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Prevalence of Vitamin B_{12} Deficiency in Pregnant Women & Its Effect on Fetal Outcome

Annapoorna Yalla*, Sunanda Kasula, P. Ravinder***, Madhavan K. Nair******

Abstract

Introduction: Anemia is one of the most commonly encountered medical disorders during pregnancy. The fact that some of the pregnant women do not respond to iron therapies, implies deficiency or abnormalities of other factors involved in the hemoglobin/RBC generation and its function. One of the important factors is Vitamin B12 *Aims and Objectives:* 1.To find out the prevalence of vitamin B_{12} deficiency in primigravid pregnant women in first and early second trimester. 2.To study the effect of B_{12} deficiency on pregnancy outcome. *Results:* The prevalence of anemia is 57% with 29.5% mild, 25.5% moderate and 2.1% severe anemia (Hb%: mild 10-11,moderate 7-10 and severe <7gm%). Serum folate was normal (>/= 3ng/dl) in 93.3% and low(<3ng/dl) in 5.7%. Vitamin B_{12} was normal in 70% (>200pg/dl) and low(<200pg/dl) in 30% of the study group. *Conclusion:* Anemia is still a major complication of pregnancy with a very high prevalence of 57%. This study revealed that there is significant B_{12} deficiency in pregnancy of 30%.B_{12} deficiency is associated with preeclampsia but not with low birth weight. There was folic acid deficiency with a prevalence of 5.7% Folate deficiency is associated with early abortions and low birth weight. The study suggests that apart from iron and folate, vitamin B_{12} also is a major factor affecting maternal and perinatal outcome and needs further evaluation.

Keywords: Folic Acid; Haemoglobin; B_{12} and Fetal Outcome.

*Assistant Professor, Department of Obstetrics and Gynecology, G.S.L. Medical College, Rajahmundry, Andhra Pradesh 533296, India. **Assistant Professor, Department of Obstetrics and Gynecology, Gandhi Medical College, Secunderabad, Telangana 500003, India. ***Department of Biophysics, National Institute of Nutrition, Hyderabad, Telangana 500007, India. ****Scientist E, National Institute of Nutrition, Hyderabad, Telangana 500007, India.

Corresponding Author:
Dr. Annapoorna Yalla,
Flat no-103, Dno-3-321/5, JSN Raju Residency, Spinning mill colony-2 Lalacheruvu, Rajahmundry. Andhra Pradesh- 533106
E-mail: drsannapoorna@gmail.com

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Introduction

Anemia is one of the most commonly encountered medical disorders during pregnancy. In developing countries it is a cause of serious concern as besides many other adverse effects on the mother and the fetus it contributes significantly to high maternal mortality. According to United Nations declaration 1997, anemia is a major public health problem that needs total elimination. It is estimated that globally two billion people suffer from anemia or iron deficiency [1].

A crude estimate is that 500 million women between 15 and 49 years of age worldwide are anemic [2]. According to World Health Organization estimates, up to 56% of all women living in developing countries are anemic [3]. In India, National Family Health Survey-3 in 2005-06 shows that 52% of women -in rural and 46% of women in urban areas are anemic. In US 12 to 16% non pregnant women between ages 16 to 48 are iron deficient and 2 to 4% women are anemic [4]. Prevalence of anemia during pregnancy is much higher and has far reaching consequences, especially the severe degrees of anemia. It is estimated that 60 million pregnant women world wide are anemic. Only 4 million of these are in developed countries.

The prevalence of anemia among pregnant women in India according to the NFHS -2 in 1998 -99 & NFHS-3 in 2005-06 is nearly 58%

and 56.4% in Andhra Pradesh. Further, the striking observation is that the percentage of prevalence of anemia is increasing in pregnant women despite the mandatory supplementation of iron-folic acid as part of anemia prophylaxis program.

