Prevalence of Vitamin B12 Deficiency and Its Associated Risk Factors among Pregnant Women of Rural South India: A Community-based Cross-sectional Study

Anitha Mohanraj Barney^{1,2}, Vinod Joseph Abraham¹, Sumita Danda², Anne George Cherian^{1,3}, S. Vanitha⁴

Departments of 1Community Health, 2Clinical Genetics, 3Obstetrics and Gynecology and 4Clinical Biochemistry, Christian Medical College, Vellore, Tamil Nadu, India

Abstract

Introduction: Vitamin B12 is essential for the normal functioning of the nervous system and for the formation of red blood cells. Vegetarian diet, low socioeconomic status, and social and religious reasons are known risk factors of its deficiency. Pregnant women, children, and the elderly are vulnerable groups. Indians have the highest prevalence, but the data among pregnant women in the rural setting is lacking. **Objectives:** The objective of this study is to assess the prevalence of Vitamin B12 deficiency and its associated factors among pregnant women of rural South India. **Materials and Methods:** A cross-sectional study was conducted to recruit consecutive 120 multigravida women with \leq 20 weeks of gestation, attending the mobile doctor run clinic of Kaniyambadi block, Vellore. A structured questionnaire was administered, and blood samples were collected. **Results:** The prevalence of Vitamin B12 deficiency (<200 pgm/ml) and anemia (Hb \leq 10.5 g/dL) was 55% and 17.5%, respectively. Only 11.7% were B12 deficient and anemic. Past history of abortion (odds ratio [OR] = 0.5), fatigue (OR = 0.4), and low B12 intake (OR = 2) was associated only in the bivariate analysis. First trimester (OR = 3.9) and obesity (OR = 9.6) were found to be independent risk factors of Vitamin B12 deficiency. **Conclusion:** Our study showed a high prevalence of Vitamin B12 deficiency in pregnancy in rural India. Some risk factors were identified. However, studies with a higher sample size will be beneficial to study the associated risk factors better.

Keywords: Anemia, B12 deficiency, nutrition, pregnancy

INTRODUCTION

Ouick I

Vitamin B12 is a water-soluble micronutrient, which helps in the formation of red blood cells and is also essential for the normal functioning of the nervous system and brain.^[1] Along with folic acid, Vitamin B12 is needed for fatty and amino acid metabolisms and DNA synthesis and also plays a significant role in the conversion of homocysteine to methionine,^[2] which is required for the synthesis of neurotransmitters and phospholipids.^[3] It is naturally produced by microbial synthesis, and the main dietary sources are of animal origin.^[4] Other important sources are fermented foods and uncooked plant-based food contaminated with B12 producing bacteria^[5] or algae. Vitamin B12 deficiency can result from malabsorption, intestinal disorders, and low levels of binding proteins^[6] and the use of medications such as proton-pump inhibitors^[7] and metformin. People consuming vegetarian diet^[8] are at a higher risk. Other common causes^[9] are low socioeconomic

Ac	Access this article online				
Response Code:	Website: www.ijcm.org.in				
	DOI: 10.4103/ijcm.IJCM_403_19				

status and social and religious reasons for nonconsumption of meat. Several studies highlight South Asian ethnicity as a risk factor.^[10] India has the highest prevalence of Vitamin B12 deficiency, ranging from 47% to 71% in adults.^[11]

During pregnancy, mother needs more nutrients, especially micronutrients. The Indian Council of Medical Research recommends a dietary intake of 1 μ g/day of Vitamin B12 for adults and 1.5 and 1.2 μ g/day for pregnancy and lactation, respectively. Fast and processed food intake and decreased consumption of fruits, vegetables, and meat lead to

Address for correspondence: Ms. Anitha Mohanraj Barney, Department of Clinical Genetics, Christian Medical College, Vellore - 632 004, Tamil Nadu, India. E-mail: anithaisaac99@gmail.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Barney AM, Abraham VJ, Danda S, Cherian AG, Vanitha S. Prevalence of Vitamin B12 deficiency and its associated risk factors among pregnant women of rural South India: A community-based cross-sectional study. Indian J Community Med 2020;45:399-404. Received: 26-09-19, Accepted: 21-04-20, Published: 28-10-20 micronutrient deficiencies. In pregnancy, it leads to adverse outcomes.^[12] We decided to conduct this study since there is a lack of studies to assess the prevalence of Vitamin B12 deficiency and its risk factors in pregnancy in rural South India.

