STUDY OF VITAMIN B12 DEFICIENCY IN PREGNANCY AND ITS IMPACT ON THE MATERNAL AND FOETAL OUTCOME

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Abstract

Vitamin B12 deficiency in reproductive age of women poses a vast impact on their obstetric profile. This deficiency is frequently found but not sought for in our patients routinely. The simple test of measurement of these levels can prevent many untoward complications. Mainly belonging to a strictly vegetarian diet in our culture and practices, this deficiency is only seen as a tip of an iceberg. Our study aims at the detection of its deficiency and provides a guideline to take care of antenatal patients. We have measured the levels of vitamin B12 and its impact on pregnancy it’s maternal and foetal outcomes and presence of complications.

Keywords: Vitamin B12, Diet, Pregnancy, Supplements.

Introduction

Vitamin B12 is a water-soluble vitamin required for maintenance of normal erythropoiesis, nucleoprotein and myelin synthesis, cell reproduction and normal growth. Not frequently sought for, Vitamin B12 deficiency is frequently reported in pregnancy due to inadequate dietary intake of vitamin B12 and also a physiological decline of maternal vitamin B12 concentrations. It is well recognized that requirement for B12 increases during pregnancy and lactation. Vitamin B12 needs during pregnancy and infancy are so high that it is virtually impossible for these to be met through diet alone, especially in low and middle income countries. Vitamin B12 deficiency during pregnancy is associated with preeclampsia, foetal growth restriction, preterm labour, neural tube defects, neonatal megaloblastic anaemia and neonatal neurological symptoms. Further work is needed to introduce guidelines for vitamin B12 supplements in pregnancy as these deficiencies may be largely preventable if appropriately addressed. Screening of deficiencies in pregnancy & supplements of vitamins may prevent many complications.

This study reviews vitamin B12 levels during pregnancy, its effect on pregnancy, and the health of the offsprings.

Many studies showed maternal vitamin deficiency and the importance of detecting and treating maternal vitamin deficiency during pregnancy in at-risk patients. Failure to diagnose and institute treatment may carry significant risks to both mother and child.

Aims and Objectives: The objectives of the study were

1) To find prevalence of vitamin B12 deficiency in pregnancy and its relationship with socio-demographic and dietary intake.
2) To correlate the maternal complications due to vitamin B12 deficiency.
3) To evaluate perinatal outcome due to deficiency.

Material and Methods

The study was undertaken among patients attending OPD and admitted in Obstetrics and Gynaecology Department of M.Y. Hospital and M.G.M College Indore.

The study was conducted over a period of six months from September 2013 to March 2014 among patients attending the OPD and emergency department in Obstetrics & Gynaecology.

Sample Size

110 patients between 28 to 40 weeks of gestational period were included in this study. Information on age, education, parity, occupation, income and obstetric history was obtained from the mother using a close ended questionnaire. Gestational age (in weeks) at enrolment was calculated from the reported first day of the last menstrual period. Gestational age at birth was calculated using an ultrasonography report. Diet history was taken, vegetarian; mix includes consumption of egg and non-vegetarian taking meat, chicken, fish. History of iron and calcium intake was also taken. Blood investigations such as haemoglobin, mean corpuscular volume (MCV), haematocrit, serum vitamin B12 was done. Any complaint like numbness, bony pain, neurological symptoms and generalised weakness were asked. High risk factors like anaemia, preeclampsia and diabetes were identified. Patients were followed up for mode of termination of delivery. Details like normal delivery/LSCS(Lower segment Caesarean section)/PTL (preterm labour)/ spontaneous vaginal delivery (SVD) noted,
baby weight was measured at birth and the baby was also looked for any congenital anomaly.

Sample Technique: Specimens for B12 analysis were taken. Analysis of plasma vitamin B12 was done. Vitamin B12 was measured by fully automated electro-chemiluminescence method (Elecsys 2010, Roche Diagnostics Mannheim, USA). The intra- and inter-day assay coefficients of variation for vitamin B12 were 4.0% and 4.4% respectively. Low vitamin B12 concentration was defined as plasma vitamin B12 concentration < 203pg/ml.

