

Comparative Study of Maternal and Fetal Outcome in Nutritional Anemia through the Course of Pregnancy

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Abstract:

Background: Maternal anemia is an important cause of maternal mortality in developing countries like India. Anemia is also responsible for complications like infections, heart failure, pre term labor, etc as well as adverse fetal outcomes. Prevalence of anemia is different among different socioeconomic backgrounds. Hence this study was conducted to assess the maternal and fetal outcomes in anemic women and to compare these outcomes in women presenting with anemia in first and third trimesters.

Methods: 51 pregnant women attending OBG OPD were classified into three equal groups of 17 with first group having non anemic women, 2nd group having women anemic throughout pregnancy and 3rd group with women anemic in 3rd trimester alone.

Results: Women presenting with anemia in 1st trimester tend to have lower hemoglobin values and blood indices throughout pregnancy. Moreover, there was significant association between those who had anemia throughout pregnancy and preterm deliveries, lower birth weights and lower APGAR scores.

Conclusion: Thus, anemia control measures should start preconceptionally so that women enter the state of pregnancy with adequate iron reserves. An intergenerational approach towards anemia control should hence be adopted for healthier mothers.

Keywords: Anemia, maternal, fetal outcome, comparison

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I. Introduction

According to the WHO, approximately 18 percent of the women population in developed nations is found to be anemic.¹ Maternal anemia is a very common problem in pregnancy in developing countries like India where 61-90% of the pregnant women are anemic.^{2,3} The reason for this is the poor nutritional status of the people and the high incidence of parasitic infestation.^{4,5} In low income countries, most of the risk factors for anemia in pregnancy are related to chronic poverty.

Dilutional anemia due to the physiologic increase in blood volume is an important reason for anemia in pregnancy.⁶ Reduced iron reserves in a woman, which maybe present from the time before conception is believed to be the main cause of anemia in pregnancy.¹ Anemia shows itself only in the last stage of severe iron deficiency.⁷ The huge amount of blood loss during labor and puerperium along with repeated pregnancies often at smaller intervals aggravate the problem of maternal anemia.

Adverse fetal such as preterm labor, low birth weight, Intrauterine Growth Restriction (IUGR), Small for Gestation Age (SGA) and anemia are reported by some studies.^{8,9,10} A meta-analysis showed that only women who were anemic at the beginning of pregnancy had increased risk of preterm labor (PTL) and Low birth weight but that this was not seen in those who developed anemia later in pregnancy.¹¹ A recent study conducted in Bangalore also found increased incidence of neonatal sepsis in pregnant anemic patients¹², while another recent study from Bangalore showed an increase in the number of birth asphyxia cases in babies born to anemic mothers.¹³

In India anemia is directly or indirectly responsible for 40% of maternal deaths. MMR increases 8-10 fold when hemoglobin falls below 5gm/dL. Early detection and effective management of anemia in pregnancy can effectively reduce maternal mortality rate.¹⁴ A study conducted in Andhra Pradesh in India had observed numerous maternal complications not only during pregnancy, like intercurrent infections, heart failure, pre-eclampsia and eclampsia, abruptio placenta, preterm labor and intrauterine deaths (IUD), but also during labor like postpartum hemorrhage (PPH), cardiac failure and maternal death.¹⁵ Caesarean rates also are found to be higher in the population with lower PCV and hemoglobin values.^{16,17}

Prevalence of anemia and the severity of its outcome are different in different places with different socioeconomic conditions. More studies are required from both rural and urban populations. Hence, this study was conducted in rural Kanyakumari district to identify nutritional anemia in gravid women; to assess the maternal and fetal outcome in gravid women with and without anemia and to compare the maternal and fetal outcome in anemic gravid women presenting in the first trimester and third trimesters.

II. Material And Methods

This prospective comparative study was carried out on antenatal patients attending the Outpatient Department of Obstetrics & Gynecology at SreeMookambika Institute of Medical Sciences, Kulasekharam, Kanyakumari, Tamil Nadu from May 2015 to April 2016. A total of 51 women were included in the study with 17 women in each of the three groups.

