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CORRELATION OF VITAMIN B12 LEVELS IN PRETERM LABOUR – A PROSPECTIVE OBSERVATIONAL STUDY.

Obstetrics & Gynaecology

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ABSTRACT

Background: Vitamin B12 are involved in the one-carbon metabolic cycle, which controls fetal development and promotes a healthy pregnancy, the birth, and perinatal outcomes. The study done to assess vitamin B12 levels during pregnancy and their association with preterm delivery. **Methodology:** This prospective study was conducted in Ballari Medical college and research centre, Ballari during 6months(1st July 2023 to 31st December 2023) study period among 65 pregnant women at 28-37 weeks of gestation. Clinico-demographic data and serum vitamin B12 levels were assessed, and perinatal outcomes were noted. Appropriate statistical tests were used for analysis and comparison. **Results:** The average age of 65 women included was 23.9 ± 3.5 years, with 90.8% having a mixed diet. At 36 weeks of gestation (63.1%) and 35 weeks (21.5%), the majority of women (87.7%) arrived at the labour room complaining of abdominal pain. 61.5% had low B12, and the average B12 level was 223.3 ± 56.4 pmol/L. Weeks of gestation at birth and B12 levels did not correlate (rs=0.05; p>0.05). Additionally, there was no significant association between NICU admission and neonatal death. The APGAR score at 1 and 5 minutes showed a weak positive correlation, although it was not statistically significant. **Conclusion:** Low maternal vitamin B12 level is very common in the Indian population. For long-term improvements in pregnancy outcomes and the health of the offspring, the study suggests including vitamin B12 into current nutritional programs.

KEYWORDS

Vitamin B12, preterm, perinatal outcome

INTRODUCTION

Maternal undernutrition is still an alarming public health concern. Pregnant women's health, nutrition, and well-being are critical to the success of a pregnancy and the long-term health of both mother and child. The prevalence of anemia, underweight, and micronutrient deficiencies varies greatly by area and within a nation worldwide. These discrepancies are caused by a variety of intricate and multifaceted factors, such as the underlying social, economic, and political background as well as access to food poverty, women's status, water, sanitation, and health care [1]. In India, public health measures place a high priority on improving maternal nutrition during pregnancy. Furthermore, the significance of maternal micronutrients (iron, vitamin B12, folate, vitamin C, vitamin D, pyridoxine, and choline) in fetal growth and development has recently become well recognized [2].

Microbes produce vitamin B12, also known as cobalamin, which is a water-soluble vitamin. Plants and fungi provide very little vitamin B12 to the human diet, whereas foods of animal origin, such as meat, milk, eggs, and fish, are the main sources of the vitamin. Because the human body cannot synthesize vitamin B12, it must be obtained from an external source [3]. It is necessary for the development, differentiation, and proliferation of cells. The conversion of homocysteine to methionine is a crucial step in the synthesis of DNA, RNA, lipids, and proteins, involving B12 in addition to folate [4, 5].

Low levels of vitamin B12 in the blood have been linked to complications during pregnancy that include neural tube defects, spontaneous abortion, preterm delivery, and potentially low birth weight [6].Placental function, gestational age at delivery, and maternal vitamin B12 status throughout pregnancy all affect the neonate's vitamin B12 status [7]. It has been suggested that B12 may have an impact on fetal development and placentation [8].

Premature births occur before the 37th week of pregnancy. Early preterm is before 34 weeks and late preterm is between 34 and 36 weeks. In 2019, preterm birth complications accounted for around 900,000 fatalities, making them the top cause of mortality for children under five. Preterm birth rates for 2020 newborns vary per country, ranging from 4 to 16% [9]. Over half of long-term morbidity and 75% of neonatal deaths are caused by preterm births. Although preterm neonates frequently survive, they are more likely to experience respiratory, gastrointestinal, and cognitive problems [10]. Therefore, it could be necessary to use a more focused micronutrient supplementation strategy.

There is little evidence to support the concept that a lower level of maternal B12 during pregnancy increases the risk of preterm delivery. Therefore, the purpose of this study is to evaluate vitamin B12 levels throughout pregnancy and their relationship to preterm birth.