The fact that some of the pregnant women do not respond to iron therapies, implies deficiency or abnormalities of other factors involved in the hemoglobin/RBC generation and its function. One of the important factors is Cyanocobalamin otherwise called Vitamin B_{12} whose deficiency causes megaloblastic anemia.

Only 3-4% of women with anemia during pregnancy have megaloblastic variety. Only 1 of every 8500 pregnant women with anemia has B_{12} deficiency anemia [5]. Vitamin B_{12} absorption is said to be unaltered in pregnancy [6].

A deficiency syndrome is described in breastfed infants of mothers with B_{12} deficiency. It is usually apparent by 6 months of age and is characterized by failure to thrive, developmental regression and anemia [7]. The reference values for nonpregnant individuals are often used to assess the vitamin B12 status during pregnancy as there are no proper studies [8].

There have been very few studies regarding B_{12} deficiency in India. A recent study conducted in a rural area of Harayana has concluded that as high as 74.1% of pregnant women had poor B_{12} stores [9] and 16.2% had B_{12} deficiency

Aims and Objectives

1. To find out the prevalence of vitamin B_{12} deficiency in primigravid pregnant women in first and early second trimester.
2. To study the effect of B_{12} deficiency on pregnancy outcome

Materials & Methods

This was a hospital-based study conducted in Gandhi hospital. We screened 4000 antenatal women and 525 women were fit for study, inclusion criteria being primigravida and before 20 weeks gestation. Women already with anemia and medical disorders were excluded. After taking written informed consent, details of their nutritional history, menstrual history, obstetric history, medical history & socio demographic history is noted. Detailed obstetric examination and calculation of height, weight done. HIV and HbsAg screening is done. A fasting venous blood sample is taken for assessment of hematological parameters. These women are followed up until their delivery and complications of pregnancy and outcome of pregnancy is recorded. Women needing immediate medical attention based on the results of the data are called and treated accordingly.

Methods

Analysis of B_{12}: By dual count method using solid phase no boil assay from kit obtained from Siemens medical solutions diagnostics was used.

Analysis of Hemoglobin: By cyanmethemoglobin method.

Analysis of Folic acid: By dual count method using solid phase no boil assay from kit obtained from Siemens medical solutions diagnostics was used.

Results

General Information

The minimum age of the subjects is 16, maximum age is 38 with a mean of 22.13 and a SD of 3.02.The minimum monthly income is 1500 and a maximum of 8000 with a mean of 3382 and a SD of 1,109rupees. The minimum body mass index is 12.5 and a maximum of 30.6 with a mean of 19.9 and a SD of 3.14. The first antenatal checkup was at a minimum of 4 weeks gestation and a maximum of 20 wks with a mean gestational age of 15.22 and a SD of 4.07. 93% of the women were taking nonvegetarian diet i.e atleast 100gm of meat twice weekly. Only 2% were pure vegetarians.

Hematological Parameters

The prevalence of anemia is 57% with 29.5% mild, 25.5% moderate and 2.1% severe anemia (Hb%: mild 10-11, moderate 7-10 and severe <7gm%). 53% had low packed cell volume. Peripheral smear showed predominantly normal platelets (97.9%)and White blood cells (81.07%). Red blood cell morphology was normocytic normochromic in 68.8%, microcytic hypochromic in 20.9%, normocytic mild hypochromic in 4.8% and a mixed picture in 5.3%.

Serum folate was normal (>/= 3ng/dl) in 93.3% and low(<3ng/dl) in5.7%. Vitamin B12 was normal in 70% (>200pg/dl) and low(<200pg/dl) in 30% of the study group.

Perinatal Outcome

Most of the women reached to term with 55%

vaginal births, 37% cesaerian delivery, 6% abortions and 2% intrauterine fetal demise. Of the live births, 14% had low birth weight (<2 kgs) and 86% had normal birth weight (2kgs-4 kgs). Maternal compilcations includes preecclampsia in 25 (23.36%), anemia needing blood transfusion in 4 (3.7%), preterm delivery in 3 (2.8%), eclampsia in 3(2.8%) and abruption in 2 women (1.8%).

