Perinatal outcome in relation with laboratory findings in pregnancy induced hypertension(PIH)

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Abstract

Background: Perinatal mortality is an important indicator of the status of maternal and child health, the conditions of obstetric care and the level of economic development of a community. The perinatal mortality rate (PMR) reflects both the characteristics of reproductive health and the quality of antenatal care, delivery, and newborn care.

Objective: To find out the corelation between laboratory parameters with perinatal outcomes in PIH cases.

Method: 320 patients having an average systolic blood pressure ≥ 140 mm hg and/or diastolic blood pressure ≥ 90 mm Hg were included in the study and biochemistry parameters like serum AST, ALT analysed by UV kinetic, LDH by UV kinetic IFCC, Uric acid by modified Trinder's method and calcium by arsenazo III methods, were measured by Xl 300 autoanalyzer.

Result: In our study overall incidence of PIH was 14.3 %. Maternal death occurred in 09 cases(2.8%). Perinatal mortality occurred in 86(23.3%) with 57(17.8%) Stillbirth and 29(9.0%) Neonatal deaths. Low birthweight<2.5Kg 73(84.8%) was the common complication observed followed by prematurity 64(74.4%) and IUGR 40(46.5%) leading to perinatal deaths. PMR increased as the BP increased. It was 14.9% for BP 140/90 to 149/94, to 57.3 % at BP >160/110 and above (Table 2). Perinatal death increased significantly in PIH women with increased levels of serum AST, ALT, uric acid, LDH and with a significant decrease in serum calcium levels. Perinatal death occurred in 63(73%) cases with Uric acid >6.0 mg/dl, 48(55.8%) in cases with > 600U/l LDH and in 48(55.8%) cases with < 8.0 mg/dl Calcium.

Conclusion: A positive correlation has been made out between serum AST, ALT, uric acid, LDH, calcium and perinatal deaths in relation to the severity of PIH and these may be useful markers and diagnostic tools for predicting the progression of PIH

Keywords: Preeclampsia, uric acid, LDH, calcium, Perinatal mortality

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Introduction

PIH is the most important cause of maternal and neonatal morbidity and mortality. In developing countries they rank second only to anaemia with approximately 7-10% of all pregnancies complicated by some form of hypertensive disorder.(1,2,3) In India incidence of preeclampsia as recorded from hospital statistics vary widely from 5-15%.(4) Approximately 10-15% of maternal deaths in developing countries are associated with pre-eclampsia and eclampsia.(5) Intrauterine growth retardation (IUGR), pre-term delivery, low birth weight, foetal deathand neonatal death due to complications of pre-term delivery are common perinatal outcomes associated with pre-eclampsia. (6) Pre-eclampsia and eclampsia is still regarded as "a disease of theories" and its etiology is still obscured. Endothelial cell dysfunction appears to be a central feature in the pathophysiology of pre-eclampsia. (7) The analysis of a combination of biochemical markers particularly markers related to vascular dysfunction such as increased uric acid, LDH, AST concentration may enrich the ability to predict and prevent PE in near future. (8,9) Therefore the present study was designed to assess the association of different biochemical parameters like uric acid, LDH, AST, ALT and calcium with perinatal outcomes in PIH cases.

Materials & Methods

Study setting, study type: This prospective study was carried out in Obstetrics and Gynaecology department and Biochemistry department of Shree Krishna Hospital attached to Pramukhswami Medical College, Karamsad, Gujarat, India.

Study participants & study period: All pregnant woman admitted between January 2006- March 2008 in the hospital were examined. Blood pressure was measured by mercury sphygmomanometer in reclining position in right brachial artery. Three readings were taken at 10 minutes interval. Participants having average systolic blood pressure ≥ 140 mm hg and/or diastolic blood pressure ≥ 90 mm Hg were included in the study.

Exclusion criteria: Patients with history of hyperuricemia, diabetes, renal diseases, cardiovascular illness, and symptomatic infectious diseases were excluded.

Sample size and sampling: Purposively out of 2237 of total pregnant women admitted in SK hospital, Karamsad, in the defined study period, a total of 320 Participants having average systolic blood pressure ≥ 140 mm hg and/or diastolic blood pressure ≥ 90 mm Hg were included in the present study.

Definitions[10]: Pre-eclampsia is hypertension presenting after 20 weeks with significant proteinuria. Severe pre-eclampsia is pre-eclampsia with severe hypertension and/or with symptoms, and/or biochemical and/or haematological impairment. Eclampsia is a convulsive condition associated with pre-eclampsia

Data collection: After enrollment participants were grouped into preeclampsis, severe preeclampsia and eclampsia. Informed consent was taken from all the participants. The history of all participants was taken. Blood samples of participants were taken from right or left cubital vein and collected in plain vial. Serum Aspartate transaminase (AST) and Alanine transaminase (ALT) was measured by UV kinetic method (11). Uric acid was measured by modified Trinder's test(12), lactate dehydrogenase (LDH) was measured by UV kinetic IFCC (13) method and calcium by Arsenazo III method (14)

Participants were observed throughout pregnancy and maternal and perinatal outcome was observed. This study was approved by the institutional ethical committee.

