International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2018): 7.426

Study of Maternal High Risk Factors in Vitamin B_{12} Deficient Pregnant Women in a Tertiary Care Centre

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Abstract: ***Background**: Vitamin B_{12} deficiency is highly prevalent during pregnancy and is associated with poor maternal outcome. The study was conducted to determine prevalence of Vitamin B_{12} deficiency and association of Vitamin B_{12} deficiency with maternal high risk factors. **Methodology**: A randomized cohort observational study was conducted in the Post Graduate Department of Obstetrics and Gynaecology from October 2017 to September 2018 after getting approval from ethical committee. 200 pregnant females with term gestation admitted in the labour room of S.M.G.S. Hospital were randomly included in the study. Results: Prevalence of Vitamin B_{12} deficiency was 45%. Mean age of pregnant females with Vitamin B_{12} deficiency was 25.7 years. Vitamin B_{12} deficiency was more prevalent among vegetarians (83.33%), in urban population (74.44%), and those belonging to lower middle and lower (76.67%) socio-economic class. Mean serum vitamin B_{12} levels were 145.1 ± 32.44 in vitamin B_{12} deficiency cohort. Moderate/Severe anaemia was present in 98.89%, Gestational hypertension in 27.78% pregnant females, Preeclampsia in 2.22%, Gestational diabetes mellitus in 11.11%, Tingling in 17.78% and Bony pain in $_{12}$, 22% Vitamin B_{12} deficient pregnant females. **Conclusion**: Vitamin B_{12} deficiency is highly prevalent in pregnant women especially with vegetarians and is significantly associated with high risk conditions.***

Keywords: Vitamin B_{12} deficiency

1. Introduction

Vitamin B_{12} is a water soluble vitamin required for maintenance of normal erythropoiesis, nucleoprotein and myelin synthesis, cell reproduction and normal growth. Vitamin B_{12} deficiency is frequently reported in pregnancy due to inadequate dietary intake of vitamin B_{12} and also a physiological decline of maternal vitamin B_{12} concentration. Strict vegetarian diet do not provide adequate amount of Vitamin B_{12}. Human requirement for vitamin B_{12} is 2-3 micro gram per day. Serum vitamin B_{12} levels less than 150 pmol/L (203 pg/mL) is defined as Vitamin B_{12} deficiency according to WHO. (Refsum et al., 2001)[1]. Megaloblastic anemia in Vitamin B_{12} deficiency develops as a result of disrupted DNA synthesis and the resultant maturation disorder of the cell nucleus, whereas cytoplasm develops normally.

2. Literature Survey

Vitamin B_{12} deficiency causes hyperhomocysteinemia leading to vascular changes associated with pre-eclampsia and include atherosis and endothelial dysfunction resulting in blunted vasorelaxation mechanisms.

Mitochondrial conversion of methyl malonyl–COA requires vitamin B_{12} as a coenzyme and in its absence accumulation of methyl malonyl-COA inhibits fatty acid oxidation and promotes lipogenesis (Adaikalakoteswari A et al., 2014)[2]. Vitamin B_{12} deficiency is associated with greater adiposity, which in turn is associated with an increased risk of diabetes during pregnancy and follow-up (Krishnaveni GV et al., 2009)[3]. Vitamin B_{12} deficiency leads to excess of methylmalonic acid, which is myelin destabilizer leading to central and peripheral neuropathy. Vitamin B_{12} deficiency affect bone metabolism and stimulate osteoclasts. The current analysis was therefore undertaken to examine association of Vitamin B_{12} status with maternal high risk factors.

3. Material and Methods

The study was conducted in Postgraduate Department of Obstetrics and Gynaecology, S.M.G.S. Hospital, Jammu over a period of one year i.e. October 2017 to September 2018 after approval from Hospital Ethical Committee. 200 pregnant females with term gestation were included in the study after taking written consent. Pregnant females who were already treated for Vitamin B_{12} deficiency and who took medications containing vitamin B_{12} were excluded from the study. Patients were divided into two cohorts. Cohort 1 comprised of Vitamin B_{12} deficient pregnant females. Cohort 2 comprised of pregnant females without vitamin B_{12} deficiency. Maternal high risk factors identified were Gestational Diabetes Mellitus, Gestational Hypertension, moderate to severe anemia, tingling and bone pain. Specimens for Vitamin B_{12} analysis were collected from the subjects at the time of admission. Vitamin B_{12} was measured by fully automated Electro-chemiluminescence method. In our laboratory, normal range is 187-883 pg/ml. Values less than 187 pg/ml was taken as vitamin B_{12} deficiency.

