"MATERNAL AND FETAL OUTCOMES IN PREGNANT WOMEN WITH ANEMIA: A CROSS-SECTIONAL OBSERVATIONAL STUDY"

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ABBREVIATIONS

ANC	–	Antenatal Care
AGA	–	Appropriate for Gestational Age
AKI	–	Acute Kidney Injury
APH	–	Ante Partum Haemorrhage
BMI	–	Body Mass Index
CI	–	Confidence Interval
CKD	–	Chronic Kidney Disease
EDD	–	Expected date of delivery
EDTA	–	Ethylene Diamine Tetraacetic Acid
EFW	–	Expected Fetal Weight
FD	–	Fetal distress
FSB	–	Fresh Still Birth
Hb	–	Hemoglobin
HIV	–	Human Immunodeficiency Virus
IDA	–	Iron Deficiency Anemia
IFA	–	Iron Folic Acid
IQR	–	Inter-quartile range
IUD	–	Intra Uterine Death
IUGR	–	Intra Uterine Growth Restriction
LBW	–	Low Birth Weight
LMP	–	Last Menstrual Cycle
LSCS	–	Lower segment caesarean section.
MCHC	–	Microcytic Hypochromic
NCNC	–	Normocytic Normochromic

NFHS	–	National Family Health Survey
OR	–	Odds Ratio
PCV	–	Packed Cell Volume
PPH	–	Post Partum Haemorrhage
RBC	–	Red Blood cell Count
RR	–	Relative Risk
SD	–	Standard Deviation.
SGA	–	Small for Gestational Age
SPSS	–	Statistical Package for Social Sciences
TB	–	Tuberculosis
TTP	–	Thrombotic Thrombocytopenic Purpura
WHO	–	World Health Organization

ABSTRACT

Background: Anemia is the most common medical disorder among all age groups in India. Anemia during pregnancy has major impact on public health as it affects both mother and the child. The evidence regarding effects of maternal anemia on perinatal outcomes is not robust. So, we studied the effects of anemia on maternal and fetal outcomes.

Materials and methods: A cross sectional observational study was done among pregnant mothers presenting to labour room in a tertiary care hospital in North Karnataka from January to December 2017. Their anemic status was correlated with various maternal and fetal complications.

Results: Of the 282 women enrolled, 87.2% had moderate and 12.8% had severe anemia. Microcytic hypochromic anemia was the most common 100 (35.4%). Pre-term labour (30.6%) was the most common maternal complication followed by pre-eclampsia (21.3%). 48.2% women required blood transfusion, with higher requirement in severe anemia ($p<0.05$). Among neonatal complications, low birth weight was seen in 56.7%. Median birth was lower in severe anemia group when compared to moderate anemia group {(2.6 (2.2,2.9) Kgs 2.35(2.0,2.7)Kg, $p<0.05$}. Women in severe anemia group had 2.62 times (95% CI: 1.2- 5.4) and 2.98 times (95% CI: 1.46- 6.08) more chance of having a LBW baby and preterm delivery respectively compared to women with moderate anemia.

Conclusion: Iron deficiency is the most common cause of anemia during pregnancy. The risk of pre-term delivery, pre-eclampsia, abruptio placenta, eclampsia, postpartum hemorrhage, HELLP syndrome, CCF and maternal mortality increases with anemia in pregnant women. The risk of prematurity, LBW, less than 5 APGAR score, respiratory distress, IUD and FSB increases with anemia. Early detection and effective treatment of anemia during pregnancy are the keystones in improving neonatal and maternal outcomes.

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INTRODUCTION

Anemia is the most prevalent disorder worldwide across all the age groups. As per global reports nearly 50% of all the pregnant women are anemic. Directly or indirectly, maternal anemia has a huge impact on the outcomes of both mother and the fetus. According to 2011 World Health Organization (WHO) estimate, prevalence of anemia in pregnant women is 47.8%[1].South East Asia and African regions top the list with respect to anemia during pregnancy. India, being a developing nation and owing to its high population have the highest burden of maternal anemia. According to the recent National Family Health Survey-4 (NFHS-4) survey, prevalence of anemia in pregnant women was 50.3% (45.7% in urban and 52.1% in rural areas)[2].

Anemia during pregnancy can be because of many reasons; Physiological Anemia occurring due to inappropriate hemodilution is the most common. Next to physiological anemia, which is more of a benign entity, deficiency of Iron is the most common cause of maternal anemia worldwide. A study done by Shoberi et al has shown that suboptimal daily intake of Iron is the main reason[3]. It has been found that only 45% of women have completed the recommended 100-day course of Iron Folic acid tablets[3]. Iron deficiency does not only limit to low income groups; Kalaivani et al found that 50% of children, adolescent and pregnant women were anemic even in high income groups[4]. Apart from Iron deficiency, Folic acid and vitamin B12 deficiency are the important nutritional causes of maternal anemia. Other causes of anemia in pregnancy include acute or chronic loss of blood; infections like malaria, Tb; haemolytic disorders and bone marrow suppression.