METHODS

This study was approved by the Institutional Review Board. This is a cross-sectional study done from August 2017 to May 2018. The calculated sample size was 100, based on a prevalence of 51%,^[13] with a relative precision of 20%. In order to account for a dropout rate of 20%, 120 samples were included. Multigravida <20 weeks of gestational age who were the residents of a rural block of Vellore district were included in the study. Known Vitamin B12 deficiency, those on Vitamin B12 supplements and known cases of malabsorption, gastrectomy, and irritable bowel syndrome or any other gastric disorders which is known to cause Vitamin B12 deficiency were excluded from the study.

Consecutive pregnant women from the mobile clinic in Kaniyambadi block, which covers a population of approximately 120,000 were recruited. An informed consent was obtained. A structured questionnaire which included a 24-h dietary recall was administered. Calibrated vessels and spoons were used to quantify the intake of solids (rice) and liquids (milk or ghee, etc.). A blood test was obtained to check for serum Vitamin B12 levels and hemoglobin. Estimation of Vitamin B12 and hemoglobin was done in a NABL accredited laboratory by Roche e602 and Sysmax KX 21, respectively, the instruments are calibrated daily. Vitamin B12 <200 pgm/ml was taken as deficient and hemoglobin ≤ 10.5 g/dL was diagnosed as anemia. Although the WHO recommends 11 g/dL as the cutoff for anemia all throughout pregnancy, the CDC^[14] recommends a trimester based cutoff. The latter recommends 10.5 g/dL in the second trimester. Since 60% of the pregnant women in our study were in the second trimester and since 10.5 g/dLwas used as the cutoff to treat B12 deficiency with anemia in pregnancy, we took 10.5 g/dL as the cutoff. In view of recent literature showing a possible increased risk of autism to the yet-to-be born child^[15] due to high maternal Vitamin B12 levels, only those with B12 deficiency and anemia were treated with 500 µg of Vitamin B12 orally, once a day till delivery. If there was a deficiency in Vitamin B12 but the absence of anemia, the hemoglobin was repeated after 1-2 months. If there was a significant drop in hemoglobin of >1 g/dL (more than what is explainable by the physiological effects of pregnancy), then the treatment was commenced with Vitamin B12 at similar doses.

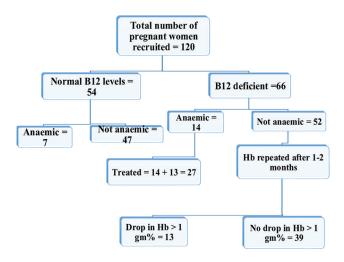
The data were entered using epidata V 3.1 and analyzed using IBM SPSS 25.0 (SPSS South Asia Pvt Ltd., Kacharkanhalli, Bangalore, Karnataka, India). Descriptive statistics for the continuous variables were calculated as mean and standard deviation. Frequencies and percentages were calculated for the categorical variables. Continuous variables were dichotomized for bivariate analysis. The Chi-square test was performed to assess the statistical significance of the risk factors, and odds ratio was calculated to assess the strength of association. Multiple logistic regression analysis was performed to find out the independent risk factors.