4. Results

The present observational prospective randomized study was conducted on 200 pregnant females with term gestation. Cohort 1 comprised of 90 (45%) pregnant females with vitamin B_{12} deficiency, while Cohort 2 comprised of 110 (55%) pregnant females without vitamin B_{12} deficiency. Values less than 187 pg/ml was considered vitamin B_{12} deficiency. Normal range was taken as 187-883 pg/ml. Following observations were made during the culmination of the study.

Out of 200 pregnant females, 90 were found to be vitamin B_{12} deficient (<187 pg/ml) with a prevalence of 45%. (Table 1)

Majority of pregnant females in Cohort 1 (88.89%) and Cohort 2 (78.18%) were in the age group of 20-29 years. Mean age of Cohort 1 was 25.7 years and that of Cohort 2 was 26.06 years. Statistically, both age groups were comparable (p>0.05). (Table 2)

In Cohort 1, majority of pregnant females were vegetarians (83.33%), while in Cohort 2, majority of pregnant females were non-vegetarians (60.91%). Difference in choice of diet between the two cohorts was statistically highly significant (p<0.0001). Vitamin B_{12} deficiency was observed more in pregnant females consuming vegetarian diet. (Table 3)

Most of the pregnant females in Cohort 1 and Cohort 2 had parity 0 (56.67% and 54.54% respectively), followed by parity 1 (27.78% and 33.64% respectively) and multiparity (15.55% and 11.82% respectively). Statistically, there was no difference in two cohorts according to parity (p=0.52). (Table 4)

There were more lower-middle socioeconomic class pregnant females in Cohort 1 (61.11%), followed by middle (23.33%) and lower socioeconomic class (15.56%). In Cohort 2, there were more middle socioeconomic class pregnant females (70%), followed by lower-middle (26.36%), lower (1.82%) and upper-middle socioeconomic class (1.82%). The difference of socioeconomic class between the two cohorts was statistically highly significant (p<0.0001). Vitamin B_{12} deficiency was significantly more in lower/lower-middle socioeconomic class pregnant females. (Table 5)

In Cohort 1, most pregnant females were from urban areas (74.44%), while in Cohort 2, most were from rural areas (58.18%). Statistically, the difference was highly significant (p<0.0001). Vitamin B_{12} deficiency was found more in urban pregnant females. (Table 6)

In Cohort 1, Severe and moderate anemia was present in 98.89% pregnant females. Gestational hypertension was present in 27.78% and pre eclampsia in 2.22% pregnant females. Gestational diabetes mellitus was present in 11.11%, tingling in 17.78% and bony pain in $_{12}$.22% pregnant females. In Cohort 2 (without vitamin B_{12} deficiency), Severe and moderate anemia was present in 92.73% pregnant females. Gestational hypertension was present in 10% and pre- eclampsia in 0.91% pregnant females. Gestational diabetes mellitus was present in 3.64%, tingling in 11.82% and bony pain in 3.64% pregnant females. (Table 7)

Severe/moderate anaemia was present in 98.89% pregnant females in Cohort 1 (with vitamin B_{12} deficiency) compared to only 92.73% pregnant female in Cohort 2 (without vitamin B_{12} deficiency), the difference being statistically highly significant (p<0.0001). (Table 8)

Mean serum vitamin B_{12} of pregnant females in Cohort 1 was significantly less as compared to those of pregnant females in Cohort 2 (145.1 vs 273.05 pg/mL; p<0.0001).Mean haemoglobin of pregnant females in Cohort 1 was significantly less as compared to those of pregnant females in Cohort 2 (8.08 vs 8.72 g/dL; p<0.0001).Mean corpuscular volume was in normal range in both the groups, though it was significantly more in Cohort 1 as compared to Cohort 2 (89.39 vs 88.$_{12}$ fL; p=0.0003). (Table 9)

Table 1: Prevalence of vitamin B_{12}deficiency in the study

Total pregnant females (No.)	Vitamin B_{12} deficiency (No.)	Prevalence (%)
200	90	45%

