FETOMATERNAL OUTCOME OF SEVERE ANEMIA IN PREGNANCY WITH SPECIAL REFERENCE TO MACROCYTIC ANEMIA

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ABSTRACT

Anemia in pregnancy has been synonymous with iron-deficiency anemia but there appears to be a changing trend with emerging evidence of macrocytic anemia. The aim of this study was to evaluate the clinical profile of patients having severe anemia in pregnancy and its fetomaternal outcome with special reference to macrocytic anemia.Our study was prospective cohort study which 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, KGMU, Lucknow, India.On comparing the results it was found that maternal and fetal morbidity and mortality is higher in subjects with macrocytic anemia as compared to iron-deficiency anemia. Hence all pregnant women with severe anemia should be investigated for serum Vitamin B12, which can help in early diagnosis and prevention of progression of severe anemia and optimizing both maternal and perinatal outcomes.

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INTRODUCTION

Anaemia is the most common nutritional deficiency disorder in the world. In India prevalence of anemia at all ages remains very high e.g. pregnant women (rural) - ICMR (11 states; 1998-2000) 84.9% with 9.9% severe anemia. The data is supported by Nutrition Foundation of India study in 7 states (2002- 2003).

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 .

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. 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.

There is usually a 2 to 3-fold increase in perinatal mortality rate when maternal hemoglobin levels fall below 8.0 g/d1 and 8-10 fold increase when maternal hemoglobin levels fall below 5.0 g/dl. A significant fall in birth weight due to increase in prematurity rate and intrauterine growth retardation has been reported when maternal hemoglobin levels were below 8.0 g/d1.

In our study we intend to determine the prevalance of Vitamin B12 deficiency and its fetomaternal outcome signifying its need 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, KGMU, Lucknow, India.All pregnant women admitted with Hb < 7g/dl,Gestational age 20 weeks onwards were included in the study and investigated and evaluated. Known cases of sickle cell anemia or thalessemia, bone marrow diseases, coagulopathy, chronic malabsorption syndrome or "chronic disease" such as severe arthritis, inflammation, chronic liver disease etc. , patients with recent (<3weeks) h/o blood transfusion or parenteral iron administration or corticosteroids and patients who presented with APH (placenta previa or abruption placenta) were excluded from the study.

STUDY METHOD

Detailed history was taken from all the patients and were clinically assessed and investigated for Complete blood count, Serum iron profile and serum Vitamin B12 and Folic Acid.

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. As per 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). 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) .Iron deficiency was seen in 146 (74.9%) subjects while vitamin B12 deficiency was seen in 110 (56.4%) which is statistically significant.

Number of subjects with Microcytic hypochromic anemia was 126 (64.6 %), macrocytic anemia was 41 (21 %) and dimorphic anemia was 18 (9.2 %). (p-value= <0.001). Only 10(5.1%) subjects had normocytic mormochromic blood picture.

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Table 1

Sr.No.	Maternal complication/ outcome	Microcytic hypochromic anemia (n=126)		Macrocytic anaemia (n=41)		Dimorphic anaemia (n=18)		Total (n=195)		P-value
		No.	%	No.	%	No.	%	No.	%	
1.	Congestive heart failure	14	1.1	5	12.2	3	16.6	22	11.3	0.79
2.	Hypertensive Disorders	13	10.3	13	31.7	1	5.5	27	13.8	0.002
3.	Abruptio placenta	3	2.4	2	4.9	1	5.5	6	3.1	0.62
4.	PROM	7	5.6	3	7.3	-	-	10	5.1	0.51
5.	Preterm labour	15	11.9	9	22	2	11.1	26	13.3	0.25
6.	Dysfunctional labour/uterine inertia	2	1.6	1	2.4	0	0	3	1.54	0.79
7.	PPH	5	3.9	3	7.3	-	-	8	4.1	0.41
8.	Puerperal sepsis	3	2.4	1	2.4	1	5.5	5	2.6	0.73
9.	Lactation failure	1	0.8	1	2.4	-	-	2	1.02	0.61
10.	Maternal mortality	3	1.6	3	4.8	-	-	6	2.04	0.36

Congestive heart failure, Abruptio placenta ,PROM , Preterm labour, Dysfunctional labour/uterine inertia, PPH, Puerperal sepsis , lactation failure and maternal mortality were more common in macrocytic anaemic subjects than microcytic and dimorphic anaemic subjects. But Hypertensive disorders were found to be significantly more in macrocytic anemic group than microcytic and dimorphic anemic group (p = 0.002).