RESULTS

A total of 120 pregnant mothers were included. By B G Prasad Scale, 15% of the mothers were in the lower class of socioeconomic status (SES), 35% of the mothers were in the lower middle-class SES, and 22.5% of them were in the middle class. Eighty-three percent of the mothers had completed at least high school. Eighty-eight percent of the mothers were homemakers, despite many being qualified. Ten percent of the mothers were obese, 19.2% were preobese, and an additional 18.3% were overweight. Sixty percent of the mothers were in their second trimester. In all half of them had not consumed folic acid at the time of recruitment into the study. The mean days of folic acid consumption were only twenty. The most common clinical manifestations were fatigue (25%), pallor (24.8%), breathlessness (20.8%), and fainting (19.2%). Among the known risk factors of B12 deficiency, consanguinity was the most prevalent (25%) followed by the usage of RO water (13.3%). The most prevalent previous maternal and neonatal risk factors/outcomes were previous one or two abortions (32.5%), low birth weight (15.8%), short stature (11.67%), and previous LSCS (9%).

The prevalence of B12 deficiency and anemia was 55% and 17.5%, respectively. Only 11.67% had B12 deficiency with anemia and were treated with Vitamin B12 supplements. As shown in the consort diagram in Figure 1, 52 women underwent repeat hemoglobin in 1 or 2 months. Thirteen of them had a drop in hemoglobin of more than 1 g% and were also treated. The rest 39 with low B12 levels were not treated for reasons mentioned previously.

In the bivariate analysis [Table 1], those with obesity $(BMI > 30 \text{ kg/m}^2)$ had higher odds ratio (OR = 4.6) of being B12 deficient. Low PCV (OR = 2.3) and the presence of any comorbidity (OR = 3.4) also had a positive association for