Table 2: Age distribution of pregnant females

Age group (in years)	Cohort 1 (with vitamin B_{12} deficiency) (n=90)		Cohort 2 (without vitamin B_{12} deficiency) (n=110)	
	No.	%	No.	%
<20	0	0.00	2	1.82
20 – 29	80	88.89	86	78.18
30 – 39	10	11.11	22	20.00
Total	90	100.00	110	100.00
Mean age ± SD (in years)	25.7 ± 3.56		26.06 ± 3.98	
Statistical Inference (Unpaired t test)	t=0.50; p=0.61; NS			

NS – Not significant

Table 3: Distribution of pregnant females according to choice of diet

Choice of diet	Cohort 1 (with vitamin B_{12} deficiency) (n=90)		Cohort 2 (without vitamin B_{12} deficiency) (n=110)		Statistical inference (Fisher's exact test)
	No.	%	No.	%	
Vegetarian	75	83.33	43	39.09	p<0.0001; HS
Non-vegetarian	15	16.67	67	60.91	
Total	90	100.00	110	100.00	

HS – Highly significant

Table 4: Distribution of pregnant females according to parity

Parity	Cohort 1 (with vitamin B_{12} deficiency) (n=90)		Cohort 2 (without vitamin B_{12} deficiency) (n=110)		Statistical inference (Fisher's exact test)
	No.	%	No.	%	
Parity 0	51	56.67	60	54.54	p=0.52; NS
Parity 1	25	27.78	37	33.64	
Multiparity	14	15.55	13	11.82	
Total	90	100.00	110	100.00	

NS – Not significant

Table 5: Distribution of pregnant females according to socioeconomic class

Socioecoonomic class	Cohort 1 (with vitamin B_{12} deficiency) (n=90)		Cohort 2 (without vitamin B_{12} deficiency) (n=110)		Statistical inference (Fisher's exact test)
	No.	%	No.	%	
Lower	14	15.56	2	1.82	p<0.0001; HS
Lower-middle	55	61.11	29	26.36	
Middle	21	23.33	77	70.00	
Upper-middle	0	0.00	2	1.82	
Total	90	100.00	110	100.00	

HS – Highly significant

Table 6: Distribution of pregnant females according to place of residence

Place of residence	Cohort 1 (with vitamin B_{12} deficiency) (n=90)		Cohort 2 (without vitamin B_{12} deficiency) (n=110)		Statistical inference (Fisher's exact test)
	No.	%	No.	%	
Urban	67	74.44	46	41.82	p<0.0001; HS
Rural	23	25.56	64	58.18	
Total	90	100.00	110	100.00	

HS – Highly significant

Table 7: Association of Vitamin B_{12} deficiency with maternal high risk factor

Maternal high risk factor	Cohort 1 (with vitamin B_{12} deficiency) (n=90)		Cohort 2 (without vitamin B_{12} deficiency) (n=110)		Statistical inference (Fisher's exact test)
	No.	%	No.	%	
Severe +Moderate anaemia	89	98.89	102	92.73	p-0.041; S
Gestational hypertension	25	27.78	11	10.00	
Preeclampsia	2	2.22	1	0.91	
Gestational diabetes mellitus	10	11.11	4	3.64	
Tingling	16	17.78	13	11.82	
Bony pain	11	12.22	4	3.64	

S –Significant

Table 8: Distribution of pregnant females according to haemoglobin level (g/dL)

Haemoglobin (g/dL)	Cohort 1 (with vitamin B_{12} deficiency) (n=90)		Cohort 2 (without vitamin B_{12} deficiency) (n=110)		Statistical inference (Fisher's exact test)
	No.	%	No.	%	
4 – 6.9 (severe anaemia)	10	11.11	0	0.00	<0.0001
7 – 9.9 (moderate anaemia)	79	87.78	102	92.73	
10 – 10.9 (mild anaemia)	1	1.11	7	6.36	
>11(normal)	0	0.00	1	0.91	
Total	90	100.00	110	100.00	

