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EFFECT OF MATERNAL FIRST TRIMESTER HEMOGLOBIN CONCENTRATION ON NEWBORN SIZE: DOES IT AFFECT OR SAFETY HEMOGLOBIN RANGE NEEDS ANALYSIS?

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ABSTRACT

Background: India has reported high prevalence of anemia in pregnancy.

Methods-Prospective observational study, included 150 mothers registered for antenatal care (ANC) and willing to continue till confinement were recruited, and subjected to complete hemogram & red cell indices. We followed up these mothers till delivery and looked into the gestation and newborn anthropometry. Statistical analysis was done using Student's *t*-test and chi x^2 test.

Observation and analysis- In study of 150 cases, 54% were anemic. In first trimester, prevalence of anemia was 68/150 cases (45.34%). In anemic mothers, low birth weight babies were 25/37 (67.56%) while in non-anemic mothers low birth weight babies were 12 /37 (32.43%) ($p<0.01$).

Conclusion-Increased incidence of low birth weight and preterm babies is seen if the mother is anemic in her first trimester with significant association when hemoglobin is less than 8 gm%.

KEYWORDS : Anemia, first trimester pregnancy, newborn size, low birth weight

Introduction-

Anemia is one of the most frequently observed nutritional deficiency disease in the world today. It is present among women in reproductive age group, particularly during pregnancy, and often become a contributory cause for maternal death (WHO, 1992). Evidence from stable-isotope studies suggest that the percentage of non-heme iron absorbed from food during normal pregnancy increases from 7% at 12 weeks of gestation to 36% at 24 weeks and 66% at 36 wks. These dramatic changes enable the healthy pregnant woman to cope with the extra demands of pregnancy without becoming anemic[1], but only if there is adequate iron in her diet.[1] Prevalence of anemia in South Asian countries is the highest in the world. WHO estimates that even among the South Asian countries, India has the highest prevalence of anemia.[2] NNMB (National Nutrition Monitoring Bureau), DLHS (District Level Household Survey) and ICMR (Indian Council of Medical Research) surveys showed that over 87% of pregnant women suffer from anemia and about 10% have severe anemia.[2]

The importance of adequate plasma volume expansion in allowing adequate fetal growth is attested by several studies that showed an increased incidence of low birth weight in association with either a high maternal hemoglobin concentration [3,4,5] or high hematocrit.[6] The mechanism by which this effect is mediated is unknown but may be related to blood viscosity. Maternal blood is supplied to the intervillous space of the placenta by spiral arteries, which are adapted to provide an almost continuous low pressure flow. Failure of the plasma volume to expand (and of the hemoglobin concentration to drop) is associated with a ≤3-fold increase in the incidence of preeclampsia in pregnancy.[7] It has been suggested that a high blood viscosity may reduce the perfusion of the placenta, which may lead to intrauterine growth restriction. There are some controversial reports about the association between maternal hematocrit and adverse outcome of pregnancy[8,9]

Materials and Methods-

Prospective observational study, conducted in department of Obstetrics, Government medical college, Latur India, during January 2015 to June 2016 after ethical committee approval, included 150 mothers registered for antenatal care (ANC) and willing to continue till confinement were recruited after written informed consent as per routine protocol.

In this study, cases with hemoglobin >11 gm% and <11 gm% were classified as normal and anemia respectively in first trimester of pregnancy.

Inclusion criteria:

1. All pregnant women registered to our institute for ANC till delivery were included in the Study.
2. Cases of all types of anemia including hemolytic anemia.
3. Singleton pregnancy
4. Having had a USG in first trimester to accurately confirm / adjust dates and assign gestational age accordingly

Exclusion criteria:

Pregnant women with one of the following at booking were excluded:

1. Diabetes mellitus.
2. Hypertension (including pregnancy-induced hypertension).
3. Toxoplasmosis, Rubella, Cytomegalovirus, Herpes infection.
4. Diagnosed renal or cardiac illness.
5. Smoker or alcoholic.
6. Multiple gestation.