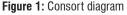


Table 1: Association between variables and Vitamin B12 deficiency status							
Variables	Groups	Vitamin B12 deficient (<200 pg/ml) (<i>n</i> =66), <i>n</i> (%)	Vitamin B12 normal (200-950 pg/ml) (<i>n</i> =54), <i>n</i> (%)	Р	OR	95% CI	
Sociodemographic variables							
Age (years)	≥26 (<i>n</i> =57)	57.9	42.1	0.59	1.3	0.6-2.5	
	<26 (<i>n</i> =59)	52.4	47.6		1	0.3-1.3	
Education	\leq High school (<i>n</i> =57)	49.1	50.9	0.22	0.22 0.6		
	\geq Higher secondary (<i>n</i> =63)	60.3	39.7		1		
Occupation	Homemaker (n=102)	55.2	44.2	1.0	1.1 0.4-3.		
	Working (n=18)	53.3	46.7		1		
Per capita monthly income	≤2500 (<i>n</i> =82)	54.9	45.1	1.0	1.0	0.4-2.1	
(INR)	>2500 (<i>n</i> =38)	55.3	44.7		1		
BMI (kg/m ²)	\geq 30 kg/m ² (<i>n</i> =12)	83.3	16.7	0.03	4.6	1.0-22.1	
	<30 kg/m ² (n=108)	51.9	48.1		1		
Obstetric history							
Gestational age	First trimester (n=48)	43.8	56.2	0.04	0.5	0.2-0.9	
	Second trimester (<i>n</i> =72)	62.5	37.5		1		
Folic acid consumption	No (<i>n</i> =56)	53.6	46.4	0.86	0.9	0.4-1.9	
1	Yes (<i>n</i> =64)	56.2	43.8		1		
Number of abortions	≥ 1 (n=42)	42.9	57. 1	0.05	0.5	0.2-1.0	
	No abortion (<i>n</i> =78)	61.5	38.5		1		
High-risk pregnancy	Yes (<i>n</i> =30)	60	40	0.67	1.3	0.6-3.0	
0 10 9	No (<i>n</i> =90)	53.3	46.7		1		
Dietary intake (24 h recall)					-		
Calories (Kcal)	≤1600 (<i>n</i> =57)	63.2	36.8	0.06	1.9	0.9-3.9	
	>1600 (<i>n</i> =63)	47.6	52.4	0.00	1	0.9 0.9	
Iron (g)	$\leq 22 (n=78)$	55.1	44.9		1.0	0.5-2.1	
non (g)	$\geq 22 (n - 73)$ >22 (n=42)	54.8	45.2	1.0	1 0.5-2	0.5 2.1	
Vitamin B12 (µg)	$\leq 1.5 \ (n=79)$	60.8	39.2	0.05	2.0	1.0-4.2	
vitalilli D12 (µg)	>1.5 (n=41)	43.9	56.1	0.05	1	1.0 4.2	
Calcium	$\leq 800 \ (n=77)$	59.7	40.3	0.11	1.7	0.8-3.6	
Calcium	$\geq 800 (n - 43)$	46.5	53.5	0.11	1.7	0.0-5.0	
Known risk factors	>800 (<i>n</i> -43)	40.5	55.5		1		
Consanguinity	Yes (<i>n</i> =29)	58.6	41.4	0.4	1.2	0.5-2.8	
Consanguinity	No $(n=91)$	53.8	46.2	0.4	1.2	0.3-2.8	
Consumption of RO water	NO(n=91) Yes (n=22)	54.5	45.5	1.0	0.9	0.3-2.4	
Consumption of KO water				1.0		0.3-2.4	
Equily history of D12	No (<i>n</i> =98)	55.1	44.9	1.0	1	0 1 12 2	
Family history of B12 deficiency	Yes (n=2)	50.0	50.0	1.0	0.8	0.1-13.3	
-	No (<i>n</i> =118)	55.1	44.9		1		
Clinical manifestations	X. (05)	40.0	52.0	0.5	0.7	0.2.1.7	
Nocturnal cramping	Yes (<i>n</i> =25)	48.0	52.0	0.5	0.7	0.3-1.7	
	No (<i>n</i> =95)	56.8	43.2	0.04	1		
Fatigue	Yes (<i>n</i> =30)	40.0	60.0	0.04	0.4	0.2-1.0	
~	No (<i>n</i> =90)	60.0	40.0	· · -	1		
Pallor	Yes (<i>n</i> =29)	41.4	58.6	0.07		0.5 0.2-1.1	
	No (<i>n</i> =91)	59.3	40.7	<u>.</u>	1		
Angular stomatitis	Yes (<i>n</i> =6)	33.3	66.7	0.4	0.4	0.1-2.2	
_	No (<i>n</i> =114)	56.1	43.9		1		
Premature greying	Yes (<i>n</i> =6)	83.3	16.7	0.16	4.3	0.5-38.3	
	No (<i>n</i> =114)	53.5	46.5		1		
Blood cell parameters							
PCV (%)	≤35 (<i>n</i> =58)	65.5	34.5	0.02	2.3	1.1-4.8	
	>35 (<i>n</i> =62)	45.2	54.8		1		

Contd...

Table 1: Contd							
Variables	Groups	Vitamin B12 deficient (<200 pg/ml) (<i>n</i> =66), <i>n</i> (%)	Vitamin B12 normal (200-950 pg/ml) (<i>n</i> =54), <i>n</i> (%)	Р	OR	95% CI	
Hemoglobin (g/dL)	≤10.5 (<i>n</i> =21)	66.7	33.3	0.17	1.8	0.7-4.9	
	>10.5 (<i>n</i> =99)	52.5	47.5		1		
MCV (fL)	≤82 (<i>n</i> =55)	58.2	41.8	0.32	1.3	0.6-2.6	
	>82 (<i>n</i> =65)	52.3	47.7		1		
MCH (pg)	≤28 (<i>n</i> =55)	61.8	38.2	0.11	1.7	0.8-3.5	
	>28 (<i>n</i> =65)	492	50.8		1		

MCV: Mean corpuscular volume, PCV: Packed-cell volume, MCH: Mean corpuscular hemoglobin, OR: Odds ratio, CI: Confidence interval

being B12 deficient with statistical significance. Gestational age in the first trimester (OR = 0.5), past history of abortion (OR = 0.5), and fatigue (OR = 0.4) had a protective effect. In the multiple logistic regression [Table 2], after adjusting for confounding factors, first trimester (OR = 3.9; 95% CI 1.4–10.6) and obesity (OR = 9.6; 95% CI 1.3–63.1) were found to be independent risk factors of Vitamin B12 deficiency.