Statistical Analysis
Data were collected through specially designed performa after taking verbal consent. Descriptive data were presented as number and percentages with mean and standard deviation wherever required. Chi-square test was used for analyzing categorical data. Student’s ‘t’ test was used for comparing mean between two groups. A p-value of 0.05 or less was considered statistically significant.

Estimated Average Requirements (EAR), (WHO CRITERIA)

The concentrations suggested for defining folate and vitamin B12 deficiencies based on metabolic indicators are:
- < 10 nmol/L (4 ng/mL) for serum folate
- < 340 nmol/L (151 ng/mL) for RBC folate
- < 150 pmol/L (203 pg/mL) for plasma vitamin B12

Observation tables
Data of table 1 and figure 1 shows that 110 subjects participated in the study in which 46(41.8%) were found deficient with vitamin B12.

Table 1. Deficiency of Vitamin B12

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number of pregnant women screened</th>
<th>Number of pregnant women with Vitamin B12 deficiency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>110</td>
<td>46</td>
<td>41.8</td>
</tr>
</tbody>
</table>

Data in table 2 shows that vitamin B12 deficiency was more in primi para (69.5%), Deficiency was common in Urban (82.7%) as compared to rural population (17.3%). Deficiency was more common in Hindus (78.3%) compared to Muslims (21.7%), deficiency was more in anaemic (69.57%) as compared to non-anaemic (30.43%), and in vegetarian (52.17%) than mix (32.60) or non-vegetarians (15.21).

Table 2. Demographic variables of woman with vitamin B12 deficiency

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total no. (n%)</th>
<th>Deficient (n=46) n%</th>
<th>Chi square value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Para 0 1 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural  Urban</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hindu  Muslims</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetarian Mix</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Vegetarian</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaemic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-anaemic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Vitamin B12 deficiency was higher in patients with oligohydramnios, IUGR, gestational hypertension, diabetes mellitus, congenital anomaly and patients complaining of neurological symptoms like numbness and tingling as shown in table 3.

Table 3. Vitamin B12 deficiency in high risk patients

<table>
<thead>
<tr>
<th>High risk patients</th>
<th>Total</th>
<th>Vitamin B12 deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tingling, numbness</td>
<td>28</td>
<td>23</td>
</tr>
<tr>
<td>Gestational Hypertension (GHTN)</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Bony pain</td>
<td>37</td>
<td>12</td>
</tr>
<tr>
<td>Oligohydramnios</td>
<td>34</td>
<td>23</td>
</tr>
<tr>
<td>IUGR</td>
<td>21</td>
<td>12</td>
</tr>
<tr>
<td>Diabetes</td>
<td>02</td>
<td>02</td>
</tr>
<tr>
<td>Congenital anomaly</td>
<td>05</td>
<td>05</td>
</tr>
</tbody>
</table>

Out of the total, 88 vaginally delivered patients 35 patients had low levels of vitamin B12. Out of 22 caesarean deliveries 11 patients had low vitamin B12 levels. These data shows that there is 1.5 to 2 fold risk of LSCS in Vitamin B12 deficient
pregnant women as compared to normal delivery as shown in table 4.

**Table 4. Mode of Delivery**

<table>
<thead>
<tr>
<th>Mode of delivery</th>
<th>Total</th>
<th>Vitamin B12 deficiency (46)</th>
<th>Normal Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal delivery</td>
<td>88</td>
<td>35</td>
<td>53</td>
</tr>
<tr>
<td>LSCS</td>
<td>22</td>
<td>11 (23.91%)</td>
<td>11</td>
</tr>
</tbody>
</table>

Fifty babies weighed less than <2.5kg at birth (45.5%) and there were 2 IUD. Three babies were diagnosed to have Neural Tube Defects (NTD) in USG reports and 2 had other congenital anomalies. Out of 50 newborns below 2.5 kg baby weight 36 (72%) were vitamin B12 deficient as compared to normal baby weight as shown in table 5.