The investigations done were:

1. Blood-

a) Measurement of hemoglobin concentration was done by cyanomethemoglobin method (Analyzer–Coulter).
b) Complete blood picture- MCV, MCH, MCHC, RDW.
c) Hematocrit (Hct).
d) Peripheral smear for typing of anemia.
e) Hemoglobin electrophoresis whenever required.

Birth weight was recorded in grams using a digital scale with a scale of 1 gram. As per weight of newborns categorization was done as normal if birth weight is above 2.5 kg and low birth weight if less than 2.5 kg.

Statistical analysis-

The correlation between hemoglobin concentration and birth weight and other anthropometric parameters was measured by using chi test and students-t test. P value was considered significant if it was below 0.05 and highly significant in case <0.001.

Observations and analysis-

Of 150 pregnant women enrolled in study after their consent, 123 of them belong to age group 21-30 years (82%), elderly primigravida cases were 6 (4%), 117 cases (78%) were primiparous and remaining 33 cases (22%) were multiparous.

Table1: Percentage of severity of anemia in our study as per severity assessment by WHO classification-

Hemoglobin Level	First Trimester (n=150)
Normal > 11.1 gm%	82 (54.66%)
Mild (9.1-11.0 gm %)	54 (36.00%)
Moderate (7.1-9.0 gm %)	14 (9.33%)
Severe (4.1 -7.0 gm %)	0

In our study, observed mild anemia during first trimester were 36.00%, moderate anemia were 9.33% and none case of severe anemia.

Table 2: First trimester hemoglobin concentration and outcome in the form of birth weight of baby and maturity-

Hemoglobin (gm %)	<7.0 gm% (N=0)	7.1 to 9.0 gm% (n=14)	9.1 to 11.0 gm% (n=54)	11.1 to 13.0 gm% (n=68)	>13 gm% (n=14)
	-	**8.35 ± 0.52**	**10.07 ± 0.67**	**11.92 ± 0.55**	**13.85 ± 0.82**
Mean Birth Weight in gram	-	2250 ± 323.32	2770 ± 401.42	2861 ± 378.67	2645 ± 216.53
Birth Weight < 2500 gram (n=37)	-	2181 ±205.33 (n=13)	2212 ±142.90 (n=12)	2280 ±111.05 (n=10)	2270 ±210.41 (n=2)
Birth Weight > 2500 gram (n=113)	-	3140 ± 0.00 (n=1)	2930 ± 292.36 (n=42)	2962 ± 311.43 (n=58)	2707 ± 142.58 (n=12)
Preterm (n=21)	-	5	10	5	1
Term (n=129)	-	9	44	63	13

Values of Hemoglobin & Birth weight = Mean± SD

In first trimester women with severe anemia (Hb < 7.0gm %) were nil. In 14 cases with moderate anemia (Hb -7.1-9.0 gm%) mean Hb was 8.35± 0.52gm% and mean birth weight was 2250±323 gm, and in 14 cases, 9 were term and 5 were preterm deliveries.

Total 54 women were with mild anemia (Hb range 9.1-11.0 gm%) with mean Hb of 10.07± 0.67gm% and mean birth weight of 2770±401gm and among them 44 were term and 10 were preterm deliveries.

Discussion-

Effect of first trimester hemoglobin percentage on newborn size and pregnancy outcome-

In first trimester prevalence of anemia i.e. Hb <11 gm% were 45.34% (68 cases) and normal range Hb> 11gm% (non-anemic) were 54.66% (62 cases). In anemic mothers low birth weight babies were 25 out of total 37 i.e. 67.56% while in non-anemic mothers low birth weight babies were 12 of 37 i.e.32.43%, statistically significant difference noted (p<0.01). Of total 113 normal birth weight babies, born in anemic and non-anemic mothers were 43 (38.05%) and 70 (61.95%) respectively, difference is statistically significant (p<0.01). Out of 21 preterm babies, 15 babies (71.42%) born to anemic mothers and 6 babies (28.57%) born to non-anemic mothers, difference is statistically significant (p<0.01)