DISCUSSION

High prevalence of Vitamin B12 deficiency (55%) among pregnant mothers observed by us is similar to studies previously published from a semiurban area in Bangalore,^[13] with a prevalence of 51% and in Pune^[16] among rural and urban pregnant women, with 80% and 65% prevalence of Vitamin B12 deficiency, respectively.

The prevalence of anemia was 17.5%. However, only 11.7% had B12 deficiency and anemia. Our study results match a previous study done by Remacha *et al.*,^[17] where only 18% of the participants had both anemia and B12 deficiency. In our study, the mean MCV was 82.07 (normal range 63.5–97.9) and hence normal. Literature agrees that macrocytosis^[18] is not always present in cobalamin deficiency. MCV is normal or low also in mixed anemias. However, iron studies were not done in our study to demonstrate this.

A total of 27 mothers (22.5%) were treated with oral Vitamin B12 supplements 500 µg once daily till delivery. Others who were Vitamin B12 deficient but not anemic were not treated because of the evolving evidence of the risk of autism to the unborn child, in those with higher maternal serum B12 levels at delivery. In a cohort study from the United States,^[15] the risk of autism in the child increased by 17 times with higher B12 levels (>600 pmol/L) in the mother. In our study, Vitamin B12 was supplements orally because the gastrointestinal absorption in pregnancy is higher,^[19] and it is economical, practical, and convenient.

In the bivariate analysis, the mothers with obesity (BMI >30 kg/m²) had higher odds (OR = 4.6) of being B12 deficient with statistical significance. This finding persisted in the multiple logistic regression with increasing odds (OR = 9.6; 95% CI 1.3–63.1) and statistical significance (P = 0.023). A retrospective study conducted by Prameela *et al.*^[20] in Mysore, India, found that obese women have increased risk

of eclampsia, instrumental delivery, LSCS, IUGR, and PPH. Another prospective study by Koduri *et al.*^[21] among 262 pregnant women with BMI >30 also found an increased risk of complications among obese patients. Hence, it could be postulated that B12 deficiency could be one of the pathways for adverse maternal outcomes in the obese group. However, this remains to be studied further.

Among the parameters of the obstetric history, the gestational age and the past history of abortion were associated with B12 deficiency with statistical significance. In the multivariate analysis, mothers in the first trimester had nearly four times higher odds of being B12 deficient when compared with those in the second trimester (OR = 3.9; 95% CI = 1.4--10.6). Forty percent of our mothers were in the first trimester at the time of recruitment. A study^[22] which was done to examine the changes in dietary intake from the first to the second trimester of pregnancy found that intake of many micronutrient intakes increased substantially from the first to the second trimester. The increased requirement of Vitamin B12 coupled with decreased intake in the first trimester due to reasons such as morning sickness could have resulted in the increased odds of Vitamin B12 deficiency in the first trimester.

Those who had a history of at least one abortion in the past had a lower prevalence of B12 deficiency with odds of 0.5 (95% CI = 0.2-1.0) when compared to the mothers who had no previous abortion. However, after adjusting for confounders, this association did not persist (OR = 2.0; 95% CI = 0.8-4.7). A well-conducted French case-control study^[23] looked at Vitamin B12 as a risk factor for early recurrent abortion. They also conducted an analysis of five similar studies including theirs and concluded that there was a significant relationship between Vitamin B12 deficiency and early recurrent abortion. A genetic study by Puri et al.^[24] from North India found that methylenetetrahydrofolate reductase C677T (MTHFR C677T) genetic polymorphism was associated with higher homocysteine levels which leads to recurrent abortions. Since Vitamin B12 deficiency also causes the elevation of homocysteine levels, this could be the reason for recurrent pregnancy loss in these women.

