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Research Article

Association between Serum Homocysteine Concentration in Pregnant Women and Neonatal Birth Weight

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Abstract: Maternal total homocysteine concentrations have been linked to a wide range of adverse pregnancy outcomes and could possibly influence birth weight. Keeping this in mind the present study was done to find the association of serum levels of homocysteine with neonatal birth weight in Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur. It was a hospital-based analytical study. 162 pregnant women with gestational age of 28 weeks or more, normotensive or with pre-eclampsia were included. S homocysteine levels were measured and results were analyzed to find association of homocysteinewith neonatal birth weight. At normal homocysteine level (5-15 3 μmol/L) mean neonatal weight was 2.60 ± .39 kg. Mean neonatal weight decreases as the maternal serum homocysteine concentration increases. The difference in the neonatal weight, in various groups was statistically significant (p - 0.01). There was a negative correlation between neonatal birth weight and serum homocysteine levels. Serum homocysteine levels have a negative correlation with neonatal birth weight. With normalisation of elevated homocysteine levels we can provide better maternal and perinatal outcome.
Keywords: Pregnancy, Homocysteine, Neonatal birth weight, Preeclampsia

INTRODUCTION

Hyperhomocysteinemia has been implicated in a variety of clinical conditions in obstetrics like neural tube defects, spontaneous abortion, placental abruption, intrauterine fetal death and fetal growth restriction [1].

Homocysteine is a sulfur containing amino acid which is an intermediate product in methionine metabolism. It is essential amino acid required for growth of cells and tissues in the human body [2]. Our body cannot store methionine so it is demethylated to homocysteine in liver for storage until needed. About 50% of it is remethylated back into methionine and other 50% is trans-sulfurated into cystathionine and then cysteine.Various defects in remethylation or transsulfuration leads to hyperhomocysteinemia and associated adverse effects [3].

The concentration of plasma homocysteine is regulated by several factors which include genetically determined metabolic enzyme alterations and environmental factors [4]. There is fall in levels of maternal serum homocysteine with increasing gestation. This can be due to a physiological response to the pregnancy like increase in estrogen, hemodilution from increased plasma volume, or increased demand for methionine by both the mother and fetus [5]. Elevated homocysteine, which can result from genetic abnormalities and suboptimal folate, vitamin B-12, or vitamin B-6 status [6] was associated with preeclampsia [7-10]. The adverse pregnancy outcomes implicated because of increase homocysteine levels are all possibly related to increase predisposition to thrombosis. Arterial and venous thromboembolic phenomena may affect birth weight of foetus. So the aim of the present study was to determine total homocysteine levels in pregnant women and its association with neonatal weight.

MATERIALS AND METHODS

The present study was done to find the association of serum levels of homocysteine with neonatal birth weight in Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur from April 2012 to March 2013. It was a hospital-based analytical study. 162 pregnant women with gestational age of 28weeks or more, normotensive or with pre-eclampsia, willing to participate in the study were included after taking written informed consent. Women with multiple pregnancies, IUFD, in active labor or with rupture of membranes, signs of infection, pre-existing hypertensive, cardiovascular or renal disease, diabetes mellitus or chorionic disease and treatment with antifolate drugs (antiepileptics and methotrexate) were excluded from the study.

A detail history and examination was done for all included women. We collected 10 ml of maternal venous blood in standard sampling tube, centrifuged at 3439 g for 10 min. Separated serum was used to measure homocysteine by Erba 360 auto-analyzer machine. This Fully automated system automatically calculated the homocysteine concentration of each sample. Hemolysed, turbid or severely lipemic specimens were discarded.

The mean of the values was subjected to statistical analysis to find out the correlation between serum homocysteine and neonatal weight. All pair-wise multiple comparison procedures were done using Tukey test. Correlation analyses were performed using Pearson correlation coefficient. Significance level for tests was determined as 95% ($p< 0.05$). Normal S. Homocysteine value in pregnancy is 5 – 15 µmol/L.

