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Original Research Article

The Role of Potassium to Creatinine Ratio as Diagnostic Test in Pre-Eclampsia

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Abstract

Pre-eclampsia is defined as hypertension associated with proteinuria arising *de novo* after the 20th week of gestation in a previously normotensive woman and resolving. completely by the 6th postpartum week. It is a major cause of morbidity and mortality during pregnancy. There are many ways to diagnose the disease, based on clinical diagnosis and conduct some tests; measurement of the amount of protein in urine sample that had been collected for a period of twenty-four hours. Evaluate urinary K^+ to creatinine ratio as a diagnostic and screening test in PE.

Our study was carried out at Babylon Teaching Hospital for Gynecology and Pediatrics, in Babylon Province, Hilla City from February-August- 2016. The total number of all cases was 88,44 among them women with normal pregnancy, 44 cases with PE.Every patient was sent for urinary K^+ and creatinine in spot urine which both were determined by ion selective electrode and Moorehead and Briggs derived *O*-Cresol Pthalien Complexone method respectively, and the ratio K^+ to creatinine were calculated. Data are given as mean ± SD, and t-test were used as statistical method to test the result. Urinary K^+/creatinine ratio was significantly higher in patients with pre-eclampsia compared to control groups (*P value* <0.01). The sensitivity of urinary K^+/creatinine ratio to detect PE was (77%) while, its specificity was (68%).

Urinary K^+/creatinine ratio is significantly increase in preeclamptic women.

Key Words: Pre-rclaqmpsia, urinary Potassium, urinary Creatinine, K^+ /creetinine ratio.

الخلاصة

تسمم الحمل (ما قبل الأرتعاج) هو ارتفاع ضغط الدم المرتبط بارتفاع البروتين بالإدرار بعد الأسبوع ٢٠ من الحمل في المراة ذات ضغط الدم الطبيعي سابقاً و الذي ينتهي تماماً قبل الأسبوع السادس بعد الولادة. وهو سبب رئيسي للوفاة أثناء الحمل. هناك طرق كثيرة لتشخيص المرض، تعتمد على التشخيص السريري وإجراء بعض الفحوصات وفحص مسحي يتضمن قياس كمية الزلال الموجود في نموذج إدرار تم جمعه لمدة أربع وعشرين ساعة.

الغرض من الدراسة هو حساب نسبة البوتاسيوم إلى الكرياتينين في نموذج إدرار عشوائي كفحص مسحي وتشخيصي لمرض ما قبل الإرتعاج.

تم إجراء هذه الدراسة على مجموعة من المرضى في مستشفى بابل التعليمي للنسائية والأطفال، في محافظة بابل، مدينة الحلة. وقد تم جمع العينات من شباط ٢٠١٦ حتى آب ٢٠١٦. شملت الدراسة مقارنة الحالة ل ٨٨ امرأة، أربع وأربعون حالة مرضية تم تشخيص إصابتهم بمرض ما قبل الإرتعاج والأربع واربعين الأخرى من نساء حوامل صحيحة وقد تم أخذ عينات إدرار عشوائية من كل الحالات لغرض إيجاد البوتاسيوم والكرياتينين في الإدرار وبعد ذلك حساب النسبة بينهما وقد تم إجراء عمليات إحصائية متعددة للحصول على النتائج وقد وجد مايلي: نسبة البوتاسيوم إلى الكرياتينين كانت مرتفعة بشكل معنوي في المرضى الذين يعانون من تسمم الحمل مقارنة بالأصحاء قيمة ($P < 0.01$). وكانت قيمة االخصوصية (٧٧%) بينما القيمة النوعية كانت (٦٨ %).

الكلمات المفتاحية : تسمم الحمل ، البوتاسيوم في الإدرار ، الكرياتينين في الإدرار ، البوتاسيوم الى الكرياتينين.

Introduction

Pre-eclampsia (PE) is defined as hypertension associated with proteinuria arising de novo after the 20th week of gestation in a previously norrmotensive woman and resolving completely by the 6th postpartum week . It is a leading cause of fetal and maternal morbidity and mortality [1].

Pre-eclampsia is an idiopathic disorder of pregnancy. Recent studies indicate that over 63000 women die worldwide each 3year due to PE and its complications, with 98% of them occurring in developing countries. In UK, PE is the second most common cause of both direct maternal death and perinatal loss, responsible for the death of six to nine women annually and over 175 babies. More than 10% of women will have PE in their first pregnancy and although the majority of these will have successful pregnancy outcomes, the conditions can give rises to severe multisystem complications including cerebral haemo-rrhage, hepatic and renal impairment and respiratory compromise. The development of strategies to prevent and treat the disorder has been challenging due to an incomplete understanding of the underlying pathogenesis [2-5].