Among parameters assessing the nutritional status, low B12 intake (OR = 2) showed a significant association with Vitamin B12 deficiency, whereas low calorie intake (OR = 1.89) and a lower calcium intake (OR = 1.7) showed a trend toward

Variables	Groups	Vitamin B12 deficient (<200 gm/ml) (<i>n</i> =66), <i>n</i> (%)	Vitamin B12 normal (200-950 pg/ml) (n=54), n (%)	Crude OR (95% CI)	Adjusted** OR (95% CI)	Р
BMI (kg/m ²)	\geq 30 kg/m ² (<i>n</i> =12)	83.3	16.7	4.6 (1.0-22.1)	9.6 (1.3-63.1)	0.02
	<30 kg/m ² (<i>n</i> =118)	51.9	48.1	1	1	
Gestational age	First trimester (<i>n</i> =48)	43.8	56.2	0.5 (0.2-0.9)	3.9 (1.4-10.6)	0.007
	Second trimester (<i>n</i> =72)	62.5	37.5	1	1	
Abortion	≥1 (<i>n</i> =42)	42.9	57. 1	0.5 (0.2-1.0)	1.9 (0.8-4.6)	0.16
	No abortion (n=78)	61.5	38.5	1	1	
Calories (Kcal)	≤1600 (<i>n</i> =57)	63.2	36.8	1.9 (0.9-3.9)	0.4 (0.2-3.1)	0.16
	>1600 (<i>n</i> =63)	47.6	52.4	1	1	
Calcium	≤800 (<i>n</i> =77)	59.7	40.3	1.7 (0.8-3.6)	1.6 (0.5-5.1)	0.42
	>800 (<i>n</i> =43)	46.5	53.5	1	1	
Vitamin B12	≤1.5 (<i>n</i> =79)	60.8	39.2	2.0 (0.9-4.2)	1.0 (0.2-1.8)	0.53
(µg)	>1.5 (<i>n</i> =41)	43.9	56.1	1	1	
Pallor	Yes (n=29)	41.4	58.6	0.5 (0.2-1.1)	0.7 (0.2-2.1)	0.5
	No (<i>n</i> =91)	59.3	40.7	1	1	
Fatigue	Yes (<i>n</i> =30)	40.0	60.0	0.4 (0.2-1.0)	0.6 (0.2-1.7)	0.08
	No (<i>n</i> =90)	60.0	40.0	1	1	
Premature	Yes (<i>n</i> =6)	83.3	16.7	2.5 (0.2-24.9)	0.1 (0.1-2.1)	0.16
greying	No (<i>n</i> =114)	53.5	46.5	1	1	
Focal weakness	Yes (<i>n</i> =6)	16.7	83.3	0.1 (0.1-1.3)	0.1 (0.0-1.2)	0.08
	No (<i>n</i> =114)	57.0	43.0	1	1	
PCV (%)	≤35 (<i>n</i> =58)	65.5	34.5	2.3 (1.1-4.8)	2.3 (0.6-9.3)	0.21
	>35 (<i>n</i> =62)	45.2	54.8	1	1	
MCH (pg)	≤28 (<i>n</i> =55)	61.8	38.2	1.7 (0.8-3.4)	0.7 (0.3-1.8)	0.42
	>28 (n=65)	492	50.8	1	1	

**Adjusted for BMI (kg/m²), gestational age, abortion, calories. Calcium, Vitamin B12, Pallor, fatigue, premature greying, focal weakness, PCV, and MCH. BMI: Body mass index, PCV: Packed-cell volume, MCH: Mean corpuscular hemoglobin, OR: Odds ratio, CI: Confidence interval

positive association though not statistically significant. In the multivariate regression analysis, none of these showed statistically significant association. Nonvegetarian diet is the most important dietary source of Vitamin B12. However, in a systematic review and metaanalysis,^[3] Sukumar *et al.* found that the prevalence of Vitamin B12 deficiency was high in nonvegetarian populations as well.

