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A STUDY OF VITAMIN B12 DEFICIENCY AS A CAUSE OF SEVERE ANEMIA IN PREGNANCY: IS THERE A NEED FOR ANTENATAL SUPPLEMENTATION?

Juhi Godara Asst, Professor, Department of Obstetrics and Gynaecology, GAIMS, Bhuj, Gujarat, India

Yashodhara Pradeep Professor Department of Obstetrics and Gynaecology, King George Medical College, Lucknow, India

Renu Singh Department of Obstetrics and Gynaecology, King George Medical College, Lucknow, India

ABSTRACT Anemia in pregnancy has been synonymous with iron-deficiency anemia but there is a changing trend with emerging evidence of macrocytic anemia. The aim of our study was to evaluate the clinical profile of patients having severe anemia in pregnancy.It is a prospective cohort study included all antenatal patients presenting with severe anemia (hemoglobin <7 gm%) over a period of 1 year from July 2014 to June 2015 in the Department of OBG, KGMC, Lucknow, India.On comparing the results , it was found that although iron-deficiency remains the most important cause of severe anemia (74.9%) but there is also a high prevalence of vitamin B12 deficiency (56.4%) amongst these cases of severe anemia in pregnancy. This study done will be helpful in providing useful inputs to National Anemia Control Programme and may be helpful to evolve appropriate guidelines for adequate supplementation of vitamin B12 during pregnancy.

KEYWORDS : Pregnancy, Anemia, Vitamin B12 , Supplementation.

Introduction

Anaemia is the most common nutritional deficiency disorder in the world. Globally anaemia affects 1.62 billion people, which corresponds to 24.8% of the population.ICMR (2000) describes four grades of anemia depending upon the Hemoglobin Value (g/dl)

- Mild 10-10.9 (less than 11)
- Moderate 7-9.9 (less than 10)
- Severe 4-6.9 (less than 7)
- Very Severe < 4.

Laboratory evaluation begins with a CBC, including WBC and platelet counts, RBC indices and morphology (MCV, MCH, MCHC, RBC volume distribution width [RDW] and examination of the peripheral smear .

The peripheral smear is highly sensitive for excessive RBC production and hemolysis. It is more accurate than automated technologies for recognition of type of anemia (namely iron deficiency anemia, megaloblastic anemia and dimorphic).

Conventionally, iron-deficiency anemia has been synonymous with anemia of pregnancy and this has been well documented in literature and also in recent studies though other causes of anemia are also present. Of late, an increasing prevalence of macrocytic anemia was observed in our patients, which prompted this analysis. Megaloblastic/ macrocytic anemia, is due to a deficiency of either vitamin B12, folic acid (or both). Deficiency in folate and/or vitamin B12 can be due to either inadequate intake or insufficient absorption. Folate deficiency normally does not produce neurological symptoms, while B12 deficiency does, this fact helps to differentiate clinically that out of two which micronutrient is actually deficient. Dimorphic morphology in peripheral smear is seen when two causes of anemia act simultaneously, leading to deficiency of both iron and vitamin B12 or folic acid.

Vitamin B12 deficiency is an important cause of severe anemia during pregnancy contributing to significant maternal and fetal morbidity. Identifying the correct cause followed by appropriate treatment needs to be further underscored.

In our study we intend to determine the prevalance of Vitamin B12 deficiency and its importance in antenatal supplementation .

Materials and Methods

Subjects

The study was a prospective cohort study involving 195 pregnant women with severe anemia, that is, hemoglobin (Hb) <7 gm%, who were admitted to the maternity ward during a period of 1 year from July 2014 to June 2015 in the Department of Obstetrics and Gynaecology, King George Medical College, Lucknow, India.All pregnant women admitted with Hb < 7g/dl,Gestational age 20 weeks onwards were included in the study and investigated and evaluated.

Study method

Detailed history was taken from all the patients and were clinically assessed and investigated for CBC, Serum iron profile and serum Vitamin B12 and Folic Acid. Deficiency of vitamin B12 and folic acid was diagnosed by taking vitamin B12 = < 243 pg/ml and serum folic acid = <4.6 ng/ml.

Statistics

The data were presented as mean and standard deviations (normally distributed data) or as median and interquartile range (non-parametric data) for continuous variables, and as frequencies and proportions for categorical variables. Data were compared by 't' test , chi-square and Fisher's exact tests. All tests were two tailed and a 'p' value of < 0.05 was taken as significant. Analysis was done using statistical software packages IBM-SPSS 15.0 version .

Results

Total 195 subjects with severe anemia were enrolled as per the study design .Majority of subjects 124 (64%) belonged to rural residence while 71(36%) of subjects belonged to urban residence. (p-value =0.002) . The mean age was 24.64 years with a standard deviation of 3.75. Family's socioeconomic status was assessed according to Kuppuswamy's socioeconomic status scale. Maximum number of subjects (40%) belonged to lower class and 35% belonged to upper lower class; thus 75% patients belonged to lower class of socioeconomic status (p- value = <0.001) . Out of the 195 women enrolled for the study, nearly half (48%) were illiterate, 27% were upto 5th std and 25% were educated more than 5th standard . Some of them (9.3%) were illiterate. The majority of subjects (73 %) in the study were Hindus. 26% were Muslims and 1% were Sikhs. Out of the total subjects enrolled in the study 127 (65%) were multigravida and 68 (35%) were primigravida. (p-value = 0.003). Out of the 127 multigravida subjects 64.6 % were having spacing of less than 2 years while only 35.4% had spacing more than 2 years.(p-value < 0.001).

Number of subjects with vegetarian diet (50.7%) was more than the number of subjects with occasional non-vegetarian food habits (49.3%). (p -value = 0.75) Number of subjects who were

undernourished was found to be 40% while 55% were having normal nutritional status. (p-value = 0.003) Only 5% subjects were overnourished.

Iron deficiency was seen in 146 (74.9%) subjects while vitamin B12 deficiency was seen in 110 (56.4%) which is statistically significant. 81(81.8%) patients out of 99 with vegetarian diet had low vitamin B12 levels while only 29 (30.2%) of the 96 non vegetarians had the same finding thus low levels of vitamin B12 is significantly associated with pure vegetarian diet (p-value <0.001).

Iron deficiency (as indicated by low serum ferritin) was seen in all the patients with microcytic hypochromic anaemia and dimorphic anaemia and in 3(7.3%) patients of macrocytic anaemia. Vitamin B12 deficiency was seen in 38(92%) patients with macrocytic anaemia, 55(43.6%) patients with microcyitc hypochromic and 17(94.4%) subjects with dimorphic anaemia. Out of 41 subjects with macrocytic anaemia majority 38 (92%) were deficient in vitamin B12 , while 13(31.7%) subjects had deficiency of folic acid.

Residence	**Rural**	**124(64%)**
	Urban	71(36%)
mean age (years)		24.64+/-3.75
Socioeconomic Status	I (Upper)	2(1%)
	II (Upper middle)	10(5%)
	III(Lower middle)	38(19%)
	IV (Upper lower)	68(35%)
	V (Lower)	77(40%)
Educational level	Illiterate	93(48%)
	Upto 5th std.	53(27%)
	>5th std.	49(25%)
Religion	Hindu	144(73%)
	Muslim	50(26%)
	Sikh	2(1%)
	Christian	0(0%)
Diet	Vegetarian	99(50.7%)
	Non-vegetarian (occasionally)	96(49.3%)

Fig.1:demographic details

Sr. No.	Deficiency	Microcytic Hypochromic(n=126)	Macrocytic(n=41)	Dimorphic(n=18)	Normocytic Normochromic(n=10)	Total
1.	Vit.B12	0	25 (12.8%)	0	0	25 (12.8%)
2.	FA	0	3 (1.54%)	0	0	3 (1.54%)
3.	Iron	61 (31.3%)	0	0	0	61 (31.3%)
4.	S.Vit.B12 + S.FA	0	10 (5.13%)	0	0	10 (5.13%)
5.	Iron+ S.FA	10 (5.13%)	0	1(0.5%)	0	11 (5.64%)
6.	Iron+ S.Vit.B12	54 (27.7%)	3 (1.54%)	15(7.7 %)	0	72 (36.9%)
7.	All three	1 (0.5%)	0	2(1.02 %)	0	3 (1.54%)

Fig 2: Correlation of peripheral blood smear with various micronutrient deficiencies

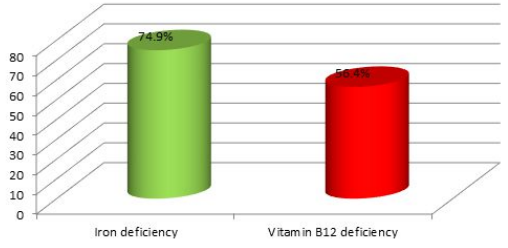

Fig 3:

The clinical details of the patients are depicted in Table 1 . Correlation of peripheral blood smear with various micronutrient deficiencies and Distribution of subjects according to Iron and VitB12 deficiency are shown in Table 2 and table 3 respectively.

Discussion

This study was intended to determine the prevalence of severe anemia and its maternal and perinatal complications and the laboratory correlation between severe anaemia with various parameters (automated blood count , iron profile and vitamin B12 and folic acid).

Our study showed that several factors are responsible for this much high prevalence of severe anemia (10.1%) in pregnant population of our study such as a illiteracy, low socioeconomic status which could be attributed to their poor dietary and hygienic conditions and increased subclinical chronic infections, undernourishment, high multiparity rate and less spacing so lost iron cannot be replenished ,vegetarian diet and late presentation for antenatal care, a lot of females becoming pregnant in adolescent or early adult age group which is a period of rapid growth and high nutritional demand for mother herself. Poor dietary status reflected by low socio-economic and literacy status makes micronutrient deficiency both clinical and subclinical, relatively, more common

In most of the severely anaemic subjects , blood picture was suggestive of iron deficiency anaemia, but biochemical studies in all the severely anemic patients showed a significant vitamin B12 deficiency along with iron deficiency, making Vitamin B12 deficiency , a significant cause of severe anemia in pregnancy. Out of all the severely anemic patients, iron deficiency was seen in 74.9% (146) of patients while vitamin B12 deficiency was seen in 56.4% (110) patients, which is statistically significant (p-value < 0.001).

Vitamin B12 is present only in foods of animal origin such as meat, dairy products, and fish. In India mostly females don't take any other foods other than cereal based food. It is major factor for high prevalence of anemia and this is particularly more in pregnant women of low socio-economic status & poor nourished women. Therefore there is need to give supplementary , folic acid and vitamin B 12 and providing nutrition education to the women .Folic acid deficiency is relatively less common because of routine folic acid supplementation in pregnancy.

In conclusion, vitamin B12 deficiency is as common as iron deficiency in pregnancy in developing country like India. A general blood picture, if used as a screening parameter, may be misleading. Even with a normal film morphology, at times these investigations will reveal important diagnostic and monitoring information. Physicians must keep in mind vitamin B12 deficiency in their differential diagnosis for a relatively wide spectrum of cases, particularly for cytopenias or anaemia of presumed iron deficiency type.

The assessment of a complete blood count, serum iron profile and serum vitamin B12 and folic acid levels remains the most efficient and effective laboratory investigation in the assessment of the patient with severe anemia.

The option of fortifying foods with vitamin B12 and its antenatal supplementation may need to be considered.

Conclusions

All the pregnant women with anemia should undergo complete anemia profile, which can help in early diagnosis and prevention of progression of severe anemia.

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