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BIOCHEMICAL PROFILE AND OUTCOME IN NORMAL AND HIGH RISK SUBJECTS

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ABSTRACT

The present study was carried out to assess the biochemical profile and outcome of pregnancy and study the adverse consequences if any, among normal and high risk pregnant women. The study group included 182 normal and 168 high risk cases attending to private and Government Hospitals in Bangalore. The high risk groups were: Pregnancy induced hypertension (PIH), gestational diabetes mellitus (GDM), Adolescents and anemic cases. Lipid peroxidation was enhanced in PIH and GDM groups (5.56 nmol/ml and 3.98 nmol/ml) MDA values as compared to other groups. Vitamin E levels were significantly ($p< 0.05$) lower in PIH group (0.38 mg/dl) as compared to other groups. Caesarean as a mode of delivery indicating more number of complications were higher among GDM (61.9%) followed by PIH group. Incidences of low birth weight were observed more in PIH group. The study revealed occurrence of oxidative stress and adverse outcome among high risk pregnancy groups.

KEY WORDS

Pregnancy induced hypertension, Gestational diabetes mellitus, Lipid peroxidation, Oxidative Stress.

INTRODUCTION

Pregnancy is a physiologically demanding process characterized by dynamic changes in multiple body systems. There is some element of risk involved in all pregnancies. A 'high risk' pregnancy is one in which risk of adverse maternal or fetal outcome is greater than that in the general obstetric population. Prevalence of anemia, gestational diabetes (GDM) and hypertension during pregnancy (PIH) are considered as high risk pregnancies and hence, demand greater attention.

Pregnancy is a stressful condition in which many physiological and metabolic functions are altered to a considerable extent. In recent years, the role of decreasing anti-oxidants and increasing superoxides are gaining importance as these are the threat to normal pregnancies Oxidative stress is an imbalance between pro-oxidants and antioxidant forces resulting in an overall pro-oxidant insult. Anti oxidants are crucial in pregnancy as they have been shown to have protective effect against oxidative stress (1). There is increasing evidence that oxidative stress is an important contributing factor to the pathogenesis pre-eclampsia (2). The exact pro-oxidant and anti oxidant status in gestational diabetes is still unclear. However, lipid peroxidation is suggested to play a role in the pathogenesis of gestational diabetes also (3).

The occurrence of altered serum lipid profile in PIH women is well documented. Magnesium is an indispensable constituent of all living cells. There has been a speculation in the past about the possibility of preeclamptic women having low serum magnesium (4). Therefore, the present investigation was carried out to assess the lipid profile, oxidative stress, outcome of pregnancy and study the adverse consequences if any, among normal and high risk pregnant women.

MATERIALS AND METHODS

A total of 350 subjects belonging to both normal and high risk pregnant groups were selected on the basis of their willingness to participate in the study. Subjects represented mainly Bangalore Urban district attending to private and government hospitals. The high risk groups under the present study were pregnancy induced hypertension (PIH), Gestational diabetes

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mellitus (GDM), Anemia and adolescent pregnancies. The medical records available at the hospitals were used for classification. The subjects having more than one type of high risk or any other complications were excluded from the study.

The study group included 182 normal, 55 PIH, 25 GDM, 15 adolescents and 73 anemic cases. Blood samples were collected from the subjects in 2nd trimester of pregnancy and were analyzed for biochemical parameters viz, serum lipid peroxides, vitamin E, total cholesterol, triglycerides and magnesium.

Lipid peroxides were analyzed by quantitative assay of thiobarbituric acid reactive substances which is expressed as n moles MDA/ml (5).Vitamin E was measured by dipyridyl method which is based on the reduction of ferric chloride to ferrous chloride by tocopherols (6). Serum cholesterol and triglycerides were determined using enzymatic diagnostic kits, based on the cholesterol-oxidase-phenol peroxidase and glycerol-3-phospatase peroxide methods (Span Diagnostics, India). Serum magnesium was estimated using Wako magnesium B kit. Hemoglobin (Hb), BUN, Creatinine values were obtained from hospital records. Birth weight and crown heel length (CHL) of the neonates were taken within 24 h after birth using standard procedures (7). Gestation week, mode of delivery and APGAR scores were noted from hospital records.