Sample size calculation:

$$N = \frac{2[1.96\sqrt{2P(1-P)} + 0.842\sqrt{(P_1(1-P_1) + P_2(1-P_2))}]^2}{(P_1 - P_2)^2}$$

1.96 = Standard normal variation at 5% Type I error

0.842 = Power at 80%

P1 = Proportion of Preterm births in pregnant women with anemia⁹
=16.8%

P2 = Proportion of Preterm births in pregnant women without anemia⁹
= 7.5%

P = (P1+P2) / 2

N (Total sample size) = 51.48

Hence, sample size of each group = 17

Subjects & selection method: Consecutive sampling method was adopted for the purpose of this study. All pregnant women attending Obstetrics and Gynecology outpatient department during the study period who fulfilled the inclusion and exclusion criteria were included in the study.

Group A(N=17 patients) – non anemic mothers;

Group B (N=17 patients) –pregnant women with Hb<10.9 throughout pregnancy; and

Group C (N=17 patients) -pregnant women who were normal in first trimester and anemic in third trimester.

Inclusion criteria:

1. Antenatal patients booked for antenatal checkups in OBG OPD.
2. Antenatal women who are willing to participate in the study.

Exclusion criteria:

1. Antenatal women with medical complications of pregnancy other than anemia.
2. Antenatal women with ante partum hemorrhage.
3. Antenatal women with hemoglobinopathies, bleeding P/R or any other cause of anemia other than nutritional causes.
4. Antenatal women with multiple pregnancies.

Procedure methodology:

Data collection started after approval from Institutional Ethics Committee. After written informed consent was obtained, detailed history was taken using an interviewer administered questionnaire. A thorough general physical examination was done. Investigations including complete hemogram and urine routine were taken. According to the Hemoglobin level the women were divided into 2 groups – one group having antenatal women without anemia and 2nd group having antenatal women with anemia. The 3rd group of women consisted of those antenatal women who reported to the OP in the 3rd trimester without any regular antenatal checkups during the current pregnancy period(unbooked cases) and detected to have anemia at the time of admission. For those patients with anemia as per WHO definition, peripheral smear was taken. Antenatal checkup was done regularly and adequate antenatal care given for all women of all 3 groups and every patient was followed up till their delivery. Maternal hemoglobin, PCV and red cell indices were done in each trimester. Mode of delivery, gestational age at delivery, birth weight, incidence of PPH, APGAR scores and any neonatal complications were recorded. Finally the pregnancy outcome between the 3 groups was compared.

Statistical analysis:

Data was analyzed using SPSS trial version 20 (SPSS Inc., Chicago, IL). Chi-square tests were performed to test for differences in proportions of categorical variables between two or more groups. P value less than 0.05 was considered as the cutoff value for statistical significance.

III. Results

This was a prospective study done among 51 pregnant women attending the Obstetrics & Gynecology outpatient department of our hospital as three groups. The first group consisted of 17 women with normal hemoglobin in all the three trimesters. The second group had 17 women who were anemic throughout pregnancy. The third group of 17 women had normal hemoglobin in the beginning of pregnancy in first trimester (T1) and later became the anemic in the third trimester (T3).

Table no 1: Baseline characteristics of the three groups of pregnant women

Variables		Category of pregnant women			Total (%)	Chi square	P value
		Normal Hb in all 3 trimesters	Hb<10.9 in all 3 trimesters	Normal Hb in T1; anemic in T3*			
Age categories	21-25 years	5(29.4%)	10(58.8%)	7(41.2%)	22(43.1%)	6.87	0.33
	26-30 years	9(52.9%)	7(41.2%)	7(41.2%)	23(45.1%)		
	31-35 years	3(17.6%)	0	2(11.8%)	5(9.8%)		
	>35 years	0	0	1(5.9%)	1(2.0%)		
Education	Primary	0	0	1(5.9%)	1(2.0%)	11.7	0.304
	Middle school	2(11.8%)	3(17.6%)	4(23.5%)	9(17.6%)		
	High school	4(23.5%)	9(52.9%)	7(41.2%)	20(39.2%)		
	Diploma	5(29.4%)	4(23.5%)	4(23.5%)	13(25.5%)		
	Graduate	3(17.6%)	0	1(5.9%)	4(7.8%)		
	Professional	3(17.6%)	1(5.9%)	0	4(7.8%)		
Occupation	Unemployed	7(41.2%)	8(47.1%)	9(52.9%)	24(47.1%)	13.62	0.19
	Unskilled	3(17.6%)	4(23.5%)	3(17.6%)	10(19.6%)		
	Skilled	0	0	2(11.8%)	2(3.9%)		
	Clerical	5(29.4%)	4(23.5%)	0	9(17.6%)		
	Semi-Professional	0	0	2(11.8%)	2(3.9%)		
	Professional	2(11.8%)	1(5.9%)	1(5.9%)	4(7.8%)		

*T1-First trimester, T3- third trimester

No statistically significant difference was observed for age distribution, education or occupation among the different categories of pregnant women.