HS – Highly significant

Table 9: Mean values of pregnant females biochemical parameters

Biochemical parameters	Cohort 1 (with vitamin B_{12} deficiency) (n=90)	Cohort 2 (without vitamin B_{12} deficiency) (n=110)	Statistical inference (Unpaired t test)
	Mean ± SD	Mean ± SD	
Serum vitamin B_{12} (pg/mL)	145.1 ± 32.44	273.05 ± $_{12}$5.47	t=9.54; p<0.0001; HS
Haemoglobin (g/dL)	8.08 ± 0.76	8.72 ± 0.64	t=6.36; p<0.0001; HS
Mean corpuscular volume (fL)	89.39 ± 3.18	88.$_{12}$ ± 1.36	t=3.71; p=0.0003; HS

HS – Highly significant

5. Discussion

In this study, Vitamin B_{12} deficiency was present in 45 % of pregnant females. This study is comparable to study by Krishnaveni GV et al., (2009)[3] in Mysore (India) in which low vitamin B_{12} concentrations (<150 pmol/L) were observed in 43% of pregnant women. In study by Lindstrom E et al., (2011)[4] in a rural area in Bangladesh, Vitamin B_{12} deficiency was present in 46% pregnant women. Out of 200 pregnant females enrolled for the study, maximum number of females in cohort 1 (88.89%) and cohort 2 (78.18%) belonged to age group 20-29 years with mean age of cohort 1 being 25.7 years and that of cohort 2 being 26.06 years. Statistically, both age groups were comparable. In study by Halicioglue O et al., (2015)[5] in Turkey, mean age was 27.5 ± 4.9 years. Vitamin B_{12} deficiency was more in pregnant females consuming vegetarian diet (83.33%). In study by Pathak P et al., (2007)[6], 70% of vitamin B_{12} deficient women were vegetarian. There was no statistically significant difference in two cohorts according to parity (p=0.52). It is in accordance with study by Halicioglu O et al., (20$_{12}$)[5] who also observed no statistically significant difference between low vitamin B_{12} levels and parity(p=0.5). Vitamin B_{12} deficiency was significantly more in lower middle and lower socioeconomic pregnant females in this study (p<0.0001). Fayyaz F et al., (2018)[7] showed prevalence of Vitamin B_{12} was very low in group of high socio-economic status women in Alberts Pregnancy Outcomes and Nutrition (APrON) cohort. In this study, vitamin B_{12} deficiency was more reported in urban pregnant females than their rural counter parts (74.44% vs 25.56%). In a study conducted by Dave et al., (2016)[8], urban population showed more deficiency (82.7%) as compared to rural population (17.3%). As was expected, mean serum vitamin B_{12} in Cohort 1 (with Vitamin B_{12} deficiency) was significantly lower as compared to those pregnant females in cohort 2 (without Vitamin B_{12} deficiency) (145.1 vs 273.05pg/ml; p<0.0001). Mean Haemoglobin of patient in cohort 1(with Vitamin B_{12} deficiency) was significantly less as compared to those of pregnant females in cohort 2 (without Vitamin B_{12} deficiency) (8.08 vs 8.72g/d L; p<0.0001). Mean corpuscular volume was in normal range in both the groups, though it was significantly more in Cohort 1(with vitamin B_{12} deficiency) as compared to Cohort 2 (without Vitamin B_{12} deficiency) (89.39 vs 88.$_{12}$ fL; p=0.0003). It was consistent with study by Pardo J et al., (2000)[9] where MCV was in normal range in both vitamin B_{12} deficiency group and non - Vitamin B_{12} deficient group (88 vs 91). Garima et al., (2016)[10] observed prevalence of vitamin B_{12} deficiency was 66%, 66%, 75% and 100% for mild, moderate, severe and very severe anemia. In our study prevalence of vitamin B_{12} deficiency was 100% for severe anemia and severe/moderate anemia was present in 98.89% pregnant females with vitamin B_{12} deficiency compared to 92.73% in pregnant females without vitamin B_{12} deficiency, the difference being statistically highly significant (p<0.0001). In our study, gestational hypertension (27.78% vs 10%) and pre eclampsia (2.22% vs 0.91%) were significantly associated with vitamin B_{12} deficiency cohort than non-deficient cohort. Dave et al., (2016)[8] also showed significant association between gestational hypertension and vitamin B_{12} deficiency. GDM was significantly associated with vitamin B_{12} deficient cohort (11.11%) as compared to cohort without vitamin B_{12} deficiency (3.64%). In study by Sukumar N et al., (2016)[11] in U.K. population, vitamin B_{12} were lower in women with GDM vs non-GDM (169 vs 195.6 pmol/L) and significantly higher proportion of women with GDM had Vitamin B_{12} deficiency as compared to non-GDM women (32.2% vs 21.9%). Krishnaveni GV et al., (2009)[3] showed low vitamin B_{12} concentrations were associated with higher incidence of GDM than non-deficient women (8.7% vs 4.6%). Similar to study by Dave et al., (2016)[8], tingling was significantly associated with vitamin B_{12} deficient cohort than non-deficient cohort (17.78% vs 11.82%) in this study.