Table 1: Demographic profile of the participants

Variable	Number	Percentage
Age (years)		
20 – 25	101	62.4
25 – 30	43	26.5
30 – 35	18	11.1
Gravida		
G_1	86	53.1
G_2	41	25.3
G_3	29	17.9
$\geq G_4$	6	03.7
Socio-economic Status		
Upper	32	19.8
Middle	78	48.1
Lower	52	32.1
Literacy Status		
Illiterate	31	19.1
Literate	131	80.9

Table 2: Mean Serum Homocysteine levelsand Neonatal birth weight with Pre-eclampsia

	Normotensive women(n = 54)	Women with Mild Pre-eclampsia (n = 54)	Women with Severe Pre-eclampsia (n = 54)	p-value
	Mean ± SD	Mean ± SD	Mean ± SD	
Homocysteine	11.3 ± 4.4	12.3 ± 4.2	15.9 ± 6.3	<0.001Highly significant
Neonatal birth weight	2.8 ± 0.3	2.6 ± 0.3	2.2 ± 0.3	<0.001Highly significant

Table 3: Serum Homocysteine levels and Neonatal birth weight

	Serum Homocysteine levels (µmol/L)				p value
	5 – 15 (n = 100)	15 – 20 (n = 49)	20 – 25 (n = 8)	>25 (n = 5)	
Mean Neonatal weight	2.60	2.56	2.21	2.22	0.01 sig
SD	0.39	0.39	0.24	0.39	

Chi-square - 1.7165, d.f. 3.

Table 4: Correlation of Neonatal Birth Weight with Serum Homocyseine

n = 162	Mean ± SD	R	R Square	Equation	p-Value LS
Neonatal Weight	2.61 ± .365				
Homocysteine	13.17 ± 5.394	.122[a]	.015	y=17.9-1.8	0.12, NS

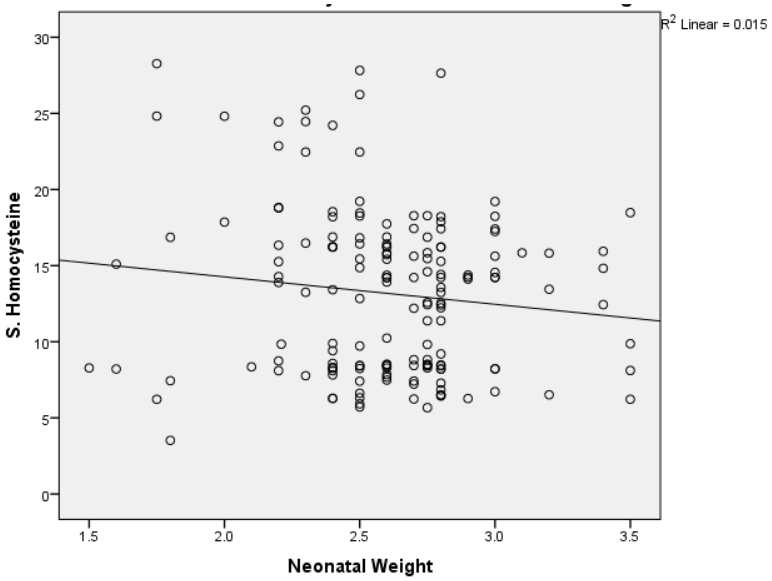

Fig. 1: Relationship between serum homocysteine levels and neonatal birth weight

RESULTS

Majority of women in the present study were literate (80.9%), gravida 1 (53.1%), belonged to middle socio-economic status (48.1%) and in the age group of 18 to 24 years with mean age 24.55 ± 3.4 years (Table 1).

The mean serum homocysteine levels in normotensive, mild preeclampsia and severe preeclampsia were11.3 ± 4.4 μmol/L, 12.3 ± 4.2 μmol/L and 15.9 ± 6.3 μmol/L respectively. The Tukey post hoc test indicated that mean serum homocysteine levels were significantly higher in severe preeclampsia than those in normotensive and mild preeclampsia ($p<.001$), but the levels of mean serum homocysteine were not significantly different between mild preeclampsia and normotensive. Mean neonatal birth weight in normotensive, mild preeclampsia & severe preeclampsia was 2.8 ± 0.3, 2.6 ± 0.3 and 2.2 ± 0.3 respectively. The difference in birth weight was highly significant ($p<0.001$) (Table 2).

At normal homocysteine level (5-15 μmol/L) mean neonatal weight was 2.60 ± .39 kg. Mean neonatal weight decreases as the maternal serum homocysteine concentration increases. The difference in the neonatal weight, in various group was statistically significant (p - 0.01) (Table 3).

Table 4 and Graph 1 revealed negative correlation between neonatal birth weight and serum Homocysteine levels.