Among the clinical manifestations, those who had the symptom of fatigue had a statistically significant lower odds (OR = 0.4; 95% CI = 0.2–1.0) of being B12 deficient compared with those who did not have fatigue, but this association did not persist on the multivariate analysis. Those who had premature greying had higher odds (OR = 2.5; 95% CI = 0.2–24.9) of being B12 deficient, though not statistically significant. This did not persist in the multivariate analysis. Case–control studies done on premature greying,^[25,26] showed that Vitamin B12 deficiency is a significant risk factor for the same.

The strength of our study is that the samples were representative of the entire Kaniyambadi block, having recruited consecutive 120 mothers spread over all the 89 villages. The limitation of the study is that the sample size was not powered to assess all the associated factors. Although obesity and first trimester were identified as the independent risk factors of Vitamin B12 deficiency, other factors such as premature greying, history of early neonatal death, and abortion, which might have had independent association could not be proved due to the limited sample size. Another limitation is that concomitant iron deficiency anemia was not looked into. Furthermore, the maternal and neonatal outcomes in the current pregnancy were not looked into, which could have assessed the impact of Vitamin B12 deficiency on these.

CONCLUSION

The prevalence of Vitamin B12 deficiency among pregnant women in rural South India is considerably high despite most of them being nonvegetarians. First trimester and obesity were found to be independent risk factors of Vitamin B12 deficiency. However, studies with a higher sample size are needed to study associated risk factors better and to consider the need for screening and supplementation of B12 in pregnancy. The genetic basis behind the low Vitamin B12 levels needs to be explored in future studies.

Financial support and sponsorship Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Gibney MJ. Introduction to Human Nutrition. 2nd ed.;

2009. Available from: https://www.wiley.com/en-af/Introd uction+to+Human+Nutrition%2C+2nd+Edition-p-9781405168076. [Last accessed on 2019 Apr 21].

- González HF, Visentin S. Micronutrients and neurodevelopment: An update. Arch Argent Pediatr 2016;114:570-5.
- Sukumar N, Rafnsson SB, Kandala NB, Bhopal R, Yajnik CS, Saravanan P. Prevalence of vitamin B-12 insufficiency during pregnancy and its effect on offspring birth weight: A systematic review and meta-analysis. Am J Clin Nutr 2016;103:1232-51.
- Gille D, Schmid A. Vitamin B12 in meat and dairy products. Nutr Rev 2015;73:106-15.
- Watanabe F, Yabuta Y, Tanioka Y, Bito T. Biologically active vitamin B12 compounds in foods for preventing deficiency among vegetarians and elderly subjects. J Agric Food Chem 2013;61:6769-75.
- Just MJ, Kozakiewicz M. Depressive disorders co-existing with addison-biermer anemia – Case report. Neuropsychiatr Dis Treat 2015;11:1145-8.
- Ingole JR, Patel RD, Ingole SJ, Pandave HT. Opportunistic screening of Vitamin B12 deficiency in IT professionals presenting for routine health check-up. J Clin Diagn Res 2015;9:OC01-2.
- Pawlak R, Parrott SJ, Raj S, Cullum-Dugan D, Lucus D. How prevalent is vitamin B (12) deficiency among vegetarians? Nutr Rev 2013;71:110-7.
- Jeruszka-Bielak M, Isman C, Schroder TH, Li W, Green TJ, Lamers Y. South Asian ethnicity is related to the highest risk of Vitamin b12 deficiency in pregnant Canadian women. Nutrients 2017;9(4):317. Published 2017 Mar 23. doi:10.3390/nu9040317.
- Wang ZP, Shang XX, Zhao ZT. Low maternal vitamin B (12) is a risk factor for neural tube defects: A meta-analysis. J Matern Fetal Neonatal Med 2012;25:389-94.
- Christian AM, Krishnaveni GV, Kehoe SH, Veena SR, Khanum R, Marley-Zagar E, *et al.* Contribution of food sources to the vitamin B12 status of South Indian children from a birth cohort recruited in the city of Mysore. Public Health Nutr 2015;18:596-609.
- 12. Lowensohn RI, Stadler DD, Naze C. Current concepts of maternal nutrition. Obstet Gynecol Surv 2016;71:413-26.
- Samuel TM, Duggan C, Thomas T, Bosch R, Rajendran R, Virtanen SM, et al. Vitamin B (12) intake and status in early pregnancy among urban South Indian women. Ann Nutr Metab 2013;62:113-22.
- Recommendations to Prevent and Control Iron Deficiency in the United States. Available from: https://www.cdc.gov/mmwr/preview/ mmwrhtml/00051880.htm. [Last accessed on 2020 Apr 09].