Menstrual history:

Around 94.1% (16) women in the first category of normal women had bleeding every 21 – 35 days and only 1 (5.9%) person had periods once in more than 35 days. In the second group, 100% of the group had bleeding at intervals of 21- 35 days. In the 3rd group 14 (82.4%) women had bleeding every 21 – 35 days and only 3 (17.6%) women had a prolonged interval of >35 days. Regarding history of passing clots during menstrual cycle, 29.4% of women in the group which was anemic throughout pregnancy and 5.9% of women in the third group gave a positive history. The first group which included normal women did not give such a history and the difference among different categories of women was statistically significant. The distribution of the number of pads changed per day during the menstrual cycle, as given below in Table 2, demonstrated a statistically significant difference across various categories of pregnant women.

Table 2: Number of pads changed/day by different categories of women

Number of pads changed/day	Category			Total
	Normal Hb in all 3 trimesters	Hb 10.9 and less in all 3 trimesters	Hb normal in T1; anemia in T3	
≤3	16(94.1%)	2(11.8%)	7(41.2%)	25(49.0%)
4-7	1(5.9%)	15(88.2%)	9(52.9%)	25(49.0%)
8-10	0	0	1(5.9%)	1(2.0%)

*Chi square value = 25.920, p value=0.000

Obstetric history:

The distribution of pregnant women according to number of pregnancies, number of deliveries and spacing between the deliveries is as given below in Table 3.

Table 3: Obstetric history across various categories of pregnant women

Variables		Category of pregnant women			Total (%)	Chi square	P value
		Normal Hb in all 3 trimesters	Hb<10.9 in all 3 trimesters	Normal Hb in T1; anemic in T3*			
Gravida	1	8(47.1%)	7(41.2%)	9(52.9%)	24(47.1%)	7.58	0.475
	2	6(35.3%)	5(29.4%)	7(41.2%)	18(35.3%)		
	3	3(17.6%)	2(11.8%)	1(5.9%)	6(11.8%)		
	4	0	2(11.8%)	0	2(3.9%)		
	5	0	1(5.9%)	0	1(2.0%)		
Parity	0	9(52.9%)	7(41.2%)	11(64.7%)	27(52.9%)	3.49	0.48
	1	8(47.1%)	9(52.9%)	6(35.3%)	23(45.1%)		
	2	0	1(5.9%)	0	1(2.0%)		
Spacing between deliveries	NA	9(52.9%)	7(41.2%)	11(64.7%)	27(52.9%)	3.79	0.435
	<2 yrs	2(11.8%)	3(17.6%)	0	5(9.8%)		
	>2 yrs	6(35.3%)	7(41.2%)	6(35.3%)	19(37.3%)		

*T1-First trimester,T3- third trimester

Clinical findings:

Women belonging to group 2 and 3 had visible pallor on general examination. We found that the presence of pallor was more (76.5%) in the third group than in the second group (64.7%) and this difference was statistically significant. Around 23.5% of the women who were anemic throughout pregnancy had tachycardia with a pulse rate of more than 100/minute, while the other two category women had normal pulse rate and this difference also was statistically significant.

On calculation of Body Mass Index (BMI), 3 (17.6%) women in the first category were underweight with a BMI of <18.5, 10 (58.8%) women had normal BMI (18.5 – 25), 2 (11.8%) were overweight (BMI=25.1 to 30) and 2 (11.8%) women were obese (BMI>30.1). In the second category, 8 (47.1%) women were underweight, 7 (41.2%) were in the normal BMI group and 2 (11.8%) were overweight. In the third category 2 (11.8%) women were underweight, 13(76.5%) women came in the normal weight group, 1 (5.9%) woman was overweight and one (5.9%) woman was obese.

