ORIGINAL ARTICLE

Serum uric acid as predictor model for pre eclampsia

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Abstract:

Objective: To determine that serum uric acid as a predictor in pre-eclampsia during pregnancy. To determine fetal and maternal outcome in pregnancy with hypertension.

Study design: Case control study.

Setting: Gyne Unit-2, Civil Hospital Karachi.

Duration: 8 months (1st March 2008 to 30 October 2008).

Patients and methods: 30-Cases of singleton primigravida with BP > 160/110 mmHg and 30-Cases of singleton primigravida with Normal BP 120/80 mmHg were studied at the time of delivery.

Results: Thirty Patients with pre-eclampsia taken along with thirty patients with normal BP, since higher proportion of un-booked woman in Pre-eclampsia group than normotensive group. Significantly low gestational age in Pre-eclampsia group mean is 34 weeks and 37 weeks for normotensive group. Mean age of marriage for both groups is 1-2 years in both groups. No difference in mean age in pre-eclampsia and normotensive group that may be due to duration of marriage and early marriage trend in our culture. History of hypertension is seen in 19 (63.3%) of patients. The average birth weight of patients with pre-eclampsia is 2.5 Kg and 3 Kg for normotensive group. Difference may be due to pre-term delivery in pre-eclampsia. Apgar score low in pre-eclampsia group. Increase caesarean rate is 93.3 % Vs 20 % in pre-eclampsia and normotensive group. This difference is due to the fact the caesarean section is considered to be safest mode of delivery for pre-eclampsia group. Uric acid level > 0.45 mmol/l was observed in 15 patients (50% of pre-eclampsia group) and 7 patients (23.3 % of woman with normal blood pressure).

Conclusion: Maternal hyper uricemia is a strong predictor of maternal disease progression and fetal outcome. Thus it can be used as useful and inexpensive marker of predicting pre-eclampsia and fetal growth retardation in women presenting with gestational hypertension.

Key Words: Pre-eclampsia, Maternal hyper uricemia, Fetal birth weight

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Introduction:

Pre eclampsia is characterized by a blood pressure of 140/90 mmHg on two separate occasion at least 4 hours apart, after the 20th week of pregnancy in a previously normotensive woman. This is accompanied by significant proteinuria (>300mg in 24 hours.) and resolves completely by sixth postpartum week.[1]

Pregnancy Induced Hypertension (PIH) occurs when new onset hypertension develops in the second half of pregnancy but in the absence of protinuria or any other feature of pre eclampsia.

Severe pre eclampsia is identified by a blood pressure of 160 /110 mmHg or more.

Eclampsia is a serious and life threatening complication of pre eclampsia. It is defined as convulsions occurring in a woman with established pre eclampsia.[1]

Imminent eclampsia, or fulminating preeclampsia, is the transitional condition characterized by increasing sign and symptoms.[1]

Pre eclampsia may be asymptomatic, symptoms include headache, visual disturbances or epigastric pain. Signs may include facial and peripheral oedema, hyper reflexia and right upper quadrant pain etc.

Hypertensive disorder complicates approximately 12% to 22% of all pregnancies. Gestational hypertension which includes pre-eclampsia and eclampsia is responsible for 70% of cases of where chronic hypertension represent 30% of hypertensive disorder of pregnancy. The exact incidence of pre-eclampsia is unknown but is approximately 5% to 8%.[2] Pre-eclampsia complicates 3 – 5 % of first pregnancies and 1% of subsequent pregnancies with 5 – 10% of cases being severe.[3,4,5]

Pre-eclampsia is a pregnancy specific syndrome and a leading cause of maternal and fetal morbidity and mortality. Clinically pre eclampsia is diagnosed by new onset gestational hypertension after the 20th week of gestation and proteinuria[6].

However pre eclampsia is a multi-systemic syndrome and far more than simply gestational hypertension and proteinuria. The presentation is very variable and can involve any organ predominantly, but hypertension and proteinuria are two signs most commonly present.[7,8,9]

In pre eclampsia, there is total or patchy failure of trophoblats invasion of myometrial segments of spiral arteries that interferes the fetal growth and oxygenation.

Identification of early pregnancy abnormalities that are associated with increased risk of pre-eclampsia would be useful to identify the women who require more monitoring which result in recognition of pre-eclampsia before life threatening complications develop. Bio chemical or hormonal changes are detectable in an early pregnancy that might also clarify the pathogenesis of super imposed eclampsia and ultimately lead to more specific mechanistically based prevention and treatment.[10]

Risk factors for the development of pre-eclampsia are broadly divided into maternal specific and fetal or pregnancy specific. These may include primigravida, multiple pregnancy, molar pregnancy,diabetes mellitus, chronic hypertension, previous history of pre eclampsia etc.