Study variables: Predictor variables were ALT, AST, calcium, LDH and uric acid. The investigations were performed in the laboratory of Biochemistry department. Outcome variables were fetal complications or fetal death.

Statistical Analysis: The data were cleaned, validated and analyzed with the help of Epi info 7. We used unpaired,,t" test for comparing the mean level of uric acid, LDH, AST, ALT, calcium with perinatal outcome. p value < 0.05 was considered statistically significant.

Result & Discussion

The total number of 2237 patients were admitted for delivery during the period January 2006 to March 2008, 1990 were livebirths during the study period while 86 were perinatal deaths.

Pregnancy induced hypertension (PIH) was diagnosed in 320 patients. Thus the incidence of PIH is 14.3 % in our institution. The total number of livebirths in these participants were 269 which included 258 singleton births and 04 sets of twins and one set of triplets(Table:1). Maternal death was noted in 09 cases, MMR in our study was 4.5/1000 livebirths. Out of the 86 (26.8%) perinatal deaths, stillbirths 57(17.8%) and 29(9.0%) Neonatal deaths (NND) cases was noted (Table: 1).The perinatal mortality rate (PMR) due to PIH in this study was 43.2/1000 livebirths.

Table 1: Demographic data

OUTCOME	Preeclampsia N=117	Severe preeclampsia N=136	Eclampsia N=67	TOTAL N=320
Live births (with NND)	102 (37.9%)	107(39.7%)	43(15.9%)	269(84.0%)
SB	15 (26.3%)	21(36.8%)	21(36.8%)	57(17.8%)
NND	04(13.7%)	15(51.7%)	8(27.5%)	29(9.0%)
Total perinatal mortality	19(22.0%)	36(41.8%)	29(33.7%)	86(26.3%)
Twins	03(75%)	--	01(25%)	04(1.2%)
Triplets	--	01	--	01(0.31%)
Low Birth weight <1.5kg	16(26.2%)	24(39.3%)	20(32.7%)	61(19.0%)
Birthweight 1.5-2.5 kg	65(34.9%)	77(41.3%)	38(20.4%)	186(58.1%)
Birthweight >2.5kg	34(43.0)%	35(44.3%)	9(11.3%)	79(24.6%)
IUGR	42(21.2%)	124(62.2%)	29(14.6%)	198(61.8%)
Prematurity	42(29.5%)	53(37.3%)	42(29.5%)	142(44.3%)

Majority of perinatal deaths was observed in PIH mothers in the age group 20-35 age group 51(59.3%), in eclamptic women 29 (33.7%), 16(18.6%) having anemia<7gm, 60(69.7%) who had not taken ANC, 76(88.3 %) from Low socioeconomic group, 56(65%) in illiterates and 33(38.3%) were primigravida.

The incidence of perinatal death was higher in infants with Low birth weight<2.5Kg 73 (84.5%), out of which 35(40.6%) infants had Birth weight <1.5Kg, Preterm birth 64(74.4%) and IUGR 40(46.5%) are also the major complications leading to perinatal mortality.

Table 2: Perinatal mortality according to Blood pressure (BP)

	140/90 to 149/94mmHg	150/95 to 159/109mmHg	>160/110 mmHg
Number of cases	127	132	61
No. of perinatal mortality	19	32	35
PMR	14.9%	24.2%	57.3 %

Table 3: Comparision of Biochemical parameters in relation to perinatal death

Parameters	Live Mean ± SD	Death Mean ± SD	P value
ALT	37.20 ± 66.34	66.28 ± 134.6	0.010
AST	54.49± 137.7	108.33 ± 309.1	0.031
Uric acid	6.07 ± 2.08	7.38 ± 2.34	0.000
LDH	482.47 ± 188.8	667.56 ± 301.90	0.000
Calcium	8.67 ± 0.67	8.27 ± 0.70	0.000

Significance P value <0.05

Perinatal mortality rate increased as severity of PIH increased (Table 02), this observation was in agreement with other studies (15,16,17). Hypertension develops through increased chemokine and cytokine expression, induction of the renin-angiotensin system and increased vascular C-reactive protein (CRP) expression in mother (18). As the severity of the PIH increases, there is increase in the severity of the patho-physiological phenomenon leading to the accentuation of blood pressure. This elevated blood pressure recovers within one month postpartum suggesting that after expulsion of placenta which is said to be the reason for PIH, the altered physiology returns to the normal (17).