METHODOLOGY:

This prospective observational study was conducted after obtaining permission from Institutional Ethics Committee. The study participants were women in labor with gestational age of 28-37 weeks and admitted to labor room in the department of Obstetrics and Gynecology, Ballari medical college and research Centre Ballari-Karnataka between 1st August 2023 to 1st January 2024. At enrolment, all study participants provided written, signed informed consent. Women who had become pregnant after IVF and who were taking B12 supplements before the trial began were not included in the study.

Pre-validated forms were utilized to prospectively record laboratory data and trained research personnel provided validated structured questionnaires to gather sociodemographic, clinical data. Calculated from the day of the last menstrual cycle, gestational age in weeks was verified by ultrasonographic measures. The pregnant women included in the study were subjected to routine antenatal workup including a complete blood examination, blood sugar levels. Furthermore, 1ml of blood sample was taken in a plain vacutainer and assessed for levels of Vitamin B12 with Coobass E4.11 machine.

Sample Size And Statistical Analysis:

Sample size was estimated by using the proportion of vitamin B12 deficiency in subjects who had preterm labor was 81.30% from the study by Spasova V et al [11]. Using the formula, $Z_{1-\alpha/2}^{2}$ P (1-P)/ d^2, where d was 10% and $Z_{1-\alpha/2}$ at 5% was 1.96. A sample size of 59 participants will be included in the study using the values at the 95% confidence level. A sample size of 59 + 5.9 = 65 people will be included in the study, taking 10% nonresponse into account.

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square was used as test of significance. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference. Correlation between serum vitamin B12 and gestational age was done using Spearman Rho test. P value <0.05 was considered as statistically significant.

RESULTS:

In total 65 pregnant women-neonate were analyzed. The average age of the pregnant women was 23.9 ± 3.5 years. The Clinicodemographic data have been enlisted in **table 1**.

Table 1: Clinicodemographic Data.

Clinicodemographic data	Description	Frequency	Percentage
Diet	Mixed diet	59	90.8
	Vegetarian	6	9.2
Obstetric score	Primigravida	32	49.2
	Gravida-2	21	32.3
	Gravida-3	9	13.8
	Gravida-4	3	4.6
Presence of risk factors	Nil	43	66.2
	Preterm premature rupture of membrane	8	12.3
	Anemia	5	7.7
	Pre-eclampsia	5	7.7
	Previous caesarean section	3	4.6
	Rh negative grouping	2	3.1
Presenting complaints	Pain abdomen	57	87.7
	Per vaginal leak	8	12.3
Gestational age (based on LMP)	31 weeks + (1-6 days)	1	1.5
	33 weeks + (1-6 days)	4	6.2
	34 weeks + (1-6 days)	5	7.7
	35 weeks + (1-6 days)	14	21.5
	36 weeks + (1-6 days)	41	63.1
Gestational age (based on per-abdomen findings)	30 weeks	1	1.5
	32 weeks	1	1.5
	34 weeks	10	15.4
	36 weeks	53	81.5
Per-vaginal finding	Active phase	17	26.1
	Latent phase	43	66.1
	Second stage	5	7.7

Modes of delivery was assessed on follow-up. The most common modes of delivery were preterm vaginal delivery in 57 women, while 8 women delivered via cesarean section.

The main objective of the study was to assess the serum vitamin B12 levels. The average B12 level was 223.3 ± 56.4 pmol/L. It was seen that 61.5% (40/65 had lower serum vitamin B12 and 38.5% (25/65) had a normal vitamin B12 level. Additionally, figure 1 shows the distribution of patients by sub-clinical deficiency (148-220 pmol/L) and deficient status (serum vitamin B12 <148 pmol/L).

