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Plasma Homocystein and vitamin B12 level comparison in normal and complicated pregnancy - A Observational study in tertiary care hospital.

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Abstract: *Periconceptionally, nutritional status influences the Vitamin B12 & folic acid level. Which may further affect the homocysteine level thus affecting pregnancy outcome. Non supplementation, poor economic condition,lack of hygiene & awareness are also contributory factors for these vitamin deficiency. Ahmedabad being a predominantly vegetarian city,its population is at higher risk for vitamin B12 deficiency. But there is no systematic study to know whether B12, folic acid, homocysteine affecting pregnancy complication like preeclamsia. This study was planned toknow tHcy and vitamin B12 level in normal and complicated pregnant women who were not supplemented with these vitamins before attending this hospital; and correlation between tHcy concentration and preeclampsia. Vitamin B12, tHcy & Folic acid was measured in all the subjects using fluorescence polarized immunoassay n AxSym Immunochemistry analyzer on 100 women of whom 50 were controls which included normal pregnant women. Study group consisted 50 women with complicated pregnancy. Study group showed highest mean 32.89, while the control group had least mean 13.14 homocysteine level. Significant difference between study group and control group (<0.001) at same gestational age was observed. Mean of vitaminB12(pg/ml) in control group was 359.69, in study group was 128.64. tHcy was found lowered in normal pregnant women and hyperhomocysteinemia was observed in pregnancy with complications.*

Key words: *Homocysteine, pregnancy, unspplemented Vitamin*

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I. Introduction

Preeclampsia, a common complication of pregnancy is one of the leading causes of feto- maternal morbidity and mortality. Vascular damage in the maternal utero-placental and fetal umbilical-placental circulation deterioration is at center of the reason of preeclampsia. On the other hand, Homocysteine is considered as an individual risk factor for arterial and peripheral vascular disease [1]. Homocysteine is a sulphar containing amino acid that is derived from demethylation of methionine an essential amino acid requiring folate, vitamin B12, B6 as a co-enzyme. Malnutrition or malabsorption of folate/ vitamin B12 / B6 / Inherited enzymes defect with methionine – homocysteine pathway such as MTHFR or cystathione B- synthase deficiency leads to increase in tHcy level [2]. Assumed mechanism for this, several factors such as oxidative stress [3], endothelial dysfunction, smooth muscle cell proliferation and coagulation abnormalities have been attributed[4] This bio-pathological mechanism that result in vascular damage, a relation between serum homocysteine level and vascular related pregnancy complications has been proposed[5].The people of Ahmedabad city fond of vegetarian diet, so they are in higher risk group of Vitamin B12 deficiency.

Our aim was to elaborate the correlation between serum tHcy and vascular related complications in pregnant women who were not supplemented with vitaminB12 and folic acids and find out tHcy level in normotensive pregnant women.

II. Materials and Methods

It was cross sectional observational study conducted at Sheth V S General Hospital & Sheth Chinai Maternity hospital which is a teaching institute attached to K M post graduate Institute and Smt NHL Municipal Medical college, Ahmedabad, initially 106 subjects were included in the present study but five were excluded because of no adherence to the study protocol. One sample was rejected because of faulty collection. So finally, 100 subjects were included, out of which 50 subjects were healthy pregnant women, on the other hand 50 antenatal women with singleton pregnancy were as study group. The study group subjects included those who

attended hospital at gestational age between 28-40 weeks. They neither took any antenatal care nor vitamin supplementation.

Exclusion criteria: Women with Diabetes mellitus, Chronic Hypertension, preexisting renal or liver disorder, H/O thromboembolism, Repeated miscarriage, H/O abruption placenta, anemia , Preterm labour, H/O smoking, and prior significant illness, **women with vitaminB12 and folic acid supplemention**.

Total homocysteine (tHcy) was measured in serum of all subjects using Fluorescence Polarized Immuno Assay technique by AxSym immunochemistry analyser.Commercial kit manufactured by same company was used . Results are assured as per standard quality control regime.The study was approved by the Institutional reviewcommittee.

For the analysis, 't' test, analysis of variance, p value has been used. For this study 95% confidence level have been chosen and corresponding 'p' value < 0.05 has been taken as significant.