Correlations

When multiple correlations were done by using post hoc analysis there was no statistically significant correlation between moderate and mild anemia and birth weight (p>0.05). There seems to be a trend of birth weight with hemoglobin percentage but it is not statistically significant (p>0.05). There was no significant correlation between vitamin b12 status and birth weight (p>0.05).

There was statistically significant correlation between serum folate levels and birth weight (p<0.05). There was statistically significant correlation between serum folate, hemoglobin percentage and vitamin B 12 levels (p<0.05). However, there was no correlation between folic acid and b12 with birth weight (p>0.05).

Table 1:

Name of the study	Hb%(cut off)	Folate(cut off)	B12(cut off)
Mathanetal.	57.4(11gm%)	73%(6ng)	52%(140pg)
Pathak etal.	67.7%(12ng)	26.3(3ng)	74.1%(200pg)
Present study	57%(11gm%)	5.7%(3ng)	30%(200pg)

Discussion

This study was based on the representative sample of women attending the antenatal clinics for their first visit and may not represent the community as a whole. However, it is a uniform sample and may indirectly represent the nutritional status of the community.

In the present study 93% of women are between 20-25 yrs of age. Although it is an optimal age for pregnancy 30% of these women have B_{12} deficiency. This indicates that the pre pregnancy stores of folate and B_{12} are significantly lower. Although 93% are said to be non –vegans, the deficiency of B_{12} is higher than expected. This may be due to the inadequate amount and poor quality of meat product consumption which may again be due to their low socio economic status, the mean average monthly income of this group being 3382 rupees only.

The study has demonstrated a very high prevalence of anemia, folate and vitamin B_{12} deficiency in the women even in the earlier weeks of their first pregnancy. The prevalence of anemia correlates with that of NFHS 3 (2006) in Andhra Pradesh (57% as compared to 56%) but, the folate levels and vitamin B_{12} levels are lower than that of previous studies.

There have been very few studies evaluating vitamin B_{12} status in pregnant women. In India a similar study was conducted in 1973 by Mathan et al[10] in Christian Medical College, Vellore and recently in 2007 a similar study was conducted in northern India by Pathak et al [10](Table 1).

Anemia

According to this study the prevalence of anemia is 57% with 29.5% mild, 25.5% moderate and 2.1% severe anemia (Hb%: mild 10-11,moderate 7-10 and severe <7gm%)

The prevalence of anemia in this population seems to be the same of that of Mathan et al (1973) but lower that of Pathak et al (2007) in northern India (67%). In spite of the routine anemia prophylaxis program and many other national programs the prevalence of anemia is not reduced. Moreover there is every chance of increase in the severity and percentage of anemia in the later part of present pregnancy and subsequent pregnancies if timely interventions are not made. Most of the cases are due to iron deficiency anemia as shown by the peripheral smear (20% vs. 5% for megaloblastosis). Since these levels correspond to the pre pregnancy status of nutrition, we can assume that even the adolescent stores of iron are deficient and they cannot tolerate the stress of pregnancy. This calls for further initiatives to prevent anemia in pregnancy.

In spite of severe degree of deficiency in 7 women in the study none of these women had any symptoms of anemia, but subsequently four of these women needed blood transfusions. This indicates that early antenatal checkups and regular follow up help early diagnosis, treatment of anemia thus reducing the later morbidity.

The reasons for high prevalence of iron deficiency are not clear. The mean daily intake of iron in an average Indian diet has been estimated anywhere between 15-30 mg per day [12,13]. Studies of body iron excretion with labeled iron have shown that iron loss in subjects working in hot humid environment are similar to that of people in temperate conditions

[14]. It therefore appears that sweat losses cannot explain low body iron stores. The most probable explanation is that the food iron is not available readily either because of its chemical form [15-18] or because of the presence of substances in the diet such as phytates and phosphates that inhibit iron absorption [16,19,20].

