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ORIGINAL ARTICLE

Serum Vitamin B12 and Folate Levels in Mothers and their Newborns: An Observational Study

[1]Priyanka H Krishnaswamy, [2]Sujatha Prabhu, [3]N Ashwini Pandith, [4]Achal Shetty

ABSTRACT

Aim: To estimate the average serum values of vitamin B12 and folate in women with a term pregnancy and the cord blood of their newborns. To find if any correlation exists between the levels of serum B12 and folate in the mother and that of the neonate.

Materials and methods: A prospective observational study of serum B12 and folate levels and the respective cord blood concentrations of 51 term, nonanemic, pregnant women and in the cord blood of their newborns at delivery.

Results: Fifteen women were B12 deficient (29.4%) with the mean being 189.25 ± 94.2 ng/mL and 14 neonates were B12 deficient (27.45%) with their mean being 321.86 ± 143.68 ng/mL. One woman was folate deficient (1.96%) with the mean being 13.13 ± 5.15 ng/mL and one neonate was folate deficient (1.96%) with the mean being 15.68 ± 4.61 ng/mL. There was a significant correlation between maternal and neonatal B12 levels with a Pearson's coefficient of 0.74 (p-value of < 0.01) and a significant correlation between maternal and neonatal folate levels with a Pearson's coefficient of 0.44 (p-value of < 0.01).

Conclusion: There is a high incidence of maternal B12 deficiency in the Indian community, which has a positive correlation with neonatal levels. Treatment of B12 and folate deficiency should be a part of routine antenatal treatment, and neonates should be followed up and treated if found to be B12 or folate deficient.

Clinical significance: In India, where large numbers of women are anemic, deficiency of vitamin B12 and folate is overlooked when treatment of anemia is undertaken in most hospitals. In addition, women with undetected and subclinical deficiency may transmit it to their newborns with a cycle that is self-perpetuating unless broken with adequate intake or supplementation.

Keywords: Cord blood, Folate, Maternal serum, Vitamin B12.

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[1]Registrar, [2]Professor, [3]Postgraduate, [4]Research Officer

[1]Department of Obstetrics and Gynecology, Rangadore Memorial Hospital, Bengaluru, Karnataka, India

[2]Department of Obstetrics and Gynecology, ESIC Medical College and PGIMSR, Bengaluru, Karnataka, India

[3]Department of Biochemistry, ESIC Medical College and PGIMSR, Bengaluru, Karnataka, India

[4]Department of RUHSA, Christian Medical College and Hospital Vellore, Tamil Nadu, India

Corresponding Author: Priyanka H Krishnaswamy, Registrar Department of Obstetrics and Gynecology, Rangadore Memorial Hospital, Bengaluru, Karnataka, India, Phone: +918026983300 e-mail: priyanextdoor@yahoo.com

INTRODUCTION

Vitamin B12 or cobalamin is a co-enzyme in folate metabolism, which is crucial to cell multiplication in pregnancy. The rapidly dividing placental and fetal tissue result in an increased need for both cobalamin and folic acid in pregnancy.[1] Folate deficiency is associated with megaloblastic anemia, low birth weight, neural tube defects, stunting,[2] and a range of mild-to-moderate neurological and psychological disorders, while potential complications of vitamin B12 deficiency in pregnancy range from miscarriages, intrauterine death to developmental, intellectual, and neurological sequelae.[3]

Folate deficiency is related mainly to a low intake of green leafy vegetables and legumes and meat,[4] while Vitamin B12 deficiency is more frequent in population with a poor or inadequate diet of animal foods.[5]

Pregnancy is associated with a steady and physiologic fall in serum folate and vitamin B12, which can be attributed to transfer to the fetus, hemodilution, and changes in binders (like folate-binding proteins, transcobalamin I, and haptocorrin).[3]

The cut-off values for the lower limit of normal serum vitamin B12 and folate levels has been different across the literature. In this study, the concentrations suggested for defining folate and vitamin B12 deficiencies based on metabolic indicators are < 10 nmol/L (4 ng/mL) for serum folate and < 150 pmol/L (203 ng/mL) for plasma vitamin B12[6] and are derived from the US NHANES III (National Health and Nutrition Examination Survey)[7] and are consistent with data in the Institute of Medicine report.[8]

Upto 20% of pregnant women are folate deficient due to fivefold increased requirements in pregnancy.[9] Cord blood values of folate are more than the maternal levels due to avid binding of the folic acid to its transporter, and the normal newborn infant has sufficient vitamin B12 stores to last for 6 to 8 months, even in the presence of inadequate dietary intake or defective vitamin B12.[10]

As vitamin B12 and folate levels decrease in pregnancy, deficiency of these micronutrients are even more

significant in these women and, therefore, their children. This is more common in pregnant and lactating women and their young children in developing countries than has been recognized previously, due to dietary restriction and malabsorption, and cause public health problems.

