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In the past few years, vitamin B12 has been identified to play a pivotal role in recurrent pregnancy loss. The implicated mechanisms are (Willianne, Katve, 2010, Lap Pez, 2003)

• B12 deficiency leads to faulty and sporadic ovulation producing a faulty oocyte.
• B12 deficiency leads to a state of homocysteinemia which leads to thrombosis within the placental microcirculation.
• B12 deficiency leads to incomplete trophoblastic invasion of spiral arteries thereby leading to defective placentation.

Material and Methods

The Sample size of 100 non pregnant women attending OPD for pre conceptional counseling during September 2012 to August 2014 by Prospective and interventional process.

Women with 2 or more recurrent pregnancy losses, who were not pregnant, and met the inclusion criteria were subjected to serum Vitamin B12 & fasting homocysteine levels estimation. Those women with low levels of Vitamin B12 and high level of homocysteine were identified. Women with consanguinous marriage, with BMI>25, with thrombophilia syndromes, autoimmune disorders, alloimmune disorders and exposure to environmental toxins.

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PCOS or other endocrine abnormality, with suspected malabsorption disorders and with an anomalous uterine cavity were excluded from the study.

- Blood collection was done by venipuncture of antecubital vein. Sample was collected in plain blub.
- Serum B12 level, fasting serum homocysteine level and folic acid levels were measured. The method used was chemiluminescence assay.
- Those patients with Vitamin B12 levels less than 211 pg/ml were identified and labeled as B12 deficient (Normal Vitamin B12 level=211-800pg/ml). Also women who had serum homocysteine level homocysteine > 10 mmol/L were identified (Normal level: 5-15mmol/L).
- They were supplemented with oral Vitamin B12 tablets in the dose of 1500 micrograms for 2 months and serum B12 levels and fasting homocysteine levels were repeated.
- If serum B12 levels were found to be more than 300 pg/ml, they were allowed to try for pregnancy. If B12 levels were not yet replete, then B12 administration was continued till B12 and homocysteine levels were normalized.
- After serum B12 levels were brought back to above normal, that is, >300 pg/ml their subsequent obstetric course was studied.
- Their subsequent pregnancies were carefully followed up and classified into repeat abortion, full term gestation or preterm delivery. They were also vigilantly followed up for any pregnancy related complications like pregnancy induced hypertension or gestational diabetes.
- Simultaneously, 100 controls were also recruited. They were tested for Vitamin B12, Homocysteine and folic acid levels and their data was separately documented.
- Controls imply those women, with 1 or more healthy issue and no history of abortion.

**RESULTS**

Chi square test was applied for comparing percentages of different groups. All the calculations were performed by using the chi square test in Quikal software. Mean and standard deviation and its probability values were

![Graph 1: Number of Cases and Percentage of Vegetarian and Non-vegetarian Women](image)
given oral vitamin B12, in the dose of 1500 microgram/day till their serum vitamin B12 levels became normal. After their B12 levels were normalized they were permitted to conceive (Graph 1).

Out of 40, 36 women conceived naturally within 6 months. Out of these 36 pregnancies achieved, 2 ended in repeated abortion (5.5%) , 25 (69.4%) ended in successful live birth, 6 (16.6%) have crossed 28 weeks uneventfully and 3 have crossed 20 weeks uneventfully (8.3%) at the time this study went into print (Table 1).

Out of 25 live births, 2 (8%) had preterm delivery: one at 35 weeks due to PROM and other had preterm labor at 34 weeks due to Dengue fever. 5 women (20%) developed PIH after 30 weeks, 1 woman (4%) developed Gestational Diabetes Milletus at 28 weeks and 1 woman (4%) had twin gestation. 17 women underwent full term vaginal delivery (68 %) while 8 (32 %) underwent Cessarean procedure.

Unpaired t test with Welch correction was applied for comparing mean B12, mean homocysteine and mean folic acid values in study and control group population. The mean B12 value in study population was significantly lower than mean B12 in control population. The mean homocysteine value in study population was significantly higher than mean B12 in control population. The mean folic acid value in study population did not differ significantly from the mean folic acid value in control population.

This goes to prove that serum vitamin B12 deficiency was the attributable factor causing recurrent pregnancy loss in the study population.

**DISCUSSION**

Vitamin B12 exists in a number of different chemical forms, all of which have a cobalt atom at the centre.
In a similar study conducted by Votre P et al, 33% of women with prior pregnancy losses had low levels of vitamin B12 and higher concentration of homocysteine. With subsequent administration of B12, their homocysteine concentration reduced, compared to those who received only folic acid or no supplementation (Votre et al., 2006)

In a study among South Indian Urban Women, 51.1% women showed impaired B12 serum concentration. Out of them, 64% were founded to be strict vegetarians, with also low consumption of yogurt (Katve P. et al., 2010)

Hubbner U et al conducted similar study in Syrian women with Recurrent Pregnancy loss. They confirmed that low levels of vitamin B12 were found in women with RPL. They found B12 deficiency prevalence around 38.4% (Hubbner U., 2013)

Vitamin B12 is extremely important for healthy cell division and normal placental function. B12 deficiency leads to a state of homocysteinemia, causing thrombosis in placental microcirculation.

CONCLUSION

Vitamin B12 is extremely important for healthy cell division and normal placental function. B12 deficiency leads to a state of homocysteinemia, causing thrombosis in placental microcirculation.

Future Scope

Due to pre-dominant vegetarian dietary pattern in our society and general neglect towards nutrition, the women in reproductive age group are prone to develop B12 deficiency which may be one of the important underlying cause of otherwise unexplained recurrent pregnancy loss. Serum B12 measurement is a relatively cheap and non-invasive procedure. The deficiency be is easily correctable by oral supplementation of vitamin B12. Hence, serum B12 measurement should be incorporated into the laboratory investigation profile of all the women with RPL.

REFERENCES


Alan et al., women with homocysteinemia have increased risk of pregnancy complications and adverse pregnancy outcome. J Nutri 2006; 136(6): 173 15-17405.


