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Original Research Article

An observational study to find association of serum vitamin B12 and folate level with neonatal weight at a tertiary care centre

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ABSTRACT

Background: In developing countries like India, low birth weight is a challenging and important public health problem as it has adverse effect on growth and development of children. Vitamin B12 and folate are micronutrients essential for normal foetal growth and development. Maternal folate and B12 concentrations have been positively associated with birth weight. The aim of this study was to evaluate maternal folate and vitamin B12 status in pregnant women in third trimester of pregnancy and to find their relation with foetal birth weight.
Methods: 171 pregnant women in their third trimester with live singleton pregnancy were included in the study. S. vitamin B12 and folate levels were measured and results were analysed.
Results: Mean maternal vitamin B12 level in mothers with LBW infants was significantly lower than that of mothers of ABW infants (143.23±91.79 vs 188.8±109.64 respectively p≤0.001) and mean maternal folate level in mothers with LBW infants was lower than that of mothers of ABW infants (8.46±8.94 vs 9.96±12.57 respectively p=0.054). There was a weak positive but statistically significant correlation between baby weight (kg) and S. vitamin B12 (rho=0.24, p=0.002) and S. folate (rho=0.17, p=0.029).
Conclusions: The present study confirms that maternal low vitamin B12 level and low S. folate levels are associated with low birth weight so during antenatal visit women should be screened for vitamin B12 and folate deficiency and vitamin supplementation should be continued throughout the pregnancy.

Keywords: Neonatal outcome, Vitamin B12, Folic acid, Birth weight

INTRODUCTION

In developing countries like India, low birth weight (LBW) is a challenging and important public health problem as it has adverse effect on growth and development of children.[1] Pregnancy is a period of increased metabolic demand when nutritional status directly influences the infant size and also the main determinant factor for the growth and development of the offspring.[2] During this period, inadequate store or intake of nutrients can have adverse effects on pregnancy and even death of the mother.[3] Furthermore, the foetus can be affected resulting in still birth, preterm delivery, IUGR, congenital malformation, reduced immunocompetence and abnormal organ development.[4] LBW infants have a higher risk of cardiovascular disease compared to normal birth weight infants. Additionally, preterm newborns have a higher risk of respiratory illness and learning disabilities compared to term infants.[5] So nutritional status during pregnancy has a direct influence upon birth weight of newborn and adequate supply of micronutrient is known to be very important in pregnancy.[6]

Vitamin B6, folate (vitamin B9), and vitamin B12 are water-soluble vitamins involved in the one-carbon metabolism that is important in cellular biosynthesis reactions.[7] Folate is essential in the synthesis of purine and thymidine nucleotides, the building blocks of DNA.[7,8] In

addition, folate and vitamin B12 are required for the conversion of homocysteine to methionine, whereas vitamin B6 is required for the conversion of homocysteine to cysteine.[8,9] Methionine is the precursor of S-adenosylmethionine, a cofactor that can alter gene expression through epigenetic mechanisms involving DNA methylation.[7,8] Insufficient concentrations of vitamin B6, folate, and vitamin B12 can thus impair cell division and methylation activity, which could subsequently interfere with foetal growth and development.[8]

Maternal folate and B12 concentrations have been positively associated with birth weight and gestational age at birth.[1,10] However, the findings are inconsistent.[10] Some studies did not find an association between maternal folate and B12 concentrations and birth weight and gestational age at birth, while others found a positive association.[6,11-13] Most of the previous studies were conducted in Western settings with limited data from Asian populations. With this view the present study was designed to evaluate maternal folate and vitamin B12 status in pregnant women in third trimester of pregnancy and to find their relation with foetal birth weight.

METHODS

This was a hospital based descriptive study conducted in the department of obstetrics and gynaecology, SMS Medical College, Jaipur. Sample size was calculated at 80% study power and alpha error of 0.05 assessing SD of 66.59 mg/dl in S. vit B12; level in LBW group as per result of seed article (Open J Obs And Gynac, 2017). For minimum detectable difference in mean S. vit B12 level of 30 mg/dl; 166 patients are required as sample size which is further enhanced to 175 cases expecting 10% dropouts/loss to follow-up/attrition. So, 175 women with live singleton pregnancy with gestational age between 37 to 42 weeks and willing to participate in the study were included. Women with medical disorders and congenital malformation of foetus were excluded from the study. On admission into labour room, thorough history was taken and examination was done. Gestational age was calculated in weeks from the first day of last menstrual period confirmed by ulltrasonography. All routine investigations were performed. Maternal blood samples were obtained from antecubital vein under complete aseptic conditions and S. vitamin B12 and folic acid levels were measured by immunochemiluminescent by using Immulite 2000 autoanalyzer and commercial kits.