DISCUSSION

The mean age of the participant in our study was 24.55 ± 3.4 years and majority of them were primigravida. Our results were comparable for age with the result observed by Guerra-Shinohara EM *et al*. [11] but in their study primigravida was only 26.5%.

Mean serum homocysteine levels were significantly higher in severe preeclampsia than those in normotensive and mild preeclampsia. Our observations are in consonance with Rajkovic Aleksandar *et al*. [8], Robert W Power *et al*. [9] and Powers RW *et al*. [12] studies in which mean homocysteine levels were greater in preeclampsia than normotensive controls ($p< 0.01$). Ingec M, *et al*. [2] also observed that the plasma levels of homocysteine in women with severe preeclampsia (16.7 ± 10.1 μmol/L) and eclampsia (16.5 ± 9.6 μmol/L) were significantly higher than those in mild preeclampsia (7.7 ± 2.4 μmol/L) and controls (6.7 ± 1.6 μmol/L) ($p < 0.0001$) but the levels of homocysteine were not significantly different between mild preeclampsia and controls. Yardanur G Acilmis *et al*. [13] observed that homocysteine levels in both maternal and fetal serum were significantly higher in the severe pre-eclampsia group compared to mild pre-eclampsia and control groups but no significant difference was found between mild pre-eclampsia and control groups. Shahid A Mujawar *et al*. [14] found a good, negative and statistically significant correlation ($r = -0.335$ and $p< 0.05$) between serum homocysteine and Vitamin B12 in preeclampsia. Similarly Ezzatalsadat Haji *et al*. [15] studied that mean serum homocysteine level was significantly higher in women with severe preeclampsia than in control group ($p<0.001$), but no significant difference between normal pregnant women and those with mild preeclampsia ($p=0.12$).

Various studies have investigated the association between maternal homocysteine and birth weight and different results were obtained. In this study we observed that mean neonatal weight decreases as the maternal serum homocysteine concentration increases. Our finding was in accordance with Yajnik CS *et al*. [16] who observed that higher maternal plasma homocysteine levels were associated with lower

offspring birth weight (r=-0.28, p<0.05).Vollset *et al*. [17] reported a strong association between low birth weight and homocysteine measured either before or after pregnancy in women 40–42 years of age. Gadhok AK *et al*. [18] revealed that increasing serum homocysteine levels in pregnancies complicated with IUGR accompanied by decreasing levels of serum Folic acid and Vit B12.

It was observed in our study that mean neonatal birth weight in normotensive, mild preeclampsia & severe preeclampsia was 2.8 ± 0.3,2.6 ± 0.3 and 2.2 ± 0.3 respectively. The difference in birth weight was highly significant. The study of Ingec et al[2] showed the mean birth weight in normotensive group was 3013 ± 530 gm, 2859 ± 490 gm in mild preeclampsia and 2346 ± 590 gm in severe preeclampsia group (P < 0.001). Similarly Melih A Guven *et al*. [19] observed that mean fetal weight in mild preeclampsia(2477gm) and severe preeclampsia (2435 gm) were significantly lower than normotensive (3485 gm) (p<0.001).

Yardanur *et al*. [20] found in their study the mean birth weight in severe preeclampsia group (1906 ± 85 gm) was lower than mild preeclampsia (2732 ± 451) and normotensive group (3226 ± 311). Sukla KK *et al*. [21] concluded that elevated Hcy (25%) and Vit B12 (65%) and Folic acid (27%) deficiency are potential risk factors for low birth weight baby.

The mechanisms by which homocysteine influence preterm delivery are not known. It is speculated that, in addition to a possible role in preeclampsia [8, 10] elevated homocysteine predisposes to thrombosis and has adverse effects on connective tissue thereby increasing the risk of preterm premature rupture of membranes [22]. Elevated homocysteine also has been linked to reduced nitric oxide concentration and glutathione peroxidase activity [23], and it is possible that such disruptions could affect the length of gestation.

The present study has demonstrated that serum homocysteine levels have positive correlation with SBP and DBP and negative correlation with neonatal birth weight, because women with severe preeclampsia have to be delivered at earlier gestational age than normotensive women. With normalisation of elevated homocysteine levels we can provide better maternal and perinatal outcome. Large intervention trials as well as prospective studies measuring homocysteine levels before and during different trimester of pregnancy are needed to establish the role of homocysteine as etiologic factor for adverse pregnancy outcomes and complications.

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