Serum uric acid an insoluble purine metabolite excreted from distal tubule is a marker of oxidative stress tissue injury and renal dysfunction.[6] The kidney is responsible of 2/3rd of total excretion is dependent upon the filtered load and the balance between proximal tubular secretion verses re-absorption. . Isotopes study have demonstrated that 18-12% of lost uric acid is not excreted in the urine but is degenerated to CO2 and ammonia and is excreted in the stool where it can be further metabolized by intestinal flora. Some uric acid excreted in the bile and subjected to de-generation by intestinal flora. The normal serum uric acid level is 3-7.5 mg/dl in a non-pregnant woman serum uric acid levels are 25-30% lower in normal pregnancy raising towards non pregnant level in the third trimester.[11]

Uric acid merely identifies more specific form of eclampsia.[12] Increments in urate level have been demonstrated to co-relate with the severity of pre-eclamptic lesion in renal biopsy, the degree of utero-placental vascular pathology, and the poor foetal outcome.[13,14] Redman et al clearly demonstrated that hyperuricemia was associated with a significant increase in peri-natal mortality. The result of many studies, but not of others (reviewed by Dekher and sibai, 1991), suggest that serum uric acid levels may begin to rise before the appearance of proteinuric hypertension. In most patients the increase in urate level appears to coincide with the increase in the blood pressure and proceed the development of proteinuria stage of the disease. As such, uric acid levels have been used for early diagnosis of pre-eclampsia.

In conclusion, uric acid is one of the most sensitive indicators of the disease severity in pregnan-

cy-induced hypertensive disorders and can be of great help in monitoring the cause of disease process. Redman et al demonstrated that for a given blood pressure level, a plasma urate level above 0.35 mmol/L (6,g/dl) identified a sub group of pre-eclampsia with a tenfold increase in perinatal mortality.[14] Uric acid is an indicator of disease severity in established pre eclampsia[7]. But the value in prediction and early diagnosis still not established.

The focus of current study is to determine the pattern of serum uric acid across the gestation and to evaluate the clinical utility of serum uric acid in the cases of gestational hypertension and pre-eclampsia in predicting maternal and fetal outcome.[7] Significant hyper uricemia greater than 2 baseline values in a pregnant women is an indication for intensive maternal and fetal monitoring.

In their near term labour should be induced in case of hypertension associated with significant hyper uricemia.[14]

The purpose of this study is to determine the values of serum uric acid as a screening test for pre-eclampsia.[7]

The rationale of this study is to evaluate the clinical utility of serum uric acid measurement in the cases of gestational hypertension in pre-eclampsia.

Results:

An increased uric acid (>0.45 m.mol/1) was observed in 15 (50%) women of PIH group and 7 (23.3%) women of normotensive women that reveals significant association of uric acid abnormality with PIH (2=4.59, p=0.032) as shown in Figure 1.

Apgar score at 1 minute and 5 minutes was found significantly higher in normotensive group (p=0.042 and p=0.037 respectively), that revealed significantly good apgar score in normotensive group than PIH group (Table 2).

Out of 30 women of PIH group, 22 (73.3%) were unbooked and only 8 (26.7%) were booked while in normotensive group 19 (63.3%) were booked and 11 (36.7%) were unbooked. Data reveals significantly high number of unbooked women in PIH group than normotensive group (2=8.15, p=0.004)

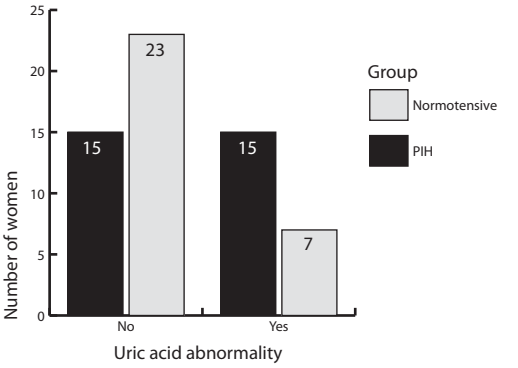
Mean maternal age of women of PIH group was 25.67±4.11 years and of normotensive group was 25.87±4.05, that reveals significant difference of mean maternal age between two groups (p=0.850)

Mean gestational age at the time of delivery of PIH group was 34.30±4.04 weeks and of normotensive group was 37.03±1.94 weeks, that reveals significantly less mean gestational age of women with PIH group (p=0.001).