After delivery women were divided into two groups on the basis of infant's birth weight: (a) group A: pregnant women who delivered low birth infant<2.5 kg and (b) group B: Pregnant women who delivered average birth infant≥2.5 kg

The data were collected and entered into MS excel sheet and analyzed. The level of significant was 0.05.

RESULTS

Out of 175 women who were included in the study 4 participants after delivery refused to participate further in the study so finally 171 women were included. 81 women (47.3%) delivered low birth infant (<2.5 kg) and 90 women (52.6%) delivered average birth infant (≥2.5 kg). Mean age of the women in group A was 25.04±3.47 years and in group B was 24.97±4.17 years. Mean age of all participant was 25.00±3.84 years. Both groups were comparable in terms of age (p=0.3).

Mean period of gestation in two groups is shown in Table 1. The mean period of gestation in group A was 37.91±0.98 weeks and in group B was 38.97±1.43 weeks. There was a significant difference between the 2 groups in terms of POG (weeks) (p≤0.001), with the median POG (weeks) being highest in the baby weight≥2.5 kg group.

Table 1: Comparison of the two groups in terms of POG (weeks).

POG (Weeks)	Group A	Group B	Total	P value
Mean (SD)	37.91 (0.98)	38.97 (1.43)	38.47 (1.34)	<0.001
Median (IQR)	38 (37-39)	39 (38-40)	38 (37-39)	
Range	37-40	37-42	37-42	

Table 2 compares S. vitamin B12 and S. folate levels in two groups. The mean S. vitamin-B12 in group A was 143.23±91.79 pmol/l and in group B was 188.80±109.64 pmol/l. There was a significant difference between the 2 groups in terms of S. vitamin B12 (p≤0.001), with the median S. vitamin B12 being highest in the baby weight ≥2.5 kg group. The mean S. folate in group A was 8.46±8.94 nmol/l and in group B was 9.96±12.57 nmol/l. Mean Folate in women with LBW was lower than mean folate in women with ABW.

The mean S. vitamin B12 in women who had normal delivery was 172.16±102.84 pmol/l and in women who delivered by LSCS was 162.21±105.17 pmol/l. There was no significant difference between the groups in terms of S. vitamin-B12 (p=0.124). The mean S. folate in women who had normal delivery was 8.03±5.59 nmol/l and in women who delivered by LSCS was 10.49±14.48 nmol/l. There was no significant difference between the groups in terms of S. folate (p=0.560) (Table 3).

Mean S. vitamin B12 and mean S. folate were significantly more in women with babies Apgar of 7 or more (168.87±100.7 pmol/l and 9.43±11.49 nmol/l respectively) than women with babies APGAR<7 (167.73±123.68 pmol/l and 8.09±7.05 nmol/l respectively) (Table 4).

Table 2: Comparison of the groups in terms of S. vitamin B12 and S. folate levels.

	Group A	Group B	Total	P value
S. vitamin-B12				
Mean (SD)	143.23 (91.79)	188.80 (109.64)	168.72 (103.67)	
Median (IQR)	123 (85.64-178)	177 (114-230)	160 (99-213)	<0.001
Range	40-604	30-857	30-857	
S. folate				
Mean (SD)	8.46 (8.94)	9.96 (12.57)	9.25 (10.99)	
Median (IQR)	6.32 (2.84-10.78)	9 (5.08-11)	7.3 (3.065-11)	0.054
Range	0.37-63	0.72-117	0.37-117	

Table 3: S. vitamin B12 and S. folate levels in relation to mode of delivery.

	Mode of delivery		P value
	NVD	LSCS	
S. vitamin B12			
Mean (SD)	172.16 (102.84)	162.21 (105.17)	
Median (IQR)	163.5 (102.75-213)	155 (79-210)	0.124
Range	30-857	40-604	
S. folate			
Mean (SD)	8.03 (5.59)	10.49 (14.48)	
Median (IQR)	7.44 (2.97-11)	7.3 (4.48-11.15)	0.560
Range	1.14-24	0.37-117	

Table 4: Comparison of S. vitamin B12 and S. folate levels in terms of Apgar score.

