outcome of patients with symptomatic AV block managed with VDD versus DDD pacing system to assess the long term stability and viability of VDD pacing [6, 9, 13].

Patients and Methods

The study was conducted during the period between April 2006 to September 2007 on 48 patients (mean age 61.4±11.2 years) with symptomatic 2nd degree or complete heart block and normal sinus node function attending the Cardiac Care Unit in Al-Kadhimia Teaching Hospital. Patients were implanted between April 2006 and September 2007. Sinus node function was judged by in-patient monitoring or out-patient referral material. Those patients are divided into two groups: DDD group who were implanted with DDD pacemakers (St. Jude Veriy ADx XL DR Model 5356) and VDD group, who were implanted with VDD pacemakers (St. Jude Veriy ADx XL VDR Model 5456). Each group consists of 24 patients.

Devices were implanted using standard implant techniques with local anesthesia. The subclavian puncture technique was used for venous access. Atrial and ventricular pacing and sensing thresholds were determined at implant using a standard programming system analyzer. In general ventricular and leads were repositioned if ventricular sensing was less than 10 mV, or the pacing threshold was greater than 1.0 V. Atrial leads were repositioned if sensing was less than 2.0 mV, or the pacing threshold was greater than 1.0V. Implant time was defined as the time from patient entry into the implant room to patient departure. The fluoroscopy time was defined the summation of the total periods of X-ray radiation exposure. Both of them were measured. Standard pacemaker function was assessed after implantation and each follow up visit, including: Atrial sensitivity, atrial lead impedance, P-wave amplitude, event histogram (% of atrio-ventricular synchronous pacing).

Initial follow up was performed on the 2nd day, then on the 10th day, and after 1 month.

Failed atrial sensing was defined as P-wave amplitude not sensed by the pacemaker programmed threshold. Sinus node dysfunction was diagnosed if at least one of the following criteria was fulfilled: (1) sinus bradycardia below the pacemaker interventional rate of 45 beats/ min, (2) intermittent sinoatrial block, or (3) sinus arrest.

Results

Pacemakers were implanted in 48 patients. Those patients are divided into two groups: DDD group; which consists of 24 patients receiving DDD type pacemakers, and VDD group; which consists the rest of the patients who receiving VDD type of pacemakers.

Atrial sensitivity, atrial lead impedance, P-wave amplitude, event histogram (% of atrio-ventricular synchronous pacing), duration of implantation, and duration of fluoroscopy were used to compare the efficacy and sensitivity of DDD pacemakers in the DDD group with VDD pacemakers in the VDD group.

At time of implantation:

The mean values of mean P-wave amplitude, atrial sensing threshold, atrial lead impedance, and % of AV synchrony were 3.42±1.1 mV; 3.46±1.3mV; 568±103.42Ω; 95%±7% respectively in DDD group, while they were 2.91±1.3 mV; 2.46±1.18mV;

624.2±136.42Ω; 90%±8% respectively in VDD group. Implant time was significantly reduced in VDD patients (61.82±14.6 min.) compared with DDD group (72.62±10.4 min.) ($p<0.05$). The exposure to radiation (fluoroscopy time) was significantly reduced in VDD patients (6.53±2.9 min.) in comparison with DDD patients (10.37±3.4 min.) ($p<0.05$)

Table 1: Shows the mean values of mean P-wave amplitude, atrial sensing threshold, atrial lead impedance, % of AV synchrony, and %of failure of AV synchronous pacing of DDD group and VDD group at implant

The parameter	VDD group Mean±SD n=24	DDD group Mean±SD n=24	P value (t-test)
Mean P-wave amplitude (mV)	2.91±1.3	3.42±1.1	0.012
Atrial sensing threshold (mV)	2.46±1.18	3.46±1.3	0.001
Atrial Lead Impedance (Ω)	624.2±136.26	568±103.42	0.305
%AV Synchronous pacing	90%±8%	95%±7%	0.011
%of failure of AV synchronous pacing	10%±8%	5%±7%	0.01

On the next day of Implantation:

The mean values of mean P-wave amplitude, atrial sensing threshold, atrial lead impedance, % of AV synchrony and % of failure of AV synchronous pacing were as shown in the following table 2:

Table 2: Shows the mean values of mean P-wave amplitude, atrial sensing threshold, atrial lead impedance, % of AV synchrony, and %of failure of AV synchronous pacing of DDD group and VDD group on the next day of implant

The parameter	VDD group Mean±SD n=24	DDD group Mean±SD n=24	P value (t-test)
Mean P-wave amplitude (mV)	2.62±1.2	3.38±1.3	0.0039
Atrial sensing threshold (mV)	2.41±1.15	3.39±1.23	0.0014
Atrial Lead Impedance (Ω)	564.2±116.2	518±86.6	0.54604
%AV Synchronous pacing	90%±8%	95%±7%	0.011
%of failure of AV synchronous pacing	10%±8%	5%±7%	0.01

After 10 days:

The mean values of mean P-wave amplitude, atrial sensing threshold, atrial lead impedance, % of AV synchrony and % of failure of AV synchronous pacing were as shown in the following table 3:

Table 3: Shows the mean values of mean P-wave amplitude, atrial sensing threshold, atrial lead impedance, % of AV synchrony, and %of failure of AV synchronous pacing of DDD group and VDD group 10 days after implantation.

The parameter	VDD group Mean±SD n=24	DDD group Mean±SD n=24	P value (t-test)
Mean P-wave amplitude (mV)	2.53±1.01	3.31±1.01	0.00615
Atrial sensing threshold (mV)	2.26±1.12	3.19±0.93	0.0014
Atrial Lead Impedance (Ω)	492.2±113.2	518±89.6	0.3085
%AV Synchronous pacing	88%±7%	94%±7%	0.0091
%of failure of AV synchronous pacing	12%±7%	6%±7%	0.01

At 1 month follow up:

The mean values of mean P-wave amplitude, atrial sensing threshold, atrial lead impedance, % of AV synchrony and % of failure of AV synchronous pacing were as shown in the following table 4:

Table 4: Shows the mean values of mean P-wave amplitude, atrial sensing threshold, atrial lead impedance, % of AV synchrony, and %of failure of AV synchronous pacing of DDD group and VDD group at 1 month follow up.

The parameter	VDD group Mean±SD n=24	DDD group Mean±SD n=24	P value (t-test)
Mean P-wave amplitude (mV)	2.46±1.01	3.21±1.00	0.00525
Atrial sensing threshold (mV)	2.09±1.02	3.05±0.83	0.0004
Atrial Lead Impedance (Ω)	462.31±106.2	508±106.4	0.0853
%AV Synchronous pacing	86%±7%	93%±7%	0.0099
%of failure of AV synchronous pacing	14%±7%	7%±7%	0.01

At 3 months follow up:

The mean values of mean P-wave amplitude, atrial sensing threshold, atrial lead impedance, % of AV synchrony and % of failure of AV synchronous pacing were as shown in the following table 4:

Table 4: Shows the mean values of mean P-wave amplitude, atrial sensing threshold, atrial lead impedance, % of AV synchrony, and %of failure of AV synchronous pacing of DDD group and VDD group at 1 month follow up.

The parameter	VDD group Mean±SD n=24	DDD group Mean±SD n=24	P value (t-test)
Mean P-wave amplitude (mV)	2.49±1.09	3.2±1.00	0.0125
Atrial sensing threshold (mV)	2.16±1.15	3.00±0.89	0.0014
Atrial Lead Impedance (Ω)	447.54±113.8	491±103.14	0.0631
%AV Synchronous pacing	87%±8%	93%±7%	0.0119
%of failure of AV synchronous pacing	13%±8%	7%±7%	0.0166

In the VDD group, the value of mean P-wave amplitude was significantly different when compared to that of the DDD group ($p<0.05$). The % o AV synchronous pacing and % of failure of AV synchronous pacing were significantly different when compared to that of DDD group ($p<0.05$), whereas there was no significant difference in the value of lead impedance when compared to the atrial lead impedance of the DDD group ($p>0.05$). On the other hand, the value of atrial sensing threshold in the VDD group showed a highly significant differences when compared to that of DDD group ($p<0.01$).

Discussion

Despite the introduction of single pass leads capable of dual sensing and ventricular pacing over 20 years ago, VDD pacing remains underutilized pacing approach in patient with AV block [5-7].

VDD pacemakers have a single pacing lead which has two floating ring electrodes located on the portion of the lead that is present in the right atrium and these electrodes are responsible for sensing intrinsic atrial P-wave unlike DDD pacemakers which employ a separate atrial pacing lead for sensing of intrinsic atrial P-waves and atrial pacing [5, 11, 13].

The advantages of using VDD pacemakers is obvious in patients with second degree or third degree heart block having normal sinus node function who do not require atrial pacing, which is offered by DDD pacemakers [3,4,9]. In addition the use of a single pacing lead reduces the time needed for implantation of the pacemaker and also reduces the time the patient is exposed to X-ray during fluoroscopy and it is also cheaper for such patients than DDD pacemakers. VDD pacing provides reliable chronic atrial sensing to permit maintenance of atriovenricular synchrony. VDD pacing may reduce the frequency of implant and long term complications because of the reduced number of leads involved [1, 2, 10].

The disadvantages of VDD pacemakers in comparison with DDD

regarding the long term efficacy, sensitivity and stability of atrial sensing as the atrial sensing electrodes of the VDD pacing lead is floating in the right atrium and not fixed to the endocardium as in the atrial lead of DDD pacemakers, and as a result changes in the posture, activity, ect. can cause changes in he atrial sensing [12, 14].

Despite the decrease in the atrial signal amplitude the VDD pacing, adequate AV synchrony was maintained in almost all patients with programming changes to maintain atrial sensing. In addition, patient selection resulted in a very low incidence of chronic atrial fibrillation or sinus node disease, a context where atrial based pacing may be beneficial in both sensing and pacing. This finding is in keeping with the previous observation by Anderson et al, who found little association of sinus node disease with AV block in patients undergoing atrial based pacing for sinus node disease who presented with intact AV node function [8, 10].

Longer term follow up may have permitted further detection and development of sinus node disease and atrial fibrillation, potential limitations of VDD pacing. Conversely, longer follow up is likely to detect "degenerative" lead related problems, including the potential need for lead replacement or extraction. The latter would have contributed to greater cost and complications in the DDD group [7, 9, 11].

Increased utilization of VDD pacing could realize significant cost savings. Although there is minimal difference in generator capabilities and cost between pacing modes, reduced lead costs may contribute to significant savings [6, 13].

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Causes of death among hospitalized children under 5 years of age in Sulaymani Pediatrics Teaching Hospital

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Abstract

Back ground: Knowledge about the causes of death in children is important to evaluate health system progress and provide what is needed for an efficient design of health care delivery system.

Objective: To find out the main causes of death in children under 5years & evaluate the effects of different variables like: age, gender, body weight, residency, and months of year for the causes of death.

Patient& Method: This is a retrospective study which was carried out in order to find out the main causes of death among admitted children younger than 5 year in Sulaymani Pediatrics Teaching Hospital for the period of 5 years from of January 1st 2001 to December 31st 2005 included. The total numbers of admitted cases was 137,739 out of which 1455 had died. We obtained the information from case files of the deceased patients.

Results: The incidence of death among admitted patients was (1.06%), the rate was higher in male gender (59.3%), while in female it was (40.7 %), with a P-value of <0.05 which is significant statistically with male to female ratio 1.48:1.

Deaths were mainly in neonates (61.8 % of all age groups in the study) with a p-value of <0.05. Death was mainly in those with body weights <2.5kg, which accounts for (42.1%). The main cause of death in neonate was prematurity (54.7%) while diarrhea and Acute Respiratory Infections (ARI) were main causes during infancy (57.4%, 15.9%) respectively.

Seasonal variation of died cases showed that were two peaks of death, one in June and another in November with a p-value of <0.05. The percentage of death in the rural and urban area were (64.5%, 35.5 %) respectively, with a p-value of <0.05 which is also significant.

Conclusion: This study has revealed that prematurity was the main cause of death among neonate while diarrhea and acute respiratory diseases were the main causes of death during infancy. Malignancy was the least common cause of death. Deaths were mainly in neonates. There was a significant association between deaths and gender, body weight, residency& the months of the year.

Key words: mortality rate, death cause, children under five.

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Introduction

The registration of birth and death is compulsory in all developed countries but it is so in only some of the developing countries. In addition to recording the fact of death, it's useful to establish the cause of death.

In the developed countries the first year of life represent the period of highest risk for death while death rate is very low in older children[(1)].

On the other hand in most of the developing countries, although the first year does represent the period of highest risk, a high mortality rate persists in older children. In 1999 the Under 5 Mortality Rate (U5MR) was 6/1000 in the developed industrialized countries but 173/1000 in Sub-Sahara and Africa [(1)].

It is estimated that in the developing countries; (50 %) of total mortality occurs in the first five years of age, of this (79 %) occur in the first year of life, of which (43 %) occurs

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within the first month, and remaining (36 %) during the other eleven months [1, 2, 3].

More than 10 million children younger than 5 die each year, most of them do so from preventable causes, nearly all in poor countries. The major killers in the developing countries have been and still are diarrhea, acute respiratory infection and neonatal diseases. Diarrhea remains a common illness among infants and children throughout the world. In developing countries, diarrhea is a common cause of mortality among children aged <5 years, with an estimated 2 million deaths annually [1, 3, 4, 5, 6].

Lower respiratory tract infection (LRTI) is frequently used interchangeably to include bronchitis, bronchiolitis, and pneumonia. The World Health Organization (WHO) estimates are 150.7 million cases of pneumonia each year in children younger than 5 years, with as many as 20 million cases severe enough to require hospital admission [7, 8] .The mortality rate in the developed countries is low (<1 per 1000 per year) [9, 10, 11]. While in the developing countries, respiratory tract infections are not only more prevalent but are also more severe, accounting for more than 4 million deaths annually [12].

The neonatal period accounts for 38% of all deaths in children younger than five [13].

Most neonatal deaths (99 %) arise in low income and middle income countries and almost half occur at home [14].

The major direct causes of Neonatal (NN) death globally are; Infection (36%), prematurity (28 %) & birth asphyxia (23 %) [15, 16, 17].

Estimation of mortality rate in children younger than 5 years published by WHO shows: (17.5 %) of death were due to diarrhea, (10.5 %) to pneumonia, neonatal causes (47.9%) & for others (24.1%) [3, 7]. While in the developed countries the major killers were prematurity which accounts for (32.1 %) and congenital abnormalities (17.1 %) [1, 3].

Accurate information for the causes of death is necessary for an effective health planning and evaluation of health care program [18]. The United Nations Children's Fund (UNICEF) consider Under five Mortality Rate (U5MR) as the best single indicator of social development and well being, as this rate reflects; income, nutrition, heath care and the basic education in the community[19].

Classification of the causes of death is always difficult; in developed countries where the registrations of all cases of death are relatively complete, necessitating international classification of diseases. While it is more difficult in developing countries, where often less than half of all cases of death are registered ,the died patient often received no medical attention ,either because they live too far from the health system services or because the establishment of the cause was of no interest to any one[20,21] .

The Aim of study is to find out the main causes of death among children less than 5year of age, to evaluated the effect of different variables like; age, sex, weight, months of the year, residency on the cause of death& to monitor health progress and provide what is needed for an efficient design of care delivery system.

Patients and Methods

The study was retrospective and hospital based done in the Pediatrics Teaching Hospital in Sulaymani; Sulaymani is one of the three governorates in Kurdistan region of Iraq. It has an average population of 1,547,071 with 265000 children being younger than 5*.

The live birth rate in Sulaymani is around 1275/month**.

Sulaymani pediatrics teaching hospital is the largest hospital for children in Sulaymani governorate. The average number of annual admission during the study period was 27547.8***, and the main reasons for admission were diarrhea, ARI and neonatal problems. The turn over rate in the hospital is relatively rapid especially during late spring and summer months when the load on admission by diarrheal diseases is too high.

All deaths in infants and children from birth to 5year of age that occurred in the Sulaymani Pediatrics Teaching Hospital form 1st of January 2001 to 31st of December 2005 were included in this study.

The final causes of death as reported on case files and death certificates were analyzed according to the number of deaths by :age groups(first 28 days,>28 days-12month, >1year – 5year), body weight (<2.5kg, 2.5kg - 4kg, >4kg - 10kg and >10), gender of the died child, residency (rural, urban). The hospital files (case sheets) of the deceased individuals were reviewed and relied upon for the information's required in the above mentioned analysis.

Data entry and analysis was carried out by using SPSS software version 10,correlation between dependant variable (causes of death) and variables such as :child age ,gender, residency, body weight and the month of the year, was assessed by using chi square test, P-value, the value <0.05 was considered statistically significant.

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* Population and target per (PHC) 2007.

** Department of birth registration.

*** Department of health statistic in hospital

Results

This study was carried out from 1st of January 2001 to 31st of December 2005; during this period 137739 children were admitted to Sulaymani Pediatrics Teaching Hospital. Of the admitted cases 1455 have died, which accounted for 1.06% of total admitted cases (Table 1). Nine hundred (61.8%) were younger than 28 days i.e. neonate, 427(29.3%) were infants, while the remaining 128(8.9%) were children between >1- 5 years of age as shown in (Table 2).

The death number varied from one year to another, the maximum number of deaths occurred in 2001, which accounts for 342 of total deaths and (1.44%) of total admitted cases while the minimum numbers of deaths occurred during 2003 which accounts for 217 of total deaths and (0.61%) of total admitted cases(Table 1). This variation was statistically significant with a P- value (<0.05).

By far the commonest cause of death was prematurity in 501cases which accounts for (34.4%) of total death during this study.

Other main causes of death in different age groups were, diarrhea in 319 cases (21.9 %), respiratory diseases mainly pneumonia & bronchiolitis in136 cases (9.3%), Cardiovascular diseases in 131 cases (9%), septicemia and meningitis in 129 (8.8%), birth asphyxia in 111 cases (7.6%), congenital anomalies in 66 case (4.5 %), and other causes apart from malignancy (trauma, poisoning, renal failure) account for 57 cases (3.9%). malignancy came at the bottom of list as a cause of death in 5 cases (0.34 %) of the total number of deaths (Figure 1).

(Table 3) present the causes of death by age group, three age groups were chosen: First28 days (neonate), >28 days-12 month and >1year-5years.The highest percent of death

occurred in the first group (28day) which accounts for 900 cases (61.8%) of total deaths, prematurity was the main cause of death among this age group which accounts for 493 cases (54.7%) of total death in this group.

While the second group constitutes for 427 cases (29.3%) and the main cause of death was diarrhea which accounts for 245 cases (57.4%) of the total deaths among the second group. The third age group accounts for 128 cases (8.9 %), still diarrhea was constituted large portion of deaths which accounts for 28 cases (21.8%). This variability was statistically significant with a p value (<0.05).

The death rate among male gender in all age groups was higher than in female gender as indicated in (Table 4). which show that in male gender 869 were dead which accounts for (59.75 %) while female deaths were 586, which accounts for (40.3 %).with male to female ratio 1.48: 1.This difference were most obvious in prematurity, birth asphyxia and malignancy which was Statistically significant with a P- value of (<0.05).

(Table 5) shows the relationship between weight of the deceased patients and cause of death, the maximum number of death occurred among those with body weight of <2.5kg which accounts for 613 cases (42.1 %), and mainly due to prematurity; the number of death decrease as body weight increase. This is also significant statistically with a P value of <0.05).

The causes of death and number vary from one month to as it shown in (Figure 2). The peak number of death occurred in June, the main cause of death during this month was diarrhea. Another peak occurred in November; here the main cause was prematurity and respiratory illnesses. This variability is statistically significant with a P-value of (<0.001).

The distribution of death varies according to residency as shown in (Table 6). the largest number of death occurred in rural areas which accounts for 938 cases (64.5 %), in which prematurity was the most common cause followed by diarrhea, while in urban area death accounts for (35.5%).. The difference was significant with P-value of (<0.05).

Table 1: Death rate among admitted patients according to years

Years	Admitted patients	Number of death		Percentage of death	Death / 1000
2001	23655	342		1.44	14/1000
2002	25628	330		1.28	12/1000
2003	35277	217		0.6	6/1000
2004	26446	275		1.04	10/1000
2005	26733	291		1..08	11/1000
Total	137739	1455	Mean	1.06	10.6/1000

Table 2: Number of deaths according to the age

Age	number of death	%
1day – 28 days	900	**61.8**
>28day-12month	427	**29.3**
>1year – 5year	128	**8.9**
Total	**1455**	**100**

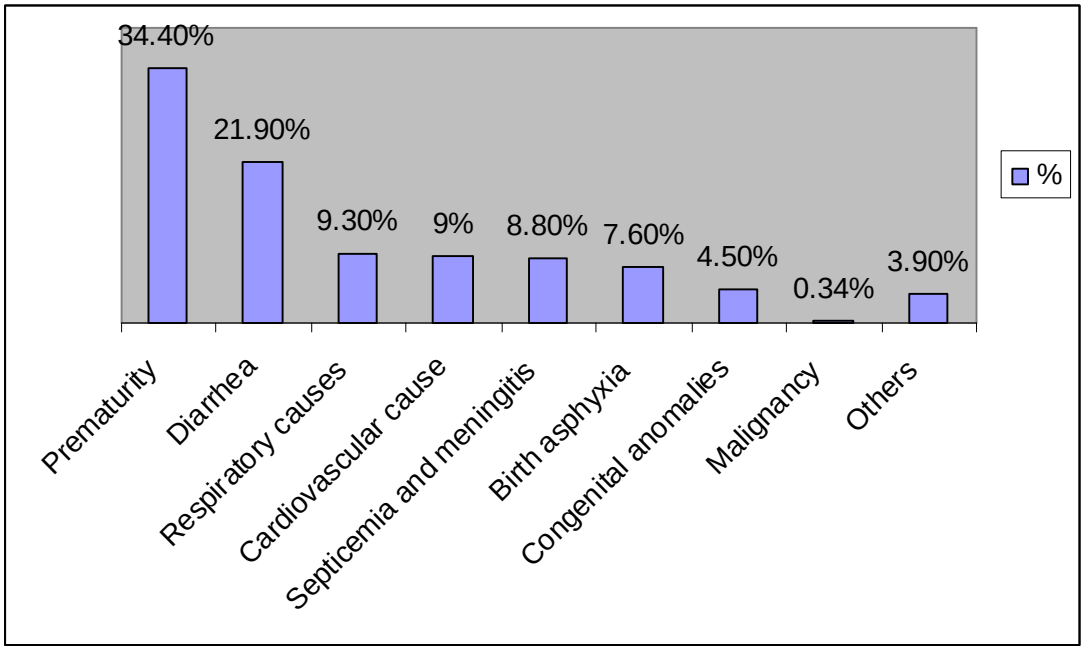

Figure 1: Proportions of percentages of different causes of death

Table 3: Relation between the age and the cause of death

Causes of death	28 days (No.)	%	>28d-12months (No.)	%	>1y-5y (No.)	%	Total
Prematurity	493	54.7	8	1.9	/	/	501
Diarrhea	46	5.4	245	57.4	28	21.8	319
Respiratory causes	54	6.0	64	15.9	18	14.01	136
Cardiovascular causes	49	5.4	58	13.6	24	18.7	131
Septicemia and meningitis	85	9.4	26	6.0	18	14.01	129
Birth asphyxia	111	12.3	/	/	/	/	111
Congenital anomalies	53	5.8	8	1.9	5	3.9	66
Malignancy	/	/	2	0.5	3	2.3	5
Others	9	1.0	16	3.7	32	25.8	57
Total	900	61.8	427	29.3	128	8.9	1455

P-value <0.05

Table 4: Relationship between Sex and the cause of death

Causes of death	Male (No.)	%	Female (No.)	%	Total
Prematurity	292	58.2	209	41.8	501
Diarrhea	198	62.1	121	57.9	319
Birth asphyxia	83	74.8	28	25.2	111
Respiratory causes	80	58.9	56	41.1	136
Septicemia and meningitis	73	56.6	56	43.4	129
Cardiovascular causes	69	52.7	62	47.3	131
Congenital anomalies	41	62.0	25	38.0	66
Malignancy	3	60.0	2	40.0	5
Others	30	52.6	27	47.4	57
Total	869	59.7	586	40.3	1455

P-value<0.05

Table 5: Relationship between body weight and the causes of death

Causes of death	<2.5kg (No.)	%	2.5 - 4kg (No.)	%	>4 - 10 kg (No.)	%	> 10 kg (No.)	%	Total
Prematurity	488	97.4	13	2.6	/	/	/	/	501
Diarrhea	30	9.4	79	24	194	60.8	16	5.0	319
Respiratory causes	20	14.7	50	36.8	58	42.6	8	5.9	136
Cardiovascular causes	13	9.9	61	46.6	45	34.3	12	9.2	131
Septicemia and meningitis	31	24.0	54	41.9	33	25.6	11	8.5	129
Birth asphyxia	3	2.7	92	82.9	16	14.4	/	/	111
Congenital anomalies	23	34.9	33	50	9	13.6	1	1.5	66
Malignancy	/	/	/	/	2	40.0	3	60.0	5
Others	5	8.7	11	19.3	23	40.4	18	31.6	57
Total	613	42.1	393	27	380	26.2	69	4.7	1455

P-value<0.05

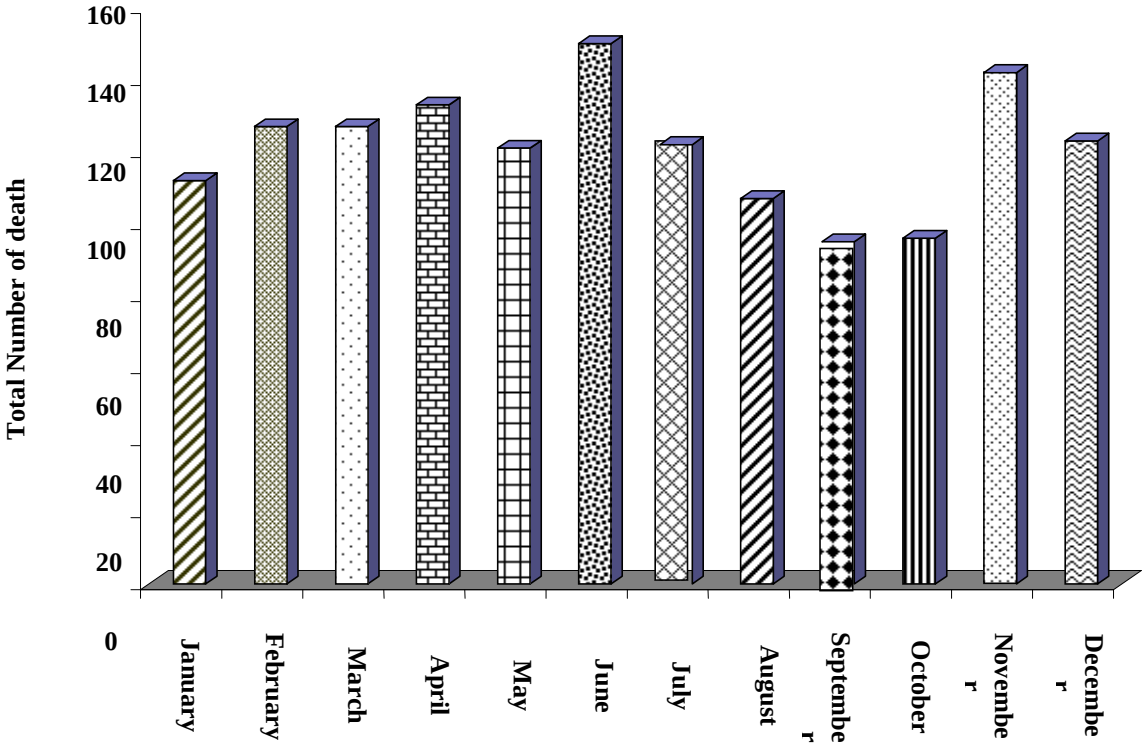

Figure 2: Total Number of death during the months of the year

Table 6: Relationship between residency and causes of death

Causes of death	Rural (No.)	%	Urban (No.)	%	Total
Prematurity	308	61.5	193	38.5	501
Diarrhea	235	73.7	84	26.3	319
Birth asphyxia	70	67.4	41	32.6	111
Respiratory causes	84	61.8	52	38.2	136
Septicemia and meningitis	87	61.8	42	38.2	129
Cardiovascular causes	81	73.1	50	36.9	131
Congenital anomalies	36	55.0	30	45.0	66
Malignancy	1	20.0	4	80.0	5
Others	36	63.2	21	36.8	57
Total	938	64.5	517	35.5	1455

P- Value (<0.05).

Discussions

Up to three-quarters of the world population live in the third world and here the proportion of the world children is even greater. Children all over the world, especially in the developing countries have been and still are under life threatening risks, most of which now a day are either preventable or treatable [1,3,7].

The great decline in the mortality among children observed in the developed countries is much less obvious in the developing countries as the availability of good medical care tend to vary inversely with the need for it in the population served [15].

In this study the average rate of death among children less than 5 year of age was 10.6/1000of total admitted cases, this result was obviously lower than the rate of death in children in children welfare Teaching Hospital in Baghdad, in which death rate was 88.6/1000 [21]. This difference of death number may be due to absence of an oncological department in Sulaymani Pediatrics Hospital while such department is present in children welfare Teaching Hospital raising the mortalities from malignancy.

The maximum number of deaths in this study was in the first 28days of life which accounts for (61.8 %) of total deaths. This rate is compatible to the fact which says that in areas where Under Five Mortality Rate (U5MR) <35/1000[3], the bulk of death occur during neonatal period. This number is higher than that which was found in a developed country like England and Wales in 1999 were (46%)confined to neonatal age [1,22], this difference due to defective management of neonates and premature with lack of essential medicine like (surfactant) , absence of modern medical equipments and inadequate antenatal care.

The degree of mortality was inversely proportional to the age. This finding was compatible with both developing and developed countries [1].

In this study the main cause of death was prematurity this accounts for (34.4%) of total causes, which contributed to increase in the number of death during neonatal period; at the same time prematurity was found to be the main cause of death in this age group, which constitute (54.7 %) of death during neonatal period . In comparison to England and Wales in 1999were prematurity constitute (32.7 %) of death during neonatal period [1,22]. this higher rate of death from prematurity in sulaymani is due to lack of well equipped neonatal intensive care unit, Surfactant therapy, mechanical ventilation and defects in the subspecialized medical and nursing staff for neonates.

Beyond the neonatal period diarrhea was the commonest cause of death, which accounts for (21.9 %). Approximately five billion episodes of diarrhea occur worldwide annually, accounting for (15 to 30%) of all deaths in some countries [4, 5, 6, 7]. This may be due to poor sanitation, using well water & incompliance with WHO program.

It is worth mentioning the hospital specialty when causes of death are considered, the malignancy as a cause of death comes at the top of most lists (23.8%) in children welfare study as it is one of referral hospital in Baghdad for malignant cases in Iraq & other studies [21, 23], while malignancy was a rare cause in this study because malignant cases were not usually treated in sulaymani due to lack of facilities, making malignancy accounts for (0.34 %) only.

The result have shown a male to female ratio among deceased children to be 1.48:1.This may be due to increased susceptibility of male babies to septicemia illness [24, 25], and higher

incidence of Hyaline Membrane Disease (HMD) among male babies [1] in this study. This result is similar to study performed in children welfare Teaching Hospital in Baghdad in 2003 [21]. The same fact has also been noticed in the other developing countries [26].

The death rate was inversely proportional to the body weight in this study particularly in premaures; this finding was similar to studies conducted in developing and developed country [1, 14,22].

The number and the causes of deaths in children varied from one month to another. There were two peaks of death one in June and the other in November as it is common to have a large number of acute diarrheas in spring and summer while a large number of acute respiratory infections (ARI) in autumn and winter this result is similar to a study conducted in Ramadi [2].

Relatively the largest proportions (64.5 %) of died children were from rural area, while only (35.5%) was from urban. This indicates a better family income, clean water supply, good sanitation, housing, and medical care in the urban children or could be due to long distance between the rural area and the hospital especially in this area leading to delay in bringing patients to the hospital. This fact is similar to the result in many similar studies carried in other developing countries including Iraq [2,17, 26,27].

Conclusions

This hospital based study has revealed the death number was significantly lower than previous study in other hospital in the same country.

The major causes of death were prematurity followed by diarrhea.

The maximum number of death occurs in the neonatal period.

The death rate was higher in males than females.

The death rate was higher among children from rural areas than urban areas.

Seasonal variance in both numbers and causes of death.

The death rate inversely proportional to body weight.

The death rate inversely proportional to age.

Recommendations

We recommend enhancement of antenatal care, planning to build a neonatal care unit that is well equipped with modern medical devices& services, improving medical care provided to rural area, encouragement of health care provider for effective management of diarrhea, acute respiratory diseases following WHO instructions and finally attempt to apply 10 revisions of international classification of disease and cause of death in order to standardize recording system.

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IFN-γ VERSUS IL-10 *IN SITU* EXPRESSION IN RECURRENT SPONTANEOUS ABORTION

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Abstract

Background: The possible immunological bases of recurrent spontaneous abortion (RSA) are still largely unknown, aberrant type 1 cytokine production; interferon-γ (IFNγ), and a defective type 2 cytokine; Interleukin-10 (IL-10) has been suggested to be related to the incidence of unexplained RSA.

Objective: To study the relation between the in situ expression of IFNγ and IL-10 in women with recurrent spontaneous abortion.

Materials and Methods: The study included three groups of women; Group A: patients had recurrent abortion (n=24), Group B: patients had spontaneous abortion for the first time (n=10), Group C: women with elective pregnancy termination (n=6). Curate samples obtained from these women were subjected for *in situ* hybridization technique to detect and determine the *in situ* expression of IFN-γ and IL-10.

Results: The *in situ* expression of IFN-γ was significantly higher in women with RSA as compared with normal pregnant and first abortion groups (p=0.000 and 0.002 respectively), while IL-10 expression was significantly lower in women with RSA as compared with first abortion group (p=0.005), and the ratio of IFN-γ/IL-10 was 1.97 in women with recurrent abortion, while that of normal pregnant and first abortion groups were 0.67 and 0.73 respectively.

Conclusion: The data of this study strengthened the possibility that type-1 immune response may have the upper hand in the pathology of RSA in association with reduction in the type-2 immune response.

Key words: RSA, IFN-γ, IL-10

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Introduction

Human pregnancy represents a semi-allograft to the maternal host. It is very interesting that the semi-allogeneic embryo/fetus is not rejected by the mother [1]. T helper (Th1)-dependant effector mechanisms such as cytotoxic T lymphocytes (CTL) activity play a central role in acute allograft rejection [2]. The production of Th2-type cytokines or regulatory cytokines such as TGF-β and IL-10 may be central to the induction and maintenance of allograft tolerance [2, 3]. So that, the physiological protection from maternal rejection, was hypothesized to be due to a Th2-type response at the materno-fetal interface [4, 5].

IL-10 was proposed to be a factor that might protect the semi-allogeneic fetus from maternal allo-recognition and rejection by driving the maternal (both local and systemic) immune reaction toward a Th2-type immune response [6,7], IL-10 is believed to play a major role in directing Th_0 cell differentiation toward a Th2 phenotype [8,9]. IL-10 inhibits pro-inflammatory cytokines production including IL-1β, IL-6, IL-8, TNF-α and IFN-γ [10-12], therefore prevents the development of Th1-type immune reactions deleterious for the maintenance of pregnancy [5-13].

In 1995, Th1-type cytokine secretion was observed for the first time in women with RSA, when peripheral blood mononuclear cells were activated by a trophoblast cell line [14]. This finding was also supported by other reporters [15-19]. Th1-type cytokines (IL-2, TNF-α, IFN-γ) can boost, and Th2-type cytokines (IL-3, IL-4, IL-10) can reduce abortion

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rate in mice [20]. But the inefficiency of NK cell, macrophage, and Th1-type cytokines in killing trophoblasts led to question the mechanism whereby the cytokines produced their effects. A target other than trophoblasts for cytokines was sought; a maternal vascular target was suggested by pathologic specimens of aborted material that showed hemorrhagic necrosis at the trophoblast-decidual interface [21].