The hemoglobin levels were normal in the women in the first category, while the hemoglobin level in the second group of women were below 7gm in 11.8%, between 7 and 9 gm in 23.5% and between 9.1 and 10.9 gm in 64.7%. However in third trimester, hemoglobin below 7 gm was found in only 5.9% of women, while 94.1% had a hemoglobin level between 9.1 and 10.9gm. In the third category, while hemoglobin level was normal in the beginning of pregnancy, nearing delivery 23.5% had hemoglobin of less than 7 gm, while 76.5% had hemoglobin between 9.1 and 10.9gm in the third trimester. The PCV and Red Blood Cell indices of the wwomen were as described below in Table 4.

Peripheral smear examination done at delivery showed that all women in the first category had normocytic normochromic peripheral smear. In the second category, at the time of delivery, only one (5.9%) woman had normocytic normochromic peripheral smear, while the remaining 16 (94.1%) had microcytic hypochromic peripheral smear. In the third category, 2 (11.8%) women had normocytic normochromic peripheral smear and 15 (88.2%) women had microcytic hypochromic peripheral smear at the time of delivery. This difference in proportions was statistically significant.

Table no 4:PCV and RBC indices across different categories of pregnant women

Variables		Category of pregnant women			Total (%)	Chi square	P value
		Normal Hb in all 3 trimesters	Hb<10.9 in all 3 trimesters	Normal Hb in T1; anemic in T3#			
PCV in T1	<33%	0	16(94.1%)	0	16(31.4%)	46.63	0.000 [†]
	≥33%	17(100.0%)	1(5.9%)	17(100.0%)	35(68.6%)		
PCV in T3	<33%	1(5.9%)	15(88.2%)	17(100.0%)	33(64.7%)	39.15	0.000 [†]
	≥33%	16(94.1%)	2(11.8%)	0	18(35.3%)		
MCH in T1	<27	0	14(82.4%)	0	14(27.5%)	38.59	0.000 [†]
	27-33	17(100.0%)	3(17.6%)	17(100.0%)	37(72.5%)		
MCH in T3	<27	0	11(64.7%)	15(88.2%)	26(51.0%)	28.4	0.000 [†]
	27-33	17(100.0%)	6(35.3%)	2(11.8%)	25(49.0%)		
MCV in T1	<80	6(35.3%)	14(82.4%)	6(35.3%)	26(51.0%)	10.04	0.007 [†]
	80-96	11(64.7%)	3(17.6%)	11(64.7%)	25(49.0%)		
MCV in T3	<80	6(35.3%)	15(88.2%)	17(100.0%)	38(74.5%)	21.27	0.000 [†]
	80-96	11(64.7%)	2(11.8%)	0	13(25.5%)		
MCHC in T1	<33	6(35.3%)	15(88.2%)	3(17.6%)	24(47.1%)	18.41	0.000 [†]
	33-36	11(64.7%)	2(11.8%)	14(82.4%)	27(52.9%)		
MCHC in T3	<33	8(47.1%)	15(88.2%)	16(94.1%)	39(76.5%)	39.6	0.000 [†]
	33-36	9(52.9%)	2(11.8%)	1(5.9%)	12(23.5%)		

*P value<0.005 –statistically significant, # T1-first trimester, T3-third trimester

Maternal outcome:

Regarding gestational age at termination of pregnancy, in the normal category of 17 women, only one (5.9%) had pre-term delivery (<37 weeks), while 16 (94.1%) women delivered after 37 weeks. In category 2, 7 (41.2%) women delivered before 37 weeks and 10 (58.8%) women after 37 weeks. In category 3, one (5.9%) woman delivered before 37 weeks and 16 (94.1%) women after 37 weeks. Statistically significant difference was noticed in the occurrence of preterm delivery among women with anemia throughout pregnancy (category 2) and the other two groups. Mode of delivery was that more than half of women in the study (58.8%) had normal delivery, 1 (2%) had instrumental delivery and 20 (39.2%) women had LSCS. In the normal category, 9 (52.9%) had normal delivery, while 8 (47.1%) women had Caesarean section. In the second group of anemic women, 9 (52.9%) had normal delivery and 8 (47.1%) women had Caesarean section. In the third category, 12 (70.6%) women had normal delivery, 1 (5.9%) had instrumental delivery and 4 (23.5%) women had LSCS.