	Apgar score		P value
	≥7 (N=148)	<7 (N=23)	
S. vitamin B12			
Mean (SD)	168.87 (100.7)	167.73 (123.68)	
Median (IQR)	158.5 (99.25-213)	160 (79-200)	0.032
Range	30-857	52-604	
S. folate			
Mean (SD)	9.43 (11.49)	8.09 (7.05)	
Median (IQR)	7.82 (3.1-11)	6.32 (2.86-10.97)	0.015
Range	0.37-117	1.14-24.21	

Table 5 shows S. vitamin B12 and folate levels in terms of NICU admission. The mean S. vitamin B12 levels were lower in women whose babies had NICU admission (161.14±55.80 pmol/l) than without NICU admission (167.51±107.09 pmol/l). There was no significant difference between the groups in terms of S. vitamin B12 (p=0.826). The mean S. folate levels in women whose babies had NICU admission was 8.12±5.59 nmol/l and in women without NICU admission 9.35±11.35 nmol/l. There was no significant difference between the groups in terms of S. folate (p=0.689).

The mean S. vitamin B12 in women where the perinatal mortality present was 109.83±116.85 pmol/l and in the perinatal mortality absent group was 169.30±103.11 pmol/l. There was a significant difference between the 2 groups in terms of S. vitamin B12 (p=0.032), with the median S. vitamin B12 being highest in the perinatal mortality: absent group. The mean S. folate in the perinatal mortality present group was 3.47±2.34 nmol/l and in the perinatal mortality absent group was 9.46±11.13 nmol/l. There was a significant difference between the 2 groups in terms of S. folate (p=0.015), with the median S. folate being highest in the perinatal mortality: absent group (Table 6).

To depict the corelation between baby weight and S. Vitamin B12 and S. Folate levels scatterplot was made (Figure 1-2), individual points represent individual cases. The blue trendline represents the general trend of correlation between the two variables. The shaded grey area represents the 95% confidence interval of this trendline. Spearman correlation was used to explore the correlation between baby weight (kg) with S. vitamin B12 and S. folate (Table 7).

There was a weak positive correlation between baby weight (kg) and S. vitamin B12, and this correlation was statistically significant (rho=0.24, p =0.002) as well as there was a weak positive correlation between baby weight (kg) and S. folate, and this correlation was statistically significant (rho=0.17, p=0.029).

Table 5: Comparison of S. vitamin B12 and S. folate levels in terms of NICU admission.

	NICU admission		P value
	Present	Absent	
S. vitamin B12			
Mean (SD)	161.14 (55.80)	167.51 (107.09)	0.826
Median (IQR)	175.5 (146.5-218.25)	157 (99-211.5)	
Range	70-604	30-857	
S. folate			
Mean (SD)	8.12 (5.59)	9.35 (11.35)	0.689
Median (IQR)	6.17 (4.66-10.92)	7.87 (3.1-11.07)	
Range	2.44-63	0.37-117	

Table 6: Comparison of S. vitamin B12 and S. folate levels in terms of perinatal mortality.

	Perinatal mortality		P value
	Present	Absent	
S. vitamin B12			
Mean (SD)	109.83 (116.85)	169.30 (103.11)	0.032
Median (IQR)	60 (56.25-89.25)	160 (100-213)	
Range	40-345	30-857	
S. folate			
Mean (SD)	3.47 (2.34)	9.46 (11.13)	0.015
Median (IQR)	2.82 (1.68-5.5)	7.77 (3.16-11)	
Range	1.14-6.34	0.37-117	

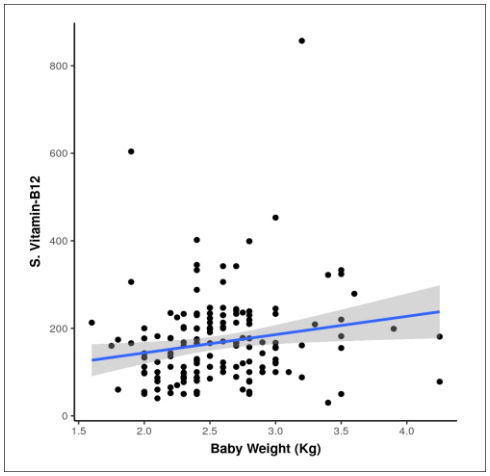

Figure 1: Correlation between baby weight (kg) and S. vitamin B12 (N=171).