In our study, we observed that as hemoglobin percentage of mother increases, birth weight of baby increases (p<0.001).In cases with Hb between 7.1 to 9 gm% (moderate anemia) mean birth weight of LBW babies were 2181±205gms, and that of normal babies was 3140±0.0gms (p<0.001). In cases with hemoglobin between 9.1 to 11 gm% (mild anemia) mean birth weight of LBW and normal babies were 2212±142gms and 2930±292gms respectively (p<0.001). **Ronnenberg AG et al** [10] 2004 (China) observed that both mild and moderate anemia were significantly associated with lower birth weight. In cases with hemoglobin between 11.1gm% to 13gm% mean birth weight of LBW and normal babies were 2280±111gms and 2962±311gms respectively (P<0.001). In cases with hemoglobin above 13.0 gm% mean birth weight of LBW babies and of normal babies were 2270±210gms and 2707±210gms respectively (p<0.002) . **Murphy JF et al** [7] studied relation of hemoglobin levels in first and second trimesters to outcome of pregnancy and found both high (greater than 13.2 g/dl) and low (less than 10.4 g/dl) hemoglobin values were associated with an adverse outcome. The frequencies of perinatal death, low birth weight, and preterm delivery were greater with high than with intermediate hemoglobin. **Blankson ML et al** [9] **and Rasmussen et al** [11] observed correlation with high hemoglobin /hematocrit and low birth weight.

Studies correlating effect of first trimester hemoglobin percentage on newborn size and pregnancy outcome with present study

Author, Year	Effect of Maternal Anemia on Newborn size and maturity
In Present Study	In anemic mothers low birth weight babies were 25 out of total 37 i.e. 67.56% while in non-anemic mothers low birth weight babies were 12 of 37 i.e.32.43%, statistically significant difference noted.(p<0.01).
Alwan et al [12] 2011 U.K	There was a positive relationship between total iron intake, from food and supplements, in early pregnancy and birth weight.
Muhammad Owais Ahmad et al [13] 2011	The number of low birth weight infants (64%) was statistically very highly significantly more (p<0.001) in the anemic group of mothers than the non-anemic group.
Umber Jalil Bakhtiar et al [14] 2007	Risk of preterm and low birth weight among anemic women was 3.4 and 1.8 times more than non-anemic women. Regular antenatal care from first trimester has a vital role in assessing and managing maternal anemia timely and it directly affects the perinatal outcome.
F Nasiri-Amiri et al [15]2007	Anemia is frequently observed during pregnancy. Anemia marked by hematocrit<34% in the first trimester was associated with a significantly increasing risk of low birth weight (<2500 g) and preterm delivery which was indicated by the gestational age of less than 37 weeks.
Levy A et al [16] (2005)	Maternal anemia influences birth weight and preterm delivery, but in our population, is not associated with adverse perinatal outcome.
Patra S et al[17](2005)	Perinatal outcomes of 130 severely anemic pregnant women who had 5 gm/dl or lower hemoglobin. Following outcomes were reported: preterm birth rate 69.2%, fetal distress 23%, low birth weight 24.6 % and neonatal death rate 35%.
Lone, F. W et al [18](2004)	The risk of preterm delivery and LBW among exposed group was 4 and 1.9 times higher among anemic women, respectively. Low maternal hemoglobin levels are associated with increased risk of preterm delivery, LBW babies
Ronnenberg AG et al[10] 2004 China	Both mild and moderate anemia were significantly associated with lower birth weight. Preconception anemia, particularly iron-deficiency anemia, was associated with reduced infant growth and increased risk of adverse pregnancy outcome.
Malhotra M et al [19] 2002	Mild anemia fared best in maternal and perinatal outcome. Severe anemia was associated with increased low birth weight babies, induction rates, operative deliveries and prolonged labor
Bondevik GT et al [20] 2001 Nepal	Severe anemia particularly in the first trimester was associated with a significantly increased risk of low birth weight (<2500 g) and preterm delivery (<37 weeks gestation)
Lindsay H Allen et al[21] (2000), USA	Maternal iron deficiency anemia increases the risk of preterm delivery and subsequent low birth weight
Zhou LM et al [22] 1998 China	Rates of LBW and preterm birth were related to early pregnancy hemoglobin concentrations in a U-shaped manner.
Schol TO et al [23] 1994 USA	Anemia diagnosed early in pregnancy is associated with increased risks of low birth weight and preterm delivery.