Table 4: Number (%) of prenatal complications in groups studied

		Calcium ≤8.0	Uricacid≥6.0	LDH ≥600
Perinatal deaths (n=86)	Perinatal deaths (n=86)	48 (55.8%)	63 (73.0%)	48 (55.8%)
	Prematurity (n=64)	31 (48.4%)	49 (76.5%)	40 (62.5%)
	IUGR (n=40)	18 (45.0%)	26 (65%)	19 (47.5%)
	Birth weight <1.5 (n=35)	24 (68.5%)	30 (85.7%)	26 (74.2%)

From the Table 3 it's obvious that there is a statistically significant relationship between perinatal death and elevated levels of serum ALT, AST, uric acid, LDH and decrease in serum calcium levels.

Hyperuricemia in preeclampsia was once thought to result solely from reduced renal clearance, but levels of uric acid are now also thought to increase through increased uric acid production caused by trophoblast breakdown, cytokine release and ischemia. Uric acid can promote endothelial dysfunction, damage and inflammation, which leads to oxidation(19).

Some study (20) observed patients with serum uric level >5.5mg/dl, 86.4% had perinatal deaths. All the mothers with serum uric acid levels above 5.5mg/dl delivered babies with birth weight less than 2.5 kg. and 60 % of patients had preterm delivery, 68% of them being Small for Gestational Age (20).

Although hyperuricemia does correlate with maternal morbidity, there is an even stronger association of uric acid with the risk for small birth weight infants and overall fetalmortality(21). Hyperuricemia patients with severe preeclampsia is a strong risk factor for several perinatal complications and increase the risk for intra uterine death by 30.4 times, cesarean section by 6 folds, maternal mortality by 21.5 times, IUGR by 6 folds and eclampsia by 14.3 fold in those with a uric acid level >6mg/dl as compared to a level <6mg/dl (22). This was in consistent with our study, those having uric acid >6.0 mg/dl showed perinatal deaths in 63(73.0%), IUGR 26(65%), LBW <1.5Kg 30(85.0%) and preterm deliveries 49(76.5%) (Table 4) In contrast, Hickman et al concluded that the serum uric acid level was an unreliable indicator of developing hypertension in the individual woman (23).

Liver function tests are found to be abnormal in 20–30% of patients with preeclampsia. They may reflect liver dysfunction resulting from vasoconstriction of the hepatic vascular bed. Some study (24) observed that the women with preeclampsia having abnormal LFT are associated with proteinuria, low platelet count

and maternal complications than those with normal liver function tests.

In our study serum calcium levels <8.0mg/dl was seen in perinatal deaths 48(55.8%), premature delivery 31(48.4%), IUGR 18(40%) and with LBW <1.5Kg 24(68.5%).(Table 4) It was noted that serum calcium levels were significantly lower in preeclamptic women and they found low levels of calcium as early as by 28 weeks and so studies concluded that calcium could be used for early diagnosis of preeclampsia (25). A relative calcium deficiency can be due to increased maternal-fetal transfer of calcium and hypocalciuria in preeclampsia (26). Some studies (27) even concluded that supplementation of calcium in diet may be of value to prevent preeclampsia, it can be explained by reduction in parathyroid calcium release and intracellular calcium concentration, thereby reducing smooth muscle contractility and promoting vasodilatation (28).

In PIH there are multisystem disorders and that lead to a lot of cellular death. LDH is an intracellular enzyme and its level is increased in these women due to cellular death. So, serum LDH levels can be used to assess the extent of cellular death and thereby the severity of disease in this group of women. This can be further used as help in making decision, regarding the management strategies to improve the maternal and fetal outcome(29,30).

Higher serum LDH levels were associated with increased incidence of perinatal deaths, preterm deliveries, IUGR and LBW in the present study. There was a significant increase in perinatal mortality with increasing serum LDH levels ($P < 0.001$). Perinatal mortality was 48(55.8%), IUGR 19(47.5%), LBW <1.5Kg 26(74.2%) and preterm delivery 40(62.5%) was when LDH levels >600 IU/l was seen in PIH mothers (Table 4). Studies showed LDH levels have significant association with various maternal and fetal outcomes in patients of preeclampsia and eclampsia, showing significant increase in neonatal complications still births and perinatal deaths(30).

Conclusions

In the present study, a positive correlation has been made out between serum AST, ALT, uric acid, LDH, calcium and perinatal deaths in relation to the severity of PIH and these may be useful markers and diagnostic tools for predicting the progression of PIH and thereby preventing and reducing fetal complications by timely intervention.

Conflict of Interest: None

Source of Support: Nil

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