EFFECT OF GESTATIONAL HOMOCYSTEINE ON FETAL GROWTH IN BANGLADESHI WOMEN

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Abstract

Hyperhomocysteinemia has been reported among the women of south Asian countries including Bangladesh. It affects fetal development through intrauterine growth retardation (IUGR) and is one of the important issues associated with low birth weight (LBW) of newborns. If its association with IUGR can be established, then maternal serum Hcy could help diagnose IUGR cases and ultimately provide scope for prevention and treatment of the cases by supplementation of B-vitamins and folic acid. In this case control study, 80 pregnant women were enrolled, of which 30 were IUGR cases while 50 appropriate for gestational age (AGA) pregnancies worked as control. Maternal Hcy at 3rd trimester of all the subjects were measured and its effects on neonatal size were analyzed. The maternal Hcy of the IUGR cases was significantly higher than the control. The babies born to IUGR cases had a significantly lower birth weight, lower height and lower OFC compared to the babies born to control mothers. Weight, length and OFC of the newborns showed significant inverse correlation with maternal Hcy. Hyperhomocysteinemia was found to be a significant risk factor for LBW (OR 5.23, 95% CI 1.92-14.23), short stature (OR 2.19, CI 0.792-6.06) and low OFC (OR 3.04, CI 1.15-8.04) of the newborns.

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Introduction

Low birth weight (LBW) of newborns is a challenging problem in developing countries like Bangladesh. Babies born with weight less than 2.5 kg is considered as LBW[1] and a major cause of infant mortality, child morbidity and impaired psychological and intellectual development. According to report of UNICEF/FAO (2004) the incidence of LBW is 58% in developing countries with the highest in South Asia (74%).[2]

LBW may be due to preterm delivery. This may also occur in full term babies due to intrauterine growth retardation. In case of IUGR, the transplacental transfer of nutrients to the developing fetus is reduced due to placental insufficiency, which finally affects the neonatal size.[3] Short stature of mothers and higher level of plasma homocysteine are usually considered as the major causes of IUGR. Homocysteine is a sulfur containing amino acid produced in the body as a metabolite of another amino acid methionine. Presence of higher level of homocysteine – more than 15μmol/L – is considered as hyperhomocysteinemia and is one of the risk factors associated with IUGR.[4]

Although hyperhomocysteinemia may be a sequel to B-vitamin deficiency, it could be due to other causes as well. Unilateral hyperhomocysteinemia with normal vitamin B_{12} and folic acid status tends to cause IUGR by placental insufficiency whereas hyperhomocysteinemia following B_{12} and folic acid deficiency appears to be associated with IUGR like a bi-directional saw. Irrespective of B-vitamin status, it is claimed that hyperhomocysteinemia can be treated successfully by

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B_{12} and folate supplementation during pregnancy, thereby preventing many cases of IUGR. With this end in view, the present study was designed to evaluate the maternal homocysteine status with respect to neonatal size in Bangladeshi pregnant women.

Materials and Methods

The present study was conducted in the Dept. of Biochemistry, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh during the period from July 2006 to June 2007. A total of 80 pregnant women in the 3rd trimester were included in the study as subjects. Using ultrasonogram, 50 were included as controls having an appropriate for gestational age (AGA) while 30 were cases of IUGR. The pregnant women suffering from diabetes, malnutrition, eclampsia and preclampsia, hepatic disorder, chronic renal disease, hypothyroidism, chronic illness and the patients taking folic acid and vitamin B_{12} supplementation were excluded from the study. At 3rd trimester, maternal serum Hcy was estimated by fluorescence polarization immunoassay (FPIA) method by Abott Ax SYM system analyzer.[5] At delivery anthropometric measurements such as weight, height and occipital frontal circumference (OFC) were taken from all newborns. Age, body weight and height of the mothers were also recorded.

Statistical analyses – The data were analyzed by using SPSS. Unpaired 't' test was done to see the significance between the groups (cases vs. control). Pearson correlation coefficient test was done to see the correlation of serum Hcy concentration with the anthropometric measurements (weight, length and OFC) of newborns at birth. OR (95% CI) was calculated to see the association of maternal serum Hcy concentration with birth weight, birth length and birth OFC of newborn.

Results

The comparison of characteristics of cases and control groups are shown in Table 1. Both the groups were matched for age, weight and height though they differed in Hcy level. Hcy level was significantly higher in the cases.

Table 2 shows the comparison of weight, height and OFC between babies born to cases and controls. All these three anthropometric characteristics were found significantly lower in the babies of cases indicating IUGR.