Multiple studies have shown that anemia has significant impact on both maternal and fetal outcomes, but the results are highly conflicting and inconclusive. Many studies have found that anemia during pregnancy influences maternal outcomes and also attributed anemia to be one of the most important cause for maternal mortality and other obstetric

complications. Various studies and even multi level analysis showed that anemia increased the odds of maternal mortality by 2.36 times[5]. Ample number of observational studies and their meta-analyses are published in literature stating the significance of maternal anemia on fetal outcomes like LBW, IUGR, Pre-term birth and birth asphyxia[6-8]. Contrary to these there are reports stating that high haemoglobin concentration also increases the risk of LBW[9,10]. Some studies found no relation between maternal anemia and fetal birth weight[11].

Despite these controversies one can easily appreciate the fact that treating anemia could change the outcomes of both mother and the baby. As the prevalence of anemia is so high among females of all age groups, treating anemia forms one of the important strategies for the holistic maternal and childcare.

AIMS AND OBJECTIVES

Primary:

1. To study the effect of maternal anemia on various obstetrical outcomes such as pre-term, pre-eclampsia, abruption, eclampsia, PPH, HELLP, CCF, AKI, maternal mortality and puerperal sepsis etc.

Secondary:

1. To study the effect of maternal anemia on fetal outcomes such as birth weight, APGAR score, distress, FSB, IUD, birth asphyxia, etc

REVIEW OF LITERATURE

The topic shall be discussed under the following headings

I. Definition and classification of Anemia in pregnancy
II. Anemia in pregnancy- Prevalence and its importance
III. Causes
IV. Maternal and fetal outcomes
V. Purpose of the study

I. DEFINITION AND CLASSIFICATION OF ANEMIA IN PREGNANCY

Anemia is defined as hemoglobin value that is lower than the threshold of 2 SD below the mean value for a healthy matched population. WHO cut off for defining anemia in pregnancy is hemoglobin value less than 11gm/dl. WHO further classifies anemia into 3 subgroups based on Hb level; Hb value between 9 and 11gm/dl is Mild anemia, between 7 and 9gm/dl is moderate anemia and Hb value less than 7gm/dl is severe anemia.[1]

II. ANEMIA IN PREGNANCY- PREVALENCE AND ITS IMPORTANCE

Globally 38.9% to 48.7% of pregnant women were anemic as per the WHO 2011 estimate, indicating that nearly half of all the pregnancies worldwide are at risk of developing either one of the maternal or fetal complication. On subgroup analysis based on WHO regions, highest prevalence was seen in South East Asian region (48.7%), followed closely by African region (46.3%).[1]Also the prevalence is higher in developing countries compared to developed nations. In a recent meta-analysis by Rahmati et al, prevalence of anemia in pregnancy in developing nations was 52%, whereas the same in developed nations is 22.5%.[6]

Among the South East Asian countries, India bears the brunt of this rampant disease. Indian figures are also similar to global numbers as was found in the recently published NFHS-4 survey. According to this, which is basically the data compiled over 2015 and 2016; overall prevalence of anemia in pregnant women was 50.3% (45.7% in urban and 52.1% in

rural areas).[3]The prevalence in India was highly variable across different regions and among various studies. In the longitudinal prospective study done in rural India by Mangla et al,98% of pregnant women were anemic.[12] In Karnataka, prevalence of anemia in pregnant women was 45.4% (39.6% in urban and 48.7% in rural areas) as per NFHS-4 data.[3]

With the prevalence being so high, the importance of treating and preventing anemia need no emphasis owing to its impact on social and economic development of the nation. Not only in pregnant women but also prevalence of anemia in non-pregnant women in South East Asia region is high (41.5%).[1] Hence it is not an exaggeration to say that treatment of anemia forms a solid component in achieving the fourth and fifth Millennium Development Goals targeting Infant and Maternal mortality.

III. CAUSES OF ANEMIA IN PREGNANCY

There are a multiple of causes for anemia in a normal pregnancy, ranging from a benign physiological hemodilution to complex hemolytic disorders complicating pregnancy. Broadly causes of anemia in pregnancy can be grouped into Physiological and Pathological as shown below.

1. Physiological
2. Pathological-
    a) Nutritional deficiencies-
        i. Iron deficiency
        ii. Folic acid deficiency
        iii. Vitamin B12 deficiency
    b) Hemorrhage-
        i. Acute- First trimester bleeding/ APH
        ii. Chronic- Hook worm infestation, GI bleeding

c) Hemolytic anemia-

   i. Hereditary-

   - Hemoglobinopathies - Thalassemias / Sickle cell anemia
   - RBC membrane defects