III. Results

In this study, pregnant women in control group I and study group II were between 28-40 weeks of gestational age and in most of them are between 36-40 weeks of gestational age. No statistical difference in age of these groups were observed in the present study. All the groups were matched according to socio-economical status and diet habits After analysis of samples and calculations of data shows control group had the mean homocysteine level of **(13.14 ± 5.09µmol / L)** while study group I had least homocysteine level of **(32.89 ± 9.90 µmol / L)** . Significant difference is observed between control and study group I ($p<0.05$). None of them supplemented with vitamin B12 and or Folic acid at the time of sampling.

Table-I : Homocysteine level in different groups :

Group	Number of cases	Mean homocysteine level (µmol / L)	Standard Deviation	P value
control	50	13.14	5.09	<0.01*
study group	50	32.89	9.90	

- **p' value statistically Highly significant. (p<0.001).**

Table II: Vitamin B12 and Folate level in different groups

Group	Number of cases	Mean Vitamin B12 Level (pg /mL)	Mean folate level (ng /mL)
control	50	360	12
study group	50	129	9

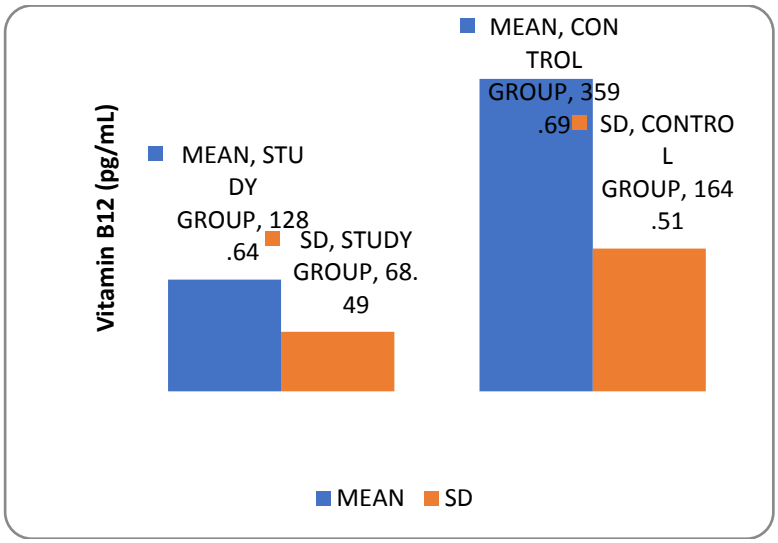

Figure 1. Mean and SD Vitamin B12 in Study and control group

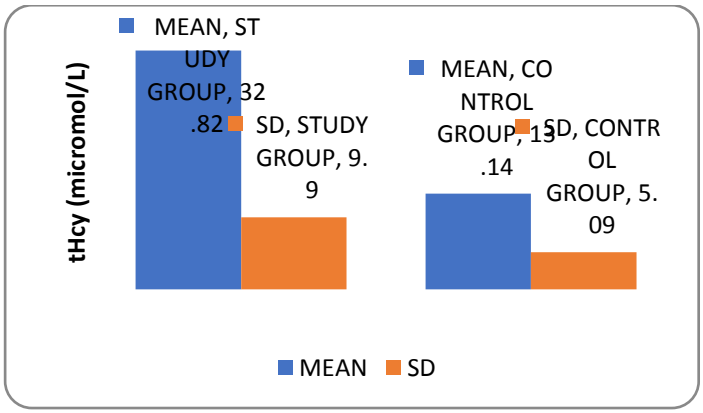

Figure 2. Mean and SD tHcy (Homocystine) in Study and control group

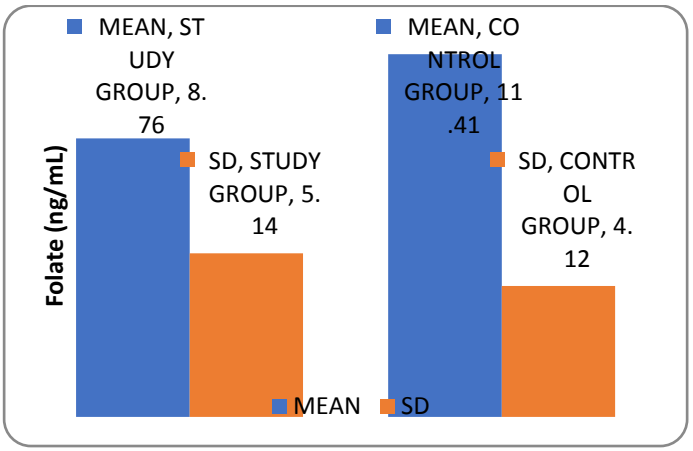

Figure 3. Mean and SD Folate in Study and control group

IV. Discussion

Since decades homocysteine found to be an independent risk factor in pathophysiology of atherothrombotic vascular disease. Its role for prediction as a risk of complication in pregnancy also has been extensively studied worldwide. As Vitamin B12 & Folic acid influence on the metabolic pathway of homocysteine they are linked. Many studies have been done in these regard, but most of these studies done on western population. There is no systematic study done in Gujarat. But considering the ethnic diversity, rapid industrialization & dietary habits of population of Gujarat may have affected the level and relation between homocysteine, vitamin B12, folic acid. Ahmedabad is the biggest city of Gujarat which caters population of different walks of life. Hence a systematic epidemiogical study of homocysteine, vitamin B12 and folate status in pregnancy with complication of Ahmedabad is necessary.

We aimed at that whether the dietary habits of people of Ahmedabad has influence on these vitamin level and thus homocystein metabolism as they are mostly. Vitamin B12 is derived from animal protein on the other hand vegetarian food is also a poor source of methionine so have reduced methylation activity. It is true that microorganism responsible for synthesis of vitamin B12 are available only in animal kingdom but poor socioeconomic, hygienic & malabsorption would affect the metabolism of Vitamin B12, Folic acid and Homocysteine and thus may lead to pregnancy related complications like IUGR, IUD, Eclampsia, Preeclampsia.

