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Estimation of plasma uric acid in pregnancy induced hypertension (PIH). Is the test still relevant?

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Summary

Plasma uric acid and creatinine were estimated at each visit of 59 consenting women attending ante-natal clinic. Results in the third trimester of pregnancy confirmed that the plasma uric acid was able to differentiate between normal pregnancy and those with PIH at $P < 0.002$. The results of those with ordinary hypertension and the women who developed pre-eclampsia were similar. Plasma creatinine was found to be able to differentiate between women with ordinary hypertension (97.45 ± 25.03 umol/L) and those with pre-eclampsia (288.75 ± 191.97 umol/L) at $P < 0.01$. For patients with pre-eclampsia who developed convulsions, there invariably was a further rise in the plasma uric acid levels. Monitoring of plasma creatinine level among patients with PH will help to predict those at risk of developing pre-eclampsia. In the same way, monitoring of plasma uric acid level in those with pre-eclampsia will help to predict those that will develop eclampsia. The tests are inexpensive but sensitive, which is in contrast to many more expensive electronic alternatives.

Keywords: *Pregnancy-induced hypertension, pre-eclampsia, eclampsia, uric acid, creatinine, fetus.*

Résumé

Le taux d'acide urique et de creatinine dans le plasma avait ete estime a chaque visite chez 59 femmes lors des visites prenatales. Les resultals au troisieme trimestre de grossessese a montre que le taux d' acide urique dans le plasma a ete capable de differentie entre les grossesses normales et celles avec Hypertension gestationelle (HTG) *(P < 0.002)*. Les resultats de celles qui avaient une hypertension simple et celles qui avaient une pre-eclampsie etaient similaire. Le taux plasmiqure de creatinine montrait la difference entre les femmes avec l'hypertension simple (97.45 ± 25.03 Umol/L) et celles avec pre-eclampsie qui developaient des convulsions, il y avait invariablement une augmentation de taux d'acide urique dans le plasma. Le control du taux de'creatinine dans le plasma chez le patients avec HTG aidera a prevenir celles a risque de developer une pre-eclampsie. De la meme maniere, le control de taux d'acide urique dans le plasma chez les patients avec pre-eclampsie aidera a prevoir celles qui pourront developer une eclampsie. Ces testes sont moins chere et sensitifs contrairement aux autre testes electroniques tres couteux.

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Introduction

Uric acid is the end product of purine catabolism in humans. Its production is mostly in the liver which has a high activity of xanthine oxidase, as does the intestinal mucosa [1]. Several cases were described in which the nitrogenous waste products measured in the serum of patients with pre-eclampsia and eclampsia suggested that these waste products presented a 'staircase' effect [2]. In pregnancy, a minimal involvement of the kidney causes an increase in the uric acid level while urea and creatinine are still normal. A moderate involvement of the kidney led to an increase in both urea and uric acid while the creatinine level remained normal. It is only in severe kidney involvement that the creatinine values are elevated in pregnancy [2].

Since these early studies, hyperuricaemia has been recognised as a biochemical index of pregnancy-induced hypertension (PIH) [3]. The higher the rise in the level of uric acid, the more severe the clinical condition [4]. The level has also been used as an index of fetal prognosis [5,6]. Low serum uric acid levels are found in early and mid-trimester of pregnancy rising to non-pregnant levels in the third trimester [7,8,9]. The excretion of creatinine and uric acid reach a maximum before the thirty- second week of normal pregnancy and then decrease during the last few weeks before delivery [3]. These normal variations must be considered where one is attempting to evaluate results of tests of patients with abnormal levels.

Suggestions as to the cause of the reduced uric acid excretion and therefore increase in uric acid in PIH is as varied as the cause of PIH itself. Vasospasm and reduced intravascular volume which leads to reduced renal blood flow seems the most plausible [10]. These in turn will cause reduced secretion and increased reabsorption of uric acid from renal tubules.

This study was undertaken to confirm if measurement of plasma uric acid can differentiate between a normal pregnant woman and a woman with PIH, and if the level of plasma uric acid can be used to differentiate the various stages of PIH.

Materials and method

Fifty-nine consenting primigravidae (mean age 23.9 ± 5.0 years) attending the ante-natal clinic of the Lagos University Teaching Hospital were recruited in their first trimester. Some were referrals from private clinics in their second trimester. The standard procedure was followed at each visit. Plasma uric acid and creatinine were the analytes of interest in the laboratory investigations. A modified uricase method incorporating 3,5-dichloro–2-hydroxybenzene sulphonic acid and 4-aminophenazone was used for the uric acid estimation [11]. The specific uricase method was preferred because approximately 11% of the colour produced by phosphotungstate reduction in filtrates of plasma resulted from other substances other than uric acid [12]. Another advantage is that haemoglobin up to 1 g/L and bilirubin up to 340 umol/L in serum do not affect the determination [11] which is an advantage in eclamptics with haemolysis. Creatinine was analyzed using the Jaffe reaction [13].

The women were divided into four groups depending on the outcome of pregnancy, (normal pregnancy and the three stages of PIH). Pregnancy-induced hypertension is defined as, "hypertension that develops as a consequence of pregnancy, and regresses postpartum" [14]. It is subdivided into: (a) Hypertension without proteinuria or pathological oedema (ordinary hypertension):(b) Pre-eclampsia – with proteinuria and/or pathological oedema - mild or severe, and (c) eclampsia - proteinuria and/or pathological oedema with convulsions or coma

Group A (Normal pregnancy – 34 cases)
These cases had a blood pressure below 140/90 mmHg throughout the duration of pregnancy. They had little or no dependent oedema and no proteinuria.