Out of 51 women included in the study, 12 women (23.5%) had PPH- 3 (17.6%) of them in the normal group, 4 (23.5%) women belonging to category-2 and 5 (29.4%) women in the third category. However, this difference was not statistically significant ($p=0.72$). Out of 12 women with PPH, 10 had atonic PPH and two had traumatic PPH. Out of cases with atonic PPH, equal numbers of women (8) had anemia either in third trimester or throughout pregnancy while there were only 2 non anemic women. But this was not statistically significant. One non anemic woman and one woman with anemia in T3 had traumatic PPH.

Fetal outcome:

In case of birth weight of babies, in the normal group only one (5.9%) baby had a weight between 2 and 2.49 kgs. 16 (94.1%) babies weighed between 2.5 and 3.5 kgs. In the second category, 11 (64.7%) babies were low birth weight weighing between 2 and 2.49 kgs and 6 (35.3%) babies weighed between 2.5 and 3.5 kgs. In the third category, 4 (23.5%) babies weighed between 2 and 2.49 kgs, while 13 (76.5%) babies weighed between 2.5 and 3.5 kgs. The difference in birth weight among the different category of pregnant women was observed to be statistically significant ($p=0.001$).

In category 1, 9 (52.9%) babies had an APGAR of 7 at 1 minute, while 8 (47.1%) babies had an APGAR of 8 at 1 minute. There was no baby with an APGAR lower than 7 at 1 minute. In category 2, 4 (23.5%) babies had an APGAR of 6 at 1 minute, 12 (70.6%) babies had an APGAR of 7 at 1 minute and 1 (5.9%) baby had an APGAR of 8 at 1 minute. In category 3, 1 (5.9%) baby had an APGAR of 6 at 1 minute, 6 (35.3%) babies had an APGAR of 7 at 1 minute and 10 (58.8%) babies had an APGAR of 8 at 1 minute. Statistically significant difference was observed among different categories of women in APGAR 1 minute score ($p=0.007$).

In category 1, 3 (17.6%) babies had an APGAR of 8 at 5 minutes, while 14 (82.4%) babies had an APGAR of 9 at 5 minutes. In category 2, 10 (58.8%) babies had an APGAR of 8 at 5 minutes and 7 (41.2%) babies had an APGAR of 9 at 5 minutes. In category 3, 5 (29.4%) babies had an APGAR of 8 at 5 minutes and 12 (70.6%) babies had an APGAR of 9 at 5 minutes. This difference also was statistically significant.

Regarding neonatal complications, all the 17 patients in category 1, who were normal, had none. In category 2 out of the 17 babies 3 (17.6%) had neonatal complications, while 14 (82.4%) were normal. In the third category, 2 (11.8%) babies had neonatal complications and 15 (88.2%) babies were normal. Neonatal complications were observed to be higher among women with persistent anemia throughout pregnancy than the other two categories and this difference was statistically significant ($P=0.02$).

IV. Discussion

In our study, the maximum number of patients in the entire study (45%) was in the age group of 26 – 30 years range, while only one patient was aged more than 35 years. There were no patients below 20 years of age due to which the effect of anemia on teenage pregnancy could not be studied. No statistically significant difference was observed in the socio-demographic profile (age, educational status and occupation) of pregnant women included in this study.

The passage of clots which indicates menorrhagia was present in 29.4% of women and 5.9% women in category 2 and 3 respectively, while none of the non anemic women had it. The results from our study have a significant correlation with findings of Bar et al. ie, heavy bleeding with passage of clots during periods is an important contributor to iron deficiency anemia. Oral contraceptives have been suggested by Bar et al as a tactic to reduce anemia, predominantly for teenagers who are at high risk of unwanted pregnancies.¹⁸

In the present study, no significant could be found between anemia and gravidity, parity and spacing between deliveries. In the second category which included women, who were anemic throughout pregnancy, two women were 4thgravidae and one woman was a 5thgravida. Repeated pregnancies may have been the reason for their anemia.