RESULTS AND DISCUSSION

Lipid peroxidation was enhanced in PIH and GDM groups (5.56 nmol/ml and 3.98 nmol/ml) as indicated by significantly higher MDA values as compared to other groups. The levels of vitamin E were measured in the groups to assess the non-enzymatic antioxidant status. Vitamin E levels were significantly lowers ($p < 0.05$) in PIH group (0.38 mg/dl) as compared to other groups. Serum magnesium levels were comparable in normal and anemic groups (1.79 mg/dl and 1.87 mg/dl respectively). Serum cholesterol and triglyceride levels were significantly ($p < 0.05$) elevated in PIH (219 and 206 mg/dl) and GDM groups (223 & 185 mg/dl) compared to normal and anemic groups (Table 1).

Several investigations have reported an increase in MDA or products of lipid peroxidation and lower vitamin E concentration in preeclampsia (8, 9). Vitamin E is a free radical scavenger and exerts its antioxidant activity in lipid phase. However, vitamin E is consumed in exerting its action. Hence, abnormal rise in lipid peroxides in pre-eclampsia could increase the consumption of antioxidants resulting in decreased vitamin E levels. Another possibility is decreased absorption of vitamin E from the gut as a result of vasoconstriction on preeclampsia (10). Current concepts of preeclampsia have been focused on dysfunction of maternal vascular endothelium as the central pathogenic factor of the disease. The hyperlipidaemia in PIH and GDM subjects has been attributed to the endocrinal response in the conditions (8, 11) and also showed a similar damage in the lipid profile among PIH patients. A higher level of Mg in PIH and GDM groups does not support the hypothesis that magnesium deficiency to be the cause of preeclampsia (12). Data pertaining to the lipid profile is classified according to NCEP guidelines (13). Majority of the subjects belonging to the normal and anemic groups had cholesterol and triglyceride levels in the optimum range (76.7% and 80% respectively). Mean total cholesterol and triglycerides were higher than the desirable range in majority of PIH and GDM subjects (> 50%) indicating a distinctive atherogenic lipid profile in these high risk pregnancies (Table 2).

Table 3 presents the hemoglobin status (initial and at term) among the anemic pregnant women. In the first trimester, 12.3% of the women were mildly anemic, 71.2% were

Table 1: Bio-chemical profile of normal and high risk pregnant groups (mean ±SD)

		High Risk Groups				
	Normal (n=30)	PIH (n=23)	Anemia (n=21)	GDM (n=15)	Combined (n=89)	F-Value
Components						
MDA (nmol/ml)	1.52 ± 0.9^{a}	5.56 ± 2.5 ^{b}	1.80 ± 0.7^{a}	3.98 ± 1.8^{c}	3.04 ± 1.4	33.86*
Vitamin-E (mg/dl)	0.89 ± 2.2^{a}	0.38 ± 1.1^{b}	0.77 ± 1.8^{a}	0.78 ± 1.4^{a}	0.71 ± 1.6	32.24*
Magnesium (mg/dl)	1.79 ± 0.5^{a}	2.12 ± 0.5^{ac}	1.87 ± 0.6^{a}	2.37 ± 0.6^{c}	1.99 ± 0.6	4.44*
Cholesterol (mg/dl)	178 ± 42.7^{a}	219 ± 43.1^{b}	178 ± 49.1^{a}	223 ± 48.7^{b}	196 ± 45.9	6.42*
Triglyceride (mg/dl)	125 ± 30.1^{a}	206 ± 67.6^{b}	153 ± 59.3^{a}	185 ± 45.5^{b}	163 ± 50.6	12.05*

*Significant at 5 % level, 0.37; Common alphabet indicate non-significant, row wise

Table 2: Classification of blood lipid profile *

Parameters	Values (range)	Normal (n=30)		PIH (n=23)		GDM (n=15)		Anemia (n=21)	
		Mean ± SD	n (%)	Mean ± SD	n (%)	Mean ± SD	n (%)	Mean ± SD	n (%)
Total Cholesterol									
Optimum	< 200	159.9 ± 28.2	23(76.7)	173.8 ± 16.5	8(34.8)	162.5 ± 38.5	4(26.7)	157.9 ± 33.1	16(76.2)
Border line	200-239	221.4 ± 6.8	5(16.7)	211.7 ± 11.9	6(26.1)	217.6 ± 8.8	5(33.3)	225.7 ± 11	3(14.3)
High	>240	273 ± 4.3	2(6.6)	263.7 ± 21.2	9(39.1)	268.3 ± 16.3	6(40.0)	271.5 ± 29	2(9.5)
Triglycerides									
Optimum	<150	113.5 ± 20.5	24(80)	128.1 ± 19.2	7(30.4)	130.0 ± 14.1	2(13.3)	113.9 ± 19.8	11(52.4)
Border line	150-199	169.2 ± 14	5(16.7)	180.8 ± 15.3	4(17.4)	174.0 ± 18.2	10(66.7)	161.3 ± 6.1	07(33.3)
High	200-499	218.0 ± 0.0	1(3.3)	260.5 ± 39.5	12(52.2)	258.0 ± 36.5	3(20)	309.0 ± 9.1	03(14.3)