Out of 30 women of PIH group, 16 (53.3%) women got marry for last one year, 10 (33.3%) for couple of years, 3 (10%) for last three years and only one (3.3%) woman had duration of marriage of 9 years. Among 30 women of normotensive group, almost same pattern was observed except one lady who had duration of marriage of 9 years (p=0.572).

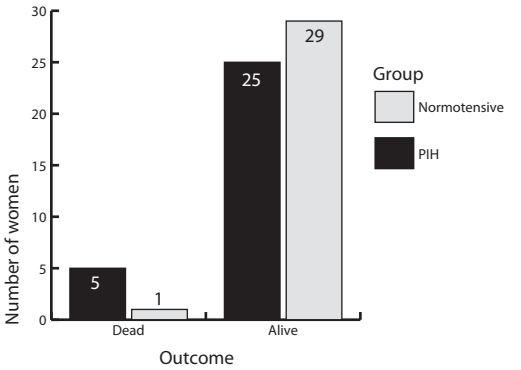
History of hypertension was present in 19 (63.3%) women of PIH group only, 12 (40%) women were on anti-hypertensive drugs. Headache was reported by 28 (93.3%) women of PIH group, visual disturbance was found in 12 (40%) women of PIH group and reflexes were found in 15 (50%) women of PIH group only.

Figure 1: *Comparison of uric acid abnormality between PIH and normotensive groups*



Significant association of uric acid abnormality with PIH (x^2=4.59, p=0.32).
PIH=Pregnancy induced hypertension

Figure 2: *Comparison of fetal outcome between PIH and normotensive groups*



Significant difference between two groups (Fisher's exact test, p=0.195).
PIH=Pregnancy induced hypertension

Mean systolic blood pressure of PIH group was 156.5 ± 17.1 which was significantly higher than the mean of normotensive group was 117.7± 5.04 (p<0.001). Mean diastolic blood pressure of PIH group was 103.0 ± 7.94 which was significantly higher than the mean diastolic blood pressure of 76.3 ± 5.07 (p<0.001).

Urine DR indicated significant number of women of PIH group was AL+ while only one woman of normotensive group had AL+. Abnormal LFT was found in 2 (6.7%) women of PIH group and PT/ APTT positive was in only one (3.3%) woman of PIH group

Per abdominal findings have shown significantly high proportion of before term women in PIH group than normotensive group (p<0.001).

Per vaginal findings have shown that significantly high proportion of long duration of labor in PIH group than normotensive group (p<0.001).

Table 1: *Comparison of sex and birth weight of baby between PIH and normotensive groups*

Finding	PIH N=30	Normotensive N=30	p-value
Sex			0.605
Male	16 (53.3)	13 (43.3)	
Female	14 (46.7)	17 (56.7)	
Mean neonatal weight (kg)	2.35=1.04*	3.10±0.82	<0.001

**Shows significantly low mean at 5% level of significance*

Table 2: *Comparison of neonatal APGAR score between PIH and Normotensive groups*

Variable	PIH N=100	Normotensive N=100	p-value
Apgar score at 1 minute	7.47± 1.32	7.78 ±0.73	0.042
Apgar score at 5 minute	8.58 ± 1.42	8.91 ±0.68	0.037

Significantly high proportion of PIH group than normotensive group were delivered with caesarean section (93.3% vs. 20%). In the group of 30 women with PIH, 5 (16.7%) fetal deaths were took place while only one (3.3%) fetal death in the group of 30 normotensive women, however this difference was statistically insignificant between two groups (p=0.195).

Of 30 PIH mothers, 16 (53.3%) were male babies and 14 (46.7%) female babies while of 30 normotensive mothers, 13 (43.3%) were male babies and 19 (56.7%) were female babies. Data reveals statistically insignificant difference of gender distribution was observed (p=0.605). However, mean neonatal birth weight was significantly low in PIH group than normotensive group (2.35 ± 1.04 vs. 3.10 ± 0.82, p<0.001).

Discussion:

Our study suggest that the increased severity and longer duration of hypertension may be the primary pathophysiologic mediator of adverse perinatal effects in pregnancy but maternal hyperuricemia is a marker which can be used not only to predict maternal disease progression from gestational hypertension to pre-eclampsia but also a reliable guide line to fetal prognosis.[12]

Increased uric acid (>0.45 mmol / 1) was observed in 15 (50%) woman with PIH and 7 (23.3%) of woman of normotensive B.P that reveals significant association of uric acid abnormality with PIH predictive value given by Warfis A. Hallark M. is 33% given in High risk pregnancy book.[2]

The prediction in this case varies, these studies shows that there is association with the development of pre-eclampsia with increased uric acid level.

Apgar score studies showed that the baby born to normotensive are good than those born to PIH patients.

