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STUDY OF FETAL OUTCOME IN VITAMIN B^{12} DEFICIENT PREGNANT WOMEN IN A TERTIARY CARE CENTRE

Ashita Punjabi* Junior Resident, Department of Obstetrics and Gynecology, GMC Jammu, J&K, India. *Corresponding Author

Indu Kaul Professor and Head (retd), Department of Obstetrics and Gynecology, GMC Jammu, J&K, India

Radhika Gupta Junior Resident, Department of Obstetrics and Gynecology, GMC Jammu, J&K, India.

ABSTRACT

BACKGROUND: Maternal Vitamin B_{12} deficiency during pregnancy is associated with adverse fetal outcome and neurodevelopmental morbidity in infancy.

METHODOLOGY: A randomized prospective observational study was conducted in the Postgraduate Department of Obstetrics and Gynaecology, S.M.G.S Hospital Jammu from October 2017 to September 2018 after getting approval from ethical committee. 200 pregnant females with term gestation were included in the study. Maternal and fetal Vitamin B_{12} levels were analyzed. Fetal outcome in Vitamin B12 deficient pregnant women were studied.

RESULTS: 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).Umbilical cord vitamin B12 levels were higher than maternal vitamin B12 levels in both cohorts. Fetal outcomes in terms of low Apgar scores at 1 min (p=0.001) and 5 min (p=0.007), fetal anomaly (p=0.02) and NICU admission at birth (0.006) were found to be statistically significant in women with vitamin B_{12} deficiency during pregnancy.

CONCLUSION: Even though neonatal cord Vitamin B_{12} levels were higher than maternal levels, still maternal vitamin B_{12} deficiency was found to be a significantly associated with fetal neural tube defects and poor fetal outcome.

KEYWORDS : Vitamin B_{12} deficiency, Fetal neural tube defects

INTRODUCTION:

Vitamin B_{12} deficiency during pregnancy may elevate plasma homocysteine levels (Waterland RA and Michels KB, 2007)[1] and is associated with increased risk for adverse outcome including neural tube defects (Ray JG et al., 2007)[2], small for gestational age (Hogeveen M *et al.,* 2012)[3], intrauterine growth retardation (Muthayya S *et al.,* 2006)[4], early miscarriage (Hubner U *et al.,* 2008)[5] and preeclampsia (Refsum H *et al.,* 2001)[6]. Studies have shown association between low maternal plasma vitamin B_{12} and pregnancy affected by anencephaly (Schorah CJ *et al.,* 1980)[7]. Throughout the lifecycle, the most serious consequence of Vitamin B_{12} deficiency is impaired development and function of neurological processes. The underlying mechanism may involve impaired myelination or demyelination; imbalance of tumor necrosis factor-alpha (TNF-alpha) and epidermal growth factor (EGF) levels; and accumulated lactate in brain cells. In general deficiency of vitamin B_{12} has been linked to a variety of abnormal neurological symptoms including: hypotonic muscles, failure to thrive, cerebral atrophy and developmental regression (Dror DK and Allen LH, 2008)[9].

METHODS

The study was conducted in Postgraduate Department of Obstetrics and Gynaecology, S.M.G.S. Hospital, Jammu from 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. Specimens for Vitamin B_{12} analysis were collected from the subjects at the time of admission. Values less than 187 pg/ml were taken as vitamin B_{12} deficiency. Newborn blood samples were collected from newborn side of severed or cut umbilical cord at time of delivery. At the end of study, the data was compiled and analyzed by appropriate statistical tests.

RESULTS:

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)(Table 1).

Mean serum vitamin B_{12} level in newborns was available in 84 cases in Cohort 1 and 109 in Cohort 2.In both, Cohort 1 (265.66 pg/mL) and Cohort 2 (397.18 pg/mL), was within normal range. However, the difference between the two cohorts was statistically highly significant (p<0.0001) (Table 2).

Apgar score <7 at 1 minute was observed more in Cohort 1 (21.11%) as compared to Cohort 2 (5.45%), the difference being statistically highly significant (p=0.001) (Table 3).

Apgar score <7 at 5 minutes was observed more in Cohort 1 (16.67%) as compared to Cohort 2 (4.55%), the difference being statistically highly significant (p=0.007) (Table 4).

Fetal anomalies were observed in 7(7.77%) cases in Cohort 1 and in 1 (0.91%) cases in Cohort 2, the difference being statistically significant (p=0.02) (Table 5).

Mean neonatal birth weight in both, Cohort 1 (2.75 kg) and Cohort 2 (2.86 kg) was comparable (p=0.06) (Table 6).

IUDs were observed more in Cohort 1 (5.56%) as compared to Cohort 2 (0.91%), however the difference was statistically not significant (p=0.09) (Table 7).

There were 5 cases of IUD and 1 mortality in Cohort 1, while there was 1 case of IUD in Cohort 2. Therefore, NICU admission was considered for 84 cases in Cohort 1 and 109 in Cohort 2. NICU admission at birth was more in Cohort 1 (16.67%) as compared to in Cohort 2 (4.59%), the difference being statistically highly significant (p=0.006) (Table 8)

Table 1. Mean values of maternal vitamin B_{12}levels

Serum vitamin B_{12} (pg/mL)	Cohort1 (n=90)	Cohort 2 (n=110)
	Mean ± SD	Mean ± SD
	145.1±32.44	273.05±125.47

Statistical inference (Unpaired t test) t=9.54; p<0.0001; HS

Table 2. Comparison of mean Vitamin B_{12} levels of newborns between Cohort 1 and Cohort 2

Biochemical parameter	Cohort 1(n=84)	Cohort 2 (n=109)
	Mean ± SD	Mean ± SD
Serum vitamin B_{12} (pg/mL)	265.66± 89.30	397.18 ± 158.76

Statistical inference (Unpaired t test) –t=6.80 p=<0.0001 HS – Highly significant

Table 3. Association of Vitamin B_{12} deficiency with Apgar score at 1 minute

Apgar score at 1 min	Cohort 1(n=90)		Cohort 2 (n=110)	
	No	%	No.	%
<7	19	21.11	6	5.45
>7	71	78.89	104	94.55
Total	90	100.00	110	100.00

Statistical Inference (Fisher's exact test)- p=0.001; HS – Highly significant

Table 4. Association of Vitamin B_{12} deficiency with Apgar score at 5 minutes

Apgar score at 5 min	Cohort 1 (n=90)		Cohort 2 (n=110)	
	No.	%	No	%
<7	15	16.67	5	4.55
>7	75	83.33	105	95.45
Total	90	100.00	110	100.00

Statistical Inference (Fisher's exact test)- p=0.007; HS – Highly significant

Table 5. Association of Vitamin B_{12} deficiency with fetal anomaly

Fetal anomaly	Cohort 1(n=90)		Cohort 2 (n=110)	
	No	%	No	%
1.Neural tube defects				
Meningo myelocele	1	1.11	1	0.91
Occipital meningocele	1	1.11	0	0.00
Spina Bifida	1	1.11	0	0.00
2.Club foot	1	1.11	0	0.00
3.Hydro- Cephalus	2	2.22	0	0.00
4.Bilateral multicystic dysplastic kidneys	1	1.11	0	0.00

Statistical Inference (Fisher's exact test)- p=0.02; S - Significant

Table 6. Association of mean vitamin B_{12} deficiency with neonatal birth weight

Parameter	Cohort1 (n=90)	Cohort 2) (n=110)
	Mean± SD	Mean± SD
Neonatal birth weight (kg)	2.75±0.40	2.86± 0.42

Stastistical Inference (Unpaired t test) t=1.88; p=0.06 ; NS – Not significant

Table 7. Association of Vitamin B_{12} deficiency with intrauterine death (IUD)

Intrauterine death (IUD)	Cohort 1 (n=90)		Cohort 2 (n=110)	
	No.	%	No.	%
Yes	5	5.56	1	0.91
No	85	94.44	109	99.09
Total	90	100.00	110	100.00

Statistical Inference (Fisher's exact test)- p=0.09; NS – Not significant

Table 8. Association of Vitamin B_{12} deficiency with NICU admission at birth

NICU admission at birth	Cohort 1 (n=84)		Cohort 2 (n=109)	
	No	%	No.	%
Yes	14	16.67	5	4.59
No	70	83.33	104	95.41
Total	84	100.00	109	100.00

Statistical Inference (Fisher's exact test)- p=0.006; HS – Highly significant

DISCUSSION:

Mean cord Vitamin B_{12} levels were higher than maternal serum levels in both the cohorts (265.66 in Cohort 1 and 397.18 in Cohort 2) .Obeid R *et al.,* (2005)[9] reported significantly higher concentrations of vitamin B_{12} in cord serum levels than in maternal serum. In study by Frery N *et al.,* (1992)[10], cord blood Vitamin B_{12} levels were 2-3 fold higher than maternal levels. It was reported that placenta synthesis transcobalamin and is rich with transcobalamin receptors (Seetharam B, Li N, 2000)[11]. Furthermore, vitamin B_{12} is efficiently sequestered in intervillous space of placenta (Giugliani ER *et al.,* 1985)[12].In this study, no significant association was found between vitamin B_{12} levels and birth. In study by Ozturk O *et al.,* (2015)[13], there was statistically no significant effect of vitamin B12 levels on birth weight (3298± 482 g with low vitamin B_{12} levels vs 3316±434g with normal vitamin B_{12} levels). In this study, Apgar score <7 at 1 min and 5 min were more associated with maternal vitamin B_{12} deficiency. In study by Ozturk *et al.,* (2015)[13], Apgar score of all newborns was 7 and above. The difference may be due to association of vitamin B_{12} deficiency with high risk factors , thereby having effect on neonatal Apgar score in this study. In this study, NTDs and other anomalies were associated significantly with maternal vitamin B_{12} deficiency than non-deficient women (p=0.02). Ray JG *et al.,* (2008)[2], nine years post-folic acid fortification in Canada reported almost a tripling in the risk for NTDs in presence of low maternal vitamin B_{12} levels suggesting that maternal Vitamin B_{12} deficiency may be an independent risk factor for NTD. In a case control study in Ireland by Molloy AM *et al.,* (2009)[14] women with either NTD affected pregnancy or history of NTD affected pregnancy, low maternal Vitamin B_{12} concentrations predicted 2.5-3 times greater odds of NTDs, independent of folate status.

Intrauterine deaths were observed more in cohort 1 (5.56%) as compared to cohort 2 (0.91%), however the difference was statistically not significant. NICU admission at birth was more in cohort 1 (16.67%) as compared to Cohort 2 (4.59%), the difference being statistically significant.

CONCLUSION:

It was interesting to note that despite maternal Vitamin B_{12} deficiency, umbilical cord blood levels were higher than maternal levels. In this study, maternal vitamin B_{12} deficiency was found to be a significantly associated with low Apgar scores, fetal neural tube defects and more NICU admissions. Further studies are required to firmly establish the fetal outcome due to maternal Vitamin B_{12} deficiency. 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.

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