*According to NCEP guidelines.

Table 3: Hemoglobin status * of anemic subjects

Hemoglobin Values	Anemic Subjects			
	Initial		At term	
	n	%	n	%
Normal	0	0	5	6.9
Mild	9	12.3	29	39.7
Moderate	52	71.2	37	50.7
Severe	12	16.5	2	2.7
Combined	73	100	73	100
χ^2 Value		25.20**		

* initial & at term, ** Significant at 5 % level

moderate and 16.4% of women were severely anemic. As indicated by the hemoglobin values at term, 7% had become normal, 40% were mild, 51% were moderate and only 2.7% were severely anemic. Marked improvement in the hemoglobin status among anemic subjects may be attributed to supplementation. The results confirm that anemic women have been compliant with respect to medicines and nutritional advice of doctors and nutritionists to improve their health status.

Table 4 depicts the presence of proteinurea among 38% of PIH subjects. Higher BUN and creatinine levels were observed in a small number of PIH subjects.

It is suggested that, decreased placental perfusion resulting in endothelial damage and generalized vasospasm leads to poor tissue perfusion, reduced renal plasma flow and glomerular filtration rate. This condition increases the blood urea level, serum creatinine, serum uric acid and protein loss in the urine (14).

The present study reveals that, majority of PIH patients had normal BUN and creatinine levels. Hence, a cause and effect relationship between increased serum urea, creatinine and the onset of PIH cannot be assumed. This needs further investigation.

A significant negative correlation was evident among both normal and high risk groups between serum lipid peroxides (MDA) and vitamin E levels (r=- 0.3654, p< 0.05) and (r=-0.4318, p< 0.01) respectively. Our findings are in agreement with earlier reports which suggest that low vitamin E is associated with the elevated MDA levels in pregnancy (8, 9 & 10). However, it is not clear whether lower levels of vitamin E-a physiological antioxidant, can cause accumulation of lipid peroxidation products. However, MDA showed a positive significant relationship with cholesterol and triglyceride among both normal (r=0.3862* and r=0.3793*) and high risk groups (r=0.4083** and r=0.4187**) (Table 5). In the present study, lipid peroxidation product (MDA) was significantly increased in PIH and GDM subjects, as compared to normal subjects.

Table 4: Selected Bio-chemical Indices of PIH subjects

Parameters	Subjects (n=55)		Mean ± SD
	n	%	
Blood pressure (mm Hg)			
Systolic (120)	55	100	139.2 ± 15.3
Diastolic (80)	55	100	91.0 ± 10.9
Proteinurea (Traces)	21	38.2	NA
BUN (mg/dl)			
Normal 7-18	51	92.7	8.3 ± 2.1
Abnormal >18	4	7.3	
S.Creatinine (mg/dl)			
Normal (0.5-1.1)	52	94.5	0.82 ± 2.3
Abnormal (>1.1)	3	5.5	

Table 5: Correlations between serum MDA and selected Biochemical parameters

Study Groups	Sample (n)	Correlation coefficients (r) between MDA and		
		Vitamin E	Cholesterol	Triglyceride
Normal	30	-0.3654*	+0.3862*	+0.3793*
High risk	59	-0.4318**	+0.4093**	+0.4187**
Combined	89	-0.3518**	+0.4018**	+0.3843**

**Significant at 1% level; *Significant at 5% level

Nevertheless, the hyperlipidaemia may contribute to increased lipid peroxidation, the precise mechanism by which the oxidant stress is increased in preeclampsia and gestational diabetes remains to be established. PIH subjects (61%) had more number of low birth weight (LBW < 2.75 kg) babies. The gestation week was less for most of the PIH subjects (41%) while it ranged from 38-40 weeks among normal group. The number of cesarean were more with GDM (62%) and PIH (61%) subjects. Seventy percent of GDM babies had CHL > 48 cm. Assessing the clinical condition of the new born baby after delivery at the time of 1& 5 min interval is termed as APGAR scoring. Abnormal APGAR score at 1 min (<5) was recorded more among infants born to PIH mothers (27.9%) and abnormal APGAR score at 5 min (<7) was more among infants born to GDM mothers (10.0%). The differences between the groups for APGAR scores were found to be statistically significant ($p< 0.05$).