6. Conclusion

Hence, it is found that Vitamin B_{12} deficiency is highly prevalent in pregnant women in our population. Its association with high risk factors in our study was significant. It is recommended that steps to prevent and to treat vitamin B_{12} deficiency should be taken so as to prevent maternal complications. There is no data to support routine screening for vitamin B_{12} deficiency in pregnancy in terms of health benefits or cost effectiveness. As the test is expensive, offering it to all women may not be cost effective compared to universal supplementation, which is regarded as being safe and may help in preventing Vitamin B_{12} deficiency and its complications.

References

[1] Refsum H, Yajnik CS, Gadkari M, Schneede J, Vollset SE, Orning L et al. Hyperhomocysteinemia and elevated methylmalonic acid indicate a high prevalence of cobalamin deficiency in Asian Indians. Am J Clin Nutr 2001; 74(2):233-41.

[2] Adaikalakoteswari A, Jayashri R, Sukumar N, Venkataraman H, Pradeepa R, Gokulakrishnan K et al. Vitamin B_{12} deficiency is associated with adverse lipid profile in Europeans and Indians with type 2 diabetes. Cardiovasc Diabetol 2014; 13:129.

[3] Krishnaveni GV, Hill JC, Veena SR, Bhat DS, Wills AK, Karat CL et al. Low plasma vitamin B_{12} in pregnancy is associated with gestational 'diabetes' and later diabetes. Diabetologia 2009; 52(11):2350-58.

[4] Lindstrom E, Hossain MB, Lonnerdal B, Raqib R, El Arifeen S, et al. Prevalence of anemia and micronutrient deficiencies in early pregnancy in rural Bangladesh, the MINIM at trial. Acta Obstet Gynecol Scand 2011; 90:47-56.
[5] Halicioglu O, Sutcuoglu S, Koc F, Ozturk C, Albudak E, Colak A et al. Vitamin B_{12} and folate statuses are associated with diet in pregnant women, but not with anthropometric measurements in newborns. The Journal of Maternal-Fetal and Neonatal Medicine 20_{12}; 1-4.
[6] Pathak P, Kapil U, Yajnik CS, Kapoor SK, Dwivedi SN et al. Iron, folate, and vitamin B_{12} stores among pregnant women in a rural area of Haryana State, India. Food Nutr Bull 2007; 28:435-38.
[7] Fayyaz F, Wang F, Jacobs RL, O'Connor DL, Bell RC, Field CJ. Folate, vitamin B_{12}, and vitamin B6 status of a group of high socioeconomic status women in the Alberta Pregnancy Outcomes and Nutrition (APrON) cohort. Appl Physiol Nutr Metab 2014; 39(12):1402-408.
[8] Dave A, Verma M, Jain N, Dave A. Study of Vitamin B_{12} deficiency in pregnancy and its impact on the maternal and foetal outcome. Indian Obstetrics and Gynaecology 2016; 6(2):12-16.
[9] Pardo J. Evaluation of low serum vitamin B_{12} in the non-anaemic pregnant patient. Hum Reprod 2000; 15:224-26.
[10] Garima, Jyala NS, Chaudhary D. A study of vitamin B_{12} deficiency in anemia in pregnancy. International Journal of Advances in Science Engineering and Technology 2016; 4(4):116-119.
[11] Sukumar N, Venkataraman H, Wilson S, Goljan I, Selvamoni S, Patel V, Saravanan P. Vitamin B_{12} Status among Pregnant Women in the UK and Its Association with Obesity and Gestational Diabetes. Nutrients2016;8(12):piE768

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