

Estimation of uric acid ,urea, creatinine and creatinine clearance in the serum of preeclamptic women

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Abstract:

Preeclampsia is one of the most frequent complication of pregnancy which manifested by high blood pressure during pregnancy for the first time after 20th weeks of gestation with presence of protein in the urine and the causative is unknown. The aim of this study is to estimate serum urea ,serum creatinine, serum uric acid and creatinine clearance in preeclamptic women for feasibility early detection of preeclampsia and prevention of it. Out of 100 pregnant women 50 of them there blood pressure is normal (uncomplicated pregnancy) and the other 50 were suffered from preeclampsia. The patients chosen when admitted to general Kirkuk hospital from July 2011 to January 2012 .In all 100 pregnant women serum urea, uric acid ,creatinine and urinary creatinine were measured by enzymatic reaction methods, then creatinine clearance rate was calculated by 24 hrs. urine collection . This study revealed that serum urea ,creatinine, uric acid in preeclamptic group were elevated significantly($p < 0.05$) in compared to normotensive pregnant group. The creatinine clearance was lower in preeclamptic women than in normotensive pregnant women, the difference was significant ($p < 0.05$). 45.33% of pre-eclamptic women had positive past medical history of preeclampsia while 64% of them had positive family history of preeclampsia. This study showed that 62% of pre-eclamptic women were primigrivda.

Conclusion: It is important to asses renal function tests especially serum uric acid for all pregnant women have high blood pressure as it is the first change and denoter for effecting of renal function in preeclampsia cases.

تقدير حامض البوليك، يوريا، كرياتينين و تصفية كرياتينين في مصل النساء المصابات بتسمم الحمل

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مفتاح البحث : حامض البوليك، اليوريا، الكرياتينين

الخلاصة

تسمم الحمل هو من أكثر تعقيدات الحمل المتكررة والذي لوحظ بارتفاع ضغط الدم للمرة الأولى بعد الأسبوع العشرين من الحمل مع وجود البروتين في الادرار وأسبابه غير معروف. الهدف من هذه الدراسة هو تقدير اليوريا، الكرياتينين، حامض البوليك، وحساب تصفية الكرياتينين في مصل النساء المصابات بتسمم الحمل لإمكان الكشف المبكر عنه ومنعه. من مجموع 100 امرأة حامل خمسون منها كان ضغط الدم لديها طبيعياً (حمل بدون مضاعفات)، والآخرى كانت تعاني من تسمم الحمل، تم اختيار المرضى من بين الذين كانوا يراجعون مستشفى كركوك العام أثناء الفترة من تموز 2011 ولغاية كانون الثاني 2012. في 100 امرأة حامل تم قياس اليوريا، وحامض البوليك في المصل، ونسبة الكرياتينين في المصل والإدرار بواسطة طرق التفاعل الأنزيمي وتم حساب تصفية كرياتينين باستخدام تحليل تجميع البول خلال 24 ساعة. فقد تبين من هذه الدراسة زيادة معنوية في تركيز مصل اليوريا، الكرياتينين ($p < 0.05$) والحامض البولي ($p < 0.01$) في مجموعة قبل التشنج الحلمي مقارنة بمجموعة النساء الحوامل ذوات الضغط الطبيعي. وكانت تصفية الكرياتينين في النساء المصابات بتسمم الحمل أقل مقارنة بمجموعة النساء الحوامل ذوات الضغط الطبيعي وكان فرق معنويًا ($p < 0.05$). كان 45.33% من النساء المصابات بتسمم الحمل التاريخ الطبي الماضي من تسمم الحمل في حين أن 64% منهن لديها تاريخ عائلي إيجابي من تسمم الحمل. وأظهرت هذه الدراسة أن نسبة 62% من النساء المصابات كانت في الحمل الأول.

الاستنتاج :- من المهم إجراء فحص لوظائف الكلية وخاصة الحامض البولي لكل النساء الحوامل المصابات بارتفاع ضغط الدم كونه التغيير الأول والثابت كدليل على إصابة الكلية في حالات تسمم الحمل.

Introduction

Preeclampsia is a clinical disorder that occurs only during pregnancy and the postpartum period. Affecting at least 5% of all pregnancies, it is a rapidly progressive condition characterized by high blood pressure and the presence of protein in the urine. The only effective treatment is delivery of the fetus and placenta. Typically, preeclampsia occurs after 20 weeks gestation (in the late 2nd or 3rd trimester), [1,2,3] though it can occur earlier. Globally, preeclampsia and other hypertensive disorders of pregnancy are a leading cause of maternal and infant illness and death. [4]. There are many theories concerning the etiology of preeclampsia. Inadequate blood supply to the placenta, abnormalities in the immune system and maternal endothelial cell dysfunction are suspected to be involved. The cause however, is still considered to be unknown [5].