Symptoms which predicate imminent eclampsia including headache, visual disturbances, epigastric andright upper abdominalpain or may be asymptomatic **[6]**. Signs is included elevation of blood pressure, fluid retention, brisk reflexes and uterine and fetal size may be feel smaller for gestational age [7].

A two-stage model of PE has been proposede as a means of addressing it's pathophysiology. The first was placental perfusion reduced in PE. Evidence for this came originally from clinical findings. The second was The clinical features of PE appear to arise from a generalized systemicc inflammatory response, of which endothelial dysfunction is a prominents components. Several serum markers of endothelial activations are alterede in women with PE, including Von Willebr and antigen, cellular fibronectin, and endothelin [8-12].

The relation between two stages is completed before the 20th week and prior to the appearance of clinical signs. In the second and third trimesters of pregnancy, the placenta requires increasing access to the maternal blood supply. As a result of the first stage, leading to a reduced uterine perfusion, the placenta becomes increasingly hypoxic. This hypoxic and dysfunctional aplacenta is considered to release factors into the maternal circulation that eventually cause the clinical features of PE. These released factors act as the linkage between the two stages and their identifications could hopefully enable the development of therapies for prevention of the clinical stages development [13,14].

Potassium (K^+) is an essential mineral micronutrient and the main intracellular ion for all types of cells. It is important in maintaining fluid and electrolyte balance in the bodies of humans and animals **[15]**. The body in steady state K^+ balance with K^+ intake (normally 60-80 mmol/day) equal to K^+ excreetion. The kidney excrete the bulk of ingested K^+ (renal excration 50- 65 mmol /day, stool 10-15 mmol/day, and small amount is lost via the skin in sweat). Urinary K^+ excretion rises in response to increased intake. Under normal circumasance, 180 L plasma are filtered per day, resulting in the entry of 720 mmol K^+ in the lumen of the nephron. The majority of the filtered K^+ (around 500 mmol) is reabsorbed in the proximal tubule. The control of K^+ secretion occurs primarily in the principle cells of the cortical collecting duct. K^+ secretion is dependent on the delivery of Na^+ and water to the cortical collecting duct and on the action of hormone aldosterone. Aldosteron increases Na^+ reabsorption from the lumen and promotes K^+ secretion into the lumen, restoring electrical neutrality [16-18].

Creatinine is formed from creatine and creatine phosphate in muscle and is excreted into the plasma at a constant rate related to muscle mass. Plasma creatinine

is inversely related to GFR and, although an imperfect measure, it is commonly used to assess renal filtration function Small amounts of creatinine are secreted by the proximal tubule and reabsorbed by the renal tubules [19-21]. A creatinine urine test can measure amount of creatinine in urine. It can be done on its own or with other tests that establish the amount of other substances in the urine [22].

Materials and Methods

This prospective study was carried at Babylon Teaching Hospital for Maternity and Children, Babylon Province, Hilla City from February 2016 till August 2016. 88 cases were divided into two groups: 44 of them were patients diagnosed with PE in the 2nd and 3rd trimester and the other 44 normal pregnancy.

The following inclusion criteria were followed: pre-eclampsia was diagnosed by blood pressure elevation equal to or more than 140/90 mm Hg in combination with protienuria ++ and/or oedema after 20 weeks gestation in previously normotensive non protienuric patients. Their ages ranges from 21 – 30 years, the gestational ages from 21 – 37 weeks..

The exclusion criteria were: Age over 35 years, multiple pregnancy, history of essential hypertension, diabetes mellitus, renal disease, hepatic disease, blood disorder, epilepsy and other medical disease, body mass index > 30, and any history of drug intake other than supplement.

Body mass index (BMI) was calculated as: BMI = Weight (kg) / Height (m^2) [23]. Blood pressure was recorded in the study in the sitting position with cuff that is large enough for the subjects arm on at least 2 occasions 6 hours apart. Protienuria was diagnosed by collecting clean catch mid-stream urine sampled in clean dry container then urine protein was determined using the strips [Albustix] reading at 2+ [1 gm/l] or more was considered to be positive result for protein urea, the urine samples were centrifuged at 1000 g for approximately 5 minutes then the supernatant was taken to estimate of potassium and creatinine, by using electrolyte analyzeris dependent upon the ion selective electrode principle, and spectrocolormetric method Jaffe reaction respectively **[24,25]**. K^+/creatinine ratio was calculated by the following equation: Result of K^+ (mmol/L) / Result of creatinine (g/L). Unit of the ratio: mmol/g. Data are given as mean ± SD, and t-test were used as statistical method to test the result. All analyses were performed using commercially available software (SPSS version 20th). P-value of <0.01was considerede to be statistically significant.

Results

Table 1 showed the mean differences of socio-demographic characteristic including (age, body mass index and gestational age) between to studied groups (patients with PE and control group).