The mechanisms that operate by which poor iron status may affect birth weight and preterm births remains poorly understood. A few tested hypotheses are (I) Poor iron status may affect immune function adversely and thus increase the host susceptibility to genital tract infections. (ii) Iron deficiency may increase the stress hormones norepinephrine and cortisol. (iii) Low hemoglobin concentration may cause chronic hypoxia, which can activate the body's stress response and thus increase circulating levels of corticotrophin releasing hormone, and (IV) iron deficiency may increase oxidative stress of the placenta.[19,24]

Other important observations-

1. Prevalence of anemia in study population.

Prevalence of anemia in our study in urban setting in tertiary care hospital in India, especially in pregnant women is 54%. The FOGSI-WHO[25] has estimated that prevalence of anemia in developed and developing countries in pregnant women as 14% and 51% respectively

and 65-75 per cent in India. National Nutrition Monitoring Bureau (NNMB)[26] DLHS and ICMR surveys showed that over 70 per cent of pregnant women and adolescent girls in the country were anemic.

Various studies conducted by Kalaivani K et al [27] & Patra, Puri & Trivedi et al [17] observed prevalence of anemia as 87% & 56.9% respectively.

2. National programme to give iron supplementation to all pregnant women.

Programme for prevention and management of anemia (NACP) [30] India was the first developing country to take up a national programme to prevent anemia among pregnant women and children. The programme envisaged that all pregnant women will be screened for anemia. Non anemic women would get iron (100 mg) and folate (500 microgram) and those with anemia should get two tablets daily.

3. Safe hemoglobin range, where no intervention is necessary.

We observed better neonatal outcome in the form of weight and anthropometry if maternal preconception hemoglobin is in range of 10 to 13 gm%. After extrapolating neonatal outcome in study group and available data from other studies, we recommend iron prophylaxis in this group and no treatment above this hemoglobin percentage.

4. U shape correlation between hemoglobin concentration and newborn size-

In several studies, a U-shaped association was observed between maternal hemoglobin concentrations and birth weight. Abnormally high hemoglobin concentrations usually indicate poor plasma volume expansion, which is also a risk for low birth weight. Lower birth weights in anaemic women have been reported in several studies.[7,15,21,31]

In our study, in first trimester clustering of normal birth weight was observed in hemoglobin (Hb) range of 9.0 to 13.0gm% and percentage of LBW was increased as hemoglobin drops below 9.0 gm% and also when hemoglobin is above 14 gm%. We also observed, high hemoglobin percentage above 14 gm% was not positively associated with proportionate increase in newborn size as noted with U shape correlation of maternal hemoglobin with newborn size and gestational age. Such correlation was unable to draw because sample number in our study was not sufficient enough to make meaningful conclusions.

Conclusion:

Anemia in pregnancy has a recognizable association with fetal outcome. Increased incidence of low birth weight babies is seen if the mother is anemic in her first trimester with significant association when hemoglobin is less than 8 gm%. Increased incidence of preterm deliveries is seen if the mother is anemic in her first trimester.

We observed better neonatal outcome in the form of weight and anthropometry if maternal hemoglobin is in range of 10 to 13 gm%. Supplementing iron earlier during antenatal period and maintaining optimal hemoglobin concentration between 10 to 13 gm percent has overall better outcome regarding premature deliveries and low birth weight babies.

Regular antenatal care from first trimester has a vital role in assessing and managing maternal anemia timely and it directly affects the perinatal outcome.

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