- Raghavan R, Fallin MD, Wang X. Maternal plasma folate, Vitamin B12 levels and multivitamin supplementation during pregnancy and risk of autism spectrum disorder in the Boston Birth Cohort. FASEB J 2016;30 Suppl 1:151.6.
- 16. Katre P, Bhat D, Lubree H, Otiv S, Joshi S, Joglekar C, *et al.* Vitamin B12 and folic acid supplementation and plasma total homocysteine concentrations in pregnant Indian women with low B12 and high folate status. Asia Pac J Clin Nutr 2010;19:335-43.
- Remacha AF, Sardà MP, Canals C, Queraltò JM, Zapico E, Remacha J, et al. Combined cobalamin and iron deficiency anemia: A diagnostic approach using a model based on age and homocysteine assessment. Ann Hematol 2013;92:527-31.
- Nagao T, Hirokawa M. Diagnosis and treatment of macrocytic anemias in adults. J Gen Fam Med 2017;18:200-4.
- Bolaman Z, Kadikoylu G, Yukselen V, Yavasoglu I, Barutca S, Senturk T. Oral versus intramuscular cobalamin treatment in megaloblastic anemia: A single-center, prospective, randomized, open-label study. Clin Ther 2003;25:3124-34.
- 20. Prameela HJ, Madhuri S.Obesity in pregnancy: maternal and perinatal outcome. Int J Reprod Contracept Obstet Gynecol 2017;6:141-4.
- Koduri A, Subbalakshmi TD, Shaik MK. Increasing trend of maternal obesity in India: A prospective study, department of anaesthesia, Andhra Medical College, Visakhapatnam. Journal of Dental and Medical Sciences. Volume 14, Issue 3 Ver. II (Mar. 2015), PP 100-3.
- Rifas-Shiman SL, Rich-Edwards JW, Willett WC, Kleinman KP, Oken E, Gillman MW. Changes in dietary intake from the first to the second trimester of pregnancy. Paediatr Perinat Epidemiol 2006;20:35-42.
- Reznikoff-Etiévant MF, Zittoun J, Vaylet C, Pernet P, Milliez J. Low Vitamin B (12) level as a risk factor for very early recurrent abortion. Eur J Obstet Gynecol Reprod Biol 2002;104:156-9.
- Puri M, Kaur L, Walia GK, Mukhopadhhyay R, Sachdeva MP, Trivedi SS, *et al.* MTHFR C677T polymorphism, folate, Vitamin B12 and homocysteine in recurrent pregnancy losses: A case control study among North Indian women. J Perinat Med 2013;41:549-54.
- Daulatabad D, Singal A, Grover C, Chhillar N. Prospective analytical controlled study evaluating serum biotin, Vitamin B12, and Folic acid in patients with premature canities. Int J Trichology 2017;9:19-24.
- 26. Sonthalia S, Priya A, Tobin DJ. Demographic characteristics and association of serum Vitamin B12, ferritin and thyroid function with premature canities in Indian Patients from an Urban Skin Clinic of North India: A retrospective analysis of 71 cases. Indian J Dermatol 2017;62:304-8.