The aim of this analysis is to describe the mean values of vitamin B12 and folate in a pregnant population in India and their newborn children, percentage of women and their babies who are deficient in these micronutrients, and if a correlation between levels of the mother and baby exists. Data from this study could help plan strategies and policies focused on the control and reduction of these micronutrient deficiencies.

AIMS AND OBJECTIVES

- To find the average levels of serum B12 and folate in women with 37 to 41 weeks of gestation and the percentage of women deficient in them.
- To study the levels of serum B12 and folate in cord blood of newborns at delivery and the percentage deficient in them.
- To find if any relation exists between the levels of serum B12 and folate in the mother and that of the neonate.

MATERIALS AND METHODS

A prospective comparative study of 51 term pregnant women attending the Obstetrics Outpatient and Labour Division at ESIC Medical College & PGIMSR, Rajajinagar, Bengaluru, Karnataka, India, during the period April 2013 to January 2014 irrespective of the place and frequency of prior antenatal checkup. We obtained permission from the Hospital and Departmental Clinical Research Committee before starting this study.

Clinical Management and Data Collection

Participants who fulfilled the inclusion and exclusion criteria were included in the study. Hospital staff and participants were all aware of the study being conducted and an informed consent was taken from the patient.

Ethical Approval

We obtained approval from the Hospital and Departmental Clinical Research Committee on May 18, 2013, before starting this study.

Study Population and Setting

Women between 21 and 35 years of age, with a single live intrauterine pregnancy of 37 to 41 weeks of gestation who had consented to be included in this study. The exclusion criteria were multiple pregnancy, preterm delivery, and women on treatment for detected iron, vitamin B12, or folate deficiency.

A total of 51 pregnant attending the Outpatient Antenatal Clinic at ESIC Medical College & PGIMSR either for the first time or are booked in the institution were examined, investigated, and if fulfilled the inclusion and exclusion criteria were registered into the study. Informed written consent was obtained for the procedure. Venous blood of 3 mL was drawn into a plain vacutainer and maternal serum B12, and folic acid was estimated using the International Federation of Clinical Chemistry (IFCC).

When the patient came in labor or was admitted for obstetric indications and delivery was planned, the inclusion criteria were again checked, procedure explained, and written informed consent obtained. Cord blood of 3 mL was drawn into a plain vacutainer within 90 seconds of birth and 30 seconds of clamping the cord. Serum B12 and folate levels were estimated using the IFCC method. (Normal values: < 4 ng/mL for serum folate and < 203 ng/mL for plasma vitamin B12).

The results of her blood test as well as her baby's were informed to the woman before discharge and suitable treatment was given.

Statistical Analysis

The data obtained was fed into Microsoft Excel and proportions estimated. It will be further analyzed using Statistical Package for the Social Sciences (SPSS) – Correlation statistics.

Study Outcomes

The primary outcomes studied are the average levels of serum B12 and folate in women and their newborns along with the percentage of them deficient in these micronutrients. The secondary outcome was to find out if any relation exists between the levels of serum B12 and folate in the mother and that of the neonate.

RESULTS

Study Group (Table 1)

Demographic characteristics were analyzed with respect to age, weight, hemoglobin status, and parity.

Table 1: Demographics of the study population

Demographic characteristics	*Group (range)*
Age (years)	25.7 (18–35.5)
Weight (kg)	55.9 (38–82)
Hemoglobin (gm/dL)	11.5 (10.5–13.2)
Parity	*No. of women (%) (n = 51)*
Primigravida	20 (39.2)
Parous	31 (60.8)

Table 2: Antenatal supplementation of folic acid, iron, vitamin B_{12}, and calcium in study population

Supplements	*Preconception (%)*	*6–12 weeks (%)*	*12–20 weeks (%)*	*20–37 weeks (%)*	*Nil (%)*	*Total*
Folic acid	5 (9.8)	28 (54.9)	15 (29.4)	0 (0)	3 (5.8)	51
Iron	0 (0)	1 (1.9)	29 (56.8)	19 (37.2)	2 (3.9)	51
Vitamin B12	0 (0)	0 (0)	0 (0)	0 (0)	51 (100)	51
Calcium	1 (1.9)	1 (1.9)	25 (49)	14 (27.4)	10 (19.6)	51

Table 3: Mean, standard deviation, and range of vitamin B_{12} and folate values in the mother and baby