Pro-inflammatory cytokines such as IL-1, TNF-α and INF-γ collaborate to activate procoagulant expression in endothelial cells that are in direct contact with maternal blood. Prothrombin is converted to thrombin; thrombin then catalyzes generation of fibrin and activates IL-8 secretion by endothelial cells. IL-8 recruits polymorphonuclear leukocytes (PMNs) which kill endothelium that has been activated by IL-1, TNF-α and INF-γ [22]. The end result of unchecked thrombin production is clot formation occluding blood supply to the embryo leading to its death [23]. The procoagulant stimulated by these cytokines, which is responsible for prothrombinase activity in abortions, has been identified as the prothrombinase called fibroleukin gene (fg) l2 [21-24]. The fgl2 is present in both decidua and trophoblasts of aborted but not control tissue [23]. Clotting initiated by fg12 is known to lead to ischemic damage in a variety of inflammatory disease models such as hepatitis and endotoxic shock [25].

Patients and Methods

Patients were collected from Al-Kadhimya and Al-Ulwiya teaching hospitals in Baghdad in the year 2004, and were divided into three groups; **Group A:** 24 pregnant ladies presented with incomplete first trimester abortion, all of whom gave a history of previous 3-6 consecutive first trimester abortions, with no medical diseases, family history of genetic diseases or uterine anatomical anomaly, also all of them were negative for acute infection with rubella, cytomegalovirus and toxoplasmosis. **Group B:** 10 pregnant ladies presented with incomplete first trimester abortion and had at least three previous normal pregnancies with no previous abortion, and no history of any medical illness. And **Group C:** 6 pregnant ladies with elective termination of pregnancy in the first trimester for a maternal indication under approved consent of two senior gynecologists and a physician. Curate samples of the materno-fetal interface were taken from all these women at the end of evacuation curate operation, samples were embedded in paraffin and subjected for *in situ* hybridization technique.

***In situ* Hybridization:** For *in situ* hybridization technique (ISH), DNA Probe Hybridization/Detection System In situ kit (Maxim Biotech, Inc., USA) was used. Kit contents included: biotinylated housekeeping gene probe, hybridization solution (ready to use), protein block, detergent wash buffer, RNase A (15 μg/ ml), streptavidin-AP conjugate, substrate (BCIP/NBT), and lyophilized proteinase K (4 mg); which is dissolved in a 2 ml DNase and RNase free dilution buffer to form 10X proteinase K, then diluted by deionized water to 1X proteinase K. The probes were biotin-labeled DNA probes for human IFN-γ (249 bp), and human IL-10 (223bp), (Maxim Biotech, Inc., USA).

Tissue sections were deparaffinized in xylene for 5 minutes and rehydrated through a series of ethanol dilutions. After digestion with 1X proteinase K at 37°C for 15 minutes, the sections were quickly dehydrated in ethanol. Hybridization was carried out by applying 10 μl hybridization mixture (0.8 μl of heat

denatured biotin-labeled DNA probe diluted in 9.2 µl hybridization solution) per slide. After overnight incubation, the slides were soaked for 10 minutes in 1X detergent wash at 37°C, followed by RNase A treatment at 37°C for 30 minutes, and then the slides were washed for 5 minutes in 1X protein blocking buffer. The biotin-labeled hybrids were detected with streptavidin-alkaline-phosphatase conjugate, and an enzyme-substrate chromogen (bromo-chloro-indolyl-phosphate/ in nitro-blue-tetrazolium salt) BCIP/NBT, yielding an intense blue-black signal appears at the specific site of the hybridized probe. The slides were counterstained with nuclear fast red stain. (Poor tissue quality or target RNA degradation may give false negative results or poor signal. This could be verified by using a probe to an abundant RNA target like the probe of a housekeeping gene which is a sequence or gene product that is constitutively expressed in most tissue types such as actin or tubulin. The specificity of the ISH signal was assessed by: 1) RNase A treatment of the tissue sections for 2 hours at 37 °C, before the *in situ* hybridization, and 2) omission of the probe in the hybridization mixture).

Evaluation of *ISH* signal: The expression of IFN-γ and IL-10 mRNAs was measured by counting the number of positive decidual and trophoblastic cells, which gave a blue-black (BCIP/NBT) nuclear staining under the light microscope. The extent of the ISH signal in the villi was determined in 10 fields (X100 magnification). In each field the total number of villi were counted and the extent of nuclear staining of the cytotrophoblast and syncytiotrophoblast in a given villous was graded as 3, (75–100%); 2, (25–75%); or 1, (<25%). The total staining score was divided by the number of whole villi per field in 10 fields. These scores (between 1 and 3) were added for each field, and a score between 10 and 30 was gained for each sample. The scorer was blinded to the clinical diagnosis of the tissues at the time of assessment, and tissues were independently assessed by two observers, and as advised by Hennessy (Personal communication, 2004). For more details, refer to the *In situ* hybridization procedure and signal evaluation in references [26-27].

Statistics:

ANOVA test was used to determine the difference in the *in situ* expression of IFN-γ or IL-10 among the three groups and in between each two groups, and the relationship between these two parameters was measured using the correlation coefficient (*r*). Values of $p<0.05$ were considered as statistically significant [26].

Results

The expression of IFN-γ and IL-10 was detected by ISH technique, (Tables 1 and 2) show the percentages of IFN-γ and IL-10 *in situ* expression respectively in the villus trophoblasts in terms of mean ± SE, median, minimum and maximum values of the three groups. (Table 3) shows the difference in the expression of IFN-γ and IL-10 among the three groups and within the groups using ANOVA analysis.

The study demonstrated no significant correlation between IFN-γ and IL-10 (p =0.23, r=0.23), however, the ratio of IFN-γ/IL-10 was 1.97 in women with recurrent abortion, while that of normal pregnant and first abortion groups were 0.67 and 0.73 in an order.

The expression of IFN-γ and IL-10 was heterogenous blue-black nuclear staining, involving both decidual and trophoblastic cells, as shown in (Figure 1).

Table 1: The expression of IFN-γ among the studied groups

IFN-γ	n	Mean ± S.E.Ψ	Median	Minimal Value	Maximal Value
Group 1	24	69.8 ± 2.96	69.4	45	93.8
Group 2	10	49.5 ± 5.07	61.4	34.7	88
Group 3	6	40.1 ± 5.6	43.7	25	62.4

Ψ Standard error

Table 2: The expression of IL-10 among the studied groups

IL-10	n	Mean ± S.E.Ψ	Median	Minimal Value	Maximal Value
Group 1	24	39.96 ± 5.85	59.8	26.2	93.3
Group 2	10	69.2 ± 2.99	62.5	45	80
Group 3	6	62.42 ± 7.1	67.5	45	90

Ψ Standard error

Table 3: The significance of difference in the expression of IFN-γ and IL-10 between groups

Groups	*p* Value	
	IFN-γ	IL-10
Among the groups	0.000	0.003
Between group 1 and 2	0.002	0.005
Between group 1 and 3	0.000	0.131
Between group 2 and 3	0.645	1.000

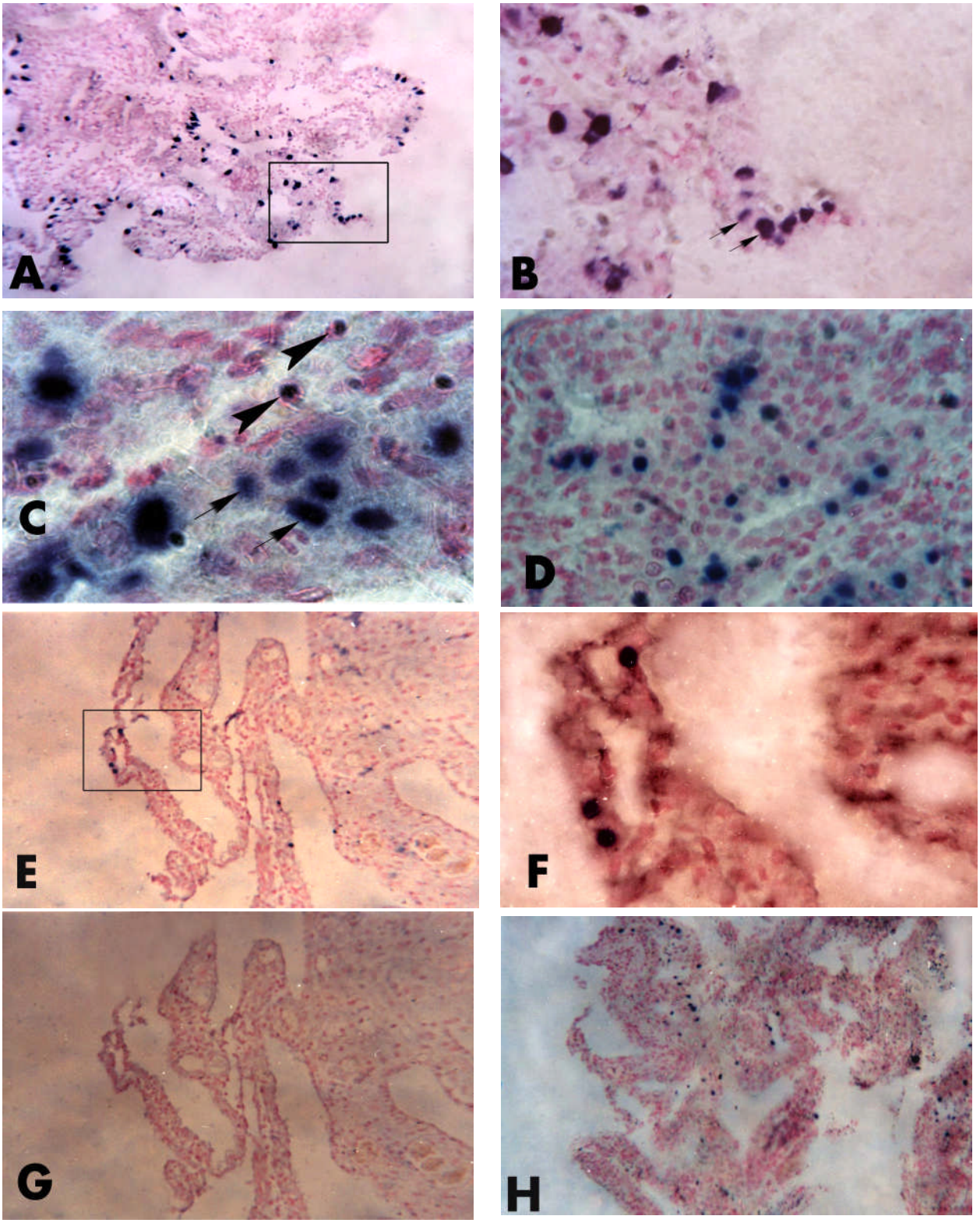

Figure (1) Detection of IFNγ and IL-10 in patients with abortion by *in situ* hybridization. Staining of IFNγ and IL-10 mRNA in the nuclei of the decidua and trophoblasts by BCIP/NBT (blue-black) counterstained with nuclear fast red. (A) Tissue from patient with RSA shows positive IFNγ hybridization signals. (B) Higher magnification of (A) demonstrates the heterogenous nuclear staining pattern (arrows). (C) Another case with RSA demonstrates IFNγ positive reactive lymphocytes and nutrophils within the tissue (arrowhead). (D) Positive control (housekeeping gene) probe. (E) And (G) hybridization in serial sections (patient had elective termination of pregnancy) in the presence of the IL-10 probe (E), and omission of the probe (G), as IL-10 positive and negative controls respectively. (F) Higher magnification of (E) demonstrates IL-10 staining near blood vessels. (H) Patient with RSA shows IL-10 expression. Magnification power of A, E, G, H (X100), B, D, F (X400), and C (X1000).

Discussion

The current study demonstrated that the *in situ* expression of IFN-γ is significantly higher in women with RSA as compared with that of normal pregnant or women with first abortion and a part from the causes of this significant increase in the *in situ* expression of IFN-γ in women with recurrent abortion, revision was made for the previous studies that examined the association between Th1 type cytokines and recurrent abortion, first studies in Hill's laboratory (14) have shown that peripheral blood mononuclear cells (PBMC) of women with a history of RSA when stimulated with a trophoblast antigen extract produced significantly higher concentrations of the Th1 cytokines, IFN-γ and TNF-α, as compared with normal pregnancy. Moreover, it has been demonstrated that stimulation of the maternal PBMC with autologous placental cells *in vitro* results in a Th1-biased production of cytokines in women undergoing unexplained RSA [15, 17, 19]. This was mirrored by the situation at the materno-fetal interface shown by other studies [28, 29].

On the other hand, this study showed a significantly higher expression of IL-10 in normal pregnant women in comparison with that of women with RSA which is in consistence with a previous study showed that IL-10 production was significantly lower in patients with recurrent miscarriage as compared with normal pregnancy [16], but the data presented by that study reflected events related to maternal blood cells in the periphery and not to the placenta itself as events at the materno-fetal interface are more representative as shown by the study of Piccinni and colleagues (28) who examined T cell clones generated from T cell infiltrating the deciduas, and found significantly decreased concentrations of IL-10 in women with recurrent abortion which is also in agreement with the results of our study. This significantly lower IL-10 expression could be attributed to defect in Th2 and Tc2 cells at the materno-fetal interface or to the accumulation failure of Th2 cells at the implantation site in women with recurrent abortion [30, 31].

The higher level of IL-10 in women with elective pregnancy termination or first abortion in this study might be due to the progressive increase of progesterone and estrogens which reach high levels during pregnancy, at these high levels, they suppress the Th1- and stimulate Th2-mediated immunological responses [32, 33]. For the same reason Th1-mediated diseases like rheumatoid arthritis, tend to improve, and Th2-mediated diseases, like systemic lupus erythematosus (SLE), tend to worsen during pregnancy [34, 35].

This study demonstrated that IFN-γ was expressed in lower levels in women with first abortion and those with elective termination of pregnancy which could be explained by previous studies showing that the pro-inflammatory cytokines act physiologically in normal pregnancy and high levels may cause recurrent miscarriage, it was found experimentally that very low concentrations of IFN-γ are required for full maturation of uterine natural killer cells which may be equally achieved by administration of 1 iu per implantation site [36,37]. Although we can not convert our findings to the corresponding values in these studies, still our results are in line with the findings given by these studies.

There are many confounding studies held the notion on the balance of Th1 and Th2 cells at the implantation site, expressing them as a ratio of Th1/Th2 cytokines, so that,

another dimension was added to the results of this study when it examined the ratio of IFN-γ/IL-10 in women with RSA which was 1.97 and about three times that of women with first abortion which lends further support to the findings of our study as it was in consistence with the previous studies [1,14,16,18].

Although this study showed that the expression of the Type 1 cytokine (IFN-γ) in women with recurrent miscarriage was significantly higher than that of normal pregnancy or first abortion groups, the current study, like many of the studies on human pregnancy failure, has not addressed a direct cause-and-effect relationship between Th1-type reactivity and pregnancy loss. However, there are many evidences support this suggestion such as, the administration of one of the Th1 cytokines like IFN-γ, TNF-α or IL-2 to normal pregnant mice causes abortion [38]. IFN-γ and TNF-α inhibit the proliferation of human trophoblast cells *in vitro* (39) and are toxic to human trophoblast cells [40]. Uterine resorption sites in a murine model of recurrent abortion were infiltrated by NK cells [41]; given the fact that the activation of NK cells has been shown to be detrimental to murine pregnancy and that NK cells are activated by the Th1 cytokine; IFN-γ [42]. Furthermore, strong Th1-dominant responses against pathogens compromise pregnancy; for example infection by *Leishmania major* results in resorptions, with a concurrent increase in the concentrations of IFN-γ in the placenta [43].

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The association of *Helicobacter pylori* mucosal density with low Serum Ferritin

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Abstract

Background: Although there are several methods to detect *Helicobacter pylori* infection, there is no simple validated test to quantify the density of infection, which is believed to play a major role in the pathogenesis of *H. pylori*-associated Gastritis and serum Ferritin level.

Objective: The aim of this study was to assess the association of low serum Ferritin level with the intensity of *H. pylori* infection.

Patients and Methods: Sixty four patients mean age of 34 years (14-66 years) who underwent upper gastrointestinal endoscopy because of gastrointestinal complaints, were studied. Patients were grouped as *H. pylori* positive group, *n*=47and *H. pylori* negative group, *n*=17.

A number of both invasive and non-invasive diagnostic tests were used for the diagnosis of *H. pylori* infection (Ultra Rapid Urease Test (URUT), slide impression smear test and *H.pylori* IgG ELISA Test).

Fasting serum Ferritin were determined using VIDAS Ferritin (Enzyme Linked Fluorescent Assay).

Results: Forty seven of the 64(73%) patients were *H.pylori* positive group. patients were classified according to the age group and gender. The rates of the *H.pylori* infection were higher in female age group 21-30 years. A total 16 of the 47 (34%) infected patients showed low serum Ferritin values with high rate in female with age group 21-30years. Twenty eight of the 47(60%) patient biopsies showed positive microscopic examination with slide impression smear test .Twenty seven of the 47(57%) infected patients showed seropositive results to anti-*H.pylori* IgG antibody and also positive with URUT,10 individuals of this group showed low serum Ferritin values. While ten of the47 (21%) infected patients showed seronegative results to anti-*H.pylori* IgG antibody but positive with URUT,5 individuals of this group showed low serum Ferritin values.

Conclusion: The possible relationship between mucosal *H.pylori* loads with low serum Ferritin level.

Keywords*: Helicobacter pylori infection*, serum Ferritin, anti-*H.pylori* IgG antibody ELISA test, Ultra Rapid Urease, Enzyme Linked Fluorescent Assay.

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Introduction

Helicobacter pylori is a gram negative, curved, microaerophilic and motile organism with multiple polar flagella. It resides in the stomach of man and other primates, lining up the gastric mucus secreting cells. It is estimated that about 50% of all humans carry *H. pylori* in their stomach [(1,2)].

The prevalence of *Helicobacter pylori* infection in developing countries is about 70 to 90% and it is only 20–50% in developed countries [(3)]. The persistent infection induces a state of chronic gastric inflammation that frequently remains asymptomatic. In some patients, however, the infection causes disease, such as peptic or gastric ulceration, the development of a mucosa-associated lymphoid tissue lymphoma, or even gastric cancer [(4)]. It is not yet clear why only some people develop more severe forms of disease despite the high prevalence of *H. pylori*

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in the human population. Certainly, host genetic factors play a role in determining the clinical outcome of the infection [5]. On the other hand, *H. pylori* virulence factors also play a role in pathogenesis, since virulent strains are associated with more aggressive tissue damage and an increased risk of a severe clinical outcome[6]. Finally, environmental factors such as nutrition are also thought to be important [7]. Epidemiologic studies have shown that the prevalence of *H. pylori* varies considerably with age [8] *H.pylori* needs to have at least four basic characteristics to be able to colonize and establish an infection in the gastric mucosa: urease, flagella, a particular shape, and adhesins. *H. pylori* is able to adhere to the surface and sites of epithelial cells and to the basement membrane of gastric epithelial cells [9]. When *H.pylori* is introduced in the stomach, a pH-neutral microenvironment around the bacteria is produced by exogenous shedding of urease, which converts urea to ammonia ions that neutralize the acidic gastric juice, and thereby enables *H. pylori* to survive and multiply in the stomach [10]. Thus, the disease outcome is determined by a combination of host, bacterial, and environmental factors.

The acute *H. pylori* infection that is dominated by abdominal pain and infiltration of polymorph nuclear leucocytes (PMNs) in the gastric mucosa only lasts for a few weeks [11-13]. Thereafter, it turns into an active chronic superficial gastritis with an increased recruitment of lymphocytes and other mononuclear leucocytes. In the humoral immune response to *H. pylori* infection, IgM antibodies to *H. pylori* are produced shortly after colonization whereas IgG antibodies to *H. pylori* seem to be delayed up to 3–6 months [14, 15]. Thus, within a few weeks of the primary exposure to *H. pylori*, a true infection can be established.

The superficial gastritis may or may not evolve to atrophic gastritis, which later may lead to intestinal metaplasia, dysplasia, and gastric cancer [16]. As the inflammation progresses, the specific immune response becomes more dominating and even the PMNs lose their ability to recognize the specific *H. pylori* strain in the host as a foreigner [17].

The diagnostic methods available for detecting *H. pylori* infection include conventional PCR and real-time PCR [18, 19]. Rapid urease test is highly specific for *H. pylori* infection and is commonly used for the detection of *H. pylori* infection at endoscopy. It requires a high density of bacteria [20]. The sensitivity of urease test is reduced in patients who are taking proton pump inhibitors (PPI), antibiotics or bismuth compounds [21, 22]. Any antibiotic active against *H. pylori* will cause a reduction in the numbers of bacteria in the stomach [23].

Increase Iron Uptake and Utilization by Bacteria

Epidemiologic studies have shown that persons seropositive for *H. pylori* infection have a significantly lower serum ferritin level [24, 25, 26, 27, 28]. Although *H. pylori* infection is common, iron deficiency anemia does not develop in all infected patients. The ability to cause iron deficiency anemia does not appear to be related to the virulence of the organism because ferritin levels did not differ between patients infected with cytotoxin-associated gene A (CagA)-positive and CagA-negative strains of *H. pylori* [24]. It may be possible that other bacterial virulence factors or host factors are responsible for the development of iron deficiency anemia.

Several mechanisms have been hypothesized to explain the possible effect of *H. pylori* infection on iron stores. A more likely mechanism is decreased iron absorption from hypo- or achlorhydria resulting from chronic gastritis [29]. Gastric hydrochloric acid facilitates iron absorption by reducing non-heme iron from the ferric to ferrous form. Another important effect of *H. pylori* gastritis that may cause reduced iron absorption is a decrease in gastric juice ascorbic acid concentration. Ascorbic acid facilitates iron absorption by reducing iron to the ferrous form [30]. Ascorbic acid is secreted into gastric juice, and it has been shown that gastric juice ascorbic acid levels are significantly lower in *H. pylori* -infected vs. uninfected persons[31,32], another mechanism to explain decreased iron absorption associated with *H. pylori* infection is increased hepcidin production from hepatocytes in response to IL-6 production associated with *H. pylori* gastritis [33]. Another possible mechanism by which *H. pylori* could result in decreased availability of iron is sequestration of iron in lactoferrin in the gastric mucosa. *H. pylori* takes up iron from human lactoferrin through a receptor-mediated method [34, 35], and lactoferrin secretion in the gastric mucosa appears to be influenced by the *H. pylori* organism [36, 37].

Another hypothesized mechanism to explain an association between *H. pylori* infection and iron deficiency is uptake of iron by the *H. pylori* organism. Like many bacteria, *H. pylori* require iron as a growth factor, and it possesses a 19-kDa iron-binding protein resembling ferritin (Pfr), that may play a role in storage of excessive iron by the bacteria [38]. Acquisition and storage of iron in *H. pylori* are controlled by the ferric uptake regulator gene product (Fur), which regulates transcription of iron uptake genes and Pfr iron storage [39].

Scientists have long known of *H. pylori*, but only in the last 10 years it has been recognized as a potential health threat. It causes stomach ulcers and gastrointestinal cancer and may play a role in the incidence of many other diseases.

Materials and Methods

Patients:

A total of 64 patients (41females and 23 males), aged between 14 and 66 years, were screened for this study. Patients attended the Gastroenterology Unit at AL-Kadhimyia teaching hospital in Baghdad from 1rst April to October 2007 because of recurrent abdominal pain and other gastrointestinal complaints, such as vomiting. All subjects filled out a questionnaire with regard to their general health and were excluded if they had been previously treated for *H.pylori* infection. The study was approved by the ethics committee of the Hospital. After an overnight fast, each patient underwent esophagogastroduodenoscopy, during which four antral biopsies were taken from within 2 cm of the pylorus using sterilized biopsy forceps (Olympus 16K; Olympus Corp., Tokyo, Japan). Biopsy specimens for the urease test were taken before those used for histological examination to avoid contamination with formalin.

Ultra rapid urease test:

Each specimen was subjected to Ultra Rapid Urease test as mentioned by Berry V, Sagar V [40] but with some modification. Briefly the medium used for the test was urea broth. It consists of urea, phenol red indicator and distilled water. 10 gm of urea was dissolved in

80ml of distilled water and final volume was made up to 100ml. To it 0.002 gm of phenol red was added, pH was adjusted up to 6.4 to 6.8 by using dilute hydrochloric acid. The broth was sterilized by using 0.22*um* Millipore filter, and dispensed in aliquot (0.5-1 ml) into a capped polypropylene tubes. The biopsy specimen for the URUT was removed from the biopsy forceps with a sterile toothpick and placed immediately into the polypropylene tube. Particular care was taken not to shake the tube after placing the biopsy into it so that a rapid positive result could be achieved [41]. A positive test result was indicated when there was a color change in the medium surrounding the biopsy from yellow to magenta. The test tube was left at room temperature and examined at intervals over 24 h. Convenient times chosen were 1, 5, 10, 20, 30 min and 1, 2, 3 and 24 h after insertion of the biopsy specimen into the urease test reagent.

Presence of H.pylori in the impression smears:

Impression smear was performed from the positive and negative specimen in the URUT test; crushed between two sterilized glass slides; heat fixed; stained with 40% carbolfuchsin for 1 min and examined under an oil immersion lens for the presence of a helical or more strikingly curved bacteria (Figure 1)

Blood samples:

The basal blood samples for assays of IgG antibodies for *H.pylori* and serum Ferritin were drawn after an overnight fast. Class antibodies to *H.pylori* were determined using specific ELISA tests (*Helicobacter Pylori* IgG ELISA Test Kit Cat. No. 601 040.01, Biohit Plc, Helsinki, Finland) according to the Instructions of the manufacturer. Samples with an ELISA value of <34 EIU (EIU=enzyme Immune Units) were considered negative, and samples with an ELISA value >42 EIU were considered positive. Samples with values between 34-42 EIU (Cut –off ~38 EIU) were considered as Borderline

Serum Ferritin was determined using VIDAS Ferritin (Enzyme Linked Fluorescent Assay Kit Cat.No.30 411, bioMerieux sa) according to the instructions of the manufacturer. Serum Ferritin values were considered as:

Iron deficiency = If concentrations are lower than 20 ng/ml in women and 30 ng/ml in men.

Inflammation = If concentrations are greater than 250 ng/ml in women and 350 ng/ml in men.

Histological evaluation of gastric biopsies

Two antrum biopsies were fixed in formalin and paraffin-embedded, and stained with hematoxylin and eosin; and subsequently evaluated by an experienced pathologist. The degree of inflammation present in the histological specimens was classified according to the updated Sydney system [42] (data not shown in this paper). A grading from absent, mild, moderate and severe was assigned for four histological variables: chronic inflammation (mononuclear cell infiltration),activity (polymorphonuclear neutrophil infiltration), glandular atrophy, and intestinal metaplasia.

Definition of H. pylori Infection

The gold standard for classifying a patient as being infected with *H. pylori* (in present study) was either detection the organism in the gastric biopsy by having the Ultra Rapid Urease test /or anti–*H. pylori* antibodies and histology results with or without visualizated by microscopic examination. Patients were considered uninfected with *H. pylori* when all tests were negative.

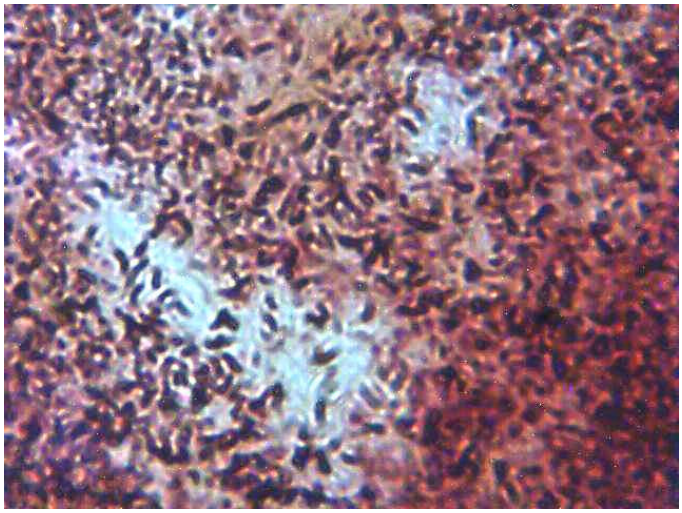

Figure 1: Antral gastric biopsy shows tufts of *H. pylori* a helical or more strikingly curved appearance and bluntly rounded ends

Results

According to the non-invasive and invasive diagnostic methods used in this study a total of 47of the 64(73%) patients were considered as *H.pylori* positive group, 37 of the 47 (80%)patients were positive with Ultra Rapid Urease test, 10 individual of this group(21%) were seronegative to *anti-H.pylori* IgG antibody,28 of the 47(60%) patients biopsies showed positive microscopic examination with impression smears and 37 of the 47(80%)patients were positive with EIA test for anti-*H.pylori* IgG antibody, 6 individual of this group(12%) showed negative results with Ultra Rapid Urease test(Table 1).

A total of 16 of the 47(34%) infected patients showed low serum Ferritin values. The results in (Figure 2) shown the percentage of low serum Ferritin in total patients among age group and gender, were found more commonly in female infected patients (15 of the 47. 32%) than male; and the rate of the *H.pylori* infection were higher in female age group of (21-30) years.

(Figure3) shown the percentage of low serum Ferritin in the infected patients when diagnosed with different methods according to the age group and gender, high rate of low serum Ferritin shown in female age group 21-30 years mainly when they were positive with Ultra Rapid Urease test.

Table 1: Prevalence (%) of *H. pylori* infected patients according to the noninvasive and invasive diagnostic used methods in this study.

Methods used	*H pylori* Infected patients, *n* (%)
Ultra Rapid Urease test	37(80)
Positive Ultra Rapid Urease test with negative EIA test	10(21)
positive Ultra Rapid Urease test with positive EIA test	27(57)
positive impression smears	28(60)
EIA test	37(80)
Positive EIA test with negative Ultra Rapid Urease test	6(12)

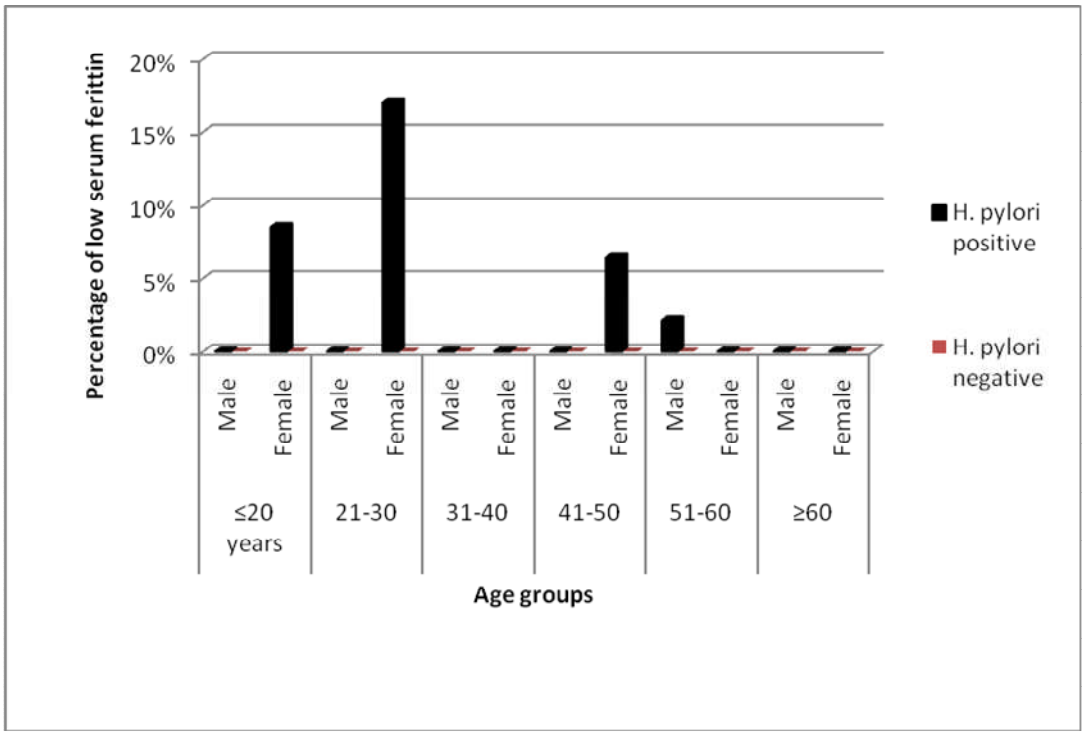

Figure 2: Percentage of low serum Ferritin in total patients among age group and gender

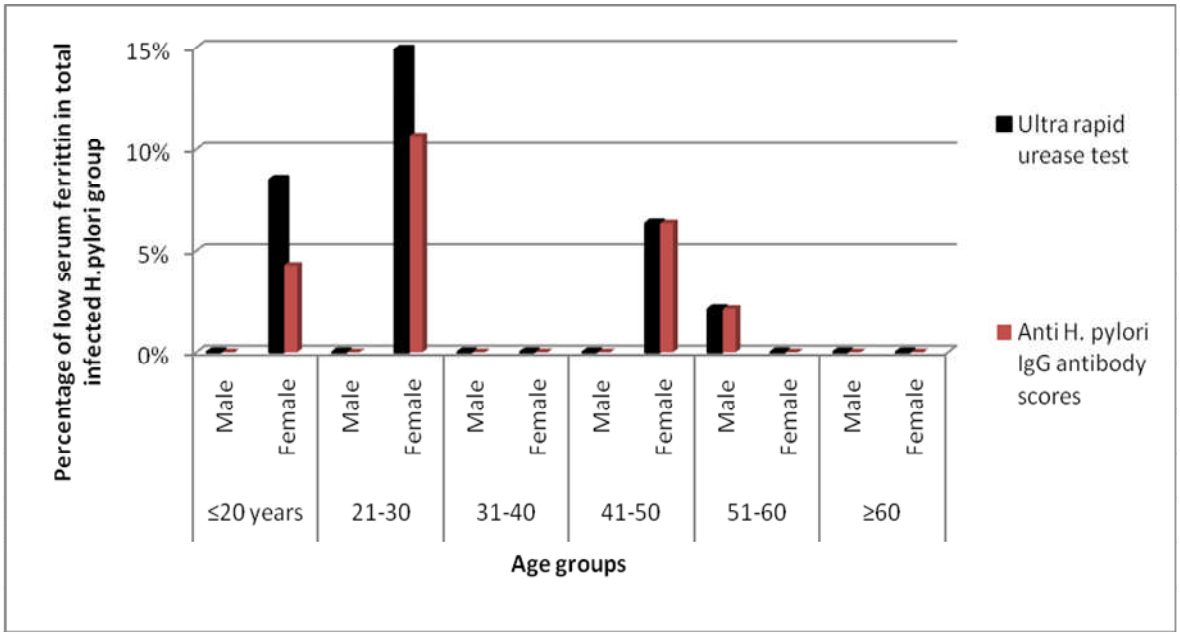

Figure 3: percentage of serum Ferritin in total *H.pylori* infected patients among gender and age groups with different diagnostic used methods.

Discussion

Currently, there are a number of both invasive and non-invasive diagnostic tests available for the diagnosis of *H. pylori* infection; each has its limitation in clinical applications. Urease-based biopsy tests require endoscopy and are not reliable in cases where patients use proton pump inhibitors. Histological examination follows endoscopy and its accuracy is dependent on the stain selected and on the pathologist's skill. Serology is inexpensive but is not reliable in determining the presence of active infection, which is important for clinical interpretation and diagnosis.

The appearance of IgG antibodies to *H. pylori* is delayed following onset of the infection and may not appear for many months [43] such that the working definition of an acute *H. pylori* infection has been a positive test for active *H. pylori* infection (e.g., histology, culture, urea breath test (UBT), or stool antigen test)and a negative IgG serology [44,45],this finding agrees with the present results as showed in (Table 1),that 10 of the 47(21%) *H.pylori* positive patients detected by URUT showed seronegative anti-*H.pylori* IgG. Also this results could be explained by Laine et al [46]. noted that sensitivity of all urease-based tests for detection of *H. pylori* is dependent upon the bacterial load in the stomach; Kobayashi *et al* [47]. used real- time PCR to estimate the total number of *H. pylori* genomes in biopsy samples and compared these with values obtained by UBT and showed a correlation between the results; other authors including Moshkowitz *et al* [48]. have reported that the intragastric bacterial density can assessed by urease activity. Moreover, the results in (Table 1) showed six individual from the37 who were positive with E I A test for anti-*H.pylori* IgG antibody, they showed negative results with URUT, this could be explained that the tissue biopsy sample contain a very low bacterial number, this finding agreed

with Karnes, et al. [49] that serologic tests may be positive in patients with gastric atrophy, in which the number of *H. pylori* organisms is so small as to be undetectable by biopsy methods.