Table-1: *Comparison between case (pregnant with IUGR: n=30) and control (n=50).*

Variables	Case	Control
	mean ± SD	mean ± SD
Age (y)	24.20 ± 3.71	24.88 ± 4.18
Weight (kg)	56.67 ± 3.11	61.36 ± 3.70
Height (cm)	150.20 ± 3.01	150.04 ± 3.74
Hcy (μmol/L)	19.36 ± 7.32	9.85 ± 4.17*

* Case v. control: t =7.4, p<0.01

Table-2: *Comparison of weight, length & OFC at birth between babies born to cases and controls*

Variables	Babies born to cases (n=30)	Babies born to controls (n=50)	*t*	*p*
	Mean±SD	Mean±SD		
Weight (kg)	2.02 ± 0.22	3.25 ± 0.42	- 5.75	.000
Height (cm)	46.65 ± 1.23	48.05 ± 1.44	- 14.57	.000
OFC (cm)	32.98 ± 1.06	34.32 ± 1.39	- 9.23	.000
Weight (kg)	2.02 ± 0.22	3.25 ± 0.42	- 5.75	.000

student's t-test

Table-3: *a) Correlations of maternal Hcy with weight, length and OFC of newborn; b) Odds ratio (OR) of Hcy for the same anthropometric variables (n=80).*

Variables	a *r, p*	b OR (95% CI)
Weight	-.781, *<0.01*	5.23 (1.92-14.23)
Length	-.563, *<0.01*	2.19 (.792-6.06)
OFC	- .538, *<0.01*	3.04 (1.15-8.04)

r – correlation coefficient, CI – confidence interval

Additionally, gestational Hcy level was found to have a significant negative correlation with weight, height and OFC of the newborn of cases but not to that of the control group (Table 3a). The risks of hyperhomocysteinemia were significant for lower weight (OR 5.2, 95% CI 1.92 – 14.23) and lower OFC (OR 3.0, 95% CI 1.15 – 8.05) but not for height (OR 2.2, 95% CI 0.80 – 6.06) of babies born to hyperhomocysteinemic mothers (Table 3b).

Discussion

This may be a pioneer study seeking an association of hyperhomocysteinemia with the fetal growth in a

Bangladeshi pregnant population. The maternal plasma Hcy concentration of the IUGR cases in the study was significantly high compared to that of control. This finding is consistent with similar studies done by Vollset *et al*. 2000, Yajnik *et al*. 2005 Murphy *et al*. 2003 and Lindblad *et al*. 2005.[6-9]

Burke *et al*. (1992) in a small study measured maternal Hcy immediately after delivery and compared it between 73 IUGR cases and 35 controls and their results did not show any difference between the cases and control.[10] Similarly, Revard *et al*. (2003) in a study compared plasma Hcy of cord blood (measured at delivery) and maternal blood (measured within 48 hours of delivery) between mothers of LBW and normal birth weight baby.[11] Unexpectedly, they found concentration of Hcy in cases to be significantly lower than that of the control. Identical view to the results of present study had also been seen by Hogg *et al*. (2000).[12] In all these studies maternal Hcy was measured just prior to or after delivery. This is a possible shortcoming, since the time interval between exposure and event may attenuate the association, because disease itself may affect the plasma Hcy concentration and because of marked changes in plasma Hcy during pregnancy.[4] To unveil the appropriate association between plasma Hcy and IUGR, maternal Hcy needs to be studied before or during pregnancy.[13,14] As such, these studies showing no association between serum Hcy and IUGR are weak while the result of the present study may be more valid as the maternal Hcy was measured during pregnancy.

This study showed a significant negative correlation of maternal serum Hcy with birth weight and birth length of fetus. These findings are consistent with the other findings.[6-9]

Hyperhomocysteinemia was found to be a significant risk for LBW, short stature and low OFC newborn, which simulate several other studies.[15-18] Gestational hyperhomocysteinemia might affect placental vasculature to cause the placental vasoconstriction, reduced placental perfusion and placental insufficiency which could be responsible for the observed IUGR.[7,19]

Conclusions

It may be concluded from the study that maternal hyperhomcysteinemia during pregnancy could be a risk factor for IUGR and small size newborns in our population. So, antenatal checkup of pregnant mothers for hyperhomocysteinemia appears to be important. Further study of similar nature with simultaneous estimation of vitamin B_{12}, B_6, B_2 and folic acid may be undertaken to confirm whether or not hyperhomocysteinemia is truly an effect of these micronutrient deficiencies.

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