Table 6: Outcome of delivery among subjects of risk groups

Out come of pregnancy	Risk groups								χ^2
	Normal		PIH		GDM		Anemia		
	N	%	n	%	n	%	n	%	
Birth wt.									
< 2.75 kg	46	35.4	26	60.5	3	15	24	47.1	20.78*
>2.75 kg	84	64.6	17	39.5	17	85	27	52.9	
Gestation week									
32-34	10	7.7	17	40.5	2	9.5	5	9.6	
35-37	59	45.4	20	47.6	12	57.1	29	55.8	37.79*
38-41	61	46.9	5	11.9	7	33.3	18	34.6	
Mode of delivery									
Caesarian	39	29.8	26	60.5	13	61.9	18	35.3	
Induced labor	23	17.6	8	18.6	1	4.8	2	3.9	33.06*
Normal	69	52.7	9	20.9	7	33.3	31	60.8	
CHL									
< 48.0 cm	70	53.9	29	67.4	6	30	28	54.9	10.33 *
> 48.0 cm	60	46.2	14	32.6	14	70	23	45.1	
APGAR-1									
5	17	13.1	12	27.9	1	5	8	15.7	
6-7	93	71.5	29	67.4	17	85	36	70.6	10.31*
8	20	15.4	2	4.6	2	10	7	13.7	
APGAR-5									
< 7	2	1.5	4	9.3	2	10	2	3.9	
7	8	6.1	5	11.6	0	0	5	9.8	25.46*
8-9	119	91.5	33	76.7	18	90	44	86.3	
10	1	0.8	1	2.3	0	0	0	0	

* Significant at 5 % level,

Intrauterine growth retardation (IUGR) is a common problem among PIH mothers and they give birth to LBW babies. PIH causes constriction of arteries throughout the mother's body, decreasing the mother's blood flow to the placenta and reducing the amount of food and oxygen reaching the baby. As a result, baby's growth slows down and leads to IUGR (15). A higher percent of Low Birth weight (LBW) cases were observed among PIH group. Many studies have reported significant maternal, fetal and neonatal complications associated with GDM (16 -18). The results of the present study showed more number of cesarean deliveries among GDM and PIH groups, indicating complications among these groups.

GDM babies were comparatively taller as large for gestational age (LGA) is one of the common conditions associated with GDM subjects. This is explained by the Pedersen Hypotheses which suggests that maternal hyperglycemia leads to fetal hyperglycemia which in turn causes the fetal pancreas to produce increased amounts of insulin. The fetal hyperinsulinemia is believed to stimulate fetal growth in utero (19).

The lower APGAR scores for the infants born to GDM and PIH mothers may be because of poor clinical condition/status. Morbidity symptoms like infections, respiratory problems and neonatal admissions were common among these groups. The findings are in accordance with earlier reports (15, 20 & 21).

Babies born to mothers with abnormal glucose levels have a higher chance of developing respiratory distress syndrome (RDS) as their pulmonary functions are not adequately matured (16).

The overall pregnancy outcome among anemic subjects was also poor. However, compared to other high risk groups in the present study, it was better. This may be because the present study included women attending antenatal check-ups in hospitals. Depending upon the severity of the anemic condition they were given regular iron supplementation or blood transfusion which resulted in improved hemoglobin status. During the 3rd trimester, the percentage of severe anemic subjects was very less. It is reported that (22) only severe anemia is associated with poor outcome. Mild or moderate anemia cause increased weakness and poor work performance but do not affect the outcome and labor.

The study reiterates the fact that altered lipid profile, oxidative stress and poor birth outcomes were predominant among subjects with high risk pregnancies. However, these are interconnected and influenced by number of factors all of which have to be considered and monitored carefully. Greater attention is required by medical practitioners, pregnant women and their families to avoid adverse consequences of high risk pregnancies.

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