The pathogenesis of preeclampsia appears to occur in two phases: abnormal implantation of the placenta leading to impaired placental blood flow, which in turn include the release of pathogenic factors in the maternal circulation results in endothelial injury in many maternal organs especially the kidney and liver [6]

It is important to identify women who are at high risk of developing the disease early in pregnancy. This is because early identification of biochemical markers of the disease would not only facilitate selective recruiting of those at increased risk for preeclampsia but also to help in determining those patients who were more likely to benefit from interventional measures should a therapeutic intervention prove successful [7,8,9].

The aim of this study were to estimate serum urea, serum creatinine, serum uric acid and creatinine clearance in preeclamptic women for feasibility early detection of preeclampsia and prevention of it

Materials and Methods:

Time & location

From of July 2011 until to January 2012. The study was carried on in Kirkuk province in which 100 sample were collected and investigated by the aid of lab. Department in Kirkuk general hospital.

The subjects included the following:

1. Normotensive pregnant women:

This group included fifty healthy pregnant women, aged ranged between (26-37) years with a mean \pm SD of (27.9 \pm 5.62) years. The mean of their blood pressure at admission was 106/71 \pm 2/1.6 mmHg, 21 of them were primigravida and 29 of them were multiparas.

2. Preeclamptic women:

This group included fifty pregnant women with signs and symptoms of pre-eclampsia, aged ranged between (25-38) years with a mean \pm SD of (31.4 \pm 5.54) years. The diagnosis of PE was made according to the criteria published by American college of Obstetricians and Gynecologists (ACOG), stated that B.p \geq 140/90 mmHg after 30 min of rest on two separate occasions at least six hours apart with proteinuria \geq +2 (100 mg/dl) on voided specimen. The mean of their blood pressure at admission was 157/103 \pm 4/2 mmHg, and urinary protein (by dipstick) averaged from (+2 to +3). 31 of them were primigravida and 19 of them were multiparas,

The subjects of group 1, 2 were in the third trimester (32-40 weeks) at the time of sampling, the gestational age was calculated according to the date of last menstrual cycle, clinical examination, and first-trimester ultrasound finding and these women were free from any disorder that effect the result of this study.

Blood sampling

After preparation general information from patients according to questionnaire form give 3ml of venous blood was drawn by the means of disposable syringe in to a clean dry sample tube. Serum were separated to assess some biochemical tests.

Methods

Serum Urea:

Urea was determined by enzymatic method (Urease–modified Berthelot reaction) [10].

Serum and urine creatinine

Colorimetric reaction (jaffe reaction) of creatinine with alkalinepicrate by kinetic according to jaffe method [11].

Serum uric acid:

Uric acid was determined by an enzymatic(Uricase) method [12] .

Estimation of creatinine clearance (C_{Cr})

Creatinine clearance was calculated using by 24hours urine collection.

Creatinine clearance (24hr Urine) in ml/min= $[\text{urine Cr (mg/dl)} \times \text{vol Ur (ml)}] / [\text{plasma Cr (mg/dl)} \times \text{time (min)}]$

Assumes 24 hr (1440 min) urine collection

Statistical analysis

The statistical analysis for this study was carried out by using the computer program (Microsoft Excel) and includes: Mean, Standard Deviation and T-test [13].

Results

The demographic and clinical characteristics:

The demographic and clinical characteristics of the present study's subjects are given in(Table 1).The difference in the mean of age between the two groups was not significant, while the difference in the mean of proteinuria at the time of sampling, was significant.

Regarding the gravidity, 42% of normotensive, 62% of pre-eclamptic, were primigravida, so there was significant difference between two groups (pre-eclamptic versus normotensive;).

When the blood pressure at the time of admission was compared, there was a significant difference between two groups (pre-eclamptic versus normotensive pregnant women) .

45.33% of pre-eclamptic women had positive past medical history of preeclampsia while 64% of pre-eclamptic women had positive family history of preeclampsia.

Regarding renal function, as presented in table (2), the mean serum urea concentration was significantly higher in women with pre-eclampsia (4.72 ± 1.01 mmol/L) than in the normotensive pregnant women (2.48 ± 0.62 mmol/l).

While the mean value of serum creatinine concentration significantly increased in women with pre-eclampsia as compared with normotensive pregnant women (88.8 ± 12.49 versus 56.61 ± 8.2 $\mu\text{mol/l}$, pre-eclamptic women versus normotensive pregnant women respectively).

In addition, serum uric acid significantly altered in the pre-eclamptic women relative to normotensive pregnant women, as increased from (207.55 ± 22.85 $\mu\text{mol/l}$) in the normotensive pregnant women to (370.83 ± 48.57 $\mu\text{mol/l}$) in the pre-eclamptic women as in table (2).

Creatinine clearance was reduced significantly from 125.3ml/min in preeclamptic women into 103.6ml/min in normotensive pregnant women in table (2).