Group B (Ordinary hypertensives – 9 cases)
Patients in this group had blood pressure of 140/90 mmHg and above taken on more than two occasions – days apart. Some of the cases in this group had little dependent oedema but no proteinuria.

Group C (Pre-eclampsia – 10 cases)
This group had hypertension as defined for group B. In addition, they had mild to moderate pathological oedema and proteinuria above 0.3 g/L (semi-quantitiative test).

Group D (Eclampsia – 6 cases)
Cases in this group had blood pressure of 160/110 mmHg or more. They also had widespread pathological oedema and proteinuria above 1.0 g/L (semi-quantitative test) with convulsions or coma.

Statistical analysis
The student t test, a parametric test and Wilcoxon rank test, a non-parametric test, were used to find out the

Table 1: Mean plasma uric acid levels of pregnant women in the third trimester

Group	Number	Plasma uric acid Mean ± SD (umol/L)	þ Values (differences between groups)
A: Normal	34	270.53 ± 53.25	
B: Ordinary hypertensive	9	431.67 ± 123.33	A and B þ ∠ 0.002
C: Pre-eclampsia	10	419.30 ± 136.91	A and C, þ ∠ 0.003
			B and C, Not significant
D: Eclampsia	6	668.67 ± 141.28	A and D, þ ∠ 0.000
			B and D, Not significant
			C and D, þ ∠ 0.002

Table 2: Mean plasma creatinine levels of pregnant women in their third trimester

Group	Number	Plasma creatinine Mean ± SD (umol/L)	þ Values (Differences between groups)
A: Normal	34	86.03 ± 32.93	
B: Ordinary hypertensive	9	97.45 ± 25.03	A and B, Not significance
C: Pre-eclampsia	10	288.75 ± 191.97	A and C þ ∠ 0.001
			B and C þ ∠ 0. 01
D: Eclampsia	6	278.45 ± 81.25	A and D þ ∠ 0.001
			B and D þ ∠ 0.001
			C and D, Not significant

significance of the difference among means of the groups with a "Statistix" software. The one-way analysis of variance (ANOVA) was also used to confirm the differences among the means with the software "SPSS/PC+". Significance was at the 5% level. Means, standard deviations and p-values of the student t test are reported.

Result

Complete results of the plasma uric acid estimations in the third trimester are presented in Table 1 The results show that Group A had a mean plasma uric acid level of 270.53 ±53.28 umol/L at the third trimester of pregnancy. This result was not statistically different from the mean of the non-pregnant females(student nurses with a mean age of 24 ±2.9 years) which was 281.27 ±50.64 umol/L. There was no significant difference between the ordinary hypertensives in Group B (431.67 ±123.33) and the women who developed pre-eclmpsia in Group C (419.30 ±136.91) The highest mean plasma uric acid level was attained by the women with eclampsia in Group D, 668.67 ±141.28 umol/L. This was significantly different from the mean of those in Group C at $P < 0.002$.

Table 2 shows the mean plasma creatinine values in the four groups. There was no significant difference between Group A with 86.03 ±32.93 umol/L, and Group B, 97.45 ±25.03 umol/L. The mean creatinine value for Group C was significantly much higher than those for Group A ($P < 0.001$) and Group B ($P < 0.01$). Group D also had much higher mean creatinine value than Groups A and B at $P < 0.001$. There was no significant difference between Group C with 288.75 ±191.97 umol/L and Group D who had 278.45 ±81.25 umol/L.

Discussion

Pregnant women are usually not sensitive prostaglandins [10]. Development of sensitivity to this substance has been thought to be what leads to vasospasm in PIH [10,15]. The vasospasm leads to reduced blood flow to the uterus and other organs inducing hypertension [10,15,16,17]. There are other conditions in pregnancy which mimic and can be confused with PIH, such as, pre-existing hypertension, chronic renal disease and primary seizure disorders. Plasma uric acid levels are helpful in differential diagnosis since hyperuricaemia is uncommon in pregnancy except in cases with gout, renal failure, sickle cell anaemia or PIH. The first three are relatively easy to diagnose by clinical and established laboratory means.

Table 1 confirms that a woman who develops PIH has a marked increase in the plasma uric acid level. Monitoring of plasma uric acid level cannot be able to predict women who are at risk of developing pre-eclampsia from among women with increased blood pressure in pregnancy. Pre-eclampsia occurs primarily after the 20th week of gestation and most frequently near term [10]. Plasma creatinine estimation has been shown in this study to be able to discriminate pregnant women with ordinary hypertension who will develope re-eclampsia (Table 2). It cannot predict who among the women with pre-eclampsia will have eclampsia. Monitoring of the plasma uric acid level among women with pre-eclampsia will be able to predict those that will develop convulsions or coma. A pre-eclamptic patient with a plasma urate level above 500 umol/L is more likely to develop eclampsia than those with lower values. Bed rest is the traditional cornerstone of preventive managdment, though the plasma uric acid level between pre-eclamptic patients who were on bed rest and those who were ambulant showed no difference [18].

More than one hundred clinical, biophysical and biochemical tests have been reported to predict pre-eclampsia [19]. Unfortunately, most suffer from poor sensitivity, and none is suitable for routine use as a screening test in clinical practice. Plasma uric acid level, especially when combined with plasma creatinine measurements, can overcome such sensitivity problem.

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