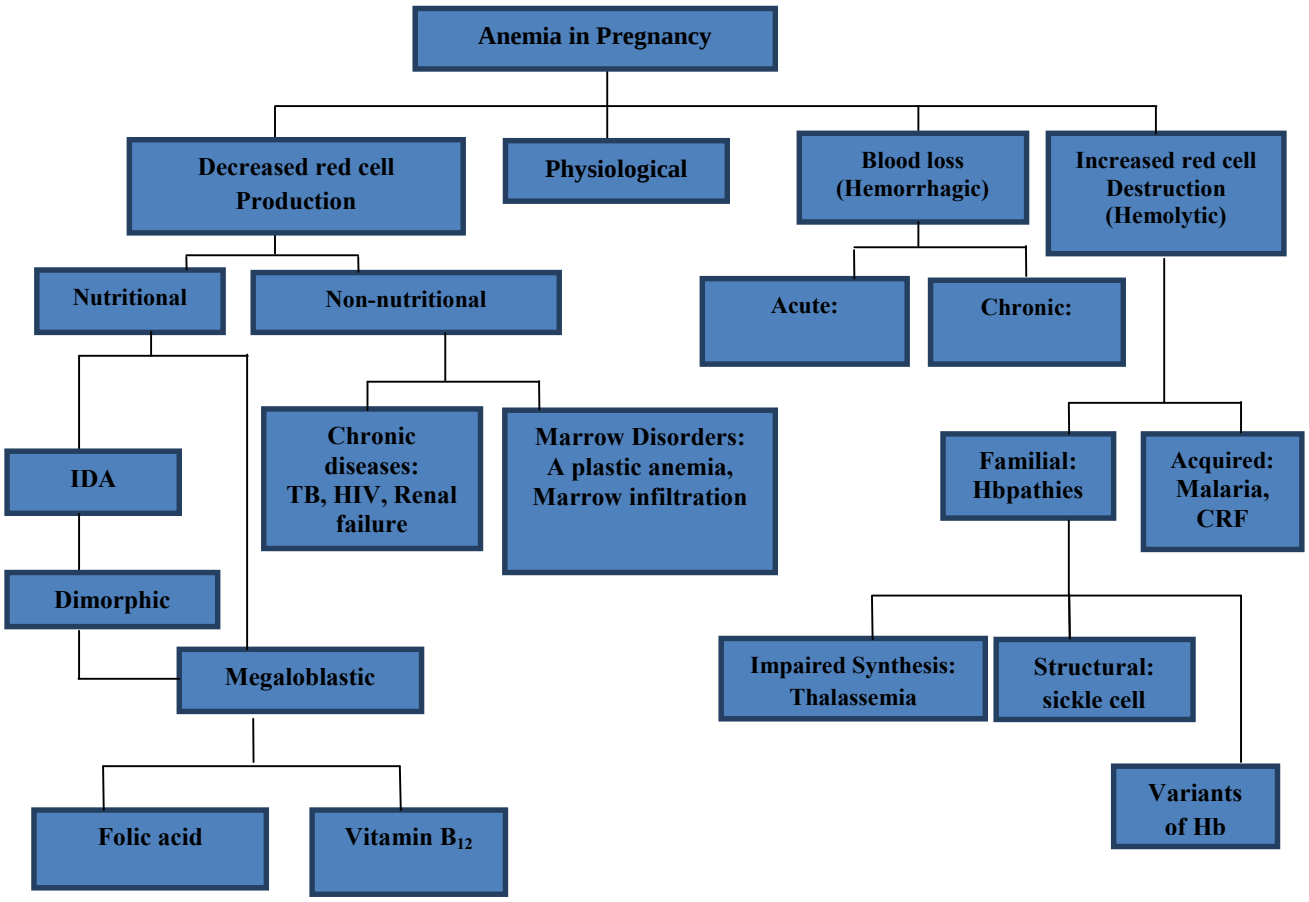
   ii. Acquired- TTP, Autoimmune

d) Infections- Malaria/ TB

e) Chronic disorders- CKD/ Aplastic anemia

Another way of classifying anemia in pregnancy is shown in Figure

Figure 1 Classification of Anemia



1. Physiological anemia of Pregnancy

During the process of normal pregnancy, the body undergoes physiological changes to facilitate the growing fetoplacental unit. Changes occurring in hematological system form an important platform for the growing fetus. Plasma volume increases to 10-15% by 6-12 weeks of gestation, rapidly increases till 30-34weeks, following which it reaches a plateau and then slightly decreases at term. On the other hand, RBC mass starts increasing by 8-10 weeks, following which it increases steadily till the term. Overall, plasma volume increases by ~30-50%, whereas RBC mass increases only by 20-30%, resulting in a state of relative hemodilution which results in what is called the Physiological anemia of Pregnancy. Final outcome of all these changes is an Hb value ~10gm/dl falling in the category of mild anemia.

Criteria for defining Physiological Anemia are:

1. Hb - 10gm/dl or less
2. RBC count- 3.5million/mm^3
3. PCV- 30%
4. Smear- Normal morphology with central pallor

In areas where non-pregnant women have normal haemoglobin and adequate Iron stores, anemia during pregnancy is predominantly because of plasma expansion and has relatively less effect on perinatal outcomes[13].

2. Pathological

a) Nutritional