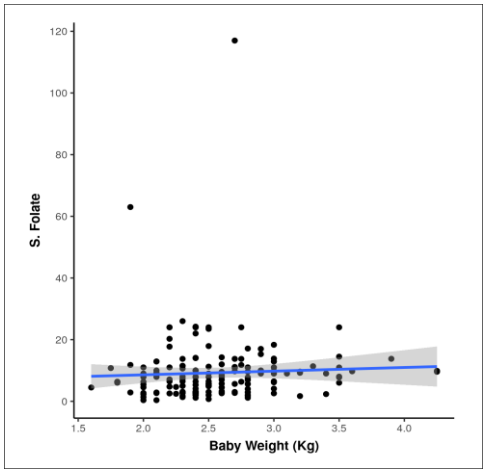

Figure 2: Correlation between baby weight (kg) and S. folate (N=171).

Table 7: Spearman correlation between baby weight and S. vitamin B12 and S. folate.

Correlation	Spearman correlation coefficient	P value
Baby weight (kg) vs S. vitamin B12	0.24	0.002
Baby Weight (kg) vs S. folate	0.17	0.029

DISCUSSION

In this study higher maternal vitamin B12 and folate concentrations in third trimester of pregnancy were significantly associated with higher birth weight. Mean age of the women in our study was comparable to the mean age observed by Muthayya et al, Youssry et al, Dwarkanath et al and Kaymaz et al but lower than that observed by Sukumar et al, Cowan et al and Chen et al.[13-19]

Mean length of gestation in our study was 38.47±1.34 weeks which is comparable with mean age observed by Dwarkanath et al, Kaymaz et al, Chen et al and Bhate et al but lower than mean age observed by Sukumar et al and Baker et al.[15-17,19-21]

Mean S. vitamin B12 in our study was 168.72±103.67. Our results were comparable with results of Sukumar et al and Mamabolo et albut lower than mean vitamin B12 levels observed by Takimoto et al, Dayaldasani et al and Hay et al.[17,22-25] Mean S. vitamin B12 in our study was higher than mean vitamin B12 observed by Kaymaz et al, Bhate et aland Yajnik et al.[16,20,26] Our results showed that the mean maternal vitamin B12 level in mothers with LBW infants was significantly lower than that of mothers of ABW infants (143.23±91.79 pmol/l vs 188.8±109.64 pmol/l respectively p≤0.001) which is in agreement with previous studies done by Muthayya et al, Dwarkanath et al, Kumari et al and Ahmed et al.[1,13,15,27]

In our study there was a weak positive but statistically significant correlation between baby weight (kg) and S. vitamin B12 (rho=0.24, p=0.002) similarly there was a weak positive but statistically significant correlation between baby weight (kg) and S. folate (rho=0.17, p=0.029). Rogne et al in their study observed that there was no linear association between maternal B12 levels in pregnancy and birth weight, but B12 deficiency (<148 pmol/l) was associated with a higher risk of LBW in newborns (adjusted risk ratio=1.15, 95% CI:1.01,1.31).[28]

Mean maternal folate level in mothers with LBW infants was lower than that of mothers of ABW infants (8.46±8.94 nmol/l vs 9.96±12.57 nmol/l respectively p=0.054). There was no significant difference between the groups in terms of S. folate in our study (p=0.054) which is consistent with the observations of previous studies done by Youssry et al, Guerra et al, Christian et al and Takimoto et al but contradicts other studies done in the past by Ahmed and Kumari et al.[1,14,23,27,29,30]. Ronnenberg et al in their study found no association of low plasma folate with low birth weight in study subjects.[31]

There was a weak positive but statistically nonsignificant correlation between Apgar and S. vitamin B12 (rho=0.11, p=0.166) and S. folate (rho=0.01, p=0.849). Our obseravations were consistant with observations made by Youssry et al where weak positive correlation of Apgar with vit B12 and folic acid was seen.[14]

CONCLUSION

The present study confirms that maternal low vitamin B12 level and low S. folate levels are associated with low birth weight. Deficient pregnant women are not capable of supporting their fetuses with necessary micronutrients particularly in low socioeconomic group. Improvement in maternal micronutrients status have the potential to improve health outcomes for infants. So, during antenatal visit women should be screened for vitamin B12 and folate deficiency and vitamin supplementation should be continued throughout the pregnancy rather than to stop at the end of first trimester as in traditional practice. These simple measures will decrease the unacceptable burden of low birth weight and other health hazards which produce adverse effect on child survival, growth and development. Further studies are needed to evaluate whether maternal B12 and folic acid supplementation in pregnancy reduces the risk of preterm birth.

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