Further, the presence of *H. pylori* was also diagnosed by slide impression smear test, (Figure 1) shown that the morphology of the *H.pylori* observed in biopsy specimens as a helical or more strikingly curved bacteria. This finding was in agreement the other study, found that *H.pylori* usually appears as a curved or straight rod in culture, whereas stained tissue biopsy samples usually reveal a helical or more strikingly curved appearance [50], also it demonstrates bluntly rounded ends [51].

In recent studies, a positive relation was detected between *H. pylori* infection and some micronutrient malnutrition in adults. Serum iron, vitamin B12, folate, vitamin A, and vitamin C levels were found to be low in the presence of *H. pylori* infection [52]. A strong association was found between *H. pylori* infection and iron deficiency [53]. However, the mechanisms by which *H. pylori* infection causes iron deficiency have not been well established. A plausible mechanism that may explain the development of iron deficiency in *H. pylori*–infected subjects might be the result of the pattern of gastritis and related effects on gastric physiology, affecting the normal process of iron absorption [54]. In the current study five of seronegative infected patients showed low serum Ferritin value. This could be explained that *H. pylori* may affect iron uptake and thus deplete iron stores in persons; this finding agree with Perez-Perez and Israel [49], reported that *H. pylori* may cause iron deficiency anemia by competing with the host for iron absorption. Iron is an essential growth factor for all bacteria, including *H. pylori*, which contains a system of iron-repressible outer membrane proteins that may be involved in iron uptake as well as a system for intracellular storage of iron that consists of the ferritin-like molecules Pfr and NapA [49].

Furthermore, the results in (Figures 2 and 3) showed that the percentage of low serum ferritin were found more commonly in female infected patients with age group of 21-30years . These results corresponding with the other studies that; an epidemiologic study of Australian women showed significantly lower ferritin levels in women with *H. pylori* infection compared to non-infected controls despite similar dietary iron intake [27], also Atherton *et al*. [55] they proposed that measurement of *H. pylori* density in gastric mucosa may be useful in determining the severity of infection and its influence on histologic changes and clinical outcomes.

In conclusion, the present results show that *H.pylori* positive results with URUT and slide impression smears test of the biopsy samples in the majority of infected patients indicates that, it has true a potential in aiding the diagnosis and management of patients with active *H. pylori* infection; as well as, the possible relationship between mucosal *H.pylori* loads with low serum Ferritin level.

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Sodium Imbalance in Preeclampsia

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Abstract

Background: Preeclampsia is a form of high blood pressure manifested during pregnancy. It is a common major complication causing significant morbidity and mortality; however, its etiology is unknown. Moreover, data on cation pattern during pregnancy are conflicting, and its relation with endothelial derived nitric-oxide and sex hormones have not been described adequately.

Objective: to demonstrate the pattern of sodium during preeclampsia with respect to normal pregnancy, and the correlation of the above parameter with nitric-oxide pathway.

Subject and methods: the present study is a cross-sectional case-control study includes measurement of nitric oxide NO), nitric oxide synthase (NOS) , serum and urinary sodium in 60 patients with preeclampsia. They were classified into two groups according to the gestational age:

- Preeclamptics in the second trimester G1: (n=30).
- Preeclamptics in the third trimester G2: (n=30,).

The results were compared with 60 apparently healthy pregnant women (as controls). They were classified according to the gestational age into two groups:

- Pregnants in the second trimester G3: (n=30).
- Pregnants in the third trimester G4: (n=30).

Results: showed a significant reduction in serum NO and NOS in the preeclamptics with significant increase in serum sodium accompanied by urinary retention of this cation (expressed as urinary sodium per urinary creatinine), as compared to the controls.

The regulatory effect of NO on fluid balance is supported by the positive correlation between NO and urinary sodium excretion indicating that NO had different effects on renal tubular reabsorption of sodium.

Conclusion: preeclamptics (in different gestational age groups) experienced vasospasm (manifested by low s.nitrite)s and altered sodium status when compared with healthy pregnant women matched with their age and gestational age.

Keywords:preeclampsia, nitric oxide , Sodium.

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Introduction

Preeclampsia is defined as the onset of hypertension and the presence of proteinuria during pregnancy, usually occurring after the 20th week of gestation in a previously normotensive woman and resolving completely by the sixth week after delivery of fetus [1, 2].

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The pathophysiology of preeclampsia is thought to represent a defective response to the physiologic demands of normal pregnancy [2, 3]. Normal pregnancy is associated with profound changes in maternal homeostasis [4]. The endpoint of these changes is to provide the fetus with the necessary environment for growth and the mother with adequate protection against pregnancy complication [4].

Early modifications in the regulation of arginine-vasopressin and the rennin-angiotensin-aldosterone system are responsible for the increase in maternal plasma volume to the extent of 50% near term [4]. The mechanisms responsible for these important changes are still

incompletely understood. The principal determinant of extracellular fluid volume is sodium and it has been calculated that normal pregnancy is associated with the net retention of some 900 mmol (3- 4 mmol /L) of sodium. Net sodium retention during pregnancy appears in some ways paradoxical in that there is a marked increment in factors which are known to enhance nartriuresis [(5)]. These include glomerular filtration rate and circulating concentrations of progesterone and atrial natriuretic peptide. One noteworthy factor opposing this change is the very substantial increase in plasma aldosterone concentrations [(5)].

It is obvious that a significant proportion of the retained sodium must be sequestered within the fetal compartment (including placenta, membranes and amniotic fluid) and it is noteworthy that the mother plasma sodium concentration decreases slightly, implying that factors other than sodium retention may also be responsible for the water retention of normal pregnancy[(4)]. Substantial alterations have been described in intracellular water and electrolyte concentrations and it is possible that these relate to changes in cell metabolism[4]. Failure to achieve these adaptational changes has been associated with intrauterine growth restriction and hypertensive disorders in pregnancy [(4)].

Nitric oxide (nitrogen monoxide) plays an important role in a wide range of physiologic processes [(6)]. NO influences renal vascular tone and blood pressure (BP), glomerular and medullary hemodynamics, and extracellular fluid volume [(3)]. This renoprotective effect was supported by several genetic and experimental studies [(3)]. Nitric oxide synthase is particularly important in the function of human kidney. It plays a role in the maintenance of normal vascular and renal function [(7)]. Not surprisingly, renal signs and symptoms from inhibiting NOS are similar to those seen in preeclampsia [(7)]. There may be a similar nitric oxide generation and sodium ion relationship in the endothelial cells of the small intestine and the tubules of the kidney cells in that when they are stressed by sodium entry, the exchange of sodium for calcium activates calcium dependent NOS[(8)]. A link between tubular absorption of sodium ions and NO generation has been shown in both in vivo and in vitro preparations [(7)].

Subjects & Methods

A-Subjects

The study was a cross-sectional, case-control study conducted on 60 patients with preeclampsia (PE) attending the Obstetric Consultant-Clinic, Antenatal Clinic, and Labor Ward at Al-Kadhimiya Teaching Hospital, for re-evaluation of newly diagnosed PE, or for delivery.

The diagnosis of PE was based on clinical criteria that were hypertension (absolute BP of 140/90 mmHg twice over 4 hr without prior comparison) [(1, 2)] and proteinuria (21.5 mg of urinary protein per µmol creatinine) [(9)].

The exclusion criteria used for cases and controls were gestational or chronic hypertension, diabetes mellitus, renal disease, multifetal gestation, intrauterine fetal death, and pregnancy less than 20 weeks of gestation.

Depending on the gestational age, the 60 patients were divided into two groups:

1. Preeclamptics in the second trimester **(G1):** They were 30 with age range from 18 to 37 years (mean age $\pm$ SD = 26.1 $\pm$ 6.4 year) and gestational age range from 20 to 28 weeks (mean gestational age $\pm$ SD = 26.3 $\pm$ 1.5 week).

2. Preeclamptics in the third trimester

(G2): They were 30 with age range from 18 to 40 year (mean age ± SD = 25.1 ± 6.9 year), and gestational age range from 29 to 40 weeks (mean gestational age ± SD = 35.6 ± 1.6 week)

The study included another 60 apparently healthy pregnant women attending the Antenatal clinic, and Labor Ward at Al-Kadhimiya Teaching Hospital, for re-evaluation of their pregnancy, or for delivery. They were included as normal controls. They were comparable with preeclamptic groups regarding the age and the gestational age. They were divided into two groups according to their gestational age:

1-.Normal pregnant women in the second trimester **(G3):** They were 30 with age range from 15 to 38 years (mean age ± SD = 24.6 + 4.5 year), and gestational age range from 20 to 28 weeks (mean gestational age ± SD = 25.5 ± 1.8 week).

2-Control pregnants during the third trimester **(G4):** They were 30 with age range from 18 to 35 year (mean age ± SD = 24.8 ± 4.6 year) and gestational age range from 29 to 40 weeks (mean gestational age ± SD = 34.6 ± 2.1 week).

B. Blood & urine samples:

Ten milliliters of random venous blood were withdrawn from each patient and control, in supine position, without application of tourniquet. Samples were transferred into clean new plane tube, left at room temperature for 15 minutes for clotting, centrifuged, and the separated sera were, then, divided into two parts:

1) An aliquot of serum was transferred into Eppendrof tube, which was used for measuring nitric oxide expressed as nitrite (the end product of NOS), this was done at the same day of collection [(10)].

2) The rest of serum was transferred into Eppendrof tube and was used for measurement of electrolytes (Na, K) [(11)]. The tubes were stored at –20° C until analysis, which was done within one month after collection [(11)].

Random urine specimens were obtained from each subject in the study to quantify urinary sodium and potassium [(11)] that was expressed as a ratio to the urinary creatinine [(11)].

As a preservative, 1-2 mls of 6M HCl was added to each random urine specimen; the samples were stored in appropriate containers at -20ºC until analysis within one month after collection [(11)].

C-Methods

Nitrite concentration measurement can be used as an index of NO synthase activity [(10)], this basic principle was used throughout the study. NO synthase activity is expressed here as the amount of nitrite (in µmoles) formed per minute, whereas the specific enzyme activity was given as the amount of nitrite (in µmoles) formed per minute per mg of protein for plasma [(10)] (µmol/min/mg protein). Serum and urinary sodium and potassium were analyzed by atomic absorption spectrophotometer [(11)].

Results

Serum Nitric oxide (NO) and nitric oxide synthase (NOS):

In preeclamptic pregnants in the third trimester G2, the maternal serum NO and NOS levels were significantly lower than those in the second trimester G1 [P< 0.001 for NO, < 0.05 for NOS]. In preeclamptic pregnants G1 & G2, the maternal serum NO and NOS were significantly lower than healthy pregnants G3 & G4 [P< 0.001 for both parameters & both groups], this difference was not found between healthy pregnants in second trimester G3 nor in third trimester G4 [P>0.05 for both parameters] as in Table 1.

Serum sodium (Na):

Serum sodium was significantly elevated in the preeclamptics (G1 & G2) with respect to their controls (G3 & G4) [P< 0.001 for the second trimester groups, < 0.05 for the third trimester groups]. Moreover, serum sodium was significantly increased in the third trimester healthy pregnant group G4 when compared with the second trimester pregnant group G3 [P= 0.01], but serum sodium was insignificantly decreased in the third trimester preeclamptic group (G2) when compared with the second trimester preeclamptic group G1 [P= 0.1] as in Table 2.

Urinary excretion of sodium expressed as sodium: creatinine ratio was significantly reduced in preeclamptics G1 and G2 when compared to corresponding controls G3 and G4. This reduction was also seen when second trimester pregnants in G3 was compared with third trimester pregnants in G4; however, the reduction in sodium excretion in third trimester preeclamptics G2 did not reach to a statistically significant level when compared with second trimester preeclamptics G1 as in Table 2.

Correlation between urinary sodium and serum NO:

A significant positive correlation between urinary sodium and serum NO level was noticed in different studied groups: in preeclamptics G1 and G2 (r=0.8, P < 0.001; r=0.8, P < 0.001) respectively and in pregnant control groups G3, and G4 (r=0.8, P < 0.001; r=0.8, P < 0.001) respectively as in Figures 1, 2, 3, and 4.

Table 1: The mean NO concentration (expressed as nitrite) and the mean NOS activity (expressed as nitrite formed per g protein per minute) in sera of different preeclamptic and control pregnant groups (presented as mean ± SD).

Variable	G1	G2	G3	G4
Nitric oxide (µmol)	6 ± 0.9	4.1 ± 2.4	8.1 ± 3	8.8 ± 3.3
NOS (µmol/g/min)	0.08 ± 0.01	0.06 ± 0.03	0.1 ± 0.04	0.11 ± 0.04

Table 2: The mean sodium values in serum and urine (expressed as urinary sodium per creatinine) of different preeclamptic and pregnant control groups (presented as mean ± SD).

Variable	G1	G2	G3	G4
Serum sodium (mmol/L)	140.9 ± 2.3	139.9 ± 2.3	136.5± 1.6	138.3 ± 3.6
Urinary sodium : creatinine	12.6 ± 6.9	11.2 ± 8.5	38.3 ± 9.4	47.7± 15.1

G1 & G2: *Preeclamptics in the second & third semesters,*
G3 & G4: *normal pregnants in the second & third semesters.*

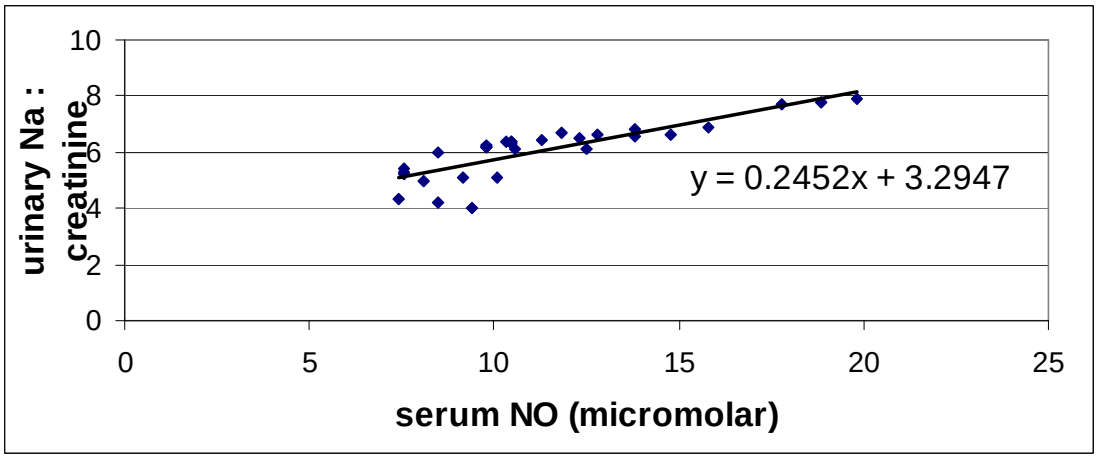

Figure 1: Correlation between serum NO & Na excretion in G1: second trimester preeclamptics (n=30; r = 0.8; P< 0.001).

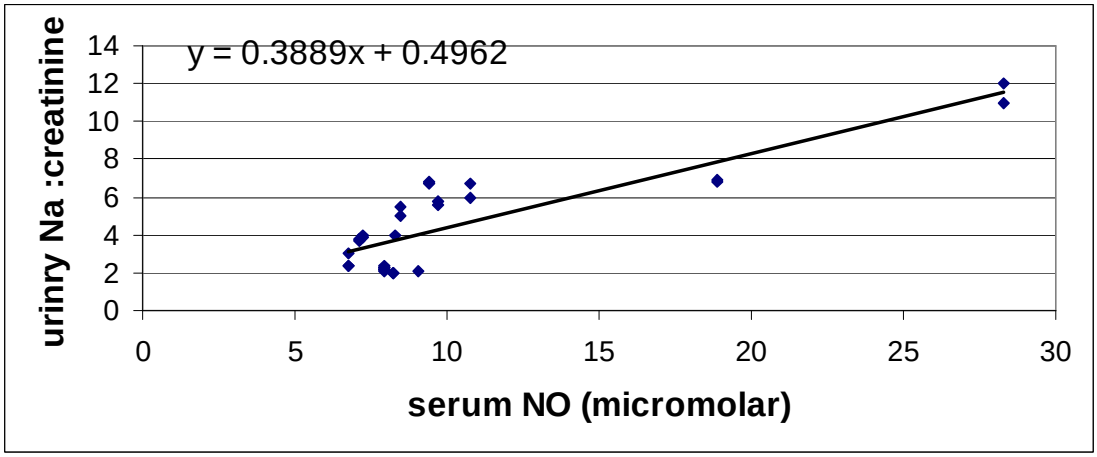

Figure 2: Correlation between serum NO & Na excretion in G2: third trimester preeclamptics (n=30; r = 0.8; P< 0.05).

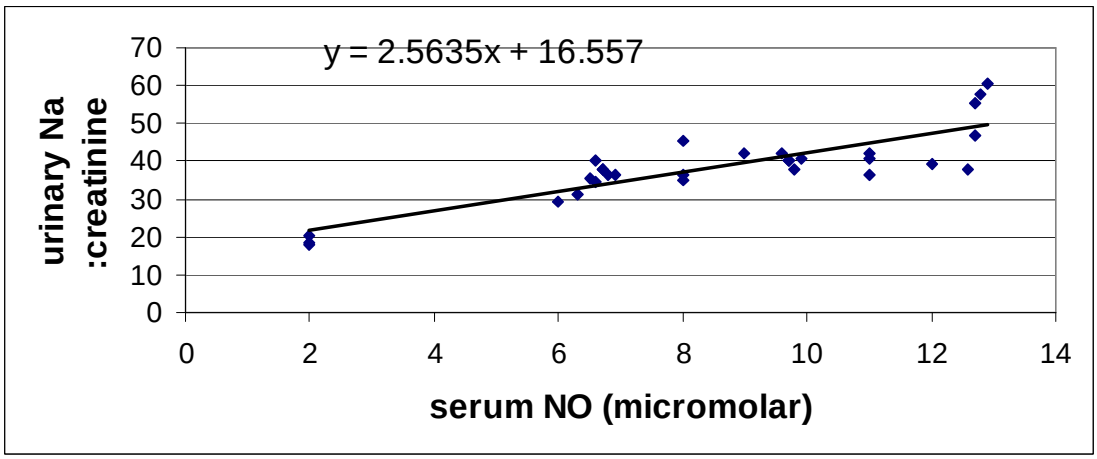

Figure 3: Correlation between serum NO & Na excretion in G3: second trimester pregnant controls (n=30; r = 0.8; P < 0.001).

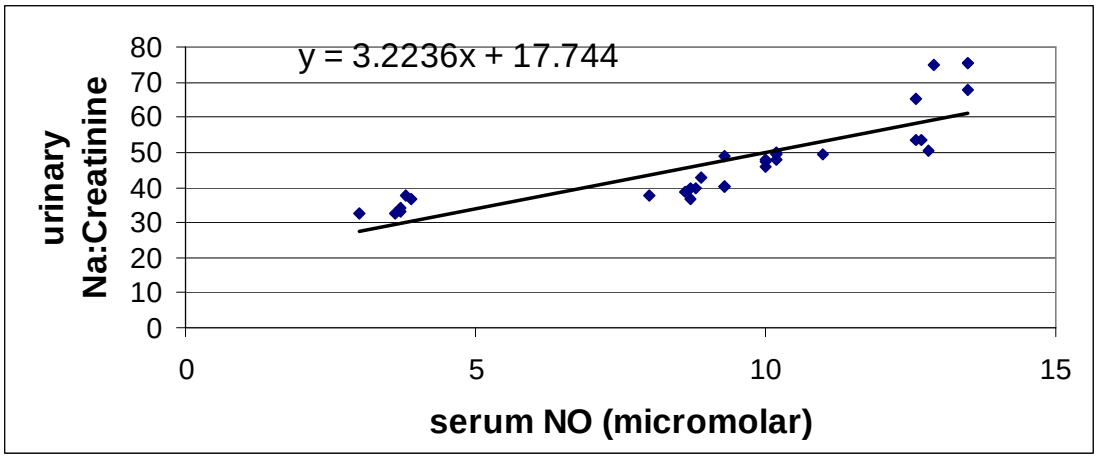

Figure 4: Correlation between serum NO & Na excretion in G4: third trimester pregnant controls (n=30, r = 0.8; P < 0.001).

Discussion

Nitric oxide mediates many functions of endothelium, including vasodilatation and inhibition of platelet aggregation [12]. Preeclampsia may be associated with nitric oxide deficiency [12], and the results of this study provide an evidence to support this hypothesis. As shown in Table 1. NO level in blood was similar in both healthy pregnants groups; it was unchanged during physiological pregnancy. During preeclampsia, the NO was decreased compared to the control level. This suggests that during preeclampsia the low activity of endothelial NO-synthases and redox-dependent transformation of NO in peroxynitrite provoke a decrease in the blood nitric oxide level [13], these results are comparable to those of Meher & Duly [12], Khetsuriani et al. [14], Choi et al.[13], Nishikawa & Miyamoto[15]

While serum Na^+ was significantly increased in normal pregnancy with advancing gestational age, it was insignificantly decreased in preeclamptics with advancing gestational age.

The observed significant low urinary excretion of sodium in the preeclamptic groups (Table 2) is comparable with Martniz et al. [16], who found that urinary excretion of sodium was lower in hypertensive than in normotensive gestation. But this finding can not be compared with the results of Halhali et al. [17], Kyey`nska et. al. [18], & Sigurdsson & Gengtss[19] who found normal range of urine Na excretion in their patients.

Preeclampsia is accompanied by amplification of the sodium retention that is a feature of a normal pregnancy [20]; which is associated with net retention of sodium with substantial alterations in intracellular water and electrolyte concentrations and possibly these are related to changes in cell membranes [21], which appear to be responsible for some pathological changes in preeclampsia. Some of the best documented alterations involve changes in the handling of sodium ion both on the systemic and intracellular levels [20, 22].

On intracellular level majority of studies support an increase in peripheral cell sodium concentration. This would suggest a defect in Na,K ATPase or sodium pump activity, leading to an increase cell sodium in vascular tissues that has been shown to enhance vascular sensitivity to vascular constricting agents or leading

directly to increased vasoconstriction [20,22].

While on the systemic level it has been suggested that blood volume depletion with subsequent reduction in the glomerular filtration rate can lead to Na retention [23]. Moreover, there is a broad agreement that component of renin-angiotensin-aldosteron pathway are markedly reduced in women with preeclampsia [16].

In this study, high serum sodium and low urinary sodium and their relation to low NO level in preeclampsia can be interpreted by understanding the role of NO in the regulation of sodium and fluid transport in the proximal tubule[24], NO functions as an inhibitor for the proximal tubular fluid and sodium reabsorption[24]. In this sense, NO is a natriuretic agent [24]. This is, in principle, consistent with the prominent role of NO in maintaining vascular tone and preventing increase in blood pressure [24]. However, the final effect of NO on proximal tubular sodium reabsorption and its role in the overall fluid and electrolyte homeostasis may vary under different circumstances [24]. The final effect of NO on proximal tubular reabsorption appears to depend on the concentration of NO and involve interaction with other regulatory mechanisms [24]. This is mainly caused by the complex effect of NO on various targets, including hemodynamics, the renin-angiotensin system, and the tubular system [24]. The above facts were confirmed by the positive correlation found between NO and sodium levels in both preeclamptics and control pregnants as seen in Figures: 1, 2, 3, and 4.

Biochemical changes in preeclampsia appear to be driven by a reduction in nitric oxide synthesis (as evident by low serum nitrite). This will, in turn, results in changes involving electrolyte metabolism and appearance of the typical pattern which may cause vasospasm of eclampsia. These changes would include relative increase in serum sodium with a reduction in its urinary excretion. These manifestations are evident by the existence of positive correlations between the parameters studied. Further study of the relation between sodium excretion and NO production by renal tissues is required. Also, Study of the membrane Na^+, K^+ ATPase and calcium pumps; as abnormalities of these pumps are also involved in the pathogenesis of preeclampsia.

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Anatomical Study of Anomalous Testicular Artery

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Abstract

Background: The testicular artery arises from aorta below the level of renal arteries, most commonly at the level of L2 vertebra.

Variations in the site of origin of the testicular artery may be accounted; it may arise from anomalous origin rather than aorta, or may originate from aorta higher than L2 level or arises from the main renal artery or accessory one.

Objectives: study the sites of origin of testicular artery and its clinical importance.

Materials & Methods: study the origins of 40 testicular arteries, in both sides of 20 male cadavers in the anatomical laboratory prepared and embalmed for teaching purposes in the medical college. Examine both sides to see the possible origins of the testicular arteries either from aorta or from somewhere else.

Results: During dissection of 20 male cadavers, examining 40 testicular arteries on both sides, a different site of origin of the testicular artery was encountered. The right testicular artery was found originated from the right main renal artery. On the other hand, the left testicular artery was found originated from the left accessory renal artery in two cases out of twenty. In the other 17 cases, all the testicular arteries whether right or left were originated from abdominal aorta.

Discussion: Variation in the renal and gonadal vasculature has been known since early days of human autopsy. The anomalous origin of testicular artery from accessory renal vessel has important clinical implications, since any surgical intervention with the kidney, during transplantation for example, may lead erroneously to injury of the anomalous testicular artery leading to atrophy of the male gonad.

Conclusion:

- Testicular artery may originate from anomalous origin rather than aorta.
- The anomalous testicular artery is the aberrant one, and no more accessory artery present.
- The encountered anomalous origin may comprise a potential risk of bleeding from injured artery during surgery.

Keywords: accessory renal arteries, testicular artery, vascular variation.

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Introduction

The renal arteries usually arise from anterolateral or lateral aspect, at right angle from abdominal aorta [1],at the level of L2 vertebra, precisly at the level of L1-L2 intervertebral disc, inferior to the origin of superior mesenteric artery[2].The left renal artery is shorter than the right ,crosses the left crus of diaphragm and psoas muscle ,behind the renal vein ,both left renal artery and vein being covered by tail of pancreas and the splenic vessels.

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The longer right renal artery crosses the right crus and psoas muscle behind the inferior vena cava and the right short renal vein.each artery reach the hilum of kidney to supply the renal segments. Each renal artery gives off small suprarenal and ureteric branches.

One or two accessory renal arteries arise frequently from the aorta, above or below the main artery [3,4].

The testicular artery usually arises from near the front of aorta, below the origin of renal artery and well above the origin of inferior mesenteric artery, the testicular artery arises most commonly from abdominal aorta at the level of the second lumbar vertebra [5, 6], then it travels through the retroperitoneal space and the entire length of the cord to the testicle [7].

In the abdomen the testicular artery supplies the perirenal fat, ureter, and iliac lymph node in the inguinal canal, it supplies the cremasteric muscle (خطأ! الإشارة المرجعية غير معرّفة.).

The testicular veins originated from a plexus in the scrotum called the pampiniform plexus (8-12 veins)which usually unite at the level of internal inguinal ring and drain into the inferior vena cava on the right and the left renal vein on the left (خطأ! الإشارة المرجعية غير معرّفة., 8).

Variations in the pattern of renal and gonadal arteries have been reported more frequently than other large vessels in the literatures and alternative nomenclatures have been used to describe the same. These include aberrant artery (9), supernumerary artery, any artery arising from the aorta in addition to the main renal artery should be named "accessory" and the renal arteries arising from sources other than aorta should be called "aberrant. The frequency of aberrant renal arteries has been reported to be much lower than accessory renal arteries (10). The testicular arteries may have anomalous origin rather than from aorta, or it may have a high aorta origin above the level of L2 vertebra in about 5-20% of cases, on the other hand, the testicular artery may arises from renal artery; main or accessory renal artery, in about 5-6% (خطأ! الإشارة المرجعية غير معرّفة., 11).

Materials and Methods

Twenty human cadavers (forty sides) are examined to study the possible variations in the origin of the testicular artery. The gender of cadavers is male. All cadavers are embalmed well and prepared for teaching purposes in the medical college. The bowel and its mesentry all are removed to view the posterior abdominal wall clearly and to make identification for the testicular artery easier.

By gross anatomical dissection, we try to identify the origin of fourty (40) testicular arteries on both sides, which may come from aorta directly or indirectly.

For those testicular arteries come directly from aorta we try also to verify if they are aberrant or accessory testicular arteries.

We use a 6 megapixels digital sony camera to take pictures of work.

Results

During examination of a 20 male cadavers (40 sides) in the anatomical laboratory, the testicular artery found to have more than one site of origin. In all of the cadavers examined. We found three cases when the testicular arteries not originate directly from abdominal aorta. One case out of twenty (40 testicular arteries examined) the right testicular artery arises from the right renal artery. In two cases out of twenty cases examined, the left testicular artery is originated from the left accessory renal artery. In the remaining cases the testicular arteries are originated directly from the anterolateral aspect of abdominal aorta.

In the three cases identified with abnormal origin testicular artery evidently it was the main artery and no more accessory testicular artery from abdominal aorta. This is defined as aberrant testicular artery.

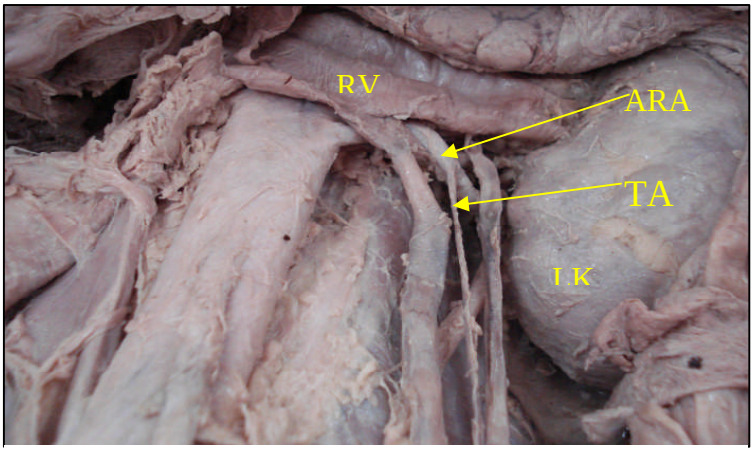

Figure 1: TA, anomalous testicular Artery, ARA, accessory renal Artery, RV, renal vein, LK: left kidney.

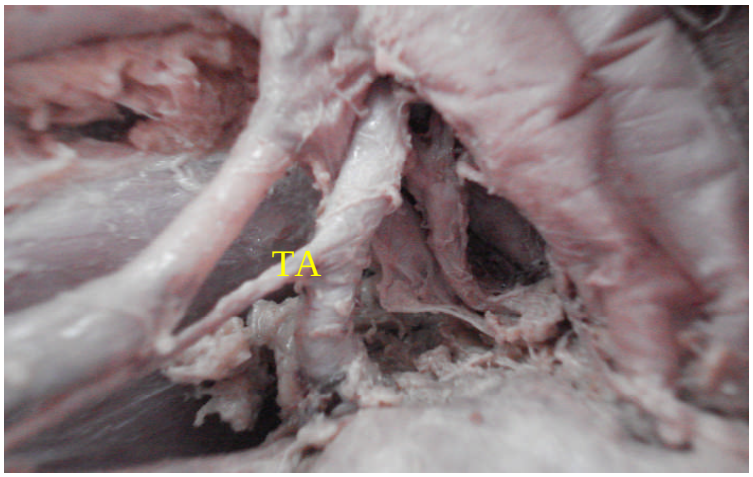

Figure 2: left testicular artery originated from left accessory renal artery, TA

The testicular artery arises at a right angle from the accessory renal artery in mid-distance of its course. *(Figure 1).*

Left accessory renal artery was found came from anterolateral aspect of abdominal aorta in three cadaver *(figure3)*.the accessory renal artery originated from abdominal aorta approximately 5 mm inferior to the origin of the main renal artery in two cases and runs toward the lower pole of the kidney

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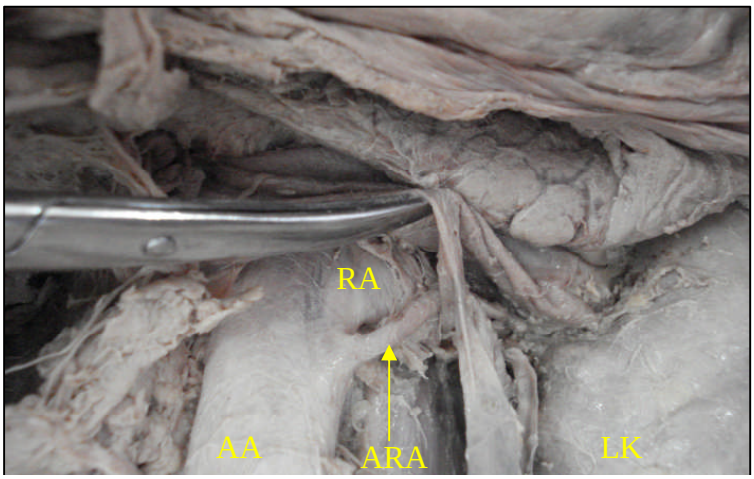

Figure 3: AA: abdominal aorta, RA: renal artery. LK: left kidney, ARA: accessory renal artery.

There is one testicular artery and two veins accompanying the artery on the left side of the cadaver

Table.1: shows number of cases with anomalous testicular arteries in 40 testicular arteries examined.

No. of cases examined	Origin from aorta	Origin from main renal artery	Origin from accessory renal artery	Others
20 cases (40 testicular arteries)	37	1 (right testicular artery)	2 (left testicular artery)	

Discussion

Careful knowledge of the embryological basis of the renal and testicular vasculatures and structural development of kidney and tesitcles is essential to understand the multitude of anomalies that may occur .variations in the origin ,course and branches of the testicular arteries are attributed to the embryological development .during fetus development, the lateral splanchnic arteries on each side supply the mesonephros, metanephros ,the testis or ovary and suprarenal glands, all these structures develop ,either totally or in part from the intermediate mesenchyme of the mesonephric ridge.one testicular or ovarian artery and three suprarenal arteries persist on each side(خطأ! الإشارة المرجعية غير معرّفة.[12]).

Four main varieties of testicular arteries are identified according to the site of origin from aorta or renal vessels.

1. a single testicular artery arising from aorta(type A)

2. a single testicular artery arising from renal artery(type B)

3. two testicular arteries arising from aorta(type C)

4. two testicular arteries penetrating the testis ,one arising from the aorta and other from the renal artery(type D)[13]

Many descriptions of abnormal origin of left testicular artery are made, Shinohara et al describes the high origin from aorta, higher to the origin of left inferior phrenic artery [14] or higher to the level of L2 vertebra in 5-20%, or it may be originated from renal arteries, either from principle left renal artery or from accessory renal artery, as well in 5-6% (خطأ! الإشارة المرجعية غير معرّفة.,خطأ! الإشارة المرجعية غير معرّفة., 15).

The accessory renal artery has been known since the early days of human dissection and autopsy. It has been reported that it occurs in 26% of individuals and originates mostly directly from aorta [16, 17].

Rarely, the accessory renal artery arises from celiac or superior mesenteric arteries near the aortic bifurcation or from common iliac arteries (خطأ! الإشارة المرجعية غير معرّفة.).
In this study, the left testicular artery was found to be originated from accessory renal artery and we define it as aberrant testicular artery.
The anomalous origin of testicular artery from accessory renal vessel has important clinical implications.

Risk of renal ischemia, lower segment infarction due to injury of anomalous testicular artery during urological or oncological surgical intervention and renal transplantation. if the surgeon is not aware of such anatomical variation. Surgeon may face unexplained bleeding from the jeopardized anomalous testicular artery

Such variations in the testicular and renal arteries have clinical and surgical significance in regard to their in influence on the blood flow to the kidney and testis and hemorrhagic complications following retroperitoneal operations [18, 19]

In addition to that ,another risk of left testicular atrophy or infarction due to unexpected loss of blood supply because of erroneous ligation or division of renal artery and/or testicular artery is clearly hazardous to result in infarction of testicle since the main blood supply of testes comes from testicular artery although cremasteric artery and differential artery may share in blood supply (خطأ! الإشارة المرجعية غير معرّفة.,خطأ! الإشارة المرجعية غير معرّفة.,20).

Due to the emergence of such critical vascular anomalies, it is widely advisable to do angiographic examination of renal arteries prior to operation on the kidney,transplantation or nephrectomy to detect any such variation of testicular artery origin to preserve the blood supply to the testis(خطأ! الإشارة المرجعية غير معرّفة.).