**Table 5. Outcome of babies**

<table>
<thead>
<tr>
<th>Weight</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2.5KG</td>
<td>60</td>
</tr>
<tr>
<td>&lt;2.5Kg</td>
<td>50</td>
</tr>
<tr>
<td>Intrauterine death (IUD)</td>
<td>2</td>
</tr>
<tr>
<td>Neural tube defects (NTD)</td>
<td>3</td>
</tr>
<tr>
<td>Congenital Anomaly</td>
<td>2</td>
</tr>
</tbody>
</table>

Discussion

Vitamin B12 is a basic nutrient required for maintenance of normal erythropoiesis, cell reproduction, nucleoprotein and myelin synthesis. B12 deficiency is associated with adverse pregnancy outcomes and neurodevelopmental morbidity during infancy. The correlation of its deficiency with few obstetric conditions has been clearly found in our observational study.

Prevalence

Of the total 110 patients 46 patients had vitamin B12 deficiency. This forms a high proportion of about 41.8 %. It is difficult to quantify the prevalence of deficiency in pregnant women partly due to the gradual decline in the plasma B12 concentration throughout gestation. Based on gestational week, prevalence of deficiency worldwide may vary from 5% (<28 days gestation) to 72% (immediately prior to delivery).²³

In South Asia, examples of reported prevalence of deficiency include 27% of pregnant woman at early to late pregnancy (i.e. gestational week, GW 10.2 ± 4.1 to 32.6 ± 3.9) in rural Nepal, 74% in Haryana, 65% at GW 18-28 in Pune and 51% at GW =14 in urban south India.⁷ The MINIMat study in Matlab, a rural area in Bangladesh showed that B12 deficiency was 46% in pregnant women at third trimester.⁸

Demographic parameters

Vitamin B12 deficiency in pregnancy was more in primigravida in our study (69.5%) suggesting an ongoing vicious cycle of malnutrition from the breast feeding up to first pregnancy, which happens at an early age commonly in the Asian subcontinent. Urban patients showed more deficiency (82.7%) as compared to the rural population (17.3%). A Muslim diet essentially contains non-vegetarian food making them less susceptible to the deficiency (21.7%) as compared to the Hindu population (78.3%) in the area. Vegetarians clearly showed a marked deficiency of vitamin B12 (52.17%). The degree of vitamin B12 deficiency was related to the degree of animal product restriction, resulting in the highest risk for vegans as reported by Hermann et al.¹⁰ Vegetarians still had a 4.4 times higher risk of hyper homocysteinemia than their non-vegetarian counterparts as reported by Yajnik et al., 2006.¹⁰

Effects of Vitamin B12 Deficiency on Pregnancy

**Congenital malformations and NTDs**

Vitamin B12 plays a key role in normal functioning of brain and nervous system. There were five patients with congenital malformations in our study. Three of them had neural tube defects and all the five patients had vitamin B12 deficiency. Schorah et al. found an association between low maternal plasma vitamin B12 and pregnancies affected by anencephaly.¹¹ Nine years post-folic acid fortification, a population based case-control study in Ontario, Canada reported almost a tripling in the risk for NTDs in the presence of low maternal B12 status, measured by serum holoTC (holotranscobalamin).³ Lower maternal vitamin B12 concentrations (Geometric mean: 130 pmol/L) were associated with higher total homocysteine (THcy) and lower SAM:SAH (S-adenosylmethionine/S-adenosylhomocysteine) in newborn suggesting that methylation could be impaired in mother-infant pairs.¹² Maternal plasma B12 in pregnancy is also predictive of offspring cognitive performance at 9 years.¹³ In rural Kenyan women (n=138), B12 intake during pregnancy was correlated with improved scores on the infant’s Brazelton Neonatal Behavioural Assessment reflex subscale score (R =-0.19, p=0.05; with adjustment for gestational age) within 3 days after birth.¹⁴ The babies of the deficient mothers were not followed beyond their hospital stay which could have revealed more information on the children’s performance at school and infant milestones and reflexes.
Twenty-three mothers out of 28 presenting with tingling and numbness had Vitamin B12 deficiency suggesting the role in neurological integrity.