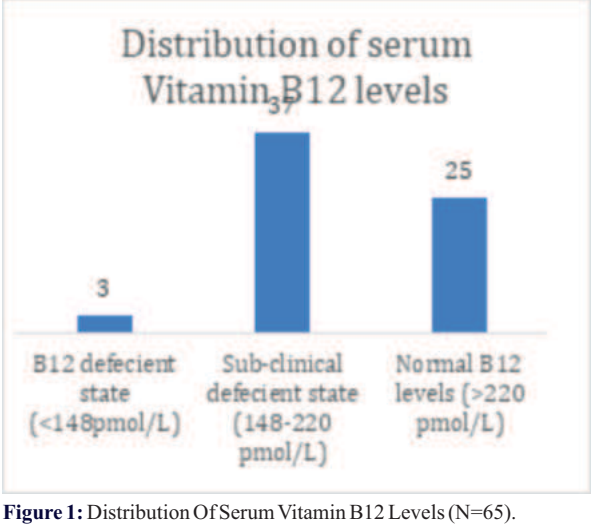

Figure 1: Distribution Of Serum Vitamin B12 Levels (N=65).

Further we found that the 32 pregnant women who had delivered in 36 weeks of gestation were having a low vitamin B12 status. The distribution has been depicted in figure 2.

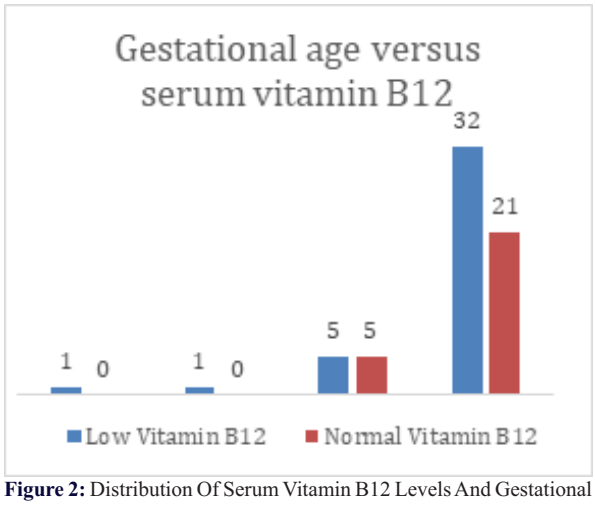

Figure 2: Distribution Of Serum Vitamin B12 Levels And Gestational (N=65).

On assessing correlation using Spearman's Rho calculator, we found no statistically significant relation between serum vitamin B12 and the gestational age at delivery with rs=-0.05, p=0.65. Figure 3 represents the Correlation of gestational age with serum vitamin B12 levels.

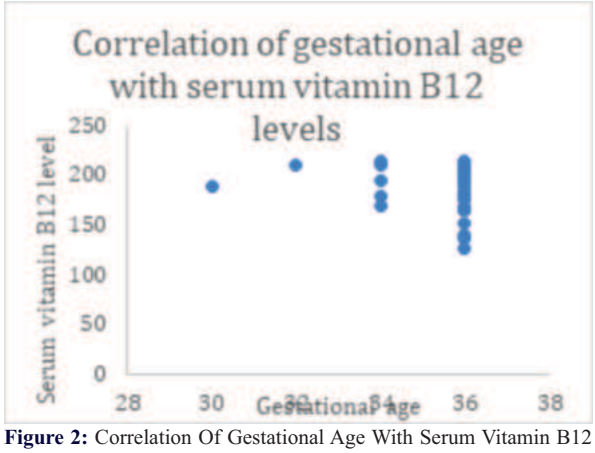

Figure 2: Correlation Of Gestational Age With Serum Vitamin B12 levels.

Association of serum vitamin B12 with Neonatal outcomes:
We found that there was no neonatal mortality in the current investigation, regardless of vitamin B12 levels. We assessed the NICU referrals sent after the delivery. However, no association was found between lower levels of serum vitamin B12 and NICU referral (p=0.88 on Chi-square test). The most common indications for NICU referrals were for respiratory distress (6 cases), Low birth weight (1 case), prematurity (8 cases). Figure 3 describes the association between serum vitamin B12 and NICU referrals.