Micronutrient studied	*Mean ± σ (standard deviation)*	*Range*
Maternal B12 (ng/mL) at 37 weeks	189.25 ± 94.2	2.78–375.72
Maternal folate (ng/mL) at 37 weeks	13.13 ± 5.15	2.93–23.32
Baby B12 (ng/mL) in cord blood	321.86 ± 143.68	37.44–606.28
Baby folate (ng/mL) in cord blood	15.68 ± 4.61	6.56–24.81

Table 4: Number of mothers and babies with normal and deficient values of serum vitamin B_{12} and folate

Micronutrient studied	*Number with normal values (%)*	*Number with deficient values (%)*
Maternal B12	36 (70.58)	15 (29.4)
Baby B12	37 (72.55)	14 (27.45)
Maternal folate	50 (98.03)	1 (1.96)
Baby folate	50 (98.03)	1 (1.96)

Maternal Supplementation with Folic Acid, Iron, Vitamin B12, and Calcium (Table 2)

Out of 51 antenatal women tested, 38 had taken folic acid, 49 had taken iron, and 41 calcium supplementation in their pregnancy. No patient had taken vitamin B12 supplementation in their pregnancy.

Serum B12 in Women (Table 3)

In the 51 term antenatal women tested, the mean maternal B12 level was 189.25 ± 94.2 ng/mL. Of these, 15 (29.4%) women were serum vitamin B12 deficient – 12 of whom were gravida 2 and higher.

Serum Folate in Women (Table 3)

In the 51 antenatal women tested, mean maternal folate levels were 13.13 ± 5.15 ng/mL. One woman (1.96%), who was gravida 3, was folate deficient and had not taken folic acid supplementation but had taken iron and calcium supplementation during her pregnancy.

Serum B12 in Neonates (Table 3)

In the 51 neonates tested, the mean neonatal B12 level was 321.86 ± 143.68 ng/mL. Fourteen neonates (27.45%) were serum vitamin B12 deficient, out of whom 10 neonates had mothers who were also deficient in vitamin B12.

Serum Folate in Neonates (Table 3)

In the 51 neonates tested, the mean neonatal folate level was 15.68 ± 4.61 ng/mL. One neonate (1.96%) was serum folate deficient and was born to the mother with low serum folic acid.

Relation between Serum 12 and Folate in Women and Neonates (Table 4)

There was a significant correlation between maternal and neonatal B12 levels with a Pearson's coefficient of 0.74 and a p-value of <0.01. There was also a significant correlation between maternal and neonatal folate levels with a Pearson's coefficient of 0.44 and a p-value of <0.01.

DISCUSSION

Main Findings

A high percentage of both mothers and neonates were vitamin B12 deficient, i.e., 29.4 and 27.45% respectively. There was a significant correlation between maternal and neonatal B12 levels with a Pearson's coefficient of 0.74 (p-value of <0.01) and a significant correlation between maternal and neonatal folate levels with a Pearson's coefficient of 0.44 (p-value of <0.01).

Strengths and Weaknesses of the Study

The major strength of this trial was that the trial population was homogeneous with strict inclusion and exclusion criteria.

Some limitations to this study may apply as this was a small study conducted in a unit of a teaching hospital. Large multicentric studies with a mixed ethnic population would be of value in this field. Another limitation to the current study may be that the outcomes evaluated were all short-term with no long-term follow-up of deficient women and babies.

Interpretation

Before applying the results to other populations and settings, several factors have to be considered. Overall, the study population had a low body mass index and was very homogeneous, and the study aimed to include only healthy women with no a priori risks.

CONCLUSION

In India, where large numbers of women are anemic, deficiency of vitamin B12 and folate is overlooked when treatment of anemia is undertaken in most hospitals. In addition, women with undetected and subclinical deficiency may transmit it to their newborns with a cycle that is self-perpetuating unless broken with adequate intake or supplementation.

A study conducted by Johns Hopkins Bloomberg School of Public Health, published in May 2016,[11] suggested that high levels of vitamin B12 and folate during pregnancy (either in the form of folate fortified food, excessive multivitamin intake, or altered metabolism of these vitamins) was related to increasing chances of autism in the baby. As this study was a longitudinal cohort study, further high-quality research in this subject is needed before change in nutritional supplementation guidelines can take place across the globe. This is especially pertinent in developing counties like India where nutritional deficiencies are high and routine measurement of serum vitamin B12 and folate for all pregnant women is not feasible and might not be cost-effective.

To provide the best outcome for pregnant women in our population with a high incidence of anemia, we recommend administration of vitamin B12 along with the administration of folate in pregnancy as a high percentage of women were found to be deficient in vitamin B12 with a direct correlation between maternal and neonatal B12 and folate levels.

CONTRIBUTION TO AUTHORSHIP

All authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors reviewed and approved the final version of the paper.

DETAILS OF ETHICS APPROVAL

The study was approved by ESI Hospital Ethical Committee.

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