Table 1: The Mean Differences of Socio-Demographic Characteristics in Studied Groups

Variable	Study groups	No.	Mean ± SD	*P*-value
Age (years)	**preeclampsia**	44	26.18 ± 2.67	> **0.01**
	control group	44	25.75 ± 2.91	
BMI (kg/m^2)	**preeclampsia**	44	28.22 ± 1.11	> **0.01**
	control group	44	28.56 ± 1.41	
Gestational age (weeks)	**preeclampsia**	44	29.79 ± 3.23	> **0.01**
	control group	44	28.77 ± 4.95	

*p value < 0.01 was significant

There were no significant differences between means of age, body mass index and gestational age (*P*. value > 0.01).

Table 2: The Mean Differences of Systolic and Diastolic Blood Pressure in Studied Groups.

Variable	Study groups	No.	Mean ± SD	P-value
Systolic blood pressure (mmHg)	**preeclampsia**	44	147.5 ± 8.03	**< 0.01***
	control group	44	123.59 ± 5.14	
Diastolic blood pressure (mmHg)	**preeclampsia**	44	89.31 ± 5.23	**< 0.01***
	control group	44	61.13 ± 3.38	

*p value < 0.01 was significant

Table-2 showed that there were significant differences between means of systolic and diastolic blood pressure in studied groups.

Figure-1 shown there were statistically significant difference between the mean of K^+/creatinine ratio (mmol/g) between controls (77.88 ± 9.16) and patients (84.51 ± 4.21) (**P< 0.01**).

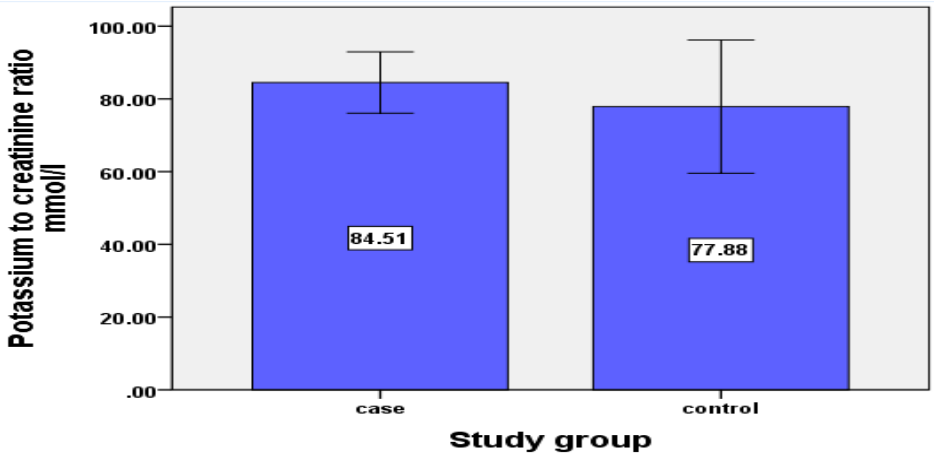

Figure 1: Mean Differences of Potassium to Creatinine Ratio (mmol/g) in Studied Groups.

Table-3 showed the sensitivity and specificity of potassium to creatinine ratio findings in comparison to clinical diagnosis. The sensitivity of potassium to creatinine ratio to detect preeclampsia was (77%) that mean the positive result of potassium to creatinine ratio (81.2 mmol/g or more) was able to detect approximately (77%) of patients with PE correctly meanwhile, its specificity was (68%) that mean the negative result of potassium to creatinine ratio was able to detect approximately (68%) of those women with normal blood pressure correctly.

Table 3: Comparison of Potassium to Creatinine Ratio Findings Versus Clinical Diagnosis of Pre-eclampsia

Potassium to creatinine ratio findings versus Clinical Diagnosis		**Clinical diagnosis**		**Total**
		Preeclampsia	**Normal pregnancy**	
Potassium to creatinine ratio (mmol/g)	positive	34	14	48
	negative	10	30	40
	Total	44	44	88

Sensitivity = (34/44) ×100 = 77.3%
Specificity = (30/44) ×100 = 68.2%
Overall accuracy = (34+30/88) ×100 = 72.7%

Discussion

Urine collection is more reliable than other methods to assess potassium consumption in this study, the ratio of K^+/creatinine was measured and the results that emerged showing an increased in potassium excretion in patients with PE compared with normotensive pregnant women. This might be due to activation of rennin angiotensin system that lead to increased production of aldosterone and consequently increase in K^+ excreation in urine. Increased dietary intake of vegetables and fruit (rich potassium intake) that cause increase excreation of K^+ in urine **[26]**.

Using a cutoff value of urinary K^+/creatinine ratio at 81.2 mmol/g, the

sensitivity was 77% and specificity was 68%. So the K^+/creatinine ratio in patient with PE has low sensitivity and specificity so it can't be used as a diagnostic or screening test.

Conclusion

Urinary K^+/creatinine ratio is significantly increased in pre-eclamptic women, but it can't be used as a diagnostic or screening test.

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