One study in Chinese women found that inadequate preconception vitamin B12 (<258 pmol/L) was associated with a 60% increased risk of preterm delivery. A cohort study in Bangalore, India, (n=486) showed that women in the lowest level of serum vitamin B12 concentration during each of the three trimesters of pregnancy had a significantly higher risk of IUGR. Our study showed fifty babies delivering with the weight of less than 2.5kg. Of these fifty babies 36 had deficiency of vitamin B12. A study carried out in South India (n=1838) observed that high folate and low vitamin B12 intakes (1.2 μg/d) during pregnancy are associated with small-for-gestational age infants.

Other Obstetrical Complications

**Gestational diabetes**

In our study there were two patients of gestational diabetes both of which had vitamin B12 deficiency. This data is though small but may indicate the relation between the two. An observational cohort study (n=785) carried out in Mysore, India found an interesting association of B12 deficiency during pregnancy with obesity and gestational diabetes.

**Gestational Hypertension**

In our study there were 13 patients having hypertension. Of these 10 patients had vitamin B12 deficiency indicating a significant association between the two. Strong associations have been reported between elevated plasma homocysteine and adverse pregnancy outcomes such as recurrent spontaneous abortion, intra-uterine death, abortion placenta, Neural Tube Defect (NTD) and preclampsia possibly due to disturbed methionine metabolism.

**Oligohydramnios**

Twenty-one patients had oligohydramnios in their pregnancy of which 12 patients had vitamin B12 deficiency.

**Mode of Delivery**

There is a definite 1.5 to 2 fold risk (23.9%) of delivery by a caesarean section in patients with vitamin B12 deficiency. This increase can be easily decreased by vitamin B12 supplementation.

**Summary**

The present study was carried out at department of Obstetrics and Gynaecology M.Y. Hospital MGM Medical College Indore from September 2013 to March 2014. Results were summarized as follows:

1. Prevalence of vitamin B12 deficiency was 41.8%.
2. Low level of serum vitamin B12 is more in pregnant mothers who are strict vegetarian or habitually took small proportion of non-vegetarian food. It was more in Hindus 78.2% as compared to Muslims 21.8%.
3. Patient complaining of general weakness, numbness, and tingling, bony pain were deficit with vitB12.
4. Our study showed fifty babies delivering with the weight of less than 2.5kg of these fifty babies 36 had deficiency of vitamin B12.
5. There were five patients with congenital malformations in our study. Three of them had neural tube defects and all the five patients had vitamin B12 deficiency.
6. Vitamin B12 deficiency was seen in patients with gestational hypertension, oligohydramnios, IUGR, DM, and congenital anomalies.

**Conclusion**

Routine screening of maternal vitamin B12 deficiency demonstrates the importance of detecting and treating maternal vitamin B12 deficiency during pregnancy in at-risk patients. Failure to diagnose and institute treatment may carry significant risks to both mother and child. Our review, after summarizing existing data of this study, shows a causal relation between low Vitamin B12 level and adverse maternal & neonatal outcome. Lack of VitB12 in pregnant women has been linked to GDM, Preecampsia, and increased rate of LSCS birth. In pregnant women deficiency may cause or be associated with spontaneous abortion, IUGR, IUD, preecampsia, preterm labour & anaemia while in new born LBW, NTDs or congenital anomalies (spina bifida, anencephaly etc.), anaemia or other developmental defects. Low levels of serum B12 have been documented among pregnant women in India who habitually are vegetarian or mix non vegetarians, taking small proportion of non-vegetarian food. These findings have important implications for the antenatal vitamin B supplementation policy in India.

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**Ethical approval:** The study has been approved by the institutional ethical Committee of MGM medical college, Indore.

**Conflict of interest:** The authors have no conflict of interest and all have contributed equally.

**References**

2. Ray JG, Goodman J, O’Mahoney PR, Mamdani MM, Jiang D. High rate of maternal vitamin B12 deficiency nearly a decade after Canadian folic acid flour fortification. JOM