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Increased expression of estrogen receptors at the materno-fetal interface in patients with recurrent pregnency loss

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Abstract

Background: Estrogen hormone has been implicated in the pathogenesis of different genital tract pathologies and in counteracting the progress of normal pregnancy.

Objective: Localization and semi-quantization of estrogen receptors at the materno-fetal interface in patients with recurrent pregnancy loss (RPL).

Methods: Immunohistochemistry analysis of estrogen receptors using paraffin embedded sections of curate samples obtained from 40 women, who where divided into three groups: 24 women with RPL, 10 women with abortion for the first time, and 6 women with induced abortion.

Results: The mean value of the expression of estrogen receptors was (71.2 ± 2.3), which is significantly higher than that of the second group (52.2 ± 3.2), and the third group (43.7 ± 4.2), (p=0.001).

Conclusion: High expression of estrogen receptors in women with RPL may give a clue to its prominent role in the pathology of pregnancy loss.

Key wards: Estrogen receptor, RPL.

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Introduction

Spontaneous abortion is defined as the spontaneous loss of pregnancy prior to the 20th gestational week of pregnancy. Pregnancy losses which occur during this period of time are said to occur in about 15 percent of pregnancies. At the same time, the risk of miscarriage increases proportionately to the number of previous miscarriages experienced [(1)]. Many underlying hormonal abnormalities, ovulation defects and cyclic abnormalities can also be observed in patients with multiple miscarriages [(1, 2)].

Several causes for recurrent pregnancy loss (RPL) have been hypothesized, including endocrine disorders [(2, 3)], genetic [(4)], and uterine anatomical abnormalities [(5)].

Immunological factors are thought to account for many of the remaining 40-60% of unexplained miscarriages [(6)].

The interactions between immune-endocrine and reproductive systems are heightened during pregnancy as an adaptive mechanism and are regulated by a complex array of hormones and cytokines that control the survival of a semiallogeneic conceptus [(7)]. Multiple signals synchronize the development of the blastocyst and the preparation of the uterus. During early pregnancy estrogen stimulates proliferation and differentiation of endometrial stromal and epithelial cells. Downstream effectors of steroid-hormone actions include peptide hormones, growth factors, and cytokines [(8)].

Estrogen is implicated in many inflammatory and autoimmune diseases [(9-11)] and has been shown to up-regulate IFN in activated splenocytes [(12-14)].

In vivo studies of the role of estrogen and progesterone in the

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regulation of the uterine immune environment demonstrated a general pro-inflammatory effect of estrogen causing an influx of macrophages and neutrophils, which is antagonized by progesterone through its receptor [15-16].

Previous studies showed a very faint immunohistochemistry signal of the staining of estrogen receptors [17]. In this study, we attempted to detect the expression of estrogen receptor in women with RPL and compare it with that in normal pregnancy and women with pregnancy loss for the first time using monoclonal antibodies of estrogen receptor.

Patients, materials and methods

This study was conducted from November 2003 to April 2004. Patients were collected from Al-Kadhmya and Al-Ulwiya teaching hospitals, and then divided into three groups; **Group A:** 24 pregnant ladies presented with abortion during the first trimester, all of whom gave a history of previous 3-6 consecutive first trimester abortions, with no medical diseases, nor family history of genetic diseases or uterine anatomical anomaly, also all of them were confirmed by lab. Tests to be negative for acute infection with rubella, HCMV and toxoplasmosis. **Group B:** 10 pregnant ladies presented with abortion during the first trimester and had at least three previous normal pregnancies with no previous abortion, and no history of any medical illness, and **Group C:** 6 pregnant ladies with elective termination of pregnancy in the first trimester for a maternal indications under approved consent of two senior gynecologists and a physician (as control group). Curate samples of the materno-fetal interface were taken from all these women at the end of evacuation curate operation then embedded in paraffin and confirmed by a pathologist, and then subjected for immunohistochemistry technique using DAKO cytomation detection kit (Denmark).

Immunohistochemistry procedure: 5µm thickness tissue sections on positively charged slides were deparafinized in xylen then rehydrated in a series of ethanol concentrations. And then, 2-3 drops of peroxidase block were applied onto the tissue sections a step which is followed by application of the primary antibody (anti-estrogen receptor in a dilution of 1:30) (BioGenex-USA), then the secondary antibody was added, followed by application of the hoarse reddish peroxidase (HRP) conjugate, and then its substrate DAB chromogen. Sections were counterstained with hematoxyline, dehydrated and mounted to be finally examined under the microscope. For more details refer to the immunohistochemistry procedure in reference [18].

Evaluation of the immunohistochemistry signal: The expression of estrogen receptors was measured by counting the number of positive decidual and trophoblastic cells, which gave a dark-brown nuclear staining under the light microscope. The extent of the immunohistochemistry signal in the villi was determined in 10 fields (X100 magnification). In each field the total number of villi were counted and the extent of nuclear staining of the cytotrophoblast and syncytiotrophoblast in a given villous was graded as 3, (75–100%); 2, (25–75%); or 1, (<25%). The total staining score was divided by the number of whole villi per field in 10 fields. These scores (between 1 and 3) were added for each field, and a score between 10 and 30 was gained for each sample [19], and to be simplified as percent, the

percentage of positively stained villi was calculated for each case by taking the mean of the percentages of the positively stained villi in the 10 fields as advised by Hennessy (Personal communication, 2004). The scorer was blinded to the clinical diagnosis of the tissues at the time of assessment, and tissues were independently assessed by two observers.

Negative controls were obtained by omitting the monoclonal antibody and using phosphate buffer saline to verify the signal specificity. Positive control signal was obtained using normal healthy ovarian tissue.

Statistics: ANOVA test was used to determine the difference in the expression of estrogen receptor among the three groups. Values of $p<0.05$ were considered as statistically significant.

Results

Table (1) shows the percentages of the expression of estrogen receptors in terms of mean ± SE, minimum and maximum values of the three groups, and it is obvious that the expression was higher in the recurrent loss group (mean=71.2 ± 2.3) than that of group B and C. (Table 2) shows the differences in the expression of estrogen receptor among the three groups and within the groups using ANOVA analysis. Estrogen receptors expression was heterogeneous dark-brown nuclear staining involving the trophoblasts, both cyto- and synsytiotrophoblasts in the three groups of women but it was more significant and obvious in the recurrent loss group (Figure 1).

Table 1: The expression of estrogen receptor among the studied groups

Estrogen Receptor	n	Mean ± S.E.$^{\Psi}$	Min. Value	Max. Value
Group A	24	71.2 ± 2.3	50	90
Group B	10	52.2 ± 3.2	35	70
Group C	6	43.7 ± 4.2	30	60

Total mean = 62.3 ± 2.4 %

$^{\Psi}$ Standard error

Table 2: The significance of differences in the expression of estrogen receptor in between the groups

Estrogen Receptor	*P* Value
Among the groups	0.001
Between group A and B	0.001
Between group A and C	0.001
Between group B and C	0.134

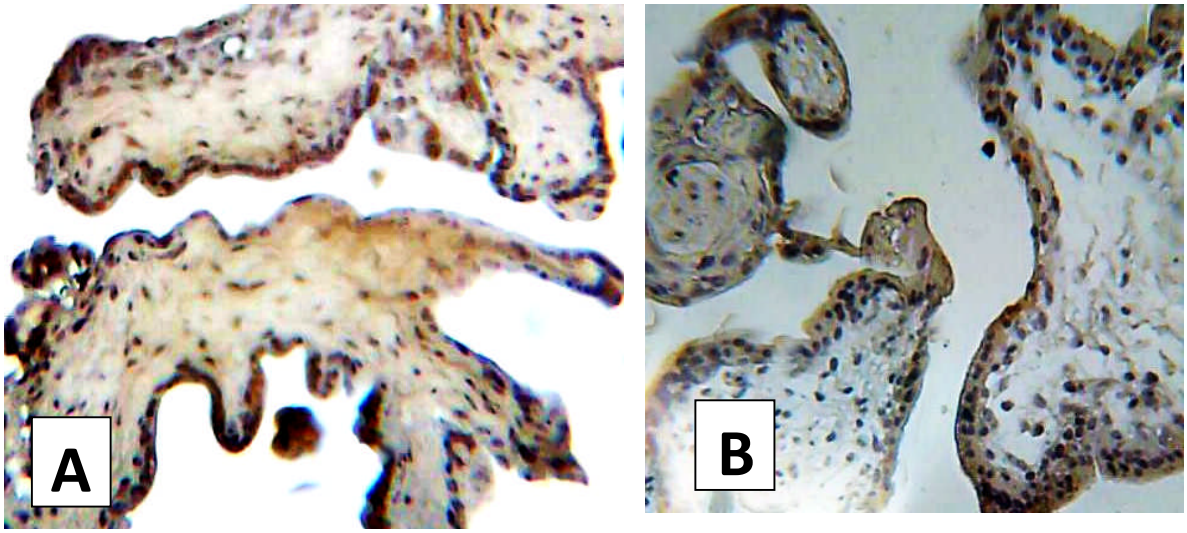

Figure 1: Detection of Estrogen Receptor by immunohistochemistry in women with pregnancy loss. (A & B) Expression of estrogen receptor in the trophoblasts in women with RPL and normal pregnancy respectively. Estrogen receptors expression was diffuse heterogeneous dark-brown nuclear staining involving the trophoblasts, both cyto- and synsytiotrophoblasts in the three groups of women but with darker and higher percentage of expression in the recurrent loss group. Magnification power of A and B (X400).

Discussion

It is well known that sex steroids have significant impact on the development of autoimmune diseases in both humans and rodents. In particular, estrogen has been suggested to be responsible for the strong female preponderance of the human rheumatoid arthritis, systemic lupus erythematosus, scleroderma, and Sjo¨gren's syndrome, but the role of estrogens in the female has not been fully characterized [20-22].

Sex hormones influence both humeral and cell-mediated immune response, and estrogen is one of potential factors in this immunological dimorphism [23].

The data of this study showed a significant increase in the expression of estrogen receptor in the tissue of women with RPL, in which estradiol has been shown to selectively enhance the development of IFN-γ-producing cells through an ER (estrogen receptor)-dependant mechanism [24]. In fact, estrogen is known to increase activity of the IFN-γ promoter and cause increase in the expression of IFN-γ mRNA in the stimulated murine spleen cells [25]. All these studies goes with the previous studies on these cases that showed a significant increase in the expression of the Th1 cytokine (IFN-γ) in women with RPL as compared with the control groups [26].

In addition another study showed that estrogen treatment up-regulates IFN-γ inducible-iNOS (nitric oxide synthase) gene expression, iNOS protein, nitric oxide, and cyclooxygenase-2 as an indirect consequence of activation of T cells [14]. Besides, estrogen may promote inflammatory conditions by altering the levels of chemokines, providing evidence for an additional mechanism by

which estrogens can regulate inflammation [27].

Recently, a study showed an inappropriate immune response to sex hormones especially estrogen and progesterone in RPL women as compared with the control group due to hypersensitivity to sex hormones [28].

On the contrary, a study compared the serum level of progesterone and estrodiol between a group of non-pregnant women with history of RPL during the follicular phase, and nulligravid females with tubal or male-factor infertility without miscarriage, showed comparable results in both groups with very few cases showing higher estrogen and lower progesterone levels in the study group [29]. But our data come from the local expression of the hormone at the materno-fetal interface meaning that we try to study the actual hormonal environment during pregnancy. Also apart from systemic changes in the maternal immune system, local immunomodulation at the materno-fetal interface via wide array of hormones and cytokines and immune effector cells also play a very critical role in maintaining the balance of a desirable immune response [30, 31].

In conclusion, increased expression of estrogen receptor in women with RPL could give a clue to its role as a pro-inflammatory stimulant augment the effect of Th1 cytokines participating in the pathology of RPL.

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The role of Testosterone in Preeclampsia

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Abstract

Background: Preeclampsia is a form of high blood pressure manifested during pregnancy, it is a common major complication causing significant morbidity and mortality; however, its etiology is still unknown.

The systemic vasculature is a target tissue for sex steroid hormone. Estrogen, androgen, and progesterone all influence the function and pathophysiology of the systemic circulation by influencing endothelial derived nitric-oxide pathway.

Objective: *was* to demonstrate the pattern of sex steroid (testosterone) in preeclampsia with respect to normal pregnancy, and the correlation of the above parameter with nitric-oxide pathway.

Subject and methods: The present study is a cross-sectional case-control study includes measurement of nitric oxide, nitric oxide synthase, and sex steroid (testosterone) in 60 patients with preeclampsia. They were classified, according to the gestational age, into two groups:

*Preeclamptics in the second trimester G1: (n=30).

*Preeclamptics in the third trimester G2: (n=30).

The results were compared with 60 apparently healthy pregnants (control group), who were, also, classified according to the gestational age into two groups:

- Pregnants in the second trimester G3: (n=30).
- Pregnants in the third trimester G4: (n=30).

Results: showed a significant reduction in serum NO and NOS in the preeclamptics as compared to the controls which was accompanied by a significant increase in serum testosterone. The inhibitory effect of testosterone on NO production is supported by negative correlation between these parameters.

The disturbance in vasodilation state and testosterone can be attributed to malfunction placenta, and it varies according to the gestational age and advancing disease state; being the best in G4 (normal pregnants in the third trimester), and the worse in G2 (preeclamptics in the third trimester) as indicated by NO measurement.

Conclusion: preeclamptics (in different gestational age groups) experienced vasospasm, hyperandrogenemia when compared with healthy pregnants matched with their age and gestational age.

Key words: preeclampsia, nitric oxide, testosterone,Testosterone in preeclampsia.

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Introduction

Preeclampsia is defined as the onset of hypertension and the presence of proteinuria during pregnancy, usually occurring after the 20th week of gestation in a previously normotensive woman and resolving completely by the sixth week after delivery of fetus [1, 2].

The pathophysiology of preeclampsia is thought to represent a defective response to the physiologic demands of normal pregnancy [2, 3]. Endocrine changes in pregnancy are largely dependent on the concerted production of protein and steroid hormones by the fetoplacental unit [4]. These endocrine changes support the successful establishment, maintenance, and termination of pregnancy [4]. It has

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been established that high androgen level, primarily dependent on placental function, is a factor in the etiopathogenesis of preeclampsia [5, 6]. Nitric oxide (nitrogen monoxide) plays an important role in a wide range of physiologic processes [7]. A major mediator of endothelial function, NO, regulates vasodilatory and antithrombotic actions in the vasculature [7]. Impaired NO bioactivity has been postulated as an important pathogenic factor in preeclampsia [7]. Endothelium-dependent arterial vasodilation has been shown to be reduced and vascular impedance to be increased in preeclampsia compared with normal pregnancy [7]. Postpregnancy, women with a history of preeclampsia (3 months postpartum or later) have significantly reduced endothelium-dependent vasodilation compared with women with a history of normal pregnancy [7]. Also, NO is mainly expressed in Leydig cells where it regulates the concentration of testosterone by acting in an autocrine/paracrine fashion. In fact, NO is involved in testicular testosterone synthesis causing a significant decrease of androgen production [8].

The present study was undertaken to elucidate the role of sex steroid (testosterone) on endothelial dysfunction in preeclampsia.

Subjects & Methods

A-Patients: The study was a cross-sectional, case-control study conducted on sixty patients with preeclampsia (PE) attending the Obstetric Consultant-Clinic, Antenatal Clinic, and Labor Ward at Al-Kadhimiya Teaching Hospital, for re-evaluation of newly diagnosed PE, or for delivery.

The diagnosis of PE was based on clinical criteria that were hypertension (absolute BP of 140/90 mmHg twice over 4 hr without prior comparison) [1, 2] and proteinuria (21.5 mg of urinary protein per mmol creatinine) [9].

The exclusion criteria, which were used for cases and controls, were gestational or chronic hypertension, diabetes mellitus, renal disease, multifetal gestation, intrauterine fetal death, and pregnancy less than 20 weeks of gestation.

Depending on the gestational age, the patients were divided into two groups:

1. Preeclamptics in the second trimester (G1):

Included thirty Preeclamptics in their second trimester of pregnancy. Age range was from 18 to 37 years (mean age $\pm$ SD = 26.1 $\pm$ 6.4 year). The gestational age range was from 20 to 28 weeks (mean gestational age $\pm$ SD = 26.3 $\pm$ 1.5 week).

2. Preeclamptics in the third trimester (G2):

Included thirty preeclamptics in their third trimester of pregnancy. Age range was from 18 to 40 years (mean age $\pm$ SD = 25.1 $\pm$ 6.9 years). Gestational age ranged from 29 to 40 weeks (mean gestational age $\pm$ SD = 35.6 $\pm$ 1.6 week).

Controls: Sixty apparently healthy pregnants attending the Antenatal clinic, and Labor Ward at Al-Kadhimiya Teaching Hospital, for re-evaluation of their pregnancy, or for delivery. The control groups were comparable to the preeclamptic groups regarding the age, gestational age, Depending on the gestational age, the apparently healthy pregnants were divided into two groups:

3. Control pregnants in the second trimester (G3):

They were thirty apparently healthy pregnants in the second trimester of pregnancy. Age range was from 15 to 38 years (mean age + SD = 24.6 + 4.5 year).

Gestational age range was from 20 to 28 weeks (mean gestational age + SD = 25.5 + 1.8 week).

4. Control pregnants during the third trimester (G4):

They were thirty pregnants in the third trimester of pregnancy. Age range was from 18 to 35 years (mean age ± SD = 24.8 ± 4.6 year). Gestational age range was from 29 to 40 weeks (mean gestational age ± SD = 34.6 ± 2.1 week).

B. Blood samples:

Ten milliliters of random venous blood were withdrawn from each patient and control, in supine position, without application of tourniquet. Samples were transferred into clean plane tubes, left at room temperature for 15 minutes for clotting, centrifuged, and the separated sera were then divided into tow parts:

1) An aliquot of serum was transferred into Eppendrof tube, which was used for measuring nitric oxide expressed as nitrite (the end product of NOS), this was done at the same day of collection [10].

2) Another aliquot of the serum was transferred into Eppendrof tube, which was used for measuring sex steroids (estrogen, progesterone, and testosterone) by enzyme linked fluorescent assay (ELFA) method. The tubes were stored at -20^{o} C until analysis, which was done within one month after collection [11].

C-Methods

Nitrite concentration measurement was used as an index of NO synthase activity [10], NO synthase activity is expressed here as the amount of nitrite (in µmoles) formed per minute, whereas the specific enzyme activity is given as the amount of nitrite (in µmoles) formed per minute per mg of protein for plasma[10] (µmol/min/mg protein).

Estimation of serum total testosterone was done in the Al-Kadhimya teaching hospital laboratories by Enzyme Linked Fluorescent Assay (ELFA) methods using the VIDAS instrument [11].

Results

Serum testosterone:

Serum testosterone was significantly higher in preeclamptics (G1 &G2) compared with normal pregnants (G3 & G4) [P < 0.001 for both]. Also serum testosterone was significantly higher in G2 compared with G1 [P < 0.001 for both], but there was no significant difference between G3 & G4 [P< 0.05] as in Table 1.

Serum Nitric oxide (NO) and nitric oxide synthase (NOS):

In preeclamptic pregnants in the third trimester G2, the maternal serum NO and NOS levels were significantly lower than those in the second trimester G1 [P< 0.001 and < 0.05 respectively]. In preeclamptic pregnants G1 & G2, the maternal serum NO and NOS were significantly lower than healthy pregnants G3 & G4 [P < 0.001 for both parameters in both groups], this difference was not found between healthy pregnants in the second trimester G3 and the third trimester G4 [P < 0.05 for both parameters] as in Table 1.

3.3.1. Correlation between serum testosterone and NO in different groups:

There was a significant negative correlation between serum testosterone and serum NO in preeclamptic groups G1 and G2 [r =0.9, P < 0.001 & < - 0.05, figures. 1 & 2 respectively) however, no correlation was seen among the normotensive groups G3 and G4 [r = 0.1, P > 0.05, r = 0.06, P> 0.05; figs. 3 & 4 respectively).

Discussion

In this study the level of the potent androgen testosterone was found to be significantly higher in women with preeclampsia than in healthy controls with similar gestational age, and chronologic age as in Table 1 & Figure 1.

Several independent studies showed that androgens could cause physiologic changes strikingly similar to those seen in preeclampsia [12]. High circulating androgen concentrations (in the male range) and exogenously administered androgens have both been linked to hypertension in vivo and in vitro [6].

Maternal serum androgen levels have been shown to be elevated in healthy pregnant women compared with levels in those who were not pregnant; this can be attributed to the increase in sex hormone binding globulin concentration induced by estrogen, or to the effect of hCG hormone which results in increasing maternal and lowering fetal testosterone [13]. Other suggestions may involve the increase in inhibin –A found in preeclamptic women which leads to increase androgen synthesis by the ovarian theca cells , with a reduction in the placental aromatization enzymes for androgens in preeclamptic women[6] .

Our findings suggest a possible effect of the enzyme deficiency, as well as a possible mechanism for its association with preeclampsia [6].

Alternatively, it could be argued that the testosterone increase observed in the patients with preeclampsia could have been caused by decreased intravascular volume found in preeclampsia [6, 14].

Nitric oxide mediates many functions of endothelium, including vasodilatation and inhibition of platelet aggregation [15]. Preeclampsia may be associated with nitric oxide deficiency [15], and the results of this study provide an evidence to support this hypothesis. As shown in Table 1, NO level in blood was similar in both healthy pregnants groups; it was unchanged during physiological pregnancy. During preeclampsia, the NO was decreased compared to the control level. This suggests that during preeclampsia the low activity of endothelial NO-synthases and redox-dependent transformation of NO in peroxynitrite provoke a decrease in the blood nitric oxide level [16]; these results are comparable to those of Meher & Duly [15], Khetsuriani et al. [17], Choi et al. [16], and Nishikawa & Miyamoto [18].

The reduction of NO in preeclampsia and other cardiovascular disease can be attributed to either the association of a subset of endothelial nitric oxide synthase gene (NOS3) polymorphisms (Glu298Asp, intron 4, -786>C and -786CC) with cardiovascular disease, preeclampsia and recurrence of pregnancy negative events[19,20] , or to testosterone increment in preeclampsia[15].

Arginase is often colocalized with NOS and they maintain a complex relationship, regulating each other and competing with one another for their common substrate [21]. There is evidence that when either arginase or NOS is activated, it competitively inhibits the action of the other [21].

During late pregnancy, arginase activity increases significantly in animals [21]. Kidney arginase was also increased in these animals [21]. This suggests that the placenta is required for maximal increase in arginase activity [21].

Rats and sheep have also been shown to have an increase in arginase that peaks in late pregnancy [21].

Arginase is also found in the human placenta [21]. One study that evaluated the levels of serum hydrolases in human pregnancy found no increase in serum arginase activity in the first, second, or third trimester of pregnancy [21]. It is quite possible that arginase activity in pregnancy is increased significantly in the involved tissues, while does not increase in the serum [21]. One study on the arginase activities of various tissues in rats also found that while there was an increase in arginase activity during late pregnancy, it was not reflected in circulating urea levels [21]. Why arginase activity is increased during pregnancy is unknown. In rats, inhibiting uterine arginase activity had arrested the embryonic development [21]. This could be secondary to its effects on polyamine synthesis [21]. The timing of the increase in arginase activity at the end of pregnancy and the decrease in NO production at this time may reflect normal enzyme interaction. It is quite feasible that the increase in arginase activity is part of the trigger that normally decreases the myometrial NOS activity just prior to, and in preparation for parturition [21].

In studies on rats and mice, testosterone has been shown to stimulate arginase activity [21]. It was found that testosterone elicited a 50% decrease in the enzyme ornithine carbaomoyl transferase (OCT). Inhibiting OCT may cause a significant decrease in endogenous L-arginine production [21].

Patients with preeclampsia have been shown to have higher levels of testosterone than the level of testosterone typical of nonpreeclamptic pregnants. If testosterone stimulates the arginase in humans, then this could potentially decrease the L-arginine available to NOS and thus increase production of O_2^-; this was supported by the negative correlation between NO and testosterone serum levels found in preeclamptics, which was lost in normal gestation as seen in Figures:1.2,3 & 4

Biochemical changes in preeclampsia appear to be driven by over-production of testosterone (probably induced by placental dysfunction) which may lead to a reduction in nitric oxide synthesis (as evident by low serum nitrite). While measuring NO and testosterone before 20^{th} week gestation can be used as predictor of the disease.

Table 1: The mean serum testosterone, nitric oxide and nitric oxide synthase (NOS) in different preeclamptic and control groups (presented as mean ± SD).

Variable	G1	G2	G3	G4
testosterone (ng/ml)	1.89 ± 0.6**	2.9± 2.4**	0.85 ± 0.7	0.72 ± 0.3
Nitric oxide (µmol)	6 ± 0.9**	4.1± 2.4**	8.1 ± 3	8.8 ± 3.3
NOS (µmol/g/min)	0.08±0.01*	0.06±0.03*	0.1 ± 0.04	0.11 ± 0.04

NOS activity is expressed as nitrite / g protein / min.
** p< 0.05 , ** p < 0,01*

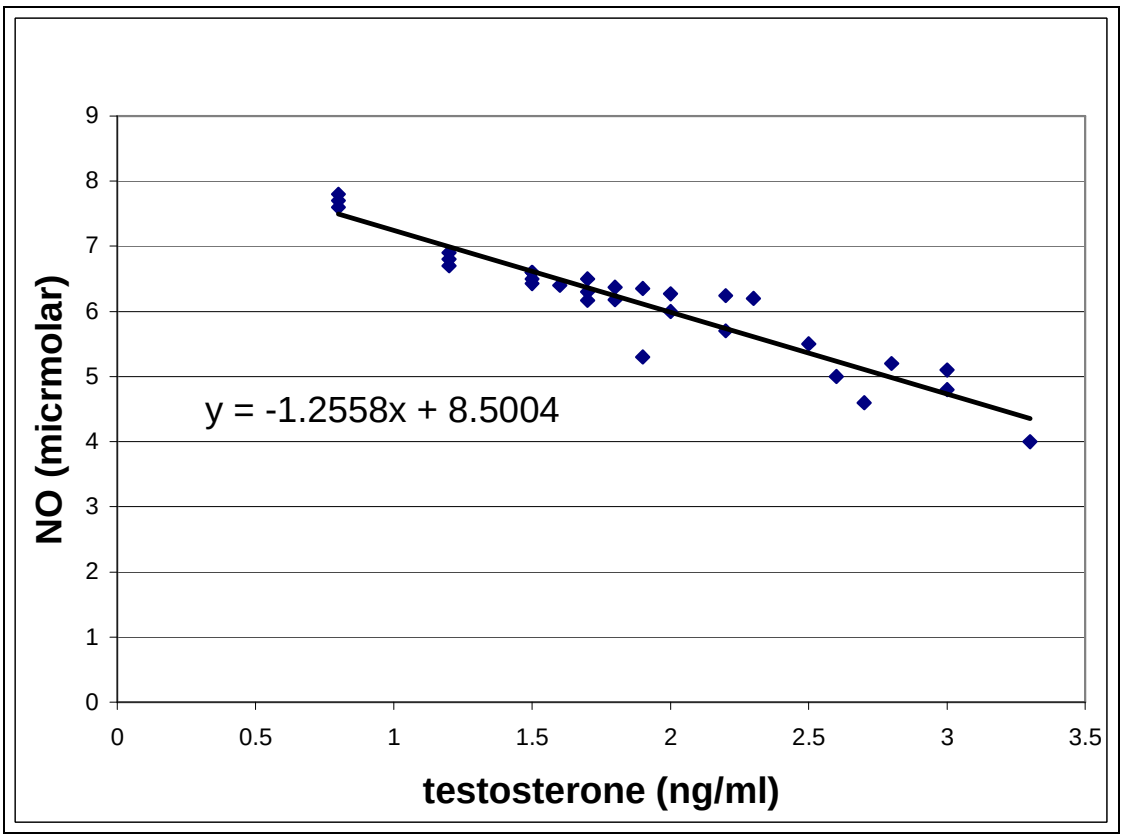

Figure 1: Correlation between testosterone & NO in sera of preeclamptics in the second trimester G1 (n = 30; r= -0.9; p< 0.001).

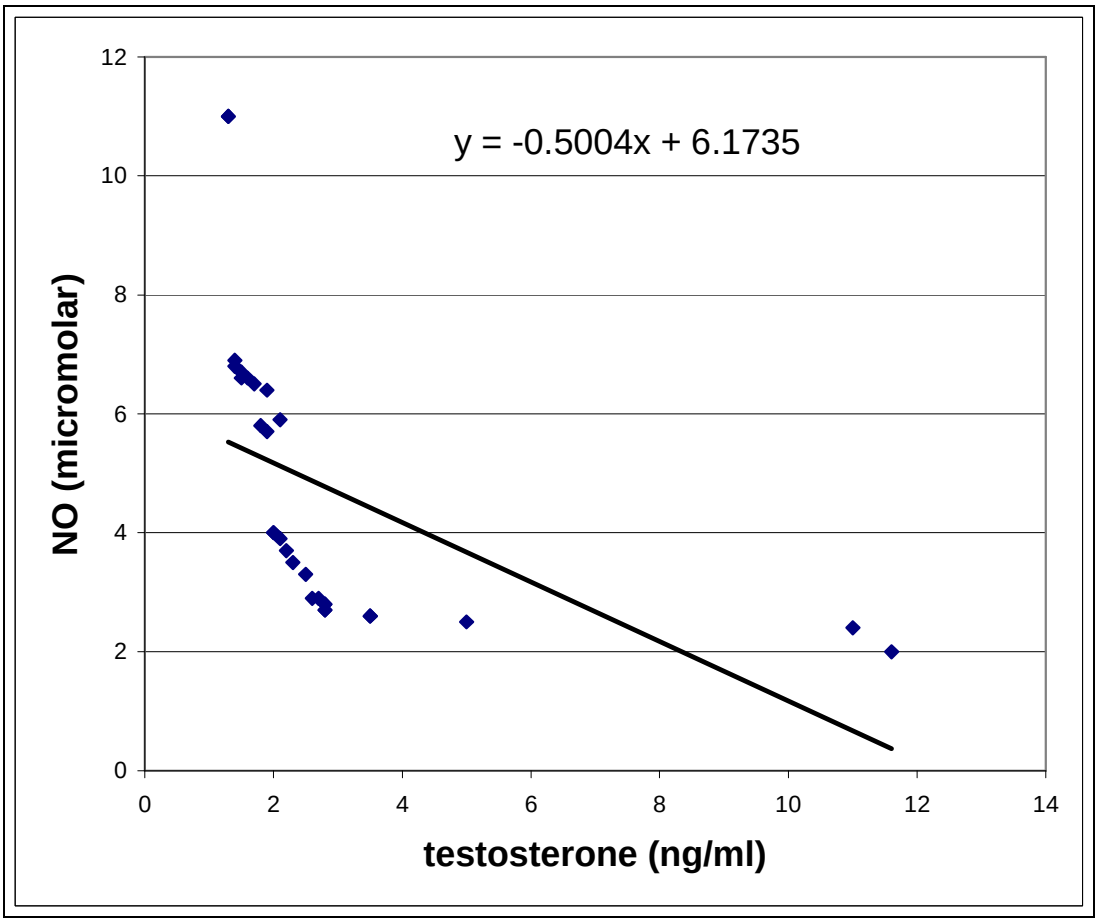

Figure 2: Correlation between testosterone & NO in sera of preeclamptics in the third trimester G2 (n = 30; r = -0.5; p < 0.01).

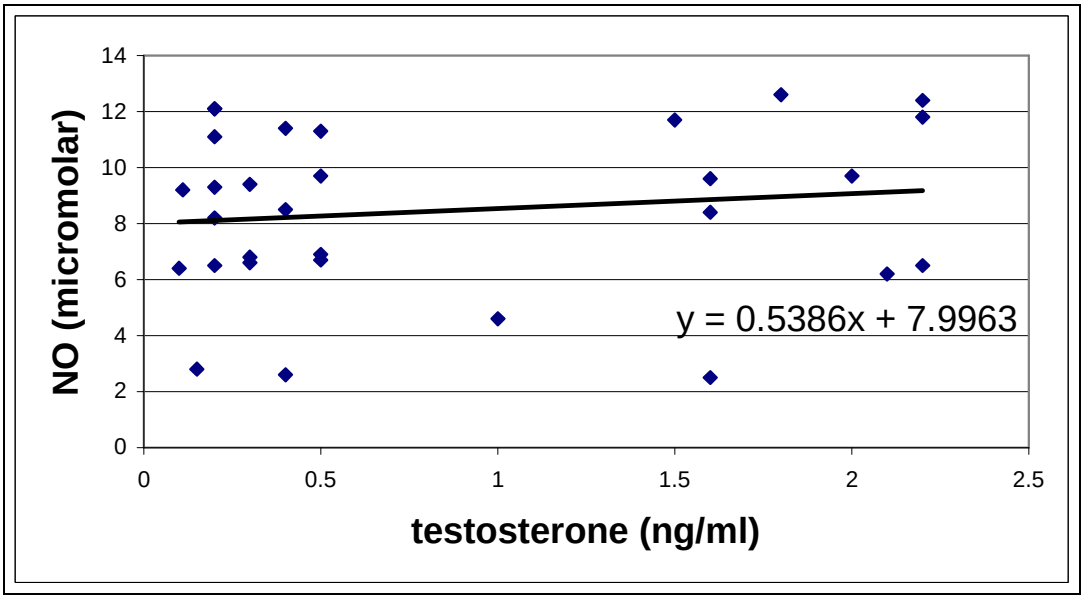

Figure 3: Correlation between testosterone & NO in sera of normotensive pregnants in the second trimester G3(n = 30; r= 0.1; p = 0.05).

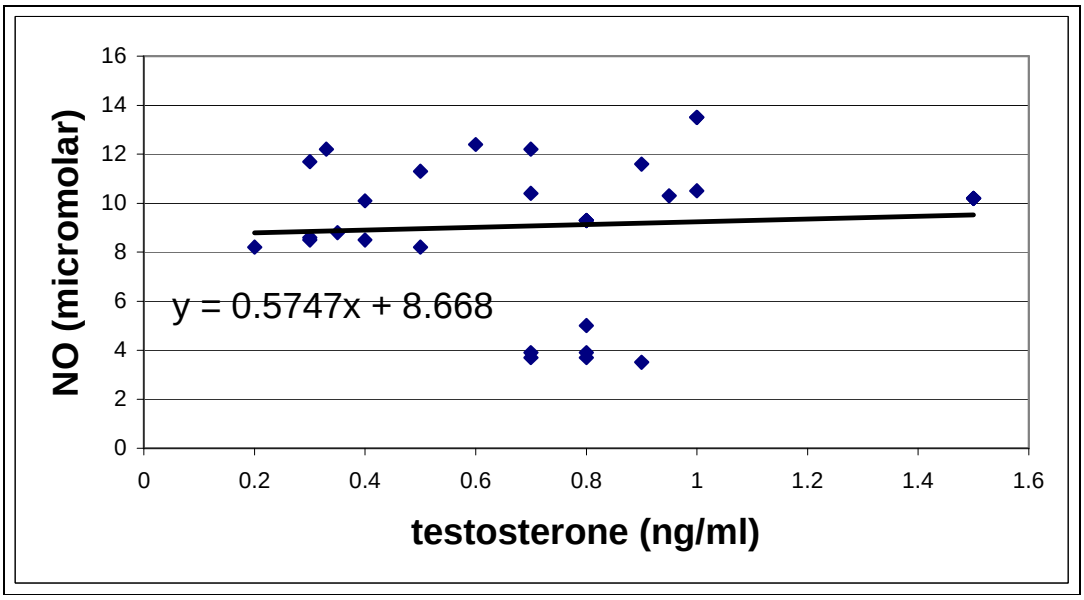

Figure 4: Correlation between testosterone & NO in sera of normotensive pregnants in the third trimester G4 (n = 30; r= 0.06; P = 0.05).

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Complications during hemodialysis in arterio-venous fistula versus temporary vascular access

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Abstract

Background: Dialysis is procedure that removes excess fluid and the toxic end products of metabolism. The major forms of dialysis are hemodialysis, and peritoneal dialysis. Access to the blood circulation is achieved by the use of central venous catheter or artificial arteriovenous fistula.