The incidence of low birth weight babies increased once the maternal plasma urate concentration crossed the normal level and this finding was in agreement with study done by Schuster et al. so that for comparison when the mean birth weight and the percentage of Intra uterine growth retardation and small for gestational age babies was compared in group of woman with gestational hypertension dividing them in those with low or normal level of serum uric acid and those with high serum uric acid all fetal parameters measured came out to be worst in the group with raised serum uric acid level as compared to those with normal serum uric acid level.

The average birth weight of patient with PIH is 2.5 Kg in my study the in normotensive patient the average weight is 3 Kg. In Augus P. Helseth et al. study the average weight for pre-eclampsia is 2.4 Kg and in normotensive is 3.0 Kg which is nearer to my study. This parameter supports my study.[10]

The majority of the patient in the study had pre-term deliveries. The main gestation age at the delivery of PIH group was 34.30+weeks and for normotensive group was 37.30 + week in my study, same results in Saeed G.Hamid R Khattak.[12] The gestational age at presentation of hypertensive woman of the three group study is between 31, 33 and 35 weeks. In my study the 16.7 % fetal death in PIH group only 3.3% in the group of normotensive, in Sameed G.Hamid R Khattak the I, II, III groups gestational hypertension. Gestational hypertension superimposed pre-eclampsia, pre-eclampsia the group three showed poor outcome.

The main maternal age of woman with PIH group was 25.67±4.11 and of normotensive group was 25.87±4.05 that reveals significant difference of mean maternal age between two groups where as Augus P. Helseth and friends demonstrated that mean maternal age for development of pre-eclampsia is 32.4±5.1 and normotensive is 32.5±5.5 age varies in my study than this study may be supported by other studies. This difference may be due to early marriage trend in our area and age of menarche.

The history of hypertension was present in 19 (63.3%) woman of PIH group only 12 (40%) woman were on anti hypertensive drugs. While as in Augus P. Helseth et al. The essential hypertension 6.8% and pre-eclampsia 16%.[10]

Woman with none of these risk factors had a probability of the development of super imposed pre-eclampsia is 16%, woman with one risk factor had a probability of 62% and a woman with all three risk factor had a probability of 86 %.[10]

Woman of PIH group 16 (53.3%) woman got married for last one year 10 (33.3%) for couple of years 3 (10%) for the last three years and only one (3.3%) woman had duration of marriage of three years. Among 30 of normotensive group same pattern was observed accept one lady had duration of marriage of nine years (p=0.572) as there is no association with duration of marriage and development of pre-eclampsia not supported by any other study.

In my study the Caesarean section rate is (93.3% vs. 20%), It varies with the study of Augus P.Helseth and friends.[10] The result comprises of (68% vs. 43%) in a patient with pre-eclampsia to normotensive patients. We considered cesarean as a safer mode of delivery to avoid further complications as in consensus with senior colleagues as well as preference by the patients

In my study the headache and visual disturbance found in 12 (40%) woman of PIH group and increased reflexes were found in 15 (50%) woman of PIH group. The other studies have not taken these parameters in consideration which are taken in my study.

In my study pre-eclampsia B.P > 160 mmHg >110 mmHg was taken and compare to group III patients of Sameed G.Hamid R Khattak.

Conclusion:

Pre-eclampsia is a pregnancy specific syndrome

and a leading cause of maternal and fetal morbidity and mortality.[6] Pre-eclampsia is a multi system syndrome and far more then simply gestational hypertension and protein urea. Identification of early pregnancy abnormalities that are associated with increased risk of pre-eclampsia would be useful to identify the woman who required more monitoring which result in recognition of pre-eclampsia before the life threatening complications developed.[10]

In our study the findings demonstrates that since higher proportion of unbooked woman in pre-eclampsia group, there is significantly low gestational age in pre-eclampsia group, most of the woman in both groups have 1-2 year of duration of marriage. There is no difference of mean age in pre-eclampsia and normotensive group that may be due to duration of marriage and early marriage trend in our culture. Higher caesarean rate in PIH group because caesarean is considered to be the safest mode of delivery in these patients.

Our study, in accordance with international literature confirms the clinical utility of serum uric acid as a marker with high predictive value to detect cases of gestational hypertension progressing to pre-eclampsia and at high risk of intra uterine growth restriction and poor fetal outcome. So that serial measurement of serum uric acid level in cases of gestational hypertension can define a group of pregnant woman exposed to greater danger of feto maternal complications. Since medical resources in our country are scarced serial measurement of serum uric acid in hypertensive pregnancies can bring forward a selected group of high risk woman to be treated by the obstetricians so that action can be taken before complications arises.[12]

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