Discussion

Preeclampsia is a human pregnancy specific disorder that adversely affect the mother by vascular dysfunction and the fetus by intrauterine growth restriction [15]

Preeclampsia is associated with atherosclerosis and abnormalities of renal ,hepatic and coagulatory function[16]

The striking normal physiological changes in renal function during normal pregnancy are accentuated in preeclampsia as a consequence of placental ischemia and impaired placental function,[17] therefore certain function tests were determined in this study including serum uric acid ,serum urea ,serum creatinine and creatinine clearance as represented in table (2)

There was a very highly significant rise in the mean value of serum uric acid concentration in the preeclamptic women as compared with the normotensive pregnant women because women with preeclampsia, renal plasma flow and glomerular filtration rate are decreased as a consequence of increased afferent arteriolar resistance and/or reduced ultrafiltration coefficient.

(Jeyabalan, *et.al.*) revealed an increase serum uric acid concentrations mainly as a consequence of reduced renal clearance. Reduced GFR leads to decreased filtered load of uric acid, and plasma volume contraction contributes to increased proximal tubular reabsorption coupled to sodium. The increase in urinary protein excretion in preeclampsia occurs secondary to alterations in the size and/or charge selectivity of the glomerular filter, possible increases in glomerular capillary pressure, and compromise of proximal tubular reabsorption. The renal histologic lesion characteristic of preeclampsia is termed "glomerular endotheliosis"[18] . Recent evidence suggests that anti-angiogenic factors emanating from the placenta in preeclampsia contribute to glomerular endotheliosis, proteinuria, and hypertension during disease. [19]. An additional possibility has been suggested that uric acid might itself be causally related to hypertension as might increase hypertension by increasing salt sensitivity and vascular smooth muscle proliferation.

This result were in accordance with the observation of(Suchanda and Kiyomiet. *al*) [14,20].

Increase in serum urea ,serum creatinine and reduction in cratinine clearance were observed in women with preeclampsia[table2]these differences were significant compared with normotensive pregnant women because preeclampsia is associated with a reduction in plasma rennin activity (PRA) and plasma rennin concentration (PRC) if compared with normal pregnancy [21], while the circulating level of angiotensin II may be normal during preeclampsia [22].

Other studies found that reducing uteroplacental perfusion pressure could increase the renal sensitivity to angiotensin II through reduction in NO or prostacyclin synthesis or by enhanced formation of TXA2 and endothelin [23]

The enhanced responsiveness leads to a significant elevation in total peripheral resistance and marked reduction in renal blood flow [24]. Recent studies showed that the systemic and renal vasoconstriction in preeclampsia is due to an increase in the serotonin level and enhanced sensitivity to serotonin [25]

Other investigators found that the activity of mono amino oxidase (MAO) is lower and serotonin is higher in the placental tissue from women with preeclampsia as compared with placental tissue from normal pregnant women [25-26]. These factors lead to a reduction in renal perfusion in a women with PIH, by an average of 20% and reduction in GFR by an average of 32% in comparison with normal pregnant women near term [27]. So, as a result of reduced GFR, serum creatinine levels and blood urea rise above normal pregnancy levels [28].

The reduction in creatinine clearance has been attributed to the diminished renal blood flow which is caused by the increase in the glomular resistance, either by mechanical effect of swelling in the cytoplasm, or by an alteration in the metabolism [29].

Present studies show that the total protein to creatinine ratio in preeclampsia increases markedly. Also albumin to creatinine ratio increased, this finding suggest that glomular barrier function is impaired in preeclampsia [30].

These results were compatible with the observations of (Pervin *et. al.* ,Wikstrom*et.al.* and Saylik*et. al*)who found a significant negative correlation between creatinine clearance and S.urea, S.creatinine [31, 32,33] .

Hussein et al and Salako,*et al* who found that no significant difference in the mean value of creatinine in preeclamptic and normotensive pregnant women [34,35].

Conclusions

Renal involvement is common complication of hypertension in pregnant women . It is important to asses renal function tests especially serum uric acid for all pregnant women have high blood pressure as it is the first change and denoter for effecting of renal function in preeclampsia cases.

Table (1)The characteristics of the study groups.

Characteristics	Pregnant (n=50)	Pre-eclamptic (n=50)
Systolic B.P, mmHg	106 ± 2	157 ± 4
Diastolic B.P, mmHg	61 ± 1.6	103 ± 2
Urine protein by dipstick	0	+ 2→ +3

Table(2)Comparison of the renal biochemical parameters (MEAN ± SD) between the pregnant and preeclamptic women

Parameters	MEAN ± SD		P-Value
	Pregnant (n=50)	preeclampsia (n=50)	
S.Urea (mmol/L)	2.48 ± 0.62	4.72 ± 1.01	P < 0.05
S.Creatinine (µmol/L)	56.61 ± 8.2	88.8 ± 12.49	P < 0.05
S.Uric acid (µmol/L)	207.55 ± 22.85	370.83 ± 48.57	P < 0.01
Creatinine clearance (ml/min)	125.30±15.14	103.6±29.63	P < 0.05

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