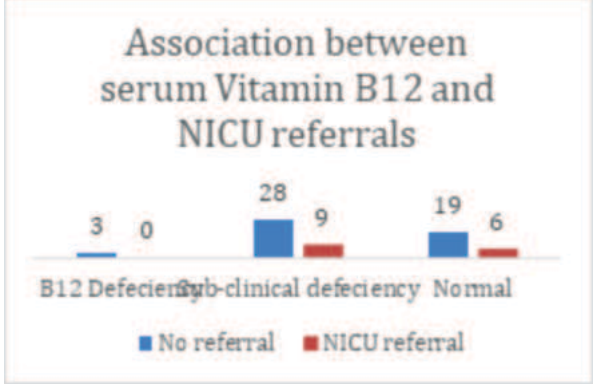

Figure 3: Association between serum Vitamin B12 and NICU referrals.

APGAR score was assessed among the neonates born at 1 and 5

minutes of birth. We found no statistical difference among neonates born to mother with low serum vitamin B12 and normal vitamin B12 ($p>0.05$ on unpaired T-test). A weak positive correlation ($rs=0.02$ and $rs=0.11$) however insignificant was noted between serum vitamin B12 and APGAR at 1 minute in low vitamin B12 and normal vitamin B12 levels. A weak positive correlation ($rs=0.01$ and $rs=0.4$) was noted between serum vitamin B12 and APGAR at 5 minute in low vitamin B12 and normal vitamin B12 levels. A significant weak positive correlation was noted between normal serum vitamin B12 levels and APGAR at 5 minutes.

DISCUSSION:

Given the very high incidence of preterm birth (5–18% of pregnancies) and its numerous causes, it is imperative that this issue be resolved for the sake of future generations' health. Serious short- and long-term health issues might result from the implications for babies born prematurely. Nonetheless, there is still debate over the available data supporting this correlation. Considering this, the current study was planned to evaluate vitamin B12 levels and their relationship to preterm birth. Only a small number of research evaluating the relationship between low blood vitamin B12 and premature deliveries have been reported, despite numerous studies showing the link between low serum vitamin B12 and other unfavorable perinatal consequences including low birth weight, intrauterine growth retardation, small for date babies etc.

According to the research, 61.5% of people had low serum B12, which indicates a serious health issue. However, the study revealed no significant correlation between vitamin B12 blood levels and the risk of preterm delivery, based on the week of gestation at which they gave birth and the measured serum concentration of vitamin B12. The study findings were in line with Spasova V et al [11], who found no association with gestational week at delivery and serum vitamin B12 levels.

The current study observed no neonatal mortality and no significant association between NICU referrals among expectant mother with low serum vitamin B12. The study found a weak positive but statistically insignificant correlation between serum vitamin B12 and APGAR score at 1 and 5 minutes. Similar trend was noted in Chaudhary A et al study [12]. They found that APGAR and S. vitamin B12 had a weakly positive but statistically insignificant connection (rho=0.11, p=0.166). Additionally, there was no discernible link between adverse perinatal outcomes and decreased blood vitamin B12 levels, according to the Finkelstein J et al. research [13]. Even a systematic review from Germany by Hajiabadi AT et al [14]showed no association between low serum B12 levels and preterm birth. Only one research by Chen LW et al. [15], however, revealed that increased B12 was linked to longer gestation and a lower risk of preterm delivery; nonetheless, the precision was limited due to the small sample size and inclusion of multi-ethnic Asian population.

The study is limited by the single-centered nature and smaller sample size. An improvement in the mother's micronutrient status may benefit the health of her unborn child. Women should thus be evaluated for vitamin B12 insufficiency during prenatal visits.

CONCLUSIONS

Maternal vitamin B-12 deficiency is a major public health problem and is associated with increased risk of adverse perinatal outcomes. During pregnancy, vitamin B12 is essential for cell growth and development. The importance of adequate vitamin B-12 status, particularly during pregnancy and early childhood, cannot be overemphasized in light of its role in neural myelination, brain development, and fetal and child growth. Research is needed to elucidate the role of vitamin B-12 in the etiology of perinatal outcomes.

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