Objective: To detect and compare prevalence of complications occurs in uremic patients using central venous catheter or arteriovenous fistula in dialysis unit in Al-Kadhimiya Teaching Hospital.

Patients and methods: One hundred patients with renal failure (chronic or acute) undergoing hemodialysis were questioned and examined for the
Complications occurred during or after the hemodialysis process using arteriovenous fistula or temporary vascular access.

Results: The results showed significant of fever and blood flow obstruction in temporary vascular access (<0.05) as a complications in hemodialysis. Other complications such as hepatitis (B&C), hypotension, exit site infection, nausea, itching, muscle cramp, vomiting, backache, fainting and disequilibrium syndrome are similar in arteriovenous fistula and temporary vascular access.

Conclusion: The main complications during hemodialysis in this study were fever, malfunction of the catheter, and exit site infection in catheter more common in temporary Catheter than arteriovenous fistula so advice to do arteriovenous fistula before end stage renal disease

Keywords: Hemodialysis, arteriovenous fistula and temporary catheter.

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Introduction

Dialytic therapy should be started when conservative management fails to maintain the patient in reasonable comfort. Usually, dialysis is required when the glomerular filtration rate drops to 5—10 ml/min. it is both unnecessary and risky to adhere to strict biochemical indications. Broadly speaking, the development of uremic Encephalopathy, neuropathy, pericarditis, and bleeding diathesis are indications to start dialysis immediately. Fluid overload, congestive heart failure, hyperkalemia, metabolic acidosis, and hypertension uncontrolled by conservative measure are also indications for starting patients patients on dialysis therapy [1].

Dialysis is procedure that removes excess fluid and the toxic end products of metabolism. Dialysis is usually prescribed to patients with significant impairment of renal function resulting from acute or chronic renal failure. It is also used occasionally to remove ingested drugs and other toxin in patients who may have normal renal function [2].

About 62.9% of patients with end stage renal disease were undergoing hemodialysis, 8.7% were being treated with peritoneal dialysis, and the rest were being sustained by functioning kidney transplant [3].

Although the basic principles of hemodialysis have not changed a great deal in the last 20 years, the technology has dramatically improved. Most patients dialyze three times per week [4].

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The use of temporary or semi-permanent hemodialysis catheters remains an essential component of dialysis practice, both for the management of acute renal failure and as temporary bridging access for patients whose other dialysis access is unavailable for use. Unfortunately the use of these catheters is often complicated by mechanical or infectious complications which may result in patient's morbidity or premature catheter removal. Catheter related bactremia is the most significant infectious complication of hemodialysis catheter [(5)].

One of the most frequent complications during hemodialysis is dialysis hypotension. It occurs in an estimated 20 % of all hemodialysis sessions. The symptoms vary from fatigue, yawning, cramps, nausea and vomiting to angina pectoris or loss of consciousness. The symptoms are generally transitory. however, dialysis hypotension can also cause permanent damage, such as a myocardial infarction, a cerebrovascular accident, intestinal infarction or an occlusion of the arterio-venous fistula[(6)].

With the advent of developments and advances in hemodialysis machine technology, dialysate water purification, and dialyzers, the clinical spectrum of intradialytic complications has changed over the decades. In the pioneering days of hemodialysis, patients were to liable develop allergic reactions to dialyzer membranes,sterilizing and reprocessing agents, coupled with machines that could not accurately control ultrafiltration rates, and chemically and bacterially contaminated dialysate[(7)].

Patients and method

A study was conducted of dialysis unit in AL-Kadhmiya Teaching Hospital from the period of February 2007 to October 2008. Complications during hemodialysis were studied in 700 hemodialysis session. The number of patients involved in this study 100 patients (56 male and 44 female) of different age group ranging from(5 to 70) years mean of age 37.3 year.

52 patients have permanent arteriovenous fistula and 48 patients have temporary catheter. Location of the catheter was subclavain vein in 28, internal jugular vein 12 and femoral vein 8. Patients were followed up for three month. Each patient subjected to hemodialysis for period of 3—4 hours in two or three sessions per week.

Using GAMBRO AK95S hemodialysis apparatus with polyflux^{TM}L dialyzer membrane with effective surface area rang from 1.4 to 2.1m^2 and flow rate rang from 200 to 300 ml/min

The composition of dialysate was as follows:

sodium	133 mmol/L
chloride	97 mmol/L
calcium	1.5 mmol/L
potassium	1.5 mmol/L
magnesium	0.8 mmol/L
acetate	40 mmol/L
glucose	2.1g/L

Special formula was prepared for each patient including: name, age, sex, and cause of renal failure, onset of renal failure, and signs and symptoms of complications during the hemodialysis process.

The following complications were given careful consideration in this study: catheter complication, hypotension, infection such as hepatitis, muscle cramps, nausea, vomiting, fainting, headache, chest pain, backache, itching, fever, chills, seizures, and disequilibrium syndrome.

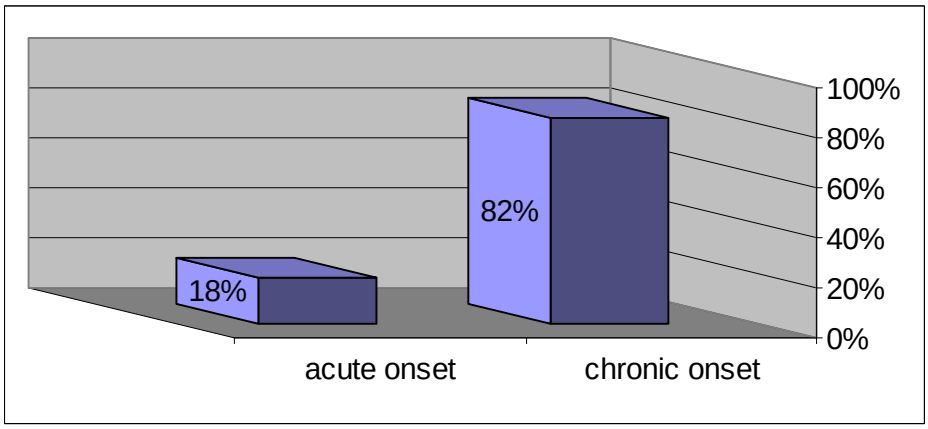
Diagnosis of these patients acute or chronic renal failure depend on history taking from the patients and relative, clinical examination also on

previous investigation and recent investigation which is done in the hospital include general urine examination, blood urea, serum creatinine, ultrasound, serum electrolyte, blood sugar, complete blood film, hepatitis screen, immunological screening (antinuclear antibody and double strand DNA), chest X ray and blood culture.

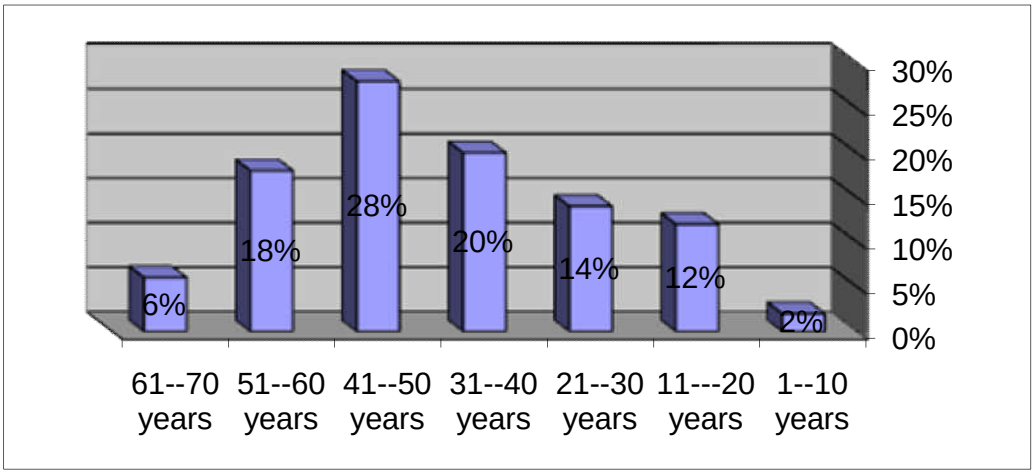
Statically analysis was performed using chi-square test. At level of significance p≤o.o5 regarded as statistically significant.

Result

The onset of renal failure for patients on hemodialysis shows in Figure 1:



The distribution of patient's age in hemodialysis unit shows in Figure 2:



The possible causes of renal failure are shown in Figure 3:

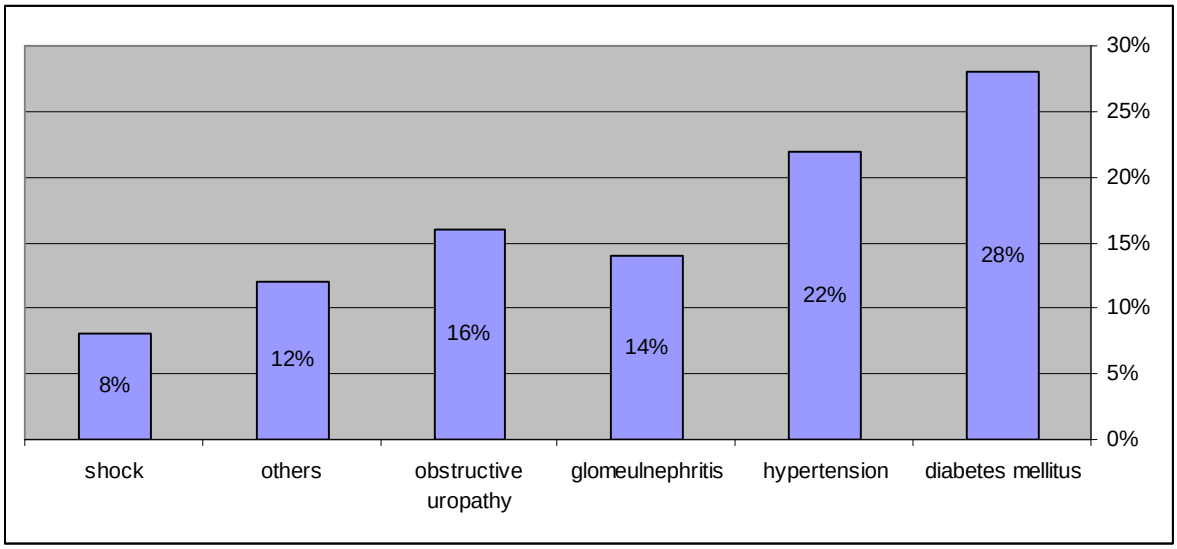


Table 1:Complications during hemodialysis 1

complication	Temporary vascular access	Atriovenous fistula	P. value
fever	30 (60%)	6 (12%)	0.0009
Blood flow obstruction	20 (40%)	3 (6%)	0.017
hypotension	12 (24%)	16 (32%)	0.80
Hepatitis B&C	15 (30%)	12 (24%)	0.08
Exit site infection	8 (16%)	3 (6%)	0.29
Nausea	15 (30%)	14 (28%)	0.29
itching	13 (26%)	11 (22%)	0.28
Muscle cramp	12 (24%)	10 (20%)	0.63
vomiting	10 (20%)	8 (16%)	0.43
Chills, rigor	27 (54%)	5 (10%)	0.0004
Chest pain	10 (20%)	7 (14%)	0.31
backache	8 (16%)	7 (14%)	0.30
fainting	6 (12%)	4 (8%)	0.54
Disequilibrium syndrome	3 (6%)	2 (4%)	0.92
Seizure	2 (4%)	1 (2%)	0.83

Discussion

The major renal replacement therapy is hemodialysis worldwide used in the management of end stage renal disease. both long-term hemodialysis and long- term peritoneal dialysis usually provide no more than about 10% of normal kidney function[8].

In this study, the incidence of chronic renal failure was high in male which is similar to other study but the age onset between 40—50 years which different from other study (usually above 60 years). This indicates the cause of chronic renal failure such as diabetes mellitus, hypertension and obstructive uropathy develop complications are

early duo to uncontrolled and late diagnosis [9].

Most of the patients in hemodialysis are diabetic (28%), hypertensive (22%) and obstructive uropathy(16%) duo to high incidence of infection, stone, , tumor and prostate hypertrophy.

Other causes (12%) patients on hemodialysis include lupus nephritis, hemolytic uremic syndrome, allport syndrome, pylonephritis and unknown cause.

The complications during hemodialysis in temporary vascular access are mainly fever 60% (p.value less than 0.05) may be duo to catheter related bacteraemia after excluding other possibility of fever such as chest infection or urinary tract infection while in patient with arteriovenous fistula the incidence of fever is less common about 12%. the high rate of fever and rigor in our study is higher than in other study by Lukas K. occurring in 18%(outcome and compilations of temporary hemodialysis catheters)[5] may be duo to high risk of infection.

Other common complications was blood flow problem 40% in temporary catheter mainly duo to obstruction in the catheter in the form of thrombosis of the catheter or stenosis or spasm in the vascular. In comparison with arteriovenous fistula there is less blood flow problem unless there are failures or aneurysm of the fistula.

Hypotension is common complications in hemodialysis in temporary catheter and arteriovenous fistula, but in temporary catheter less than in arteriovenous fistula duo to low blood flow rate in the catheter. In our study hypotensions occur in 32%which is in the same rang of other study done by andrew davenport [10].

The incidence of hepatitis (B&C) infection is high (24%) in arteriovenous fistula but in temporary catheter 30% especially hepatitis C infection because the patient exposed to blood transfusion , defect in sterilization of machine of hemodialysis and defect in facility for diagnosis of hepatitis C virus.

The incidence of hepatitis (B &C) in temporary catheter more than in arteriovenous fistula may be duo to poor sterilization, frequent replacement of the catheter or may be the patient in acute renal failure and the patient expose to multiple injury and blood transfusion.

The prevalence of hepatitis C infection in this study similar to other studies of hemodialysis patients in the United States have reported anti-HCV prevalence of 10%--36% among adults[11].

Exit site infection was common in temporary catheter 16% which is high in comparism to arteriovenous fistula (6%) because poor sterilization of the catheter and long duration of using the catheter.

Regarding other complications vomiting, nausea, headache, itching, muscle cramp, fits, seizure and disequilibrium syndrome are similar in both type and agreement with other study [12].

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Significance of Platelet Volume Indices in Patients with Coronary Artery Diseases

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Abstract

Background: Platelets play an important role in the development of intravascular thrombosis, the major cause of acute coronary syndromes. Platelet size has been considered to reflect platelet activity.

Objectives: The aim of this study is to investigate the clinical value of platelet volume indices (PVI) in the spectrum of ischemic heart diseases and the possibility of being a risk factor for acute myocardial infarction (MI).

Patients &Methods: Thirty six (36) patients were included in the study: 22 of them have myocardial infarction (MI) and 14 have unstable angina (UA). Risk factors and history of stable angina (SA) were reviewed and studied by Chi square. Complete blood count and platelet volume indices (PVI): mean platelet volume (MPV), platelet large cell ratio (P-LCR), and platelet distribution width (PDW) were done using automated hematology analysis system and studied by t-test and correlation analysis. All P values were two sided and P value of < 0.05 was considered statistically significant.

Results: It is found that MPV and P-LCR were the most significant parameters that showed statistical difference between patient with UA and those with MI (P=0.042 & P=0.031) respectively unlike other parameters (platelets count or PDW) (P=0.703 & P=0.094). There were no correlations between MPV & other platelet indices with existing past history of SA as well as other risk factors for acute coronary syndrome (P=0.811).

Conclusion: Because it is simple, economic, and practical, MPV and P-LCR can be used in predicting the possibility of acute thrombosis in patients with coronary artery diseases.

Key words: Platelets, platelet volume indices, atherosclerosis, myocardial infarction, unstable angina, coronary artery disease.

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Introduction

Coronary atherosclerosis and its complication like myocardial infarction (MI) are the major causes of morbidity and mortality in industrialized countries. Endogenous and exogenous risk factors exist but they only explain part of the case, other relevant risk factors need to be identified [1, 2, 3].

Platelets have been implicated in the pathogenesis of cardio- vascular disorders including atherosclerosis and its complication like acute myocardial infarction (AMI), unstable angina (UA) and sudden cardiac death[8].

After rupture of arteriosclerotic plaque in coronary arteries, platelets hyperactivity and local platelets activation have been suggested to play a causal role in prothrmbotic events leading to MI [1, 2, 4, 5]. An increased platelet reactivity and shortened bleeding time are associated with increased platelet volume [6], therefore; platelet size has been considered to reflect platelet level of activity [2,4] as the large platelets are metabolically and enzymatically more active than small platelets [1,7] and they have a higher thrombotic potential due to high concentration of thromboxane A2 [1,2,4,8,9].

Various studies found an association between mean platelet volume (MPV) and coronary artery disease [10] or the occurrence of an acute MI [1,2,9,10,11], while others found no such effect [12].The biological and

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prognostic value of increased MPV is still controversial and the reason for high platelet size still unclear [1].

Automated cell counter have been made the platelet volume indices (PVI) like mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR) are routinely available. The MPV can reflect changes either in the level platelet stimulation and the rate of platelet production so platelet activation can be indirectly and simply measured via MPV [4].

Patients and methods

This study was designed as cross sectional study. 36 patients admitted to coronary care unit (CCU) in Al Kadhimiya teaching hospital with state of acute coronary syndrome at the period from April –May 2008. This study was approved by the local ethics committee. Patients were divided into 2 groups according to clinical data and patient history with support of cardiac enzyme assay and electrocardiographic (ECG) changes: First group is UA group including 14 patients; Second group is AMI group including 22 patients. All individuals were reviewed for established risk factors like (smoking, diabetes mellitus (DM), hypertension, a previous diagnosis of stable angina) in addition to age and gender. Lipid profile records were not available for most of patients in this study. Those with previous or recent AMI, or cerebrovascular event or valvular heart disease were excluded.

EDTA (ethylenediamino tetra acetic acid) samples of blood drawn at first day of admission of patients were analyzed in an automated hematology analysis system (Sysmex, serial number 1544, version no. 00-17, UA). All patient samples were processed within 2 hours of venipuncture as recommended by Symth et al. [13] to avoid bias due to excessive platelet swelling which is reported in some studies secondary to effect of EDTA [14].

Statistical analysis was performed using statistical package for social science (SPSS v.10) on window XP. The chi square test used to compare differences of frequencies in patient characteristics in addition of t-test and correlation analysis. P value $\leq$ 0.05 or $\leq$ 0.001 were considered as statistically significant values accordingly.

Results

Thirty six (36) patients were included in this study, 16 were males and 20 were females. The first group, unstable angina (UA) patients, was 14 patients (38%), 4 of them were males (28.6%) and the rest were females (71.4%). Their age range was 40-65 years with mean age $\pm$ SD (standard deviation) of 52.57 $\pm$ 9.89 year. The second group, myocardial infarction (MI) patients, was 22 patients (62%), 12 were males (54.5%) while 10 were females (45.5%) with age range 46-80 years and mean $\pm$SD of 64.18 year $\pm$ 9.29 year. These two groups shows statistically significant differences concerning their age distribution (P= 0.001)

The baselines demographic data are shown in (Table 1) which demonstrate a statistically significant differences concerning the smoking history (P=0.011), and hypertension (P=0.032) with highly significant differences in cardiac enzyme elevation according to the underlying pathogenesis in the 2 groups (P=0.0001), however , there were no significant differences in terms of existing previous history of stable angina when compared with their recent presentation as acute coronary syndrome (P=0.629).

Platelets volume indices (PVI) were studied using t test between the above 2 groups of presentation and it is found that MPV and P-LCR were the most significant parameters that

showed statistical differences between patient with UA and those with MI (P=0.042andP=0.031) respectively unlike other parameters (platelets count or PDW)(P=0.703 and P=0.094) (Table 2).

It is found also that MPV will exceed 11.6 fl and 12.10 fl at percentile 95 in case of UA and MI respectively and similarly P-LCR will exceed 37.66 and 41.20 at percentile 95 in the above two groups respectively which may indicate a higher level of activity.(Table 3)

There were no correlation found between MPV and other platelets indices with existing past history of stable angina as well as other risk factors for acute coronary syndrome (P=0.811) i.e. these PVI did not altered significantly with these risk factors and their difference is related directly to acute events.

Discussion

The findings indicate that increased platelet volume is associated with a higher risk of suffering an acute coronary event independent of the extent of a previous coronary artery disease (CAD). Percentile 95 value will indicate a higher risk of getting acute coronary event with being increased platelet volume and a higher percentage of large size cells independent of existence of other risk factors. Thus MPV and P-LCR above these percentile values may represent an independent risk factors for MI similar to other studies [1, 2, 3], but there were no practical application of platelet count which had been demonstrated by Kilici-Cmur N. et al [2].

The mechanism for an increased platelet volume are not well fully understood, possibly cytokines may trigger the production of larger more reactive platelet following platelet destruction in peripheral blood including interleukin-6 (IL-6) [14], although, it is not settled completely [1].

In this study we neglected the drugs used by patients as there are limited data about the effect of pharmacological therapy on platelet count and size. It has been proved previously that standard medical treatment for coronary diseases did not significantly change platelet markers [3]. In previous studies, an increased MPV was found to be associated with coronary artery disease [10, 15, 16], UA [9, 10], AMI [1, 9] and even congestive heart failure [18] as well as in cerebrovascular diseases (18) and this can be explained on base of increased platelet hyperactivity after erosion or rupture of atherosclerotic plague leading to potentiated prothrombotic complication like MI or cerebrovascular events [1, 6].

Large platelets that contain more dense granules are metabolically and enzymatically more active than small platelet with a higher thrombotic capacity (1) as they express higher levels of prothrombotic substances, thromboxane A2, serotonin b, B-thromboglobulin and procoagulation surface protein such as P-selectin and glycoprotein IIIa [11]. An increased MPV decreases the inhibitory effectiveness of PG I_2 on both platelet aggregation and the release reaction [19]. Higher levels of P- selectin was previously reported to associate with acute MI and its measurement was promising as predictors of vascular risk due to platelet aggregation [20].

The size of platelet has been found to associate with an increased number of megakaryocyte [3]. In agreement with Kilicli-Camur observation, we did not report a significant correlation between MPV and history of stable angina, and this is in contrast to others findings like Endler G. et al and Erne P. et al [1, 17].

Similar to reported data, we found also that MPV was significantly higher in MI group than UA group (1, 2, 6, 17) but unlike the result of Mc Karns et al [3] and in contrast to finding of Mathur et al (21) who observed higher MPV in UA group than MI group. Similarly, it is noted that the time span between MI and laboratory testing did not influence platelet size and thus may suggest that MPV will not change during the acute phase reaction. The finding of this study confirm that increased MPV might be responsible for the prothrombotic state that eventually leads to thrombus formation after rupture of coronary plaque [10,16,21].

Little is known about the effect of aspirin and other platelets aggregation inhibitors on MPV (10), however, whether intervention with platelets aggregation inhibitors or other drugs are beneficial for patient with high MPV remain to be determined.

Conclusion

MPV might be a valuable risk factor for atherosclerosis and acute coronary syndrome. Since it is simple, economic & practical, MPV & P-LCR can be used in predicting the possibility of acute thrombosis in patients with coronary artery diseases.

Table 1: Demographic & clinical characteristics in the study population

Character		UA		MI		P value
		No	%	No	%	
Sex	Male	4	28.6	12	54.5	0.126
	Female	10	71.4	10	45.5	
Smoking	yes	-	-	8	36.4	0.011*
	no	14	100.0	14	63.6	
Diabetes mellitus	yes	10	71.4	14	63.6	0.629
	no	4	28.6	8	36.4	
Hypertension	yes	14	100.0	16	72.7	0.032*
	no	-	-	6	27.3	
History of CAD	yes	10	71.4	14	63.6	0.629
	no	4	28.6	8	36.4	
Cardiac Enzyme	Positive	2	14.3	18	81.8	0.0001*
	Negative	12	85.7	4	18.2	

*The Pearson Chi-Square statistic is significant at the 0.05 level.

Table 2: Distribution of hematological parameters.

Parameter	UA	MI	P value
	Mean ± SD (Min-Max)	Mean ± SD (Min-Max)	
Platelet count	280428.57 ± 76361.20 (158000-381000)	267545.45 ± 109062.55 (137000-522000)	0.703
Platelet distribution width(PDW)	13.62 ± 1.83 (10.5-15.5)	12.50 ± 1.96 (9.5-16.3)	0.094
Mean platelet volume (MPV)	10.53 ± 0.80 (9.4-11.6)	9.82 ± 1.07 (8.2-12.1)	0.041*
Platelet large cell ratio (P-LCR)	29.97 ± 5.31 (22.3-37.6)	24.43 ± 8.15 (11.6-41.2)	0.031*
ESR	35.29 ± 13.03 (12.0-55.0)	48.55 ± 35.47 (10.0-120.0)	0.190

*The Independent Samples Test statistic is significant at the 0.05 level.

Table 3: The percentile ratio of MPV & P-LCR

Diagnosis		UA	MI
Mean platelet volume	Percentile 50	10.90	9.20
	Percentile 75	11.20	10.70
	Percentile 95	11.60	12.10
	Percentile 99	11.60	12.10
Platelet large cell ratio	Percentile 50	32.40	20.10
	Percentile 75	33.90	31.40
	Percentile 95	37.60	41.20
	Percentile 99	37.60	41.20

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Hepatitis A infection and occurrence of Insulin dependent diabetes mellitus in a sample of Iraqi children

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Abstract

Background: Hepatitis A is an important endemic disease in Iraq. And Insulin dependent diabetes is one of serious chronic disease that affect children.

Objective: To study the possible relationship between viral hepatitis A infection and occurrence of diabetes mellitus in Iraqi children.

Method: A case control study was done on hundred newly diagnosed diabetic children, who were compared to hundred control children.Serological test were done to both groups to detect antibodies against Hepatitis A by using ELISA method .This study started on 1st of November 2006 and ended at 20th of December 2008 Both groups were collected from Al-Kadhymia Teaching Hospital and Al-Noor General Hospital.

Result: There was slight increase incidence of diabetes mellitus in females (56%) than males (44%) and there was significant negative correlation between Hepatitis A and diabetes mellitus since 11% of diabetic children had positive serological test while 26% of control children had positive result.

Conclusion:there was no relationship between hepatitis A infection and occurrence of IDDM.

Keywords: Hepatitis A, diabetes mellitus, children.

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Introduction

Type 1DM develops as a result of the synergistic effects of genetic, environmental and immunologic factors that ultimately destroy the pancreatic beta cells [1, 2]. Autoimmune process is thought to be triggered by an infectious or environmental stimulus and to be sustained by a beta cell –specific molecule. A number of viruses have been shown to infect the pancreas and induce acute and chronic pancreatitis [3]. The mechanism of pathogenesis of viral infections of the pancreas have been described clearly with the use of animal models of pancreatitis and Coxsackie's virus infections[4,5]. However, acute hemorrhagic pancreatitis complicating mumps infection has been reported.

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As the cell that produce insulin are destroyed the patient become permanently diabetic [6]. In addition to infection by Coxsackie virus and mumps virus infection, other viral agents such as congenital rubella, herpes simplex , varicella, hepatitis and cytomegalovirus have been proposed as being capable to triggering the development of diabetes mellitus type1[7,8].

hepatitis A is an infectious disease commonly found in many developing countries, Also it is common even in developed countries and they found that, hepatitis A infection occurred in about 40% of urban population in the united states[9].

Hepatitis A infection usually is asymptomatic in children and only small percentage has clinical hepatitis of varying severity [10].

Viral infection induces interferon α, and through a complex signal transduction pathway which induces the key antiviral enzyme 25-oligoadenylate synthetase

that then degrades viral and cellular RNA, inhibiting virus replication and promoting the death of infected cells [11].

As hepatitis A is preventable by vaccination [12].So it is important to investigate the effect of this common viral infection on occurrence of insulin dependent diabetes mellitus.

Patients and methods:

A case control study has been applied from 1st Nov.2006 to 20 th of December 2008 which was conducted in AI-Kadhymia Teaching Hospital and AL.Noor general Hospital and involve 100 newly diagnosed I.D.D.M. whose age were bellow 13 years. And one hundred control non diabetic children who were coming to both Hospitals for simple diseases, randomly chosen from both hospitals that were compatible to the diabetic group regarding, age & sex Diabetic and control children were divided into four groups according to age groups. Both groups were submitted to same questions about previous history of jaundice and laboratory investigation to detect antibodies against hepatitis A using ELISA (Bio-kit) to detect specific IgG and IgM antibodies which were done in the same hospitals.

Chi-square test was employed to test differences between proportions. And p value < 0.05 was considered significant.

Results

The study showed insignificant difference between two groups regarding to age [The youngest child in both groups

Was tow years old and the oldest child was twelve years old] since P value was >0.05 as shown in (Table 1).

Table 1: Distribution of diabetic and control group according to age group.

Age group	Diabetic		Control		Total	x^2=0.17 df=3 P=0.8
	No	%	No	%		
2-4 yr	31	31%	32	32%	63	
4-6 yr	34	34%	33	33%	67	
6-8yr	18	18%	19	19%	37	
Above 8yr	17	17%	16	16%	33	
Total	100	100 %	100	100%	200	

Also the study shows slight increase in female percentage (56%) comparing to male (44%) in diabetic group which is also statistically not significant as shown in (Table 2).

Table 2: Distribution of sex according to age group in diabetic and control group.

Age group	Diabetic group				Control group				x^2=0.15 df=3 P=0.9
	Male		Female		Male		Female		
	No	%	No	%	No	%	No	%	
2-4 yr	13	29.6%	18	32.13%	14	31.1%	18	32.74%	
4-6 yr	15	34%	19	34%	14	31.1%	19	34.54%	
6-8 yr	8	18.2%	10	17.8%	9	20%	10	18.18%	
Above 8 yr	8	18.2%	9	16.07%	8	17.8%	8	14.54%	
Total	44	100%	56	100%	45	100%	55	100%	

The study show high percentage of negative serological test for Hepatits A (IgG and IgM) in diabetic group comparing to control group and p value was 0.006 which mean that there are no relation ship between Hepatits A infection and occurance of diabetes in children as shown in (Table 3).

Table 3: Serological test for hepatitis A in diabetic and control group.

Serological test For hepatitis A (both IgG and IgM)	Diabetic group		Control group		Total		
	N O.	%	N o.	%	N O.	%	
Positive IgG	9	9%	24	24%	37	18.5%	X^2 =7.46
IgM	2	2%	2	2%			Df=1 P=0.006
Negative	89	89%	74	74%	163	81.5%	
TOTAL	100	100%	100	100%	200	100%	

Discussion:

The study showed insignificant increase infrequency of the disease in female (56%) than male (44%) which is comparable to result reported in AL-Kuwait (1993) which showed statistically significant female increase incidence rate [13].

Also the study showed significant negative relationship between Hepatitis A and occurrence of insulin dependent diabetes mellitus in children which is the first study done in Iraq to explore the relation ship between one of the common preventable viral disease in childhood and the most important chronic disease in them .we think that there is no such study in neighboring countries ,except there are two small case series from India on acute pancreatitis complicating acute viral hepatitis A, most of these patient had mild-to- moderate pancreatitis with a relatively benign course and uneventful recovery [14]. and there are studies that identify the relationship between other viruses and insulin dependent diabetes mellitus like ,long –term prospective Finnish studies have strongly suggested that infection with enteroviruses such as coxsackie virus may trigger the autoimmune process for example increased frequency of serum

enterovirus antigens and antibodies toward enterovirus were observed during prediabetic phase in children who subsequently develop diabetes[15].So in conclusion there was no positive correlation in our studied cases between hepatitis A and type 2 IDDM, and this mean that the pancreas is not affected by Hepatitis A infection or it might be mildly affected .

So preventive measures against hepatitis A may not have a beneficial value in prevention of childhood IDDM.

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Spirometric reference values in healthy, non-Smoking, Iraqi population

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Abstract

Background: Pulmonary function test depends on a number of physiological factors as height, age, gender and race. Reference mathematical equations are used to determine a normal range of spirometric results which in turn are used clinically to determine whether the results measured in any individual fall within a range to be expected in a healthy person of the same gender, height and age.

Objectives: To derive the prediction equation for healthy, non smoking Iraqi subjects.

Methods: The study was conducted in Baghdad (IRAQ) on one hundred eighty two (182) healthy, nonsmoking subjects between 20 to 60 years of age were included in the study. The subjects included were 79 males and 103 females whose pulmonary volumes and capacities were measured by spirometry.

Results: The prediction equation was derived first and then the reference values were then calculated for forced expiratory volume in 1st second (FEV1) and force vital capacity (FVC). The values for both parameters were found to be lower by about 5.58% and 6.14% in females and 4.78% and 12.65% in males, respectively, when compared to researchers done on Caucasians.

Conclusion: Pulmonary function test reference values and prediction equations for both sexes between the ages of 20-60 years were derived for a sample of healthy, nonsmoking, Iraqi population. A considerable difference was found between prediction equations and reference values obtained in present study compared with other studies conducted in western countries.

Keywords: FEV1, FVC, Spirometry, Iraqi subjects

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Introduction

Spirometry is the most frequently performed lung function test. Pulmonary function variables depend on height, age and gender. There is evidence of considerable variations in pulmonary function in different ethnic groups and across generations [(1)].Reference formulas are used to determine a normal range of spirometric results.

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The reference values so determined play an important role in establishing whether the values measured in an individual fall within a range to be expected in a healthy Person of the same gender, height and age[(2,3,4)].

The most recent American Thoracic Society [ATS] [(5)] statement on impairment and disability secondary to respiratory disorders also acknowledges the presence of documented racial and ethnic differences. Such differences must be considered when interpreting pulmonary function tests [(6)].

While some authors have described a " Plateau phase" of lung function development (9) starting from about 17 years of age to approximately 35 years of age when no lung growth takes place [(2)], others have reported a decline in lung

functions beginning at approximately 35 years of age [7,8,9,10].

A number of studies have been conducted in Europe, united state, Asia, and Mediterranean population to establish reference values for pulmonary functions in healthy subjects. To the best of our knowledge, no study was conducted in this country involving young and elderly subjects.

The aim of the present study was, thus to determine the spirometric reference formulas for a sample of young and elderly subjects living in Baghdad, and to compare the measurement of pulmonary function in those subjects with other available standards such as ECSC [European Community for Coal and Steal][11] published in 1993, predicted values of lung indices unchanged (almost universally applied in Europe), white American population (Knudson et al) [12], Mediterranean population (Roca J et al)[13], and Caucasian populations (Crapo et al)[6] .

Methods

In a total of two hundred and two healthy non-smoking subjects who met the inclusion criteria were participated in the study. Yet only one hundred eighty - two [103 females and 79 males] with an age ranged between 20 and 60 years were completed the pulmonary function tests and included in the study. The age of the male subjects was 37.10 ±9.84 years, and the females 41.30±9.44 years. The rest of the subjects were not able to perform the pulmonary function tests correctly and thus were excluded.

The lung function testing was performed in the lung function unit-at AL-Kindy Teaching Hospital, Baghdad-IRAQ. The standing height and weight was measured for all the subjects. The tested subjects were non smokers with no history of symptoms of cardiovascular or respiratory diseases that required treatment. The forced expiratory maneuvers including forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) were recorded using " Master lab body pro a universal lung function testing station- Version 4.5" in conjunction with 3 PC software. The spirometer was calibrated with a calibrating syringe. A minimum of three acceptable and reproducible maneuvers were obtained, according to the standards recommended by the American Thoracic Society [ATS].

Prediction Equation

Four sets of prediction equations were used in this study. Predicted values were derived from these equations described regression equations commonly used in Caucasian subjects. "The Crapo" equations were derived from 251 non smoking American subjects, aged 15-19 years and residing in Utah 1400 m above sea level, using a water seal spirometer (8). The Knudson equations were obtained from 746 American nonsmoking subjects, aged 8-90 years and residing in Arizona, using a Pneumotachygraph device (9). The European Community for Steel and Coal (ECSC) equations are summary equations derived for Caucasian subjects aged 5-70 years. Roca- equations were obtained from 870 adult subjects, aged 20-70 years and living in Barcelona area. Roca-equations provides reliable spirometric equations from a large Urban Mediterranean sample which were lacking so far in the literature. All four equations and this study predict FEV-1, and FVC based on gender, age, and height of a subject as primary variables. All equations, except the

Crapo and ECSC equations, are nonlinear with respect to age.