There were statistically significant correlation between hemoglobin concentration and vitamin $B_{12,}$ but not between hemoglobin concentration and folate. This may be due to IFA supplementation. There was again significant correlation between hemoglobin concentration and packed cell volume and red cell counts.

Megaloblastosis

The prevalence of megaloblastosis in the present group is low (5%) as compare to Mathan et al (60%) The highest value 75% is that of Robert et al [21] and the lowest is that of Giles [22,23] 3%. This wide variation may be due to a number of factors including differences in interpretation of morphological changes, differences in socioeconomic status and dietary habits of the population.

Folate Nutrition

The prevalence of folate deficiency is 5.7% in this study. The prevalence of folate deficiency in the present population is lower than the earlier studies, however comparison is difficult because of the various microbiological assays available. In a normal person deprived of dietary folate, the body stores are sufficient for about 4 months [24].

The low levels of folate during pregnancy indicate that the increased demands of folate outstrip the available supply from the food, rather than a preexisting deficiency of body stores. Further more the IFA program reduces the prevalence.

There is no statistically significant correlation between folic acid and vitamin B_{12}. It has been suggested that iron deficiency can cause secondary folate deficiency [25]. In the study there is association of folate deficiency with spontaneous abortions.

There has been statistically significant correlation between folic acid and birth weight.

Vitamin B_{12} Nutrition

Even though the majority of the patients were nonvegetarians by habit(93%) the prevalence of B_{12} deficiency was 30%(lower than Pathak etal and Mathan etal). This may be explained by the infrequent and low amount consumption of meat and meat products by these women. Most of these women had 100gm meat products per week, which may be inadequate for the needs of the pregnancy and to replenish the stores. And since these levels correspond to the pre pregnancy stores of $B_{12,}$ it is evident that the nutrition of adolescent women is poor. Hence the role of stressing on the dietary habits and replenishment of vitamin B_{12} should be evaluated.

The relation between maternal B_{12} status and fetal outcome has been poorly studied. It is proved that in deficiency state also cord blood levels of vitamin B_{12} are higher than that of maternal levels [26]. A deficiency syndrome has been seen in B_{12} deficient women who were breast feeding which includes failure to thrive, anemia and developmental regression [27]. Also increase in the levels of homocysteine, a metabolite of vitamin B_{12} is said to be associated with major birth defects [28]. B_{12} deficiency is also a cause of infertility [29]. Hence all adolescent women should be having adequate B_{12} stores for their safe motherhood.

The relation between maternal B_{12} levels and birth weight were not statistically significant in the present study. This was earlier proved by Muttaya etal in 2006 but there was significant correlation between fetal cord B_{12} status and IUGR. Hence maternal nutrition may indirectly effect the birth weight. Further there was an association between the maternal B_{12} levels and preeclampsia. This may be secondary to anemia caused by B_{12}. There was significant correlation between serum B12 status and serum folate levels and also with hemoglobin levels. So along with iron and folic acid supplementation, B_{12} supplementation should be considered.

Perinatal Outcome

The observation that mothers with lower hemoglobin concentration tend to have children with low birth weight suggest that maternal anemia has a detrimental effect on fetal development.

There was no statistically significant correlation between the maternal hemoglobin and birth weight but there is a trend.

Conclusions

Anemia is still a major complication of pregnancy with a very high prevalence of 57%. In addition to iron deficiency which is the major cause of anemia deficiency of micronutrients like folic acid and vitamin B_{12} is an important correctable cause of anemia. Since

vitamin B_{12} deficiency studies are not available, an attempt was made to determine the B_{12} status in pregnant women.This study revealed that there is significant B_{12} deficiency in pregnancy of 30%. B_{12} deficiency is associated with preeclampsia but not with low birth weight. There was folic acid deficiency with a prevalence of 5.7% Folate deficiency is associated with early abortions and low birth weight. The study suggests that apart from iron and folate, vitamin B_{12} also is a major factor affecting maternal and perinatal outcome and needs further evaluation.

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