Considering these facts, the present study was undertaken to know the influence of homocysteine level on pregnancy related complication. The study provides interesting insights that may be because of lack of awareness a substantial number of women attend our hospital without of antenatal care, vitamin supplementation is a far cry. More over it is difficult to ascertain the exact dose of vitamin supplementation that has been received by the patients. So, we have considered those populations who were not supplemented with vitamin during the time of sampling.This is mainly because of lack of awareness, rapid urbanization, and poor socio-economic status in certain group of population in Ahmadabad. Another major limiting factor is that to ascertain the exact dose of vitamin supplementation that has been received by the patients is difficult. So, we have considered those populations who were not supplemented with vitamin during the time of sampling/at the time of admission.

The association between raised homocysteine and thrombosis was demonstrated by many research workers worldwide[6]. Thrombovascular abnormality in homocystinuria patients is an established fact now. **Boushy et al**[7] showed homocysteine as an independent graded risk predictor for atherosclerotic disease in coronary, cerebral and peripheral vessels.[8] Hyperhomocystenemia and their relationship with vitamin B12 & Folic acid have also been extensively studied. In a recent study, the relation between hyperhomocysteinemia and serum level of folic acid and vitamin B 12 shown that deficient level of folic acid and Vitamin B12 raised the homocysteine[9]. It has been reported that tHcy value between 5 **µmol/L** to 15 **µmol/L** in fasting subject are considered normal.[5]

In the mean homocysteine levels in control group was **13.14 ± 5.09 µmol / L** and in study group the mean homocysteine level was **32.89 ± 9.90µmol/L** and significant difference found between these two study group (P<0.001(table I). Moreover, in the present study Vitamin B12 and Folate level have been measured and on comparison it is observed Mean Vitamin B12 Level in Study Group-(**129 pg/mL**) is low than Control group **(360 pg/mL)**. Same as Mean Folate level is low in pregnant women with complications **(9 ng/mL)** in compare with normal pregnant **(12 ng/mL).** These both will lead to increase in total homocysteine level and finally leads to pregnancy related complications. In this study, it has been found that folate has more contribution in causing high homocysteine level than Vitamin B12.

These findings correlate well with study of Singh Urmila et al [10.] In another study done by Power et al [11] analyzed the homocysteine and folate level in 21 women with pre-eclampsia and 33 women with normal uncomplicated pregnancies and found significantly higher homocysteine level in preeclampsia than in normal pregnancy (p<0.04). The study of Hogg et al [12] also showed elevated homocysteine levels in women with pregnancy-induced hypertension, PET at 37 weeks gestation. These finding correlates well with our study. In addition, vascular endotheliumin pregnant women may be more sensitive to homocysteine injury. Therefore, moderate elevation of tHcy level compare to normal pregnant may lead to endothelial injury with subsequent activation of various factors that eventually results in complications [13]. Further longitudinal interventional studies are required to know cause of hyperhomocysteinemia observed in pregnant women with complications like IUD, IUGR, Preeclampsia with or without vitamin supplementation, which may help in further management. Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent: Informed consent was obtained from all individual participants (Cases and controls) included in the study.

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