Statistical Analysis

The data was entered in computer package "Microsoft Excel" and analyzed using the statistical package for Social Science (SPSS) version-16 for window software. The data for age, height and pulmonary function parameters were expressed as mean ± Standard deviation. A graph of pulmonary function variables against the age were examined for each gender. Means and standard deviation of quantitative variables (age, and height) were compared according to gender by Student-t-test. Multiple linear regression analysis was applied to observed lung function values as a function of standing height and age. The FEV-1 and FVC were dependent variables, while height and age were independent variables. In all statistical analysis, only P-value <0.05 were considered significant.

Results

The age and gender distribution of the subjects are shown in figure 1.

Table 1 presents the indices examined, FEV-1, FVC separately for females and males. The mean values for FVC was 3.66 ± 0.49 liter and 2.52 ± 0.40 liter in males and females, respectively, while the values for FEV-1 was 3.56 ± 0.49 liter and 2.44 ± 0.42 liter in males and females, respectively. The prediction formulas for both males and females were derived and the reference values were calculated and compared with those given by ECSE (1993), Knudson (1983), Roca (1981), and Crapo (1986) as shown in table 2 and table 3.

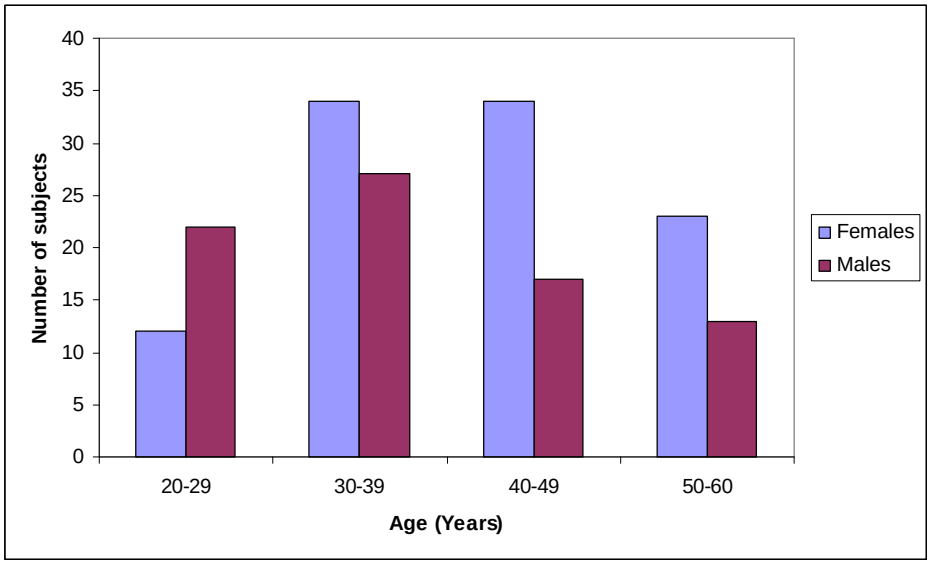

Figure 1: The age and gender distribution of the subjects.

Table 1: The lung function data in the studied subjects

	Females N =103		Males N =79	
	Mean ±SD (L)	Range (L)	Mean ±SD (L)	Range (L)
FVC	2.52 ± 0.40	1.67 – 3.14	3.66 ± 0.49	2.51 – 5.1
FEV1	2.44 ± 0.42	1.51-3.35	3.56 ± 0.49	2.51 – 5.04

FVC= Forced Vital Capacity
FEV1= Forced Expiratory Volume in the First Second

Table 2: Comparison of FEV1 and FVC prediction equations used for males in different studies.

FEV1(L)	Formula	R2	RSD
This study	-0.2935 -0.0169*A+0.0261*H	0.657	0.38
ECSC (1993)	-2.490-0.0290*A+0.0430*H	----	0.51
Knudson (1983)	-6.515-0.0292*A+0.0665*H	0.74	0.52
Crapo (1981)	-2.190-0.0244*A+0.0414*H	0.64	0.49
Roca (1986)	-3.995-0.0216*A+0.0514*H	0.56	0.45
FVC (L)			
This study	-0.3566-0.0184*A+0.0273*H	0.679	0.37
ECSC (1993)	-4.344-0.026*A+0.0576*H	-----	0.61
Knudson (1983)	-8.782-0.0298*A+0.0844*H	0.72	0.64
Crapo (1981)	-4.650-0.0214*A+0.0600*H	0.53	0.64
Roca (1986)	-6.055-0.0147*A+0.0678*H	0.52	0.53

H = height in cm; A= age in years; R2 = multiple regression coefficient; RSD = residual standard deviation.
FVC= Forced Vital Capacity
FEV1= Forced Expiratory Volume in the First Second

Table 3: Comparison of FEV1 and FVC prediction equations used for females in different studies.

FEV1(L)	Formula	R2	RSD
This study	-0.3378-0.0223*A+0.0234*H	0.672	0.28
ECSC (1993)	-2.600-0.0250*A+0.0395*H	----	0.38
Kundson (1983)	-6.575-0.0292*A+0.0665*H	0.74	0.52
Crapo (1981)	-1.578-0.0255*A+0.0342*H	0.79	0.32
Roca (1986)	-1.286-0.0253*A+0.0326*H	0.67	0.32
FVC (L)			
This study	-0.3078-0.0194*A+0.0229*H	0.659	0.28
ECSC (1993)	-2.600-0.0250*A+0.0395*H	----	0.38
Knudson (1983)	-3.195-0.0169*A+0.044*H	0.49	0.48
Crapo (1981)	-1.578-0.0255*A+0.0342*H	0.67	0.32
Roca (1986)	-2.825-0.0211*A+0.0454*H	0.56	0.40

H= height in cm; A = age in years; R2 = multiple regression coefficient; RSD = residual standard deviation.
FVC= Forced Vital Capacity
FEV1= Forced Expiratory Volume in the First Second

Comparisons of the reference values for FEV-1, FVC from this study with those of Caucasian subjects are shown in table -4. Although we found that our values for both FEV-1 and FVC were lower than in all the studies with which they were compared, the greatest difference was observed with the values given by "Roca". Our values for FEV-1 were less by about 11.78% in males and 13.56% in females while for FVC the values were 27.73% for males and 27.86% for females compared with the Mediterranean population "Roca". On the other hand , the least difference in case of FVC was found in females i.e. 3.95% when our values were compared with those of European population "ECSE" and in case of males the values of FEV-1 were 6.68% less when compared with white American population "study of " Knudson et al ". Further illustrations of the comparisons of predicted spirometric values obtained in this study and others are shown in figures (2, 3, 4, and 5).

Table 4: Mean FEV1 and FVC values and standard deviation in different studies

	FEMALES		MALES	
	FEV-1 "L"	FVC " L"	FEV-1 "L"	FVC "L"
This study	2.45 ±0.29	2.52±0.27	3.57±0.28	3.66±0.29
ECSA(1993)	2.62± 0.39	2.62±0.0.39	3.84±0.47	4.61±0.53
Knudson et al.(1983)	2.80±0.57	3.13±0.36	3.85±0.28	4.64±0.72
Crapo et al.(1981)	2.78±0.37	2.78±0.37	4.03±0.42	4.88±0.52
Roca et al.(1986)	2.83±0.36	3.49±0.39	4.05±0.46	5.07±0.53

FVC= Forced Vital Capacity
FEV1= Forced Expiratory Volume in the First Second

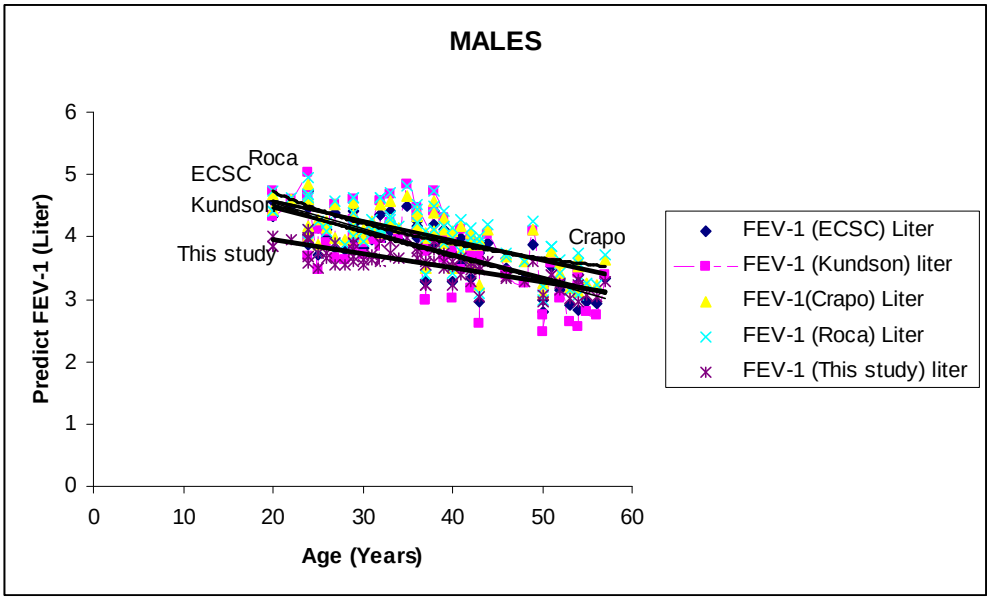

Figure 2: comparison of prediction equations of FEV-1 in males.

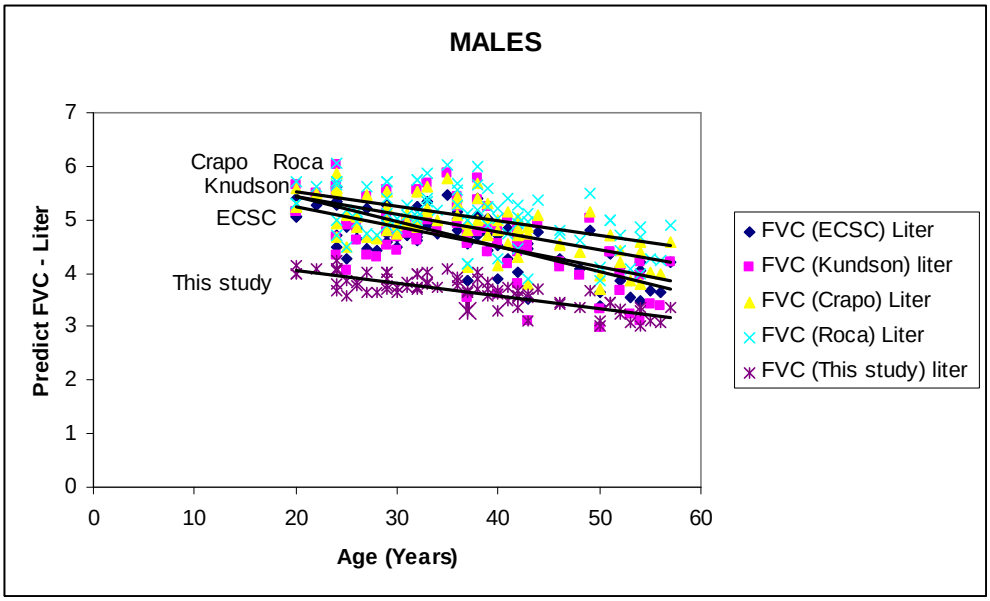

Figure3: Comparison of prediction equations of FVC in males.

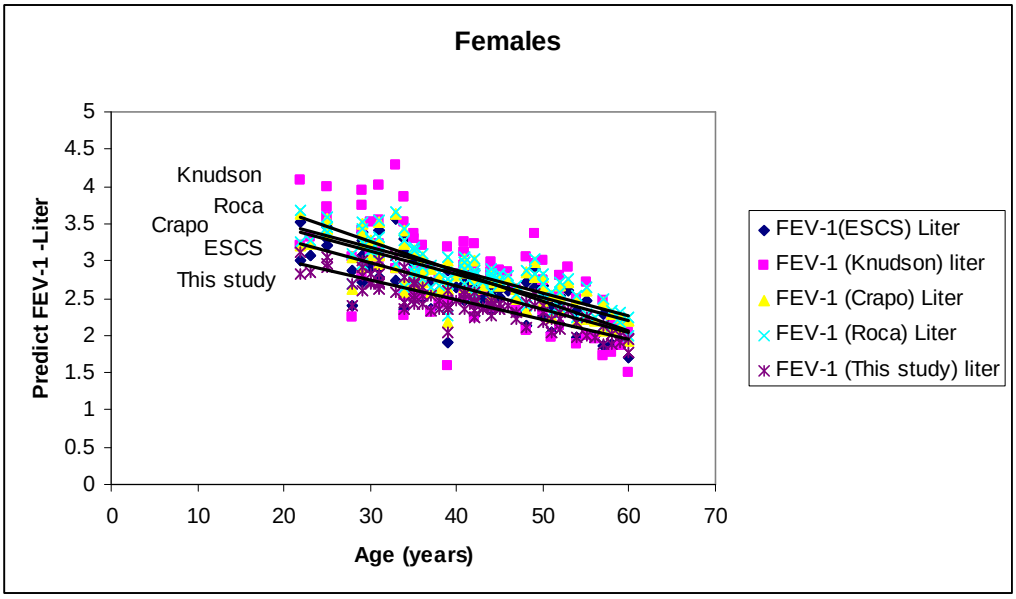

Figure 4: Comparison of prediction equations of FEV-1 in females.

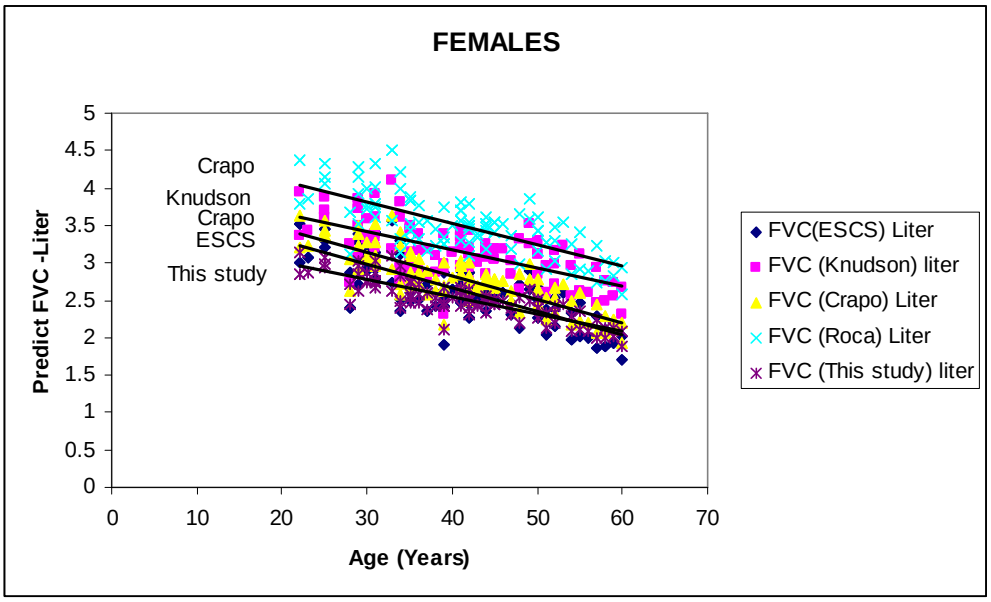

Figure5: Comparison of prediction equations of FVC in females.

Discussion

This is a study of reference values of lung function test in a random sample of healthy non smoker Iraqi subjects from Baghdad. All relevant data were obtained by trained technicians using standardized equipment & techniques that produce reproducible data. The predicted spirometric values derived from this study showed varying degrees of difference when compared with those derived from studies on Caucasians.

In the literature, the mean average difference between the Asian and Caucasian population is stated to be 16% for females and 12% for males [6]. In this study, we found that the mean difference for FEV-1 in females was 5.58% and for FVC was 6.14% ($p<0.01$) while the mean difference for FEV-1 in males was 4.78% and for FVC was 12.65% ($p<0.01$), respectively when samples were compared with that to the Caucasians. Similarly, a significant difference was found for FEV-1 7.19% and FVC 16.14% with ($P<0.01$) for females. The mean difference for FEV-1 was 6.61% and FVC 16.15% ($P<0.01$) for males when Iraqi subjects was compared with that to Mediterranean population [13].

The scatter of (R^2) was between 49% and 79% in tables 2 and 3 which mean that the strength of formulae varies in all the studies conducted. Taking that into consideration, it can be stated that non of the authors have managed to create a strong, universal formula and this again emphasizes the importance of ethnic, age, height and other variables that effect the pulmonary functions.

According to the presently accepted method of establishing predicted values for lung function indices, it is assumed that the value of FEV-1 depends on height and age. This assumption is true as it has been confirmed in several examinations in the up growth period and in subjects who outgrew this period.

Differences in the predicted values obtained in various studies may be attributed to the technical factors involved in lung function testing. For

example different lung function devices have been used with the more recent studies have employed computerized systems that portend to high precision, but between instrument variability would still exist contribute to variations in measurement [14].

The posture has also been shown to result in slightly lower spirometric values in sitting than standing [15]. However, the postural effects are small and probably much less important in determining the measurements than the quality with which the tests were conducted [15].

Similar to many previous studies in which Asians, such as Chinese, Indians, Japanese and Malaysians, have smaller lung volumes than whites [16, 17, 18, 19], we found that the FEV-1 and FVC values in samples of Iraqi subjects were lower than those of whites for all age groups with the same age and height.

When assessing lung functions values, it is also important to take into account biologic variations [20, 21, 22, 23, 24]. The most important host factors responsible for inter-individual variations in adults were sex (±30%), body size (±20%), and age (±8%) [25,26,27,28]. The age range of subjects in our study was 20 -60 years, whereas ECSC prediction equations apply to men and women of European descended aged 18-70 years.

It has been suggested that ethnic group could be an important source of inter-individual variations in the studied populations: an estimated variability due to this factor is ± 10% [21, 25].

Limitations

The limitations of this study were the age-range of the subjects and lack of anthropometric measurements. Thus, these results are not applicable to men older than 64 year and women older than 66 years. Considering that ventilatory functions vary with anthropometric variables, the measurements of anthropometric variables of Iraqi population should be introduced into research such as sitting height, weight, hip/waist circumference and ratio, and body mass index.

Conclusions

In conclusion, the reference formulas for males and females in a sample of healthy, non-smoking, Iraqi subjects have been derived. Predicted FEV1 and FVC values derived from the equations based on ECSC, Knudson , Roca and Crapo reference population are higher than the values measured in the present study. For this reason, each laboratory should have its own reference value.

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Elevated serum β-hCG levels in severe preeclampsia

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Abstract

Background: Pregnancy induced hypertensive disorders are common complications responsible for fetal, neonatal and maternal morbidity. Current hypothesis regarding the pathophysiologic mechanisms of pregnancy induced hypertension point to early placental abnormalities.

Objective: To determine whether measurement of serum human chorionic gonadotropin might reflect a different secretory trophoblastic response of preeclampsia.

Study design: A prospective study.

Setting: Department of Obstetrics & Gynecology in Al-Kadimyia Teaching Hospital.

Patients and methods: A total of 80 pregnant women were studied during the period from October through July 2005. They included 40 patients with severe peeclampsia were matched with 40 healthy normotensive women in the third trimester with singleton pregnancies and without congenital malformations. Serum levels of *β*-hCG were measured by immunoenzymometric assay before delivery and neonatal outcome was recorded.

Results: Serum *β*-hCG levels were found to be significantly higher in severe preeclamptic women compared with controls (P<0.05). Elevated *β*-hCG levels in severe preeclampsia was associated with higher rate of preterm delivery (50% vs. 7.5%), higher rate of intrauterine growth restriction of birth weight <10th centile (47.5% vs. 5%), higher rate of low birth weight of < 2500 gm (70.25% vs. 12.5%) and higher rate of fetal death (7.5% vs. 0).

Conclusion: Elevated serum *β*-hCG levels in severely preeclamptic women reflect a significantly pathologic change and abnormal secretory function of the placenta with subsequent pregnancy outcome.

Keywords: preeclampsia, Human chorionic gonadotrophin, pregnancy

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Introduction

Hypertensive disorders of pregnancy (HDP) are responsible for a significant amount of maternal and perinatal morbidity and mortality, they complicate about 7-10% of all pregnancies. Pregnancy induced hypertension (PIH) which includes preeclampsia-eclampsia is responsible for 70%, whereas chronic hypertension represents 30% of Hypertensive disorders in pregnancy [(1)].

The development of preeclampsia usually occurs after 20 weeks gestation and typically ends within 48 hours of the postpartum period [(2)].

Preeclampsia is a disease defined by hypertension, protienuria and oedema in pregnancy; or as gestational hypertension with protienuria. It is most commonly occurs during the last trimester of pregnancy, when it arises in the early second trimester (14-20 weeks), a hydatidiform mole should be considered [(3)].

It is primarily a disease of primigravida, being twice as common as multigravida and is specific to pregnancy and immediate puerperium[(4)].Preeclampsia subdivided into mild and severe forms[(5)],the differentiation between them can be

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misleading because apparently mild disease may progress rapidly to severe disease[6].

Most current hypotheses regarding the pathophysiologic mechanisms of pregnancy induced hypertension point to early placental abnormalities. Human placenta synthesizes steroid, protein and glycoprotein hormones throughout gestation [7].

Human chorionic gonadotrophin (hCG) is produced almost exclusively in the placenta but is synthesized in fetal kidney and a number of fetal tissues produce the *β*-subunit or intact hCG molecule[8].It is secreted by trophoblast cells of the placenta and its production in early pregnancy is critical for implantation and maintenance of blastocyst[9]. HCG can be detected in the maternal blood as early as 6 days after ovulation and begins to decline a nadir being reached by about 20 weeks and is maintained at this lower level for the remainder of pregnancy [10].

An association was reported between preeclampsia and elevated third trimester hCG levels[11].As preeclampsia is likely a trophoblastic disorder and hCG is secreted from the trophoblast[12], we therefore investigated whether the level of serum hCG does correlate with the severity of preeclampsia and might reflect a different trophoblastic secretary response of this disease.

Patients and methods

A prospective study was conducted on 80 pregnant women attending the department of obstetrics and gynaecology in Al-Kadimyia Teaching Hospital during the period from October through July 2005. Forty pregnant women with severe preeclampsia (group A) and forty healthy pregnant women as a control group (group B) with singleton pregnancies in the third trimester were matched for gestational age and maternal age. The patients were considered severe preeclamptic when systolic blood pressure ≥ 160 mm Hg or diastolic blood pressure ≥ 110 mm Hg, protienuria > 5 gm in 24 hours, epigastric pain, cerebral or visual disturbance, pulmonary oedema, thrombocytopenia and abnormal liver function. All women were subjected to full physical and obstetrical examination and they were followed during their admission, delivery and postnatal period.

Venous blood samples were obtained from the subjects before delivery. The blood allowed to clot and sera were separated by centrifugation and stored frozen at -20C until analysis. Serum levels of *β*-hCG levels were measured with enzymatic and immunometric assay Kits. Chi-square test and t-test were used for statistical analysis. P value < 0.05 was considered statistically significant.

Results

Table 1 shows no difference between group A and group B in terms of mean maternal age (30.57±6.78 vs. 29.52±6.59). Significant difference between the two groups was found regarding the gestational age (35.72±1.93 vs. 37.11±1.98) with P value <0.05.

Table 1: Maternal age and gestational age in preeclamptic and pregnant controls

Variables	Group A (n=40)	Group B (n=40)	P value
Age (years) Mean±SD	30.57±6.78	29.52±6.59	0.484
Gestational age (weeks) Mean±SD	35.72±1.93	37.11±1.98	0.001

Table 2 shows the mean systolic, diastolic blood pressure, serum uric acid and urea in group A and group B. statistical significant elevation was found regarding systolic, diastolic blood pressure and serum uric acid P value <0.05. No significant difference was found in blood urea levels.

Table 2: The mean systolic and diastolic blood pressure, serum uric acid and urea values in both groups.

Variables	Group A (n=40)	Group B (n=40)	P value
Systolic BP(mmHg) Mean ± SD	165.8±19.00	111.7±7.4	< 0.0001
Diastolic BP(mmHg) Mean ± SD	114.2±6.9	70.8±7.6	< 0.0001
Serum uric acid(mg/dl) Mean ± SD	8.3±1.8	4.0±1.3	< 0.0001
Blood urea (mg/dl) Mean ± SD	28.1±9.1	25.2±7.1	0.1804

Table 3 shows the mean *β*-hCG levels in both groups. There was significant difference in the mean *β*-hCG value in preeclamptic as compared to control (P value <0.05).

Table3: The mean *β*-hCG levels in preeclamptic and pregnant controls

	Group A n=40	Group B N=40	P value
β-hCG (mIu/ml) Mean ± SD	24685.000±4465.53	16209.500±2069.65	< 0.0001

Table 4 shows the neonatal outcome in group A and group B. The incidence of preterm delivery and intrauterine growth restriction were higher in severe preeclampsia (50%, 47.5%) as compared to healthy pregnant. Furthermore, about 2/3 of preeclamptic pregnant have low birth weight infants in comparison to 12.5% of the control group. The fetal death rate in preeclamptic was 7.5%.

Table 4: The neonatal outcome in group A and group B

Neonatal outcome	Group A n (%)	Group B n (%)
Preterm delivery<37week	20(50%)	3(7.5%)
Intrauterine growth restriction	19(47.5%)	2(5%)
Low birth weight<2500gm	29(72.5%)	5(12.5%)
Fetal death	3(7.5%)	0(0%)

Discussion

In this study, we found that serum β-hCG levels were significantly elevated in severe preeclampsia, compared with the controls. The placenta seems to play a fundamental role in preeclampsia, as the condition improves rapidly after its removal. Examination of the placenta in pregnancies complicated by preeclampsia has revealed focal cellular necrosis in the syncytiotrophoblast and increased mitotic activity with cellular proliferation in the cytotrophoblast [13].The proliferating syncytiotrophoblast in severe preeclampsia is rapidly transformed into syncytiotrophoblast within 72 hours [14].

The normal placenta differentiates during pregnancy with the cytotrophoblast (undifferentiated stem cell) dominant in early gestation and the syncytiotrophoblast (differentiated trophoblast) dominant in late pregnancy [15]. Although the mechanism of regulation of gestational hCG remains largely unknown, it is generally accepted that hCG is only secreted by syncytiotrophoblast [10]. Barros et al. found that the microdensitometric analysis of the section from normotensive and preeclamptic placenta indicated that there is statistically significant preeclampsia induced increased in immunohistochemical reaction intensity for hCG, which demonstrate that increase production of hCG by preeclamptic placenta is associated with strong hCG immunostaining of the syncytiotrophoblast [16]. Preeclampsia results at least in part from poor trophoblast invasion, thus Bahado et al.[17] found that hCG may play a role in trophoblast invasion and measurement of this identifies women at high risk for developing preeclampsia.In preeclampsia early placental vascular damage leading to decreased oxygen supply might result in an increased hCG production by hyperplasic cytotrophoblast cells [18].Also hCG productions has been shown to increase when normal placental villi in organ cultures were maintained under hypoxic conditions [19].

In our study we found that serum β-hCG levels were significantly elevated in severe preeclampsia compared with the controls. This finding indicates that an abnormal secretary function exists in patients with severe preeclampsia. Many authors studied serum level of hCG in preeclampsia to define an abnormal placental secretary function or to predict development of preeclampsia before this disease is manifest.

Said et al. [20] found that serum β-hCG concentration were significantly higher in preeclamptic patient compared with normotensive women matched for age and gestation, and β-HCG level were found to rise before the clinical signs of preeclampsia appeared. Gurbu et al. [21] found that the serum hCG level is especially significant in severe preeclampsia and superimposed preeclampsia.

Lee et al. [22] found that various molecular forms of hCG in serum and urine were significantly higher in preeclamptic than normotensive pregnancies. Similar results were obtained by Hsu CD et al [11].

Jaiswar et al. [23] found that there is 100% correlation between high serum β-hCG level at early gestation and development of pregnancy induced hypertension later on during pregnancy, similar results was obtained by Mullar F et al [24].

An elevation in serum β-hCG levels in the second trimester has been linked with the development of later onset of preeclampsia [25].

Wenstorm et al.[26] found that an elevated hCG level is significantly associated with preterm delivery, fetal death, and fetal growth restriction.

Lieppman et al. [27] studied a cohort of 460 women and found a four fold increase in the risk of low birth weight babies in women with high serum hCG levels. The risk of preterm delivery was 2.8 times more and risk of small for gestational age (IUGR) baby was 1.8 times more in these women.

In our study, low birth weight babies were significantly higher in hypertensive group (72.5%) than those in normotensive group (12.5%), also preterm delivery and fetal death appear to be higher in group A than in group B (50% versus 7.5%) and (7.5% versus 0%) respectively[28].

A higher incidence of preterm delivery was found among patients with severe preeclampsia in comparison to control group. This may be due to induction of labour or caesarean section because of maternal indications and complications of preeclampsia or due to fetal causes as severe intrauterine growth restriction and fetal distress. On the other hand preterm deliveries in the control group were mainly due to preterm premature rupture of membrane. This indicates that Serum β-hCG level was elevated in severe preeclamptic women and could be associated with adverse pregnancy outcome.

Conclusion

Serum β-hCG levels were found to be significantly elevated in severe preeclampsia compared with the controls and this may indicate an abnormal placental secretory function in patients with severe preeclampsia with subsequent adverse pregnancy outcome.

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Y chromosome azoospermia factors (AZF) microdeletions in azoospermic men.

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Abstract

Background: It becomes now evident that the abnormalities of chromosome Y espicially the microdeletions role the major causes of infertility and a number of studies linked the region Yq11 which contain the AZF factors to azoospermia.

Objectives: The current study was aimed to detect chromosomal abnormalities and Y microdeletions (AZFs deletions) among a number of azoospermic men.

Materials & methods: Five ml from peripheral blood was collected from 25 azoospermic men and four controls (one female and three fertile men) and used for DNA, PCR analysis and cytogenetic examinations in order to detect any kind of microdeletion in the AZF regions.

Results: Six individuals which accounts 24% of the total azoospermic men have a microdeletion in the AZF regions.The cytogenetic analysis revealed morphologically normal Y chromosome in all examined samples.

Conclusions: The microdeletions of the AZF regions cause quantitive loss in spermatogenesis.

Keywards: Infertility,AZF a,b,c , Y chromosome

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Introduction

During last few years, many Iraqi couples who are attempting pregnancy had a type of infertility. Although there is no official record about the true number of these couples. The number of men who attende the infertility clinics in Baghdad is increasing.

Men infertility can be classified into azoospermia, oligospermia, oligoastheno teratozoospermic and idiopathic and several factors behind each of them [1, 2]. Some of these factors are combined with some type of genetic abnormalities. Most of these abnormalities are associated with Y chromosome [3-5].

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It is now evident that the abnormalities of chromosome Y especially microdeletions role the major causes of infertility [6-8].

The argument of the association of Y chromosome abnormalities with infertility was strengthened by a number of studies which link the infertility to a number of microdeletions detected in the region Yq11, the region which contains the azoospermic factors AZFa,b,c and other genes such as RBM1,RBM2 and DAZ which are involved in the complex process of spermatogenesis [9-11].

AZFa,AZFb and AZFc have been identified as major cause of azoospermia leading to the disturbance of genes involved in spermatogenesis [8]. Several studies have demonstrated that microdeletion in AZF regions causes male infertility [12, 13]. Deletion of each AZF region has been found to have a different phenotypic effect [14, 15]. However, some of these deletions

are neutral which do not affect the fertility status and phenotype of the individual [16, 17].

The current study aimed to detect chromosomal abnormalities and Y microdeletions (AZF deletions) among a number of azoospermic men.

Materials and Methods

Semen and blood were collected from the azoospermic patients- aged between 20 to 51 years- who attended the infertility unit in the Institute of embryo research and infertility treatment/Al-Kadhimya from September 2006 to October 2007.

Semen sampling and analysis:

Using the 1999 WHO guidelines [18] a semen sample from each subject was collected into a clean, dry and sterile vial after abstinent of 3-4 days. After incubation at 37.5C for 30 minutes, the semen samples were centrifuged at 2500 rpm for 10 minutes and the pellets were examined under light microscope.

The azoospermia was defined as no sperm was present in the semen.

Blood Collection:

Five ml from peripheral blood was collected from 25 azoospermic men and four controls (one female +three fertile man).Each blood sample was divided into two aliquots, one aliquot was added to heparinized tube for cytological examination, the other aliquot was added to EDTA tube for DNA extraction.

The EDTA blood samples were centrifuged at 2000 rpm for 10 minutes. The serum of each blood sample was collected in a clean and sterile tube and used for further assays. The WBC layer from each sample was collected in a sterile tube and used in DNA extraction.

Blood Culture:

A half milliter from each heprinized blood sample was cultured in 5 ml of standard supplemented RPMI 1640 medium containing 20% fetal calf serum and 2% of phytohemagglutinin (PHA) (prepared by the molecular biology Department\Iraqi center for cancer and medical genetic research-ICCMGR-Baghdad-Iraq) in a sterile tubes. The tubes were cultured at 37°C for 72 hours. A hundred micro liter of cholchicine (0.45 mg\ml) was added to each culture. After 20 minutes, the cells from all culture tubes were harvested by centrifugation (2000rpm\10 mins).The supernatants were discarded and the cells redissolved with the remaining solution. The cells were exposed to mild hypotonic treatment with 3ml of 0.075 M KCL at 4°C.The cells was precipitated by another centrifugation. The supernatants were discarded, cells redissolved with remaining hypotonic solution and fixed with 5 ml fixative solution (3 methanol: 1 Glacial acetic acid).Centrifugation and fixation were repeated four times at intervals of 20 minutes. Slides were stained the following day for 10 minutes in 10 ml 5% buffered Giemsa solution, pH 6.8. Three slides were prepared for each sample and 50 metaphases were examined from each sample for chromosomal abnormalities.

DNA extraction:

The WBC layers collected from the EDTA blood samples were used in DNA extraction.

The DNA was extracted according to the Wizard genomic DNA purification kit (Progema/USA).One third milliliter from the WBC suspension was mixed with 900 ul of cell lysis buffer. Samples were incubated at 20°C for 10 minutes .The nuclei were pelleted by centrifuging at 3000 rpm for 10 minutes.The supernatant was discarded and the pellet redissolved with the remaining solution. Three hundred micro liter from nuclei lysis buffer was added to the nuclei suspension with gentle

mixing for one minute then 300 ul from protein lysis solution was added with another mixing. The samples were then centrifuged, the supernatants were collected in a clean tubes and the DNA precipitated with equal volume of isopropanol alcohol. DNA samples were pelleted by centrifugation, washed with 70% ethanol alcohol, air dried and re-suspended with 100 ul of distilled water.

The DNA concentration and purity were checked.The agarose gel electrophoresis was also adopted to confirm the presence and integrity of the extracted DNA.

PCR Assay:

Six primers supplied by alpha DNA company-Canada were used in PCR to determine the presence of Y chromosome microdeletions in AZFa, AZFb and AZFc locuses. The primers sequences were shown in Table 1.

Table 1: Primers sequences and products.

STS	Left primer	Right primer	AZF interval	Products in pb
SY84	5-GTGACACACAGACTATGCTTC-3	5-ACACACAGAGGGACAACCCT-3	AZFa	320
SY127	5-GGCTCACAAACGAAAAGAAA-3	5-CTGCAGGCAGTAATAAGGGA-3	AZFb	274
SY254	5-GGGTGTTACCAGAAGGCAAA-3	5-GAACCGTATCTACCAAAGCAGC-3	AZFc	400

PCR was performed according to (19) using a thermal DNA cycler machine (Tec gene-UK). Cinagene PCR Kit (Iran) was utilized. A hundred nano grams (ng) of denaturated DNA and 40 picomole from each primer were added to the PCR master mixture. The reaction was initiated in a volume of 50 ul. A total of 20 cycles of polymerization was carried out. Ten micro liter from each amplified DNA , 0.2 ug of lambda Hind III+EcoR1 fragments as a marker were mixed with 2 ul of loading buffer and electrophoresed through a 1% agarose gel for 30 minutes at 50 Hz volts. The gel was then stained, visualized under UV light and photographed.

Results

Screening of 25 azoospermic men with the sequence tagged sites- STS-markers specific to AZF regions showed deletion in 6 individuals (Figures 1, 2 and 3) which accounts for 24% of the total azoospermic men analyzed. Of 6 individuals with AZF deletions, deletion of the AZFc region alone was detected in 2 individuals which accounted for 33.3% of the total individuals (Table 2). One azoospermic man showed deletion in the AZFb region (16.7%) and 3 azoospermic men showed deletions in the AZFa +AZFc regions (50%).None of the control men showed deletion for STS markers.

The cytogenetic analysis revealed morphologically normal Y chromosome in all examined samples.

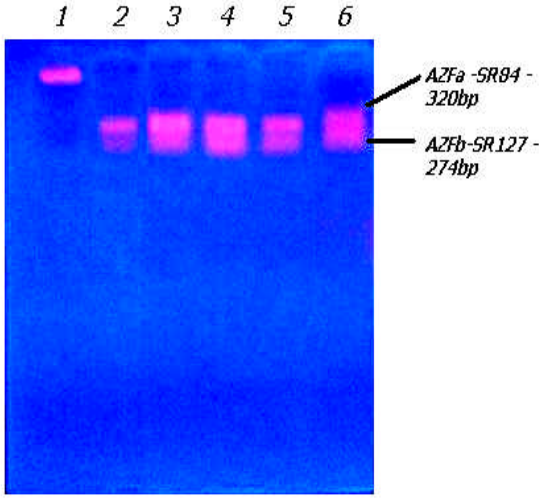

Figure-1 : Gel image showing PCR products of two markers represnting the AZFa and AZFb regions.
Line - 1: Female DNA sample without products.
Lines 2,3,4,5 and 6 azoospermic samples with normal AZFa and AZFb.

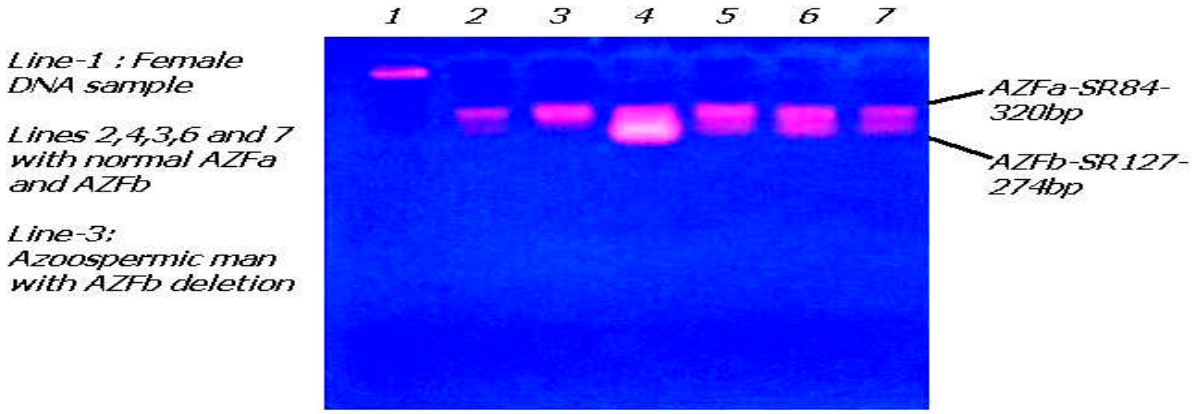

Figure-2 : PCR diplex of AZFa and AZFb products in azoospermic men.

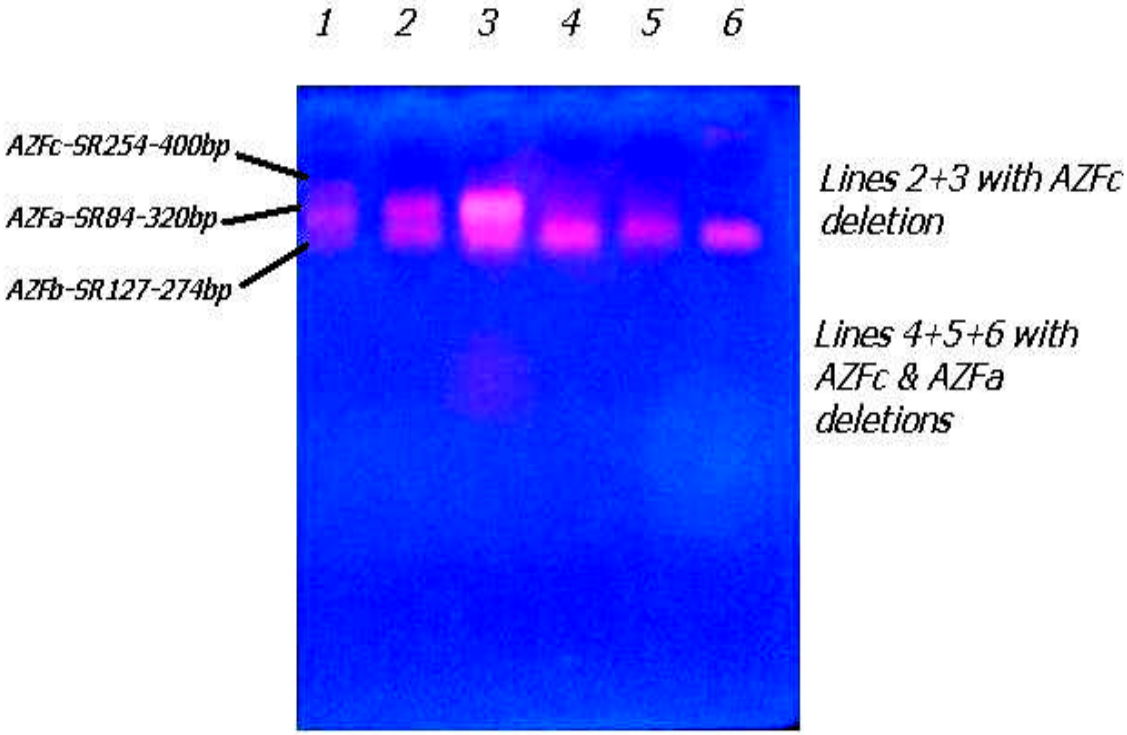

Figure- 3 : Gel image showing PCR products of three sequence-tagged sites (STS) markers representing the AZFa,AZFb, and AZFc regions.
Line-1: Fertlie man, Lines 2,3,4,5 and 6 : Azoospermic men .

Table 2: The Y chromosome deletions detected in the AZF region of azoospermic men.

Sample NO.	Y deletions		
	AZFa	AZFb	AZFc
1 (Female)	—	—	—
2	—	—	—
3	—	+	—
4	—	—	—
5	—	—	—
6	—	—	—
7	—	—	—
8 (Fertile man)	—	—	—
9	—	—	+
10	—	—	+
11	+	—	+
12	+	—	+
13	+	—	+

Discussion

PCR –based STS analysis of 25 azoospermic men revealed microdeletions on the Y chromosome in 6 individuals (Figure 1,2,3 and Table 2) accounting for 24% of the total azoospermic men analyzed . Other studies revealed that the Y chromosome microdeletions were responsible for 7% to 13% of the infertile men ([11, 20]).

Fifty five and half percentage(55.5%) of the Y chromosome deletions detected in this study were in the AZFc region, 22.2% of them with only AZFc deletion and 33.3% associated with AZFa deletion (Table-2). This indicates that gene making the AZFc region is extremely fragile comparing with other AZF regions and among the three AZF regions, deletion of AZFc has been found to be the most frequent abnormality followed by AZFa and then with AZFb. This is in agreement with the other studies showing that the incidence of deletion in the AZFc region was high compared with the AZFa and AZFb regions [8, 21, 22].

Whether the AZF deletion detected in this work associated with specific factors caused azoospermia or other types of infertility is not clear yet. However, many other studies have been found that each AZF deletion has a different phenotypic effect. Kamp et al, 2001 [23] found that AZFa is associated with sertoli cell-only syndrome type 1 (SCOS) phenotype. Also deletions in the AZFb region have been found to be associated with azoospermia, oligospermia and normozoospermia. While deletion of the AZFc region has been found to be associated with azoospermia and sever to mild oligospermia [24].

It has been found in many cases that similar deletion of AZFc region causes quantitative loss in spermatogenesis [25]. However, genotype-phenotype correlation has not been fully understood.

This high percentage of the AZF deletions accounted in our study for (24.4%) of cases suggesting that it is possible that AZFc is predominant in Iraq azoospermia. However, we believe that the etiology of male infertility may differ between ethnic populations. The deletions of AZF regions in azoospermic are not always detected. Martinez et al, 2000 [21] have analyzed 128 infertile men with SY84, SY85 and SY86 (AZFa) and found none of them had shown deletion. Dohle et al, 2002 [26], also did not see any deletion in the AZFa region during their screening of 37 azoospermic individuals with 2 STS markers for each AZF regions.

In the light of the above, further studies using other AZFc markers and more azoospermic subjects need to be done.

Most of the STS-based studies on male infertility have been carried out with a few markers for each AZF region [4]. Hence they failed to detect the Y chromosome deletion in many cases. Therefore, there is no collective opinion about the marker to be used for Y chromosome micro deletion analysis.

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Isolation and Diagnosis of the Conjunctival Normal Flora before and After Cataract Extraction Surgery

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Abstract

Background: The conjunctival flora is opportunistic microorganisms because under certain circumstances they can cause endogenous infections.

Objective: This study aimed to diagnose conjunctival flora before and after cataract surgery and their role in post-cataract surgical infections.

Method: Specimens from ninety-one patients were collected from the conjunctivas and eyelid margins of ninety-one eyes of ninety-one patients both immediately before and one day after experiencing cataract surgery. These specimens were subjected to microbiological and biochemical tests. Susceptibility of ninety isolates obtained preoperatively was performed toward fifteen antibiotics.

Results: *Staphylococcus epidermidis* followed by *Staphylococcus aureus* were the predominant bacteria isolated from the conjunctiva and eyelid margin of the eyes before and after cataract extraction surgery. Vancomycin followed by ciprofloxacin and amikacin were significantly responsive against conjunctival isolates. In this study two patients suffered from postoperative endophthalmitis with the predominant of *Staphylococcus epidermidis* and *Staphylococcus aureus.*

Conclusion: It was predicated that the most causative microbes of post cataract surgical infections were the normal conjunctival flora.

Keywords: conjunctival Normal Flora, Endophthalmitis, Ciprofloxacin, Vancomycin, Amikacin.

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Introduction

The conjunctiva is a thin mucous membrane, which lines the inner surface of the eyelids, as well as the ocular surface of the eye ball. The normal flora is a mixture of organisms regularly found at any anatomical site. The dominant conjunctival normal flora involves mostly ***Staphylococcus epidermidis*** and certain coryneforms.

Organisms from the patient's conjunctival normal flora may gain entry into the eye at the time of cataract surgery.

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These germs are the principal causative agents of postoperative endophthalmitis, which is a serious complication that threatens the visual outcome of cataract surgery. The treatment of postoperative bacterial ocular infections requires coverage for possible pathogens where this could be attained by using a combination of vancomycin, amikacin and ciprofloxacin.

Materials and Methods

Specimens from Ninety – one patients with cataracts (Forty – three males and forty – eight females) resident in Ibn – Al – Haetham Eye Hospital in Baghdad were collected during the period of November 2001 to August 2002. Their ages ranged from 9 to 92 years. All specimens were obtained by sterile – swabs under supervising the consultant physician in the operating theater. Cultures were

obtained from the conjunctivas and eyelid margins of ninety – one eyes (Forty – three left eyes and forty – eight right eyes) of ninety – one patients immediately before experiencing cataract surgery and again one day following the surgery. Swabs were soon brought to the laboratory. Blood agar, chocolate agar and MacConky's agar media were used for culturing bacteria, while sabouraud dextrose agar medium was used for cultivating fungi. Conjunctival and eyelid margin swabs were cultured by streaking each of the above media. The inoculated blood agar and MacConky agar plates were incubated aerobically at $37C^{o}$ for 24 – 48 hours. The inoculated chocolate agar plates were placed in a candle jar to offer 5 – 10 % CO_2 atmosphere with a candle flame and then incubated at $37C^{o}$ for 24 – 48 hours. The inoculated sabouraud dextrose agar plates were incubated aerobically at $25C^{o}$ for two weeks. For primary bacterial diagnosis the following morphological characteristics of colonies were recognized on blood and chocolate agar for their shape, size, color, odor [(1)]. Gram stain test was performed as mentioned in Jawetz [(2)]. Cells' shape, gram reaction and grouping were recognized. The following biochemical tests were performed: [(1)] catalase test [(2)], oxidase test [(3)], coagulase test which involved slide coagulase test and tubal coagulase test [(4)], Optochin susceptibility test to differentiate between ***Streptococcus pneumoniae*** and ***Streptococcus*** spp. [(5)] and Api system; Colonies of catalase – positive Gram – positive cocci were subjected to the identification in the Api Staph system; Colonies of catalase – negative Gram – positive cocci were identified in the Api 20 Strep system; Colonies of catalase – positive Gram – positive rods were subjected to the identification in the Api Coryne system; and colonies of catalase – positive Gram – negative rods were identified in the Api 20 E system. To determine antibiotic susceptibility, the disk diffusion test method was employed [(6)]. Mueller – Hinton agar was used [for ***Strep***. spp. Blood (5%) was added to the medium].

Results

Specimens were collected from 91 patients immediately before and one day after cataract extraction surgery. These specimens were subjected to vigorous microbiological identification and diagnosis. No fungal growth was recorded in this study. Thirteen (14.28%) out of ninty one patients showed mixed growth immediately prior to operation. Of these thirteen patients, nine patients (69.23%) exerted no growth one day after performing the surgery, one patient (7.69%) exhibited mixed growth one day following surgery, and three patients (23.07%) showed single bacterial growth one day postoperatively. Eleven out of 91 patients (12%) showed negative cultures immediately before and one day after the operation. Forty-one out of 91 patients (51.25%) revealed pre and one-day postoperative positive cultures. Thirty-six out of 91 patients (45%) exerted growth prior to surgery and no growth one-day post operation. Only 3 out of 91 patients (3.75%) showed negative cultures immediately prior to operation and positive cultures one day after surgery. This evidence suggested that these 3 patients were exposed to contamination either during the operation or after performing the surgery

Table 1 shows numbers and percentages of bacterial isolates detected immediately before experiencing cataract surgery.

Table 2 shows numbers and percentages of bacterial isolates

detected one day following cataract extraction operation.

Susceptibility of the conjunctival preoperative bacterial isolates obtained from 77 out of 91 patients was performed against 15 different antibiotics. The following antibiotics were used: vancomycin, ciprofloxacin, cephalexin, erythromycin, chloramphenicol, cefotaxime, tobramycin, amikacin, gentamicin, rifampicin, tetracycline, amoxicillin, ampicillin, penicillinG, and streptomycin. The total number of each species and the number and percentages of the sensitive isolates of each species to the antibiotics used in the study is shown in table 3.

Table 1: Numbers and percentages of bacterial isolates detected immediately before experiencing cataract surgery.

Bacterial species	Isolates	
	Number	**Percentage%**
Staphylococcus aureus	14	15.55
Staphylococcus epidermidis	51	56.66
Staphylococcus xylosus	1	1.11
Staphylococcus hominis	1	1.11
Staphylococcus sciuri	1	1.11
Staphylococcus haemolyticus	2	2.22
Streptococcus mitis 2	1	1.11
Proteus mirabilis	1	1.11
Corynebacterium xerosis	10	11.11
Corynebacterium striatum	7	7.77
Rhodococcus equi	1	1.11
Total	90	

Table 2: Numbers and percentages of bacterial isolates detected one day following cataract extraction surgery.

Bacterial species	Isolates	
	Number	**Percentages %**
Staphylococcus aureus	7	15.55
Staphylococcus epidermidis	33	73.33
Staphylococcus haemolyticus	2	4.44
Staphylococcus hominis	1	2.22
Staphylococcus sciuri	1	2.22
Proteus mirabilis	1	2.22
Total	45	

Table 3: Numbers and percentages of pre-operative bacterial isolates susceptible to antibiotics used in the study

Isolates Bacterial species	Total no. of Isolates	No. and (%) of isolates susceptible to the antibiotics used														
		VA	CF	AN	S	KF	RA	GM	CE	C	TM	TE	AMX	E	AM	PG
Staphylococcus aureus	14	13 93%	12 86%	12 86%	11 78%	9 64%	11 78%	7 50%	6 42%	5 36%	7 50%	4 28%	0 0%	1 7%	1 7%	0 0%
coagulase-negative Staphylococci																
Staphylococcus epidermidis	51	50 98%	48 94%	45 88%	39 76%	35 68%	33 65%	25 49%	26 51%	28 55%	21 41%	24 47%	12 23%	8 16%	1 2%	1 2%
Staphylococcus haemolyticus	2	2 100%	2 100%	2 100%	2 100%	1 50%	1 50%	1 50%	0 0%	2 100%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%
Staphylococcus xylosus	1	1 100%	1 100%	1 100%	1 100%	0 0%	0 0%	1 100%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%
Staphylococcus hominis	1	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	0 0%	0 0%	0 0%	0 0%	0 0%
Staphylococcus sciuri	1	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	0 0%	0 0%	0 0%	0 0%
Total no. and % of sensitive coagulase-negative Staphylococci	56	55 98%	53 94%	50 89%	44 78%	38 68%	36 64%	29 52%	28 50%	32 57%	23 41%	25 44%	12 21%	8 14%	1 2%	1 2%
Proteus mirabilis	1	0 0%	1 100%	0 0%	1 100%	1 100%	0 0%	1 100%	1 100%	0 0%	1 100%	0 0%	1 100%	0 0%	1 100%	0 0%
Streptococcus mitis 2	1	1 100%	1 100%	0 0%	1 100%	0 0%	1 100%	1 100%	1 100%	1 100%	0 0%	0 0%	1 100%	0 0%	1 100%	1 100%
Rhodococcus equi	1	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	1 100%	0 0%	0 0%	0 0%	0 0%	1 100%	0 0%
Corynebacterium xerosis	10	10 100%	9 90%	8 80%	8 80%	10 100%	8 80%	8 80%	8 80%	4 40%	9 90%	7 70%	7 70%	5 50%	6 60%	6 60%
Corynebacterium striatum	7	7 100%	4 57%	7 100%	5 71%	7 100%	2 28%	5 71%	5 71%	4 57%	6 86%	2 28%	3 43%	1 14%	1 14%	1 14%
Total and %	90	87 96%	81 90%	78 86%	71 79%	66 73%	59 65%	52 58%	50 55%	47 52%	46 51%	38 42%	24 27%	15 16%	12 13%	9 10%

VA = vancomycin; CF = ciprofloxacin; KF = cephalexin; E = Erythromycin
C = chloramphenicol; CE = cefotaxime; TM = tobramyin; AN = amikacin
GM = gentamicin; RA = rifampicin; TE = tetracycline; AMX = amoxicillin
AM = ampicillin; PG = penicillin G; S = streptomycin

Discussion

Information were obtained from 91 patients [43 males (47.25%) and 48 females (52.75%)] underwent cataract extraction surgery. Sixteen out of the 91 patients (17.6%) were diabetics. This indicates that there is a considerable correlation between development of cataracts and diabetes mellitus. Such interpretation agreed with that indicated by Cullom and Chang [7], who stated "Diabetics are at an increased risk of cataract.

Sixty five patients (71.4%) aged between 60 and 92 years. This indicates that there is an important relation between advanced ages and development of cataract. A plausible explanation is that old patients are usually suffering from senile degenerations. This quite agreed with that mentioned by Dreyer *et al*. [8] who demonstrated that senile degenerations might yield the degenerative type of cataracts.

Only one child (1.1%), who was suffering from congenital cataract, underwent cataract extraction surgery. Twenty four out of ninety one patients (26.37%) were from villages, while the remaining sixty seven (73.63%) were civilians. This reveals a significant decrease in the number of villagers in comparison with the number of civilians intending ophthalmic hospitals. It is illustrated that those rural patients had non-acceptable beliefs and worse habits concerning health care. Researches concerning the correlation between cataract patients resident in villages and cities and intending ophthalmic hospitals were not available.

Specimens were collected from 91 patients immediately before experiencing cataract extraction surgery and again one day after surgery.

Coagulase-negative staphylococci were the predominant isolates prior to surgery. This finding was similar with that found by Bialasiewicz and Welt [9]. The following coagulase-negative staphylococci were detected before surgery:

Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus sciuri, Staphylococcus xylosus.

In addition to that, the following species were isolated preoperatively:

Staphylococcus aureus, proteus mirabilis, Streptococcus mitis 2, Rhodococcus equi, Corynebacterium xerosis, **and** ***Corynebacterium striatum.***

Staphylococcus epidermidis was the predominant preoperative microorganism isolated. These results were mostly accepted by Taylor et *al*. [10], who mentioned that ***Staphylococcus epidermidis*** was the commonest microorganism isolated among the normal preoperative lid and conjunctival microbial flora.

In this study, the dominant preoperative conjunctival microbes were ***Staphylococcus epidermidis*** and ***Corynebacterium spp***. This result agreed with that found by Mims *et al*. [11], who demonstrated that

Staphylococcus epidermidis and ***Corynebacterium spp***. were the principal microbial flora of the conjunctiva. Fourteen isolates of ***Staphylococcus aureus*** and only one isolate of ***proteus mirabilis*** were detected prior to surgery, which represented 15.6% and 1.1%, respectively. The rates above were approximately accepted by those indicated by Bialasiewicz and Welt [9], who stated that coagulase-positive staphylococci and Proteus spp. represented 13.5% and 3.0% out of the total preoperative conjunctival isolates; respectively the following one day postoperative species were isolated: ***Staphylococcus aureus,*** Staphylococcus ***epidermidis,*** ***Staphylococcus haemolyticus,*** ***Staphylococcus hominis,*** ***Staphylococcus sciuri,*** **and** ***proteus mirabilis*****.**

Ocular microbial infections following cataract surgery are related predominantly to the normal conjunctival flora and to a lesser degree from air borne microorganisms or certain endogenous sources such as the genitourinary tract [13]. Herde *et al.* [14] pointed out "The conjunctival flora is of great interest for each case of intraocular operation preventing postoperative infections." In the present study, two patients suffered from postoperative endophthalmitis. Of these two patients, the conjunctival swabs showed heavy growth of ***Staphylococcus epidermidis*** **or** ***Staphylococcus aureus***, which were detected from the preoperative and one day postoperative conjunctival smears. A plausible interpretation was that the conjunctival normal flora resulted in postoperative endophthalmitis in these two patients. This explanation agreed with that found by Binder *et al.* [15] who stated "Most germs causing postoperative endophthalmitis derive from the conjunctival bacterial normal flora." Bannerman *et al.* [16] mentioned that patient's conjunctival normal flora was a major source of postoperative endophthalmitis following cataract extraction surgery. The authors Ormerod *et al.* [17], Somani *et al.* [18], and Versteegh *et al.* [19] demonstrated that organisms mostly isolated in cases of postoperative endophthalmitis were coagulase-negative staphylococci. Han *et al.* [20] documented that coagulase-negative staphylococci followed by ***Staphylococcus aureus*** played a considerable role in the pathogenesis of bacterial endophthalmitis following cataract surgery. Mandle [21] indicated that *Staphylococcus aureus* was a significant causative agent of acute infections following cataract extraction surgery. Oguz *et al.* [22] stated "The organisms most commonly recovered in cases of post-surgical endophthalmitis include primarily ***Staphylococcus aureus*** and ***Staphylococcus epidermidis, Streptococcus spp., Proteus spp***., and less frequently ***Pseudomonas spp.***". Lam *et al.* [23] documented that a diabetic patient, who underwent cataract surgery, developed endophthalmitis caused by ***Proteus mirabilis***, while Joussen *et al.* [24] indicated that diphtheroid resident in the conjunctiva were recognized as potential causatives of serious ocular diseases. However, Watkins *et al.* [25] regarded that ***Corynebacterium striatum*** was a potent microbe causing conjunctivitis. Valenton [26] indicated that infections of the sclerocorneal incision following cataract surgery could be caused by ***Staphylococcus aureus, Staphylococcus epidermidis,*** and viridans streptococci group. These results predicate that the conjunctival normal flora is the principal causative of postoperative infections; therefore preoperative microbial diagnosis is of great importance in inhibiting postoperative

infections by administering the effective prophylactic drugs and for the prescription of the best therapy in cases of postoperative infections. This suggestion agreed with that found by Herde *et al.* [14], who stated "The preoperative bacteriological diagnostic of the conjunctiva is important mainly for the prevention of postoperative endophthalmitis despite the transience and fluctuation of the conjunctival flora but also in case of endophthalmitis for rapid specific antibiotical therapy. ".

Antimicrobial resistance of bacteria has become a worldwide problem; the prevalence of resistant bacteria can lead to selection of either non-effective or expensive drugs, prolonged illness, or greater risk of death [27].

These isolated microbes exerted very high resistance to penicillin G, ampicillin, and amoxicillin. Akhter *et al.* [28] denoted that high rates of resistance were observed *among* Gram-negative and Gram-positive species to penicillin G, ampicillin, and amoxicillin.

The following antibiotics could be used as topical ophthalmic therapy: vancomycin, ciprofloxacin, tobramyin, amikacin, gentamicin, tetracycline, chloramphenicol, and rifampicin [29, 20, 8].

Gram-positive species exhibited higher sensitivity to vancomycin. All ***Corynebacterium spp.*** were responsive to this drug. Among coagulase-negative staphylococci (only one isolate) was resistant to vancomycin. Kunimoto *et al.* [30] reported similar results and indicated that all ***Corynebacterium spp.*** and high rates of coagulase-negative staphylococci were sensitive to vancomycin. In the present study, 13 out of 14 isolates of ***Staphylococcus aureus*** responded to vancomycin. A close finding was described by *Akhter et al.* [28], and Han *et al.* [20], who observed that all ***Staphylococcus aureus*** isolates complied with vancomycin.

Amikacin was effective against coagulase-negative Staphylococci and ***Corynebacterium spp***. that were detected in the study. Kunimoto *et al.* [30] pointed almost similar results when mentioned that 89.5% of coagulase-negative Staphylococci and all ***Corynebacterium spp.*** responded to amikacin. Han *et al.* [20] recognized that 81.3% of ***Staphylococcus aureus*** *microorganisms* were sensitive to amikacin. This rate was close to that observed in the study.

All ***Corynebacterium spp.*** responded to cephalexin, while the remaining isolates showed moderate sensitivity to it.

It was found that coagulase-negative Staphylococci and ***Staphylococcus aureus*** microbes obtained in the study, were highly resistant to tetracycline.

Knauf *et al.* [31] illustrated that the susceptibility of conjunctival isolates to ciprofloxacin was relatively high and represented 91.7%. This rate was almost similar with that found in this study.

The authors Kunimoto *et al.* [30] recorded that the sensitivity of ***Streptococcus spp***. to amikacin, chloramphenicol, ciprofloxacin, gentamicin, and vancomycin represented 81.8%, 92.3%, 76.9%, 53.8%, and 81.8% respectively.

The microorganism ***Rhodococcus equi*** was found to be resistant to tobramyin and tetracycline.

Gram-negative organisms do not comply to vancomycin; therefore ***Proteus mirabilis*** did not respond to it.

In this study, ***Proteus mirabilis*** exhibited intermediate resistance to amikacin. In addition, Akhter *et al.* [28] showed that ***Proteus mirabilis*** agents were highly responsive to ciprofloxacin and gentamicin and

represented 95% and 91%, respectively.

Owing to the wide use of gentamicin as the preferred ophthalmic therapy in our country, a notable decrease in the susceptibility of ***Staphylococcus aureus*** and coagulase-negative staphylococci to this drug was observed. At present time, gentamicin is currently used as a prophylactic agent preventing ophthalmic postoperative infections in Ibn-Al-Haetham Eye Hospital. As it is mentioned previously, 51.25% of patients exhibited growth pre and one day after cataract surgery. This rate indicated that gentamicin was not active sufficiently in prophylaxis and that ocular infections could appear in the first few days following the surgery.

This study suggests that gentamicin can be substituted by ciprofloxacin as a prophylactic drug, which exhibited high efficacy against the obtained isolates in the study. In addition, vancomycin and amikacin can be used in the treatment of endophthalmitis.

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المجلة العراقية للعلوم الطبية
قائمة المحتويات

المقالات

المجلد السابع، العدد الأول، ١٤٣٠ هـ، ٢٠٠٩م

المجلة العراقية للعلوم الطبية

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رقم الإيداع في دار الكتب و الوثائق ببغداد ٧٠٩ لسنة ٢٠٠٠

الهيئة الأستشارية

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CONTENTS

EDITORIAL

ARTICLES

مقارنة بين نوابض القلب الأصطناعية نوع (VDD) و نوابض القلب الأصطناعية نوع (DDD) لدى مرضى يعانون من قطع من الدرجة الثانية و قطع كامل في حزم القلب

عباس فاضل الهاشمي

الخلاصة:

خلفية الدراسة: ان نوابض القلب الاصطناعية نوع VDD تعطي فائدة فزيولوجية في التحفيز المتناسق الأذيني البطيني بواسطة نظام ملائم احادي الدليل و لكن معوقات هذا النظام هو عدم ضمان استمرار تحسس الأذين بعد مدة طويلة و حدوث اعتلال العقدة الجيبية الأذينية.

هدف الدراسة: لتقييم فاعلية و حساسية نوعين مختلفة من نوابض القلب الأصطناعية ذوات المحجرين (نوع VDD و نوع DDD) باستخدام معايير كهروفيزيولوجية و عملية في محاولة لتحديد فيما اذا يمكن لنوابض القلب نوع VDD ان تصلح بديل حيوي لنوابض القلب نوع DDD لمعالجة مرضى يعانون من قطع من الدرجة الثانية و قطع كامل في حزم القلب و لديهم عقد جيبية طبيعية.

طريقة العمل: اجريت الدراسة على خلال الفترة من نيسان ٢٠٠٦ الى ايلول ٢٠٠٧ على ٤٨ مريض يعانون من قطع من الدرجة الثانية و قطع كامل في حزم القلب حضروا الى وحدة العناية القلبية المركزة في مستشفى الكاظمية التعليمي.

هؤلاء المرضى تم قسيمهم الى مجموعتين: مجموعة ال VDD و مجموعة ال DDD كل مجموعة مؤلفة من ٢٤ مريض. تم زرع نوابض القلب الاصطناعية (VDD و DDD) كل حسب المجموعة.

اجريت اختبارات فعالية و حساسية نوابض القلب الاصطناعية خلال عملية الزرع و من ثم متابعة المرضى في فترات زمنية ثابتة (اليوم الثاني بعد العملية, ١٠ ايام , شهر و ٣ اشهر) لكلا المجموعتين. هذه الأختبارات شملت: حساسية الأذين, ممانعة الدليل الأذيني, ارتفاع موجة ال P , النسب المؤية للتحفيز الأذيني البطيني المتناسق و مدة عملية الزرع و مدة التعرض للأشعة السينية. تمت مقارنة النتائج بين المجموعتين.

النتائج: ثمانية و اربعون مريض خضعوا لعملية زرع نابض القلب الأصطناعي. نصفهم استلم نوع DDD والنصف الاخر استلم نوع VDD.

اثناء عملية الزرع و خلال فترات المتابعة التي استمرت ٣ اشهر, لوحظ ان مجوعة DDD اظهرت زيادة معنوية في فاعلية و حساسية نوابض القلب الاصطناعية مقارنة بمجموعة ال VDD.

بعد عملية الزرع كان معدل ارتفاع موجة ال P و حساسية الأذين و ممانعة الدليل الأذيني و النسب المؤية للتحفيز الأذيني البطيني المتناسق هو: ٣,٤٢±١,١ ملفولت, ٣,٤٦±١,٣ ملفولت, ٥٦٨±١٠٣,٤٢ اوم, ٩٥٪±٧٪ على التوالي في مجموعة ال DDD بينما كانت: ٢,٩١±١,٣ ملفولت, ٢,٤٦±١,١٨ ملفولت, ٦٢٤,٢±١٣٦,٢٦ اوم, ٩٠٪±٨٪ على التوالي في مجموعة ال VDD.

كما لوحظ ان مدة الزرع اظهرت انخفاضا" معنويا" في مجموعة VDD (٦١,٨٢±١٤,٦ دقيقة) مقارنة مع مجموعة DDD (٧٢,٦٢±١٠,٤ دقيقة) ($p<0.05$), و لوحظ ايضا" ان مدة التعرض للأشعاع اظهرت انخفاضا" معنويا" في مجموعة VDD (٦,٥٣±٢,٩ دقيقة) مقارنة مع مجموعة DDD (١٠,٣٧±٣,٤ دقيقة) ($p<0.05$).

الأستنتاج: ان نابض القلب الأصطناعي ثنائي المحور(DDD) يعلو نابض القلب الأصطناعي احادي المحور (VDD) من ناحية الحفاظ على للتحفيز الأذيني البطيني المتناسق على المدى البعيد لدى يعانون من قطع من الدرجة الثانية و قطع كامل في حزم القلب الكهربائية مع الحفاظ عل وظيفة العقدة الجيبية لأذينية. في حين ان انخفاض الكلفة, الجدارة العالية, و الأختصار في مدة الزرع يجعل من نوابض القلب الاصطناعية VDD بديل حيوي لنوابض القلب الاصطناعية DDD.

مفتاح الكلمات: نابض القلب الأصطناعي ثنائي المحور(DDD), نابض القلب الأصطناعي احادي المحور (VDD), انحباس الحمة الأذينية البطينية, التناسق الأذيني البطيني, و حساسية الأذين.

فرع الفسلجة [كلية الطب-جامعة النهرين]

المجلة العراقية للعلوم الطبية ٢٠٠٩ م المجلد ٧ العدد ١ ص٤-١٠

أسباب وفيات الاطفال دون سن الخامسة من العمرالراقدين فى مستشفى أطفال السليمانية التعليمي

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الخلاصة

خلفية الدراسة: معرفة أسباب الوفاة عندالاطفال مهم لتقييم مدى تقدم النظام الصحي، ولتبيان مدى الحاجة لتصميم نظام رعاية صحية كفؤة.

هدف الدراسة: لأيجاد الأسباب الرئسية للوفاة عندالاطفال دون الخامسة من العمر وتقييم تأثيرات العمر الجنس،وزن الجسم،أقامة الطفل،الشهرمن السنة على أسباب الوفاة.

طريقة الدراسة: دراسة متراجعة الغرض منها معرفة أسباب الوفاة عندالأطفال دون من الخامسة من العمر.اجريت الدراسة في مستشفى أطفال السليمانية التعليمي.فترة الدراسة من الأول في كانون الثاني عام ٢٠٠١ لنهاية الحادي والثلاثين من كانون الأول عام ٢٠٠٥. كان العدد الكلي للمرضى الرافيدين في المستشفى ١٣٧,٧٣٩ توفى منهم ١٤٥٥.جمعت المعلومات الأحصائية من طبلات المرضى.

النتائج: نسبة الوفاة كانت(١,٠٦٪) وكانت النسبة أعلى في الذكور (٥٩,٣٪) من الإناث (٤٠,٧٪) وبدرجه معتمده من الناحيه الإحصائيه. وكانت نسبة الذكور الى الإناث ١:١,٤٨, وكانت معظم الوفيات في الأطفال الحديثى الولاده(٦١,٨٪) والأطفال ذوي الأوزان أقل من ٢,٥كغم بنسبة (٤٢,١٪). الأسباب الرئيسية للوفاة كانت الولادة المبكرة (الطفل الخديج) في الأطفال الحديثي الولاده(٥٤,٧). بينما كانت الاسباب الرئيسيه للوفيات في الاطفال خلال السنة الاولى هي الأسهال (٥٧,٤) والتهابات الجهازالتنفسي (١٥,٩). كانت نسبة الوفيات مختلفة في أشهر السنة حيث كانت عالية في شهرحزيران وشهركانون الأول. كانت نسبة الوفيات في الريف (٦٤,٥٪)أعلى من الحضر(٣٥,٥٪) وكان الفرق بدرجه معتمده من الناحيه الاحصائيه.

الأستنتاجات: بينت الدراسة أن الولادة المبكرة (الخدج) سبب رئيسي للوفاة في الاطفال الحديثي الولاده, بينما الأسهال والتهابات الجهاز التنفسي كانت من الاسباب الرئيسية للوفاة في الاطفال خلال السنه الاولى أما الأمراض الخبيثة والسرطان كان أقل أسباب الوفاة في كل الاعمار. كانت معظم الوفيات فى الاطفال الحديثى الولادة, و كانت هنالك علاقة واضحة بين أسباب الوفاة وبين العمر،الوزن ، الأقامة وبعض الاشهر من السنة.

مفاتيح الكلمات: معدل الوفيات،سبب الوفاة،أطفال دون الخامسة

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٢فرع طب الاطفال [كلية طب الكندى- جامعة بغداد]
٣طب الاطفال [مستشفى اطفال السليمانية التعليمى]

المجلة العراقية للعلوم الطبية ٢٠٠٩ م المجلد ٧ العدد ١ ص١١-٢٠

التعبير الموضعي للانترفيرون كاما مقابل الانترلوكين- 10 في حالات الاجهاض التلقائي المتكرر

أسماء باقر العبيدي، منال عدنان حبيب

الخلاصة

خلفية الدراسة: لا تزال الأسس المناعية الممكنة للإجهاض التلقائي المتكرر غير معروفة بدرجة كبيرة لحد الآن. وقد أُعتبرت الزيادة في السايتوكينات من النوع الأول (Type 1 cytokines) مثل (IFN-γ), والإنخفاض في السايتوكينات من النوع الثاني (Type 2 cytokines) مثل (IL-10) من الأسباب المحتملة لعدد من حالات الاجهاض المتكرر.

هدف الدراسة: دراسة العلاقة بين التعبير الموضعي للانترفيرون كاما والانترلوكين العاشر في حالات الاجهاض التلقائي المتكرر.

المرضى وطريقة الدراسة: تضمنت هذه الدراسة ثلاثة مجموعات من النساء، المجموعة A : حالات اجهاض متكرر(n=24)، المجموعة B : حالات اجهاض تلقائي للمرة الأولى (n=10)، المجموعة C : حالات انهاء حمل ارادي (n=6). اجريت تقنية التهجين الموضعي للكشف عن وتحديد كل من IFN-γ , IL-10 في عينات الجرف الرحمي لهذه الحالات.

النتائج: اظهرت النتائج زيادة معنوية كبيرة في التعبير الموضعي IFN-γ في حالات الاجهاض المتكرر مقارنة مع حالات الاجهاض لأول مرة و الحمل الطبيعي, مع نقصان معنوي كبير في التعبير الموضعي IL-10 في حالات الاجهاض المتكرر مقارنة مع الحالات الأخرى. أما النسبة بين IFN-γ – IL-10 فقد كانت 1.97 في حالات الاجهاض المتكرر, بينما كانت 0.67 و 0.73 في حالات الحمل الطبيعي و الاجهاض لأول مرة على التوالي.

الاستنتاج: لقد قوّت نتائج هذه الدراسة احتمالية الدور المهم للنوع الأول من الاستجابة المناعية في مرضية الاجهاض التلقائي المتكرر مترابطة مع انخفاض واضح في النوع الثاني من الاستجابة المناعية.

مفاتيح الكلمات: الاجهاض المتكرر, IFN-γ, IL-10

فرع الأحياء المجهرية [كلية طب النهرين – جامعة النهرين]

المجلة العراقية للعلوم الطبية ٢٠٠٩ م المجلد ٧ العدد ١ ص٢١-٢٩

علاقه كثافه H.pylori في الغشاء المخاطي مع مستوى المصلي المنخفض للحديد

نضال رؤوف مهدي[١] ، نضال عبد المهيمن[٢]

الخلاصة

خلفيه الدراسه : بالرغم من وجود طرق عديده لتشخيص الاصابه بـ *H.pylori* لكن توجد طرق بسيطه و معتمده لتحديد كثافه الاصابه والتي من المتوقع ان تلعب دور رئيسي في نشوء امراضيه الالتهاب المعوي وعلاقته مع مستوى المصلي لمخازن الحديد.

هدف الدراسة : هدف هذه الدراسه لتحديد العلاقه بين المستوى المصلي المنخفض لمخازن الحديد مع كثافه عدوى *H .pylori*

المرضى وطريقة الدراسة : شملت الدراسه ٦٤ مريض تترلوح اعمارهم بين ١٤–٦٦ سنه تم فحصهم بناظور الجزء العلوي للمعده والامعاء بسب وجود اعتلال في منطقه المعده والامعاء. قسم المرضى الى مجموعتين (مجموعه مصابه بال *H.pylori* وعددها ٤٧) و(مجموعه سلبيه للبكتريا وعددها ١٧).عدد من الاختبارات التشخيصيه المتداخله وغير المتداخله استعملت لتشخيص العدوى لتلك البكتريا(فحص انزيم Urease السريع، مسحات مضغوطه والفحص الانزيمي لمستوى IgG المضاد لل *H.pylori*) .

حدد المستوى المصلي لمخازن الحديد في المريض بطريقه الربط الانزيمي المومض.

النتائج: مجموع٤٧ من٦٤(٧٣٪) مريض كانوا ايجابيين للمرض وصنفوا طبقا للمجموعه العمريه والجنس . نسبه العدوى للبكتريا كانت اعلى في مجموعه النساء للعمار ٢١–٣٠ سنه.

مجموع ١٦من٤٧(٤٣٪)من المصابين اظهروا مستويات منخفضه لمخازن الحديد في المصل وكانت نسبه عاليه في الاناث للمجموعه العمريه ٢١–٣٠ سنه. مجموع ٢٨ من٤٧(٦٠٪)من المصابين كانت نتائج الخزع النسيجيه موجبه ،ومجموعه ٢٧من ٤٧(٥٧٪)من المصابين كانت النتائج السيرولوجيه للIgG المضاد للبكتريا موجبه وكذلك لفحص انزيم Urease السريع. عشره من مرضى هذه المجموعه اضهروا مستوى مصلي منخفض لمخازن الحديد .مجموع ١٠من٤٧(٢١٪)مريض اظهروا نتائج مصليه سالبه للIgG المضاد للبكتريا ولكن كانت النتائج موجبه في فحص انزيم Urease السريع ، ٥ من افراد هذه المجموعه كانت النتائج المصليه لمخازن الحديد منخفضه.

الاسنتاجات: وجود علاقه محتمله بين كثافة وجود الH.pylori على الغشاء المخاطي مع مستوى المصلي المنخفض لمخازن الحديد.

مفتاح الكلمات: امراضيه الالتهاب المعوي لل*H.pylori* ، فحص انزيم Urease السريع، الفحص الانزيمي لمستوى IgG المضاد لل *H.pylori*، الربط الانزيمي المومض لقياس مستوى مخازن الحديد.

[١] فرع الاحياء المجهريه [كليه الطب البيطرى - جامعه بغداد]
[٢] فرع الاحياء المجهريه [كليه طب النهرين- جامعه النهرين]

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إختلال توازن الصوديوم عند الحوامل المصابات بارتفاع ضغط الدم اثناء الحمل (قبل الشنج)

فيصل غازي الربيعي [١], علي الربيعي [٢], مها البياتي [٣],طارق حفظي الخياط [٤]

الخلاصة

خلفية الدراسة: ضغط الدم العالي لدى الحوامل (بريإكلامبسيا أو قبل الشنج) هو نوع من أرتفاع ضغط الدم يظهر أثناء الحمل, وهو من المضاعفات الشائعة المؤدية الى نسبة وفيات ومضاضة عاليتين؛ ومع ذلك فأن سبب هذا الارتفاع غيرمعلوم. المعطيات حول الشوارد الموجبة أثناء الحمل تعتبر متناقضة. أضافة لذلك فأن علاقة هذه الآيونات مع أوكسيد النتريك المشتق من بطانة الأوعية الدموية لم توصف بشكل كامل.

هدف الدراسة: هو لبيان نمط الصوديوم في حالة ارتفاع ضغط الدم المصاحب للحمل (بريإكلامبسيا أو قبل الشنج) وعلاقته مع الحمل الطبيعي, وارتباط القياس المذكور بمسار أوكسيد النتريك.

الاشخاص وطرق الدراسة: هذه الدراسة تشمل قياس أوكسيد النتريك و الأنزيم المكوّن له والصوديوم لدى ٦٠ حاملا" مصابة بارتفاع ضغط الدم المصاحب للحمل (مجموعة الأختبار) وتم تصنيفهن الى مجموعتين حسب عمر الحمل:

- حوامل مصابات بارتفاع ضغط الدم المصاحب للحمل (قبل الشنج) خلال الفصل الثاني من الحمل (العدد٣٠ مريضة).
- حوامل مصابات بارتفاع ضغط الدم المصاحب للحمل (قبل الشنج) خلال الفصل الثالث من الحمل (العدد٣٠ مريضة).

تمت مقارنة النتائج مع نتائج ٦٠ حاملا" سليمة"ً ظاهريا"(مجموعة السيطرة)، قسمت اعتمادا" على عمر الحمل الى مجموعتين:

- حوامل صحيحات ظاهريا" خلال الفصل الثاني من الحمل (العدد٣٠ حاملا).
- حوامل صحيحات ظاهريا" خلال الفصل الثالث من الحمل (العدد٣٠ حاملا).

النتائج: أظهرت النتائج انخفاضا معنويا في مستوى اوكسيد النتريك و الأنزيم المصنع له في مصل دم الحوامل ذوات ضغط الدم العالي المصاحب للحمل (قبل الشنج)، مع زيادة مستوى الصوديوم في المصل المرتبط بأحتباس هذا الشارد في ادرار هؤلاء المرضى والمعبَّرعنه بنسبة الصوديوم الى الكرياتنين بالمقارنة مع مجموعة السيطرة المناظرة.

الدور التنظيمي لاوكسيد النتريك على توازن السوائل يتبين من خلال الأرتباط الموجب بين اوكسيد النتريك ومستوى اخراج الصوديوم في الادرار, مما يدل على ان اوكسيد النتريك ذو تاثيرات مختلفة على امتصاص الصوديوم في النبيب الكلوي.

الاستنتاجات: مما تقدم يمكن الأستنتاج أن الحوامل ذوات الضغط العالي المصاحب للحمل (قبل الشنج) يعانين من تقلّص في الأوعية الدموية و اختلال حالة الصوديوم عند مقارنتهن مع الحوامل الصحبحات المناظرات لهن في العمر وعمر الحمل.

مفاتيح الكلمات: قبل الشنج،اكسيد النتريك،الصوديوم

[١] فرع الكيمياء و الكيمياء الحياتية [كلية الطب جامعة النهرين]
[٢] مركز السموم مستشفى الجراحات التخصصية
[٣]فرع الامراض النسائية والتوليد [كلية الطب جامعة النهرين]
[٤]فرع الكيمياء الحياتية, [كلية الطب جامعة, بابل]

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دراسة تشريحية للشريان الخصوي الشاذ

ثائر محمود فرحان

الخلاصة:

خلفية الدراسة: الشريان الخصوي يتفرع من الشريان الابهر أسفل من الشريان الكلوي عند مستوى الفقرة القطنية الثانية في اغلب الحالات.التباين في طريقة منشأ الشريان الخصوي ممكن مشاهدته إما ينشا من الشريان الابهر بمستوى أعلى او أسفل من الحالة الاعتيادية أو ممكن أن ينشا من غير الشريان الابهر .

هدف الدراسة:لدراسة التباين في منشأ الشريان الخصوي والأهمية السريرية لذلك.

طريقة العمل: تم دراسة المنشأ لأربعين شريان خصوي لكلا الجهتين لعشرين جثة بشرية محنطة في كلية الطب لمعرفة التباين الممكن في ذلك.

النتائج: خلال الدراسة التشريحية لعشرين جثة ومن خلال الفحص لأربعين شريان خصوي لكلا الجهتين, تم ملاحظة اختلاف في طريقة منشأ الشريان الخصوي. الشريان الخصوي الأيمن وجد في احد الحالات ينشا من الشريان الكلوي الأيمن, في حين وجد الشريان الخصوي الأيسر ينشا من الشريان الكلوي الإضافي في حالتين من الحالات العشرين, في ماعدا ذلك فان الشريان الخصوي وجد ينشا من الشريان الابهر في كل الحالات المتبقية.

الاستنتاج:

- الشريان الخصوي ممكن ان ينشئ من منشأ شاذ غير الشريان الابهر.
- الشريان الخصوي الشاذ هوالشريان الشاذ الوحيد وليس هناك غيره
- ممكن ان يشكل الشريان الخصوي الشاذ خطر لحدوث النزف اثناء العمليات الجراحية على الكلية او شرايينها.

مفتاح الكلمات: الشرايين الكلوية الاضافية , الشريان الخصوي , التباينات الوعائية.

فرع التشريح البشري [كلية الطب _ جامعة النهرين]

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ارتفاع نسبة التعبير الموضعي لمتلقيات الايستروجين في حالات فقدان الحمل المتكرر

نضال عبد المهيمن[١]، أسماء باقر العبيدي[١], أمل هندي الفلاحي[٢]

الخلاصة:

خلفية الدراسة: اوجدت الدراسات علاقة اعتراضية لهرمون الايستروجين واستمرارية الحمل بصورة طبيعية.

هدف الدراسة: التحديد الموضعي وتقييم متلقيات الايستروجين في حالات فقدان الحمل المتكرر.

المرضى وطريقة الدراسة: استخدمت تقنية التصبيغ الكميائي النسيجي المناعي لمتلقيات الايستروجين في عينات الجرف الرحمي والتي تم الحصول عليها من ٤٠ امراة تم تقسيمهن الى ثلاثة مجاميع: ٢٤ امراة حصل لها فقدان حمل متكرر، ١٠ نساء حصل لهن اجهاض تلقائي للمرة الأولى، و ستة نساء أجري لهن عملية انهاء حمل علاجي.

النتائج: كانت مستويات التعبير الموضعي لمتلقيات الايستروجين في حالات فقدان الحمل المتكرر ذات زيادة ملحوظة مقارنة مع المجموعتين الثانية والثالثة ($p=0.001$) .

الاستنتاج: ان ارتفاع نسبة التعبير الموضعي لمتلقيات الايستروجين في حالات فقدان الحمل المتكرر قد يدل على دورها المهم والفعال في مرضية فقدان الحمل.

مفتاح الكلمات: متلقيات الايستروجين, الاجهاض المتكرر

[١] فرع الاحياء المجهريه [كليه طب النهرين- جامعه النهرين]
[٢] المعهد التقني الطبي _ المنصور _ بغداد

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دور الشحمون الخصوي عند الحوامل المصابات بارتفاع ضغط الدم اثناء الحمل (قبل الشنج)

فيصل غازي الربيعي[1] , طارق حفظي الخياط[2] , مها البياتي[3]

الخلاصة

خلفية الدراسة: ضغط الدم العالي لدى الحوامل (بريإكلامبسيا أو قبل الشنج) هو نوع من أرتفاع ضغط الدم يظهر أثناء الحمل, وهو من المضاعفات الشائعة المؤدية الى نسبة وفيات ومضاضة عاليتين؛ ومع ذلك فأن سبب هذا الارتفاع غيرمعلوم.

تعتبر الأوعية الدموية الجهازية هدفا" للهرمون الذكري (الأندروجين أو الشحمون الخصوي), الذي يؤثرعلى وظيفة وأمراض جهاز الدوران بتأثيره على مسار أوكسيد النتريك المشتق من بطانة الأوعية الدموية.

هدف الدراسة: من هذه الدراسة هو لبيان نمط الهرمون الذكري في حالة ارتفاع ضغط الدم المصاحب للحمل (بريإكلامبسيا أو قبل الشنج) وعلاقته مع الحمل الطبيعي, وارتباط القياسات المذكورة بمسار أوكسيد النتريك.

المرضى وطريقة الدراسة: هذه الدراسة تشمل قياس أوكسيد النتريك و الأنزيم المكوّن له, الهرمون الذكري "الشحمون الخصوي" لدى ٦٠ حاملة" مصابة بارتفاع ضغط الدم المصاحب للحمل (مجموعة الأختبار) وتم تصنيفهم الى مجموعتين حسب عمر الحمل:

حوامل مصابات بارتفاع ضغط الدم المصاحب للحمل (قبل الشنج) خلال الفصل الثاني من الحمل (العدد٣٠ مريضة).

حوامل مصابات بارتفاع ضغط الدم المصاحب للحمل (قبل الشنج) خلال الفصل الثالث من الحمل (العدد٣٠ مريضة).

تمت مقارنة النتائج مع نتائج ٦٠ حاملة" سليمة" ظاهريا"(مجموعة السيطرة)، وتم تقسيم مجموعة السيطرة اعتمادا" على عمر الحمل الى مجموعتين:

حوامل صحيحات ظاهريا" خلال الفصل الثاني من الحمل (العدد٣٠ مريضة).

حوامل صحيحات ظاهريا" خلال الفصل الثالث من الحمل (العدد٣٠ مريضة).

النتائج: أظهرت النتائج انخفاضا معنويا في مستوى اوكسيد النتريك و الأنزيم المصنع له في مصل الحوامل ذوات ضغط الدم العالي المصاحب للحمل (قبل الشنج) مقارنة" مع مجموعة السيطرة المناظرة, كان هذا الانخفاض مُصاحَبا لأرتفاع معنوي في مستوى الهرمون الذكري و يتضح التأثيرالمثبط للهرمون الذكري(الشحمون الخصوي) على انتاج اوكسيد النتريك من خلال الأرتباط السالب بين هذين االمتغيرين .

و يمكن للأضطرابات في حالة التوسع الوعائي ومستوى الهرمون الذكري ان تعزى الى اضطراب وظيفة المشيمة, التي تختلف حسب تقدّم عمر الحمل وتقدّم الحالة المرضية, تكون الأفضل في المجموعة الرابعة (حوامل صحيحات ظاهريا" خلال الفصل الثالث من الحمل) والأسوأ في المجموعة الثانية(حوامل مصابات بارتفاع ضغط الدم المصاحب للحمل ، قبل الشنج ، خلال الفصل الثالث من الحمل).

الاستنتاج: مما تقدم يمكن الأستنتاج أن الحوامل ذوات الضغط العالي المصاحب للحمل (قبل الشنج) يعانين من تقلّص في الأوعية الدموية مع فرط الهرمون الذكري في الدم عند مقارنتهن مع الحوامل االصحيحات المناظرات لهن في العمر وعمر الحمل.

مفتاح الكلمات: قبل الشنج، اكسيد النتريك، الشحمون الخصوي.

[1]فرع الكيمياء و الكيمياء الحياتية[كلية الطب _ جامعة النهرين]
[2]فرع الكيمياء الحياتية [كلية الطب _ جامعة بابل]
[3]فرع الأمراض النسائية والتوليد [كلية الطب _ جامعة النهرين]

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مضاعفات الديال الدموي عند المصابين بالعجز الكلوي المزمن المستخدمين الناسور الشرياني الوريدي مقارنة بالمدخل الوعائي المؤقت

جواد كاظم مناتي

الخلاصة

خلفية الدراسة: غسل الكلى هي عملية إزالة السوائل والمواد السامة الناتجة عن الايض – هنالك نوعان من غسل الكلى هما الديال الدموي والديال الصفاقي,يستخدم الناسور الشرياني الوريدي أو المدخل الوعائي المؤقت في الديال الدموي.

هدف الدراسة: تهدف هذه الدراسة لمعرفة مضاعفات الديال الدموي عن المصابين بعجز كلوي المزمن المستخدمين الناسور الشرياني الوريدي مقارنة بالمدخل الوعائي المؤقت

طريقة العمل: أجريت الدراسة في كلية الطب /جامعة النهرين/ مستشفى الكاظمية التعليمي. تضمنت الدراسة ١٠٠ مريض مصاب بعجز كلوي مزمن, ٥٢ لديهم ناسور شرياني وريدي و ٤٨ لديهم مدخل وعائي مؤقت. أجريت لهم الفحوصات السريرية والمختبرية لمعرفة أسباب العجز الكلوي والمضاعفات الناتجة عن الديال الدموي

النتائج: كانت النتائج ٦٠٪ يعانون من ارتفاع درجة الحرارة عند مستخدمي المدخل الوعائي المؤقت بينما ١٢٪يعانون من ارتفاع درجة الحرارة عند مستخدمي الناسور الشرياني الوريدي.كذلك ٤٠٪يعانون من انسداد المدخل الوعائي المؤقت. وكذلك٣٠--٢٤٪يعانون من أصابتهم بالتهاب الكبد الفيروسي(B&C)٢٤٪--٣٢٪ يعانون من انخفاض الضغط الدم أثناء الديال الدموي.بالإضافة إلى المضاعفات الأخرى التي هي متقاربة عند المستخدمين الناسور الشرياني الوريدي مقارنة بالمدخل لوعائي المؤقت كالألم الصدر ,أوجاع الرأس,القيء ,الغثيان,وكذلك الحكة

الاستنتاجات: ضرورة إجراء الناسور الشرياني الوريدي قبل أجراء الديال الدموي لمرضى العجز الكلوي المزمن لتقليل من المضاعفات.

مفتاح الكلمات: الديال الدموي,مدخل وعائي مؤقت,الناسور الشرياني الوريدي

فرع الباطنية_ شعبة الديلزة[كلية الطب_ جامعة النهرين/ مستشفى الكاظمية التعليمي]

المجلة العراقية للعلوم الطبية ٢٠٠٩ م المجلد ٧ العدد ١ ص٧٠-٧٥

أهمية فهارس حجمِ صفيحةِ الدمّ عند مرضى تصلب الشرايين التاجيةِ

وسيم فاضل التميمي , مؤيد بشيرحامد

الخلاصة

خلفية الدراسة: تَلْعبُ صفيحاتُ الدمّ دورَ مهمَ في لتخثّر الدم داخل الأوعيةِ الدموية ،السبب الرئيسي للمتلازماتِ التاجيةِ الحادّةِ. ً يعتبرَحجم صفيحةِ الدم مؤشر لنشاطِ صفيحةِ الدمّ.

هدف الدراسة: أَنْ تَتحرّى القيمةَ السريريةَ لاختبار فهارسِ حجمِ صفيحةِ الدمّ عند مرضِى تصلب شرايين القلب وإمكانية وجود عامل خطورة لحدوث احتشاء عضلة القلب.

المرضى وطريقة العمل: تُضمّنت الدراسةِ ٣٦ مريضا: ٢٢ منهم لديه احتشاء عضلة القلب و١٤ لديه ذبحة قلبيةُ غير مستقرةُ. عوامل الخطورةِ ووجود تأريخِ لذبحة قلبيةِ مستقرّةِ سابقة روجعا ودُرِسا احصائيا باستعمال Chi square. إستعمل نظامِ تحليلِ الدمّ الآليِ لإحصاء الدمِّ الكاملِ وفهارسِ حجمِ صفيحةِ الدمّ: معدل حجم صفيحةِ الدمّ ، نسبة الخلايا الكبيرةِ لصفائح الدم ، و توزيعِ قطر صفيحةِ الدمّ ودرست باستعمال إختبار t . كُلّ قِيَم P كَانتْ ذات وجهين وإعتبرتْ قيمة P الأقل من ٠,٠٥ هامّة بشكل إحصائي.

النّتائِج: ُوْجَدُ ان فهرس معدل حجم صفيحة الد م و نسبة الخلايا الكPرةِ لصفائح الدم كَانا الفهرسِين الأهمَّ التي اظهرت إختلافاً إحصائياً بين مرضِى الذبحة القلبيةُ الغير مستقرةُ و مرضِى احتشاء عضلة القلب (P =٠,٠٤٢ وP =٠,٠٣١) على التوالي على خلاف الفهارس الأخرى (عدد صفيحات الدمّ َوتوزيعِ قطر صفيحةِ الدم) (P =٠,٧٠٣ وP =٠,٠٩٤). لم يكن هناك إرتباطَ بين فهرس معدل حجم صفيحة الدم والفهارس الأخرى بوجود تأريخِ لذبحة قلبيةِ مستقرّةِ سابقة عواملِ الخطرِ الأخرى للمتلازمةِ التاجيةِ الحادّةِ ، P =٠,٨١١.

الاستنتاج: لأنه عمليُ وإقتصاديُ وبسيطُ ،اختبار فهارسِ معدل حجمِ صفيحةِ الدمّ و نسبة الخلايا الكبيرةِ لصفائح الدم ، يُمْكِنُ أَنْ يُستَعملَ في تَوَقُّع إمكانيةِ حدوث تخثّرِ حادٍّ في الشرايين التاجية لمرضى تصلب الشرايين التاجية.

مفتاح الكلمات: أصول الشرايين التاجية,فهرس الصفيحات الدموية

فرع الباطنية [كلية الطب_جامعة النهرين/ مستشفى الكاظمية التعليمي]

المجلة العراقية للعلوم الطبية ٢٠٠٩ م المجلد ٧ العدد ١ ص٧٦-٨١

إلتهاب الكبد الفيروسي نمط A والاصابه بمرض السكري عند عينه من الأطفال العراقيين

عبد الكريم جاسم محمد

الخلاصة

خلفية الدراسة: يعتبر مرض السكري من الإمراض المهمة عند الأطفال لكونه مرض مزمن وله مضاعفات كثيرة وأحيانا خطره ويحتاج إلى عناية كبيرة من الأهل والمريض كما وان التهاب الكبد الفيروسي نمط A من الإمراض المستوطنة في العراق

هدف الدراسة:لدراسة العلاقة بين التهاب الكبد الفيروسي نمط A ومرض السكري عند الأطفال العراقيين

طريقة العمل: تم فحص مئة من الأطفال المصابين حديثا بمرض السكري ومائة أخرى من الأطفال الخالين من المرض والذين يماثلونهم بالعمر والجنس حيث خضع الجميع لفحص الدم باستخدام طريقة المقايسة المناعية الأنزيمية نوع (ELISA) ضد فيروس التهاب الكبد الفيروسي نمط A .أجريت هذه الدراسة في مستشفى الكاظمية التعليمي ومستشفى النور العام من الأول من شهر تشرين الثاني عام ٢٠٠٦ وحتى العشرين من شهر كانون الأول عام ٢٠٠٨.

النتائج: أظهرت الدراسة زيادة طفيفة في عدد الإناث (٥٦٪) عن عدد الذكور (٤٤٪) المصابين بمرض السكري كما أظهرت الدراسة وجود علاقة قيمه سلبيه بين الاصابه بالتهاب الكبد الفيروسي نمط A والاصابه بمرض السكري

الاستنتاجات: لا توجد علاقة بين الاصابه بمرض التهاب الكبد الفيروسي نوع A ومرض السكري عند عينة من الأطفال العراقيين

مفتاح الكلمات: إلتهاب الكبد الفيروسي نمط A,مرض السكري , أطفال

فرع طب الاطفال [كلية طب- جامعة النهرين]

المجلة العراقية للعلوم الطبية ٢٠٠٩ م المجلد ٧ العدد ١ ص٨٢-٨٥

القيم المرجعية لفحص وظائف الرئة لعينة من العراقيين الأصحاء من غير المدخنين

منير صالح محمد النمر [١], مي فضيل إسطيفان [٢] , طلال شاكر جواد [٣]

الخلاصة

خلفية الدراسة: يعتمد فحص وظائف الرئة على عدة عوامل فزيولوجية وهي الطول, العمر,الجنس, والعرق. تستخدم المعادلات الرياضية كمرجع لأيجاد وتحديد القيم التي تمثل الحالة الطبيعية السليمة لنتائج فحص الرئة عند الاشخاص الاصحاء بأستخدام جهاز فحص الرئتين والتي بدورها تساعد العاملين في هذا المجال على معرفة فيما اذا كان قياس احجام الرئة لأشخاص لهم نفس الجنس والطول والعمر ،يقع ضمن المجال الطبيعي .

هدف الدراسة : تخمين المعادلة الرياضية لايجاد القيم المرجعية لعينة من الأشخاص العراقيين الأصحاء من غير المدخنين.

طريقة العمل: أجريت هذه الدراسة في وحدة فحص وظائف الرئة /مستشفى الكندي– بغداد على مئة واثنان وثمانون شخصاً سوياً من غير المدخنين (٧٩ من الذكور و١٠٣ من الاناث)، تتراوح أعمارهم بين (٢٠ – ٦٠) سنة، حيث تم قياس سعات وحجوم الرئة بجهاز فحص الرئتين لكل شخص.

النتائـــج : تم إشتقاق المعادلة التخمينية لكل حالة ، ومن ثم تم حساب القيمة المرجعية، والتي من خلالها يمكن حساب معدل قيمة كل من العامل" حجم هواء الزفيرالكلي" والمعرف بالسعة الحيوية للرئتين ، والعامل " حجم هواء الزفير خلال زمن ثانية واحدة ". بينت الدراسة ان معدل قيم هذين العاملين كانت اقل ب ٥,٥٨٪ و ٦,١٤٪ عند الاناث و ٤,٧٨٪ و ١٢,٦٥٪ عند الذكور مقارنة مع الدراسات التي اجريت على مجموعة من القوقازيين.

الاستنتاجات: تم إحتساب المعادلات التخمينية الرياضية وايجاد القيم المرجعية لعينة من الأشخاص العراقيين الأصحاء من غير المدخنين ومن كلا الجنسين ضمن أعمار تتراوح بين(٢٠–٦٠ سنة). المعادلات التخمينية والقيم المرجعية التي تم استنباطها في هذه الدراسة كانت تختلف عن تلك المعادلات المشتقة من قبل دراسات اخرى التي اجريت على الجنس الابيض في كل من الولايات المتحدة الامريكيه واوروبا.

مفتاح الكلمات: حجم هواء الزفير خلال زمن ثانية واحدة ، " حجم هواء الزفيرالكلي" والمعرف بالسعة الحيوية للرئتين ، جهاز فحص الرئتين ،أشخاص عراقيين .

[١]فرع الفسلجة [كلية الطب-جامعة بغداد]
[٢]فرع الفسلجة [كلية الطب-جامعة النهرين]
[٣]مستشفى الكاظمية التعليمي

المجلة العراقية للعلوم الطبية ٢٠٠٩ م المجلد ٧ العدد ١ ص٨٦-٩٥

ارتفاع الهرمون المنشط المنسلي المشيمي البشري(بيتا – اج سي جي) في حالات طليعة الارجاج الشديدة

مها محمد البياتي[١], نهى جاسم حمود[٢]

الخلاصة

خلفية الدراسه: حالات إرتفاع ضغط الدم المصاحبه للحمل تعد احد اسباب المضاعفات الانعكاسيه التي تصيب الجنين وحديثي الولاده والام الحامل مما قد يعكس وجود تغيرات مرضيه مبكره في المشيمه.

هدف الدراسة: بيان فيما لو كان قياس هرمون ال(بيتا اج سي جي) يعكس استجابة افرازية مختلفة للجذعه الاغتذائية في حالات طليعة الارجاج الشديدة .

تصميم الدراسة: دراسة مستقبلية.

مكان الدراسة: اجريت هذه الدراسة في قسم النسائيات والتوليد في مستشفى الكاظمية التعليمي , بغداد , العراق

طريقة الدراسة: شملت هذة الدراسة اربعون حالة مرضية (النساء الحوامل المصابات بطليعة الارجاج الشديدة) , قورنت مع اربعين حالة ضابطة (النساء ذوات الحمل الطبيعي) . جميع الحالات في الثلث الاخير من الحمل وذات الاحادي الجنين وغير مصاب بتشوهات خلقية . تم سحب عينات الدم من الحالات قبل الولادة وقياس هرمون ال(اج سي جي) في مصل الدم , مع ملاحظة نتائج الحمل الانعكاسية .

النتائــج: من هذة الدراسة وجد ان هرمون ال(اج سي جي) يرتفع بصورة ملحوظة في حالات الحمل المصابة بطليعة الارجاج الشديدة مقارنة مع الحالات الصحية الغير مصابة .

ان ارتفاع هرمون ال(اج سي جي) في حالات طليعة الارجاج الشديدة يرتبط بارتفاع نسبة الولادات المسبقة (٥٠٪ مقابل ٧,٥ ٪) وارتفاع نسبة اعاقة النمو داخل الرحم (٤٧,٥٪ مقابل ٥٪) وارتفاع نسبة الولادات ذات الاوزان القليلة الاقل من ٢٥٠٠ غرام (٧٠,٢٥٪ مقابل ١٢,٥٪) وارتفاع نسبة الولادات الميتة (٧,٥٪ مقابل صفر).

الاستنتاج: من هذا نستنتج ان ارتفاع هرمون ال(اج سي جي) في حالات طليعة الارجاج الشديدة يمكن ان يعكس وبصورة ملحوظة تغيير مرضي وتفاعل افرازي للمشيمة ويرتبط مع نتائج انعكاسية للحمل.

مفتاح الكلمات: طليعة الارجاج, الهرمون المنشط المنسلي المشيمي البشري, الحمل.

[١]فرع النسائيه والتوليد[كلية الطب_جامعة النهرين]
[٢]فرع النسائيه والتوليد_مستشفى الكاظميه التعليمي

المجلة العراقية للعلوم الطبية ٢٠٠٩ م المجلد ٧ العدد ١ ص٩٦-١٠١

الحذوف الدقيقة لعوامل اللانطفية على كروموسوم Y عند الرجال العقيمين.

زهره عبدالحسين[١] , عبدالحسين مويت الفيصل[٢] , باسمة محمد الجبوري[١]

الخلاصة

خلفية الدراسة: تمثل الحذوف الدقيقة في كرموسوم Y أحد أهم الاسباب المؤدية الى العقم في الذكور و تعتبر مواقع عوامل اللانطفية AZF أكثر المواقع تعرضا لهذه الحذوف.

هدف الدراسة: تحديد الحذوف الدقيقة في مواقع عوامل اللانطفية AZF التي تترافق مع العقم عند الرجال.

طريقة العمل: جمعت عينات دم من 25 مصابا بالعقم من نوع azoospermia من أجل التحليل الكروموسومي وأستخلص منها الدنا DNA أيضا لغرض فحص مواقع عوامل اللانطفية على كروموسوم Y وذلك بأستخدام تقنية PCR .

النتائج: كانت نتائج فحص الكروموسومات طبيعية لجميع العينات. بينت النتائج التي حصلنا عليها من فحص PCR أن هناك حذوف دقيقة قد شخصت في ٦ عينات . مثلت هذه ٢٤٪ من حالات العقم . فقد سجل حذف دقيق في الموقع AZFc لوحده عند ٢ من المرضى و سجل حذف دقيق لموقعين هما AZFa , AZFc عند ثلاثة مرضى و سجل حذف دقيق في الموقع AZFb عند مريض واحد.

الاستنتاج: إن الحذوف الدقيقة في الموقع AZFc هي الاكثر تكرارا عند مرضى العقم.

مفتاح الكلمات: العقم , مواقع اللانطفية AZFa,b,c , كروموسوم Y .

[١]معهد أبحاث الاجنة وعلاج العقم _ جامعة النهرين
[٢]معهد التقانة الحياتية _ جامعة بغداد

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عزل وتشخيص النبيت الطبيعي في ملتحمة العين قبل وبعد ازالة الماء الأبيض (الساد)

سندس فاضل حنتوش الناهي[1] , عبد الواحد باقر[2] , منعم مصطفى فتحي[3], فائز اسماعيل الشكرجي[4]

الخلاصة

خلفية الدراسة: النبيت الطبيعي لملتحمة العين هي كائنات ممرضة انتهازية تحت ظروف معينة تسبب امراض داخلية المنشأ .

هدف الدراسة: صممت الدراسة لعزل و تشخيص النبيت الطبيعي لملتحمة العين قبل و بعد ازالة الساد و دورها في الاصابات المرضية بعد ازالة الساد.

طريقة العمل: جمعت النماذج من ملتحمة و حافة جفن العين من احدى و تسعين من عيون المرضى مباشرة قبل ويوم بعد العملية . اخضعت العينات للفحوصات المايكروبايولوجية و الكيموحيوية . اجريت اختبارات الحساسية لخمسة عشر مضاد حيوي ضد تسعين عينة بكترية عزلت قبل ازالة الساد.

النتائج : كانت المكورات العنقودية البشروية و تلتها المكورات العنقودية الذهبية هي السائدة قبل وبعد ازالة الساد. أعطى مضاد الحيويةالفانكومايسين اعلى فعالية ' تبعه كل من السبروفلوكساسين و الاميكاسين تجاه العزلات البكتريه التي خضعت للاختبارات الحساسية. ظهرت حالتان من التهاب باطن العين بعد اجراء العملية ،اذ كان المسببان لها هما المكورات العنقودية البشروية و المكورات العنقودية الذهبية .

الاستنتاج: النبيت الطبيعي لملتحمة العين هو المسبب الرئيسي لمعظم الاصابات بعد ازالة المساد .

مفتاح الكلمات: النبيت الطبيعي لملتحمة العين ، إلتهاب باطن العين ، مضاد السبروفلوكساسين ، مضاد الفانكومايسين ، مضاد الأميكاسين .

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