The increase in plasma volume is relatively greater than the increase in red cell mass, which contributes to the drop in packed cell volume (PCV) in the first and second trimester. But in late pregnancy, plasma volume

increases at a slower rate, inducing a slight rise in hematocrit that may account for the slight rise in PCV in the third trimester especially in the 2nd category in this study.¹⁹ Our study showed that in the second category of women, who were anemic throughout pregnancy there was no marked drop in the hemoglobin percentage and PCV. This could be attributed to the regular intake of iron during the pregnancy. But the women who were normal in the beginning but became anemic in the third trimester developed a lower level of hemoglobin and PCV due to the hemodilution of pregnancy as well as irregular iron intake due to irregular antenatal checkups and non-compliance.

The RBC indices of women in the first and third groups during first trimester were normal while in 2nd group it was in anemic range. By the time of third trimester of pregnancy, only slightly more than 60% of persistently anemic women in 2nd group had improved blood indices. This may be due to iron supplementation. The reason for non-improvement in the remaining women may be due to non compliance with treatment. The first group women were still non anemic while in the third group, the blood indices of almost 88% fell to anemic range. This may also be due to non compliance, adverse effects or lack of awareness regarding the importance of iron supplementation especially in the last two trimesters.

All the women in the first category had a normal peripheral smear at the time of delivery. In the second group 94.1% of women had microcytic, hypochromic peripheral smear while in the third category 88.2% had microcytic hypochromic peripheral smear. Though the remaining patients had a normocytic normochromic smear it does not necessarily prove that there is no iron deficiency. Peripheral smear from a patient who has chronic iron deficiency anemia typically shows hypochromic, microcytic erythrocytes.²⁰ In a study reported from Turkey, of anaemic pregnant women, 38.1% had a microcytic-hypochromic anemia and 56.5% were normocytic-normochromic.²¹ Up to 40% of patients with true iron deficiency anemia will have a blood picture showing normocytic erythrocytes.²²

Only 5.9% of normal non anemic women (group 1) and those women who developed anemia later in pregnancy (group 3), had a preterm delivery (before 37 weeks of gestation), while in the 2nd category 41.2% of women had a preterm delivery. Early-pregnancy hematocrit below 37% was associated with preterm delivery.²³ There are also findings reported by Scholl et al. which shows that the odds of low birth weight were tripled and of preterm delivery more than doubled with iron deficiency, but were not increased with anemia from other causes.²⁴ Studies show that severe anemia was associated with increased low birth weight babies, increased rates of induction, higher chance for operative deliveries and prolonged labor.²⁵ But in our study the number of cesarean sections was not different between anemic and non anemic women.

In our study, the difference in birth weight among the different categories of pregnant women was observed to be statistically significant. Studies have shown that anemic women have more chance of delivering low birth weight babies.²⁶ The results have also shown that there was a positive correlation between hemoglobin concentration and weight of the infants at birth. This could also be an indication of poor food security in general.²⁷

Rusia U et al. had shown that the maternal hemoglobin concentration showed a significant correlation with APGAR score and birth asphyxia. Supplementing iron to pregnant woman and improving maternal hemoglobin concentrations were correlated with better APGAR scores and lower risk of birth asphyxia.²⁶ Our study showed that babies of anemic women had a lower 1 minute APGAR score, but the babies improved by 5 minutes with higher APGAR scores.

17.6% babies in category 2 (Respiratory distress syndrome (RDS) and neonatal anemia) and 11.8% babies in category 3 (RDS and neonatal sepsis) had neonatal complications. Normal women had normal neonates. This study revealed the effect of maternal iron deficiency anemia on fetal outcome (birth weight, APGAR scores and birth asphyxia). The maternal hemoglobin showed a significant correlation with birth weight, APGAR score, gestational age and birth asphyxia. Maternal serum ferritin also correlated positively with cord ferritin, placental weight and birth weight. Iron deficiency anemia during pregnancy had significant adverse effect on the fetal outcome.²⁸

V. Conclusion

Our findings reveal that pregnancy related complications like preterm labor, low birth weight babies and low APGAR scores at 1 minute were more in pregnant women who had been anemic from the 1st trimester, when compared to women who developed anemia only during the course of pregnancy and non-anemic pregnant women. This suggests that the outcome of pregnancy for the mother and the baby is influenced by the iron reserves of the woman prior to conception. Hence, anemia control measures should start periconceptionally so that women enter the state of pregnancy with adequate iron reserves. Thus, a comprehensive preventive approach should be adopted for prevention of anemia in order to ensure safe motherhood and healthy babies.

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