Table 2

Sr.No.	Fetal Complication/ Outcome	MCHC (n=126)		Macrocytic anaemia (n=41)		Dimorphic anaemia (n=18)		Total (n=195)		Value
		No.	%	No.	%	No.	%	No.	%	
1.	Fetal growth restriction	18	14.3	13	31.7	3	16.6	34	17.4	0.04
2.	IUD	2	1.6	2	4.9	-	-	4	2.04	0.36
3.	Small for gestational age infants	15	11.9	9	22	2	11.1	26	13.3	0.25
4.	APGAR score less than 7	6	4.8	3	7.4	1	5.5	10	5.13	0.82
5.	NNU admissions	19	15	6	14.6	2	11.2	27	13.8	0.9
6.	Early neonatal death	4	3.2	2	4.9	1	5.5	7	3.6	0.75

Table 1 depicts the maternal complications in severely anaemic women and table 2 depicst the fetal outcome in severely anaemic subjects

On observing fetal outcome it was seen that fetal growth restriction was significantly higher in fetus of macrocytic anaemic mothers (p-value = 0.04) ; other parameters like IUD, small for gestational age infants, low APGAR score, NNU admissions and early neonatal death were not statistically significant with respective p-values being 0.36,0.25, 0.82, 0.9 and 0.75. Table 3: Summarized maternal outcome in severely anaemic subjects:

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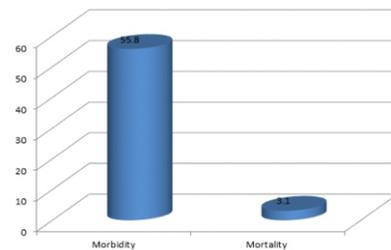| Sr. No.	Maternal outcome	No.of subjects (n=195)	%
1.	Morbidity	109	55.8
2.	Mortality	6	3.1

Fig. 1: Summarized maternal outcome in severely anaemic subjects

Out of all severely anaemic subjects a large number 64 (32.8%) had some morbidity while 6(3.1%) subjects suffered mortality.

DISCUSSION

Pregnancy itself leads to anemia by causing a state of hydremic plethora. There is disproportionate increase of plasma volume as compared to red blood cell mass leading to apparent reduction of red blood cells, hemoglobin and hematocrit value. The dilution picture is normochromic and normocytic. This is so-called physiological anemia of pregnancy.

This physiological situation can be further complicated by acquired nutritional problems, which include iron, folic acid and vitamin B12 deficiency as well as other causative factors, namely hemolytic or hemorrhagic conditions, due to acute or chronic blood loss.

Several factors are responsible for this much high prevalence of severe anemia (10.1%) as shown in results of our study in pregnant population such as a illiteracy, low socioeconomic status, undernourishment, high multiparity rate and less spacing ,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.

Types of Anemia were recognized on the basis of the morphological classification of anemia based on peripheral blood picture in present study. Morphological types showed that Microcytic hypochromic (64.6%) anemia was maximum followed by macrocytic anemia (21%) in pregnant women and dimorphic anemia (9.2%)(p-value = <0.001) (Table 16).

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. 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.

Our study shows that severe anaemia especially due to vitamin B12 deficiency or combined deficiency, is a cause of adverse foetal outcome and with increasing severity of anaemia complications. PROM (5.1%), Preterm labour (13.3%) and lactation failure(1.02%) were among the common maternal morbidities predisposing adverse fetal outcomes. On observing the fetal outcomes, 108 subjects (55.3%) showed adverse fetal outcome in one form or the other like fetal growth restriction (17.4%) , which is statistically more in macrocytic anaemia (p-value=0.04), IUD(2.04%), Small for gestational age (13.3%) , newborn with Apgar score of less than 7 at 5 mins(5.13%) , increased number of NNU admissions(13.8%) and early neonatal death(3.6%).

CONCLUSIONS

In light of these facts, the causes for increased incidence of vitamin B12 deficiency needs to be elucidated. Both the maternal and perinatal complications increase with these deficiencies, so the timely management of these deficiencies should be undertaken. It is essential for clinicians to be aware of this problem as treating all cases of pregnancy-related anemia as microcytic and due purely to iron deficiency may have serious implications as patients of macrocytosis will show suboptimal response to therapy and lead to persistence of problems, even with advancing gestation.

Given the increasing 'discovery' of vitamin B12 deficiency, the option of fortifying foods with vitamin B12 and its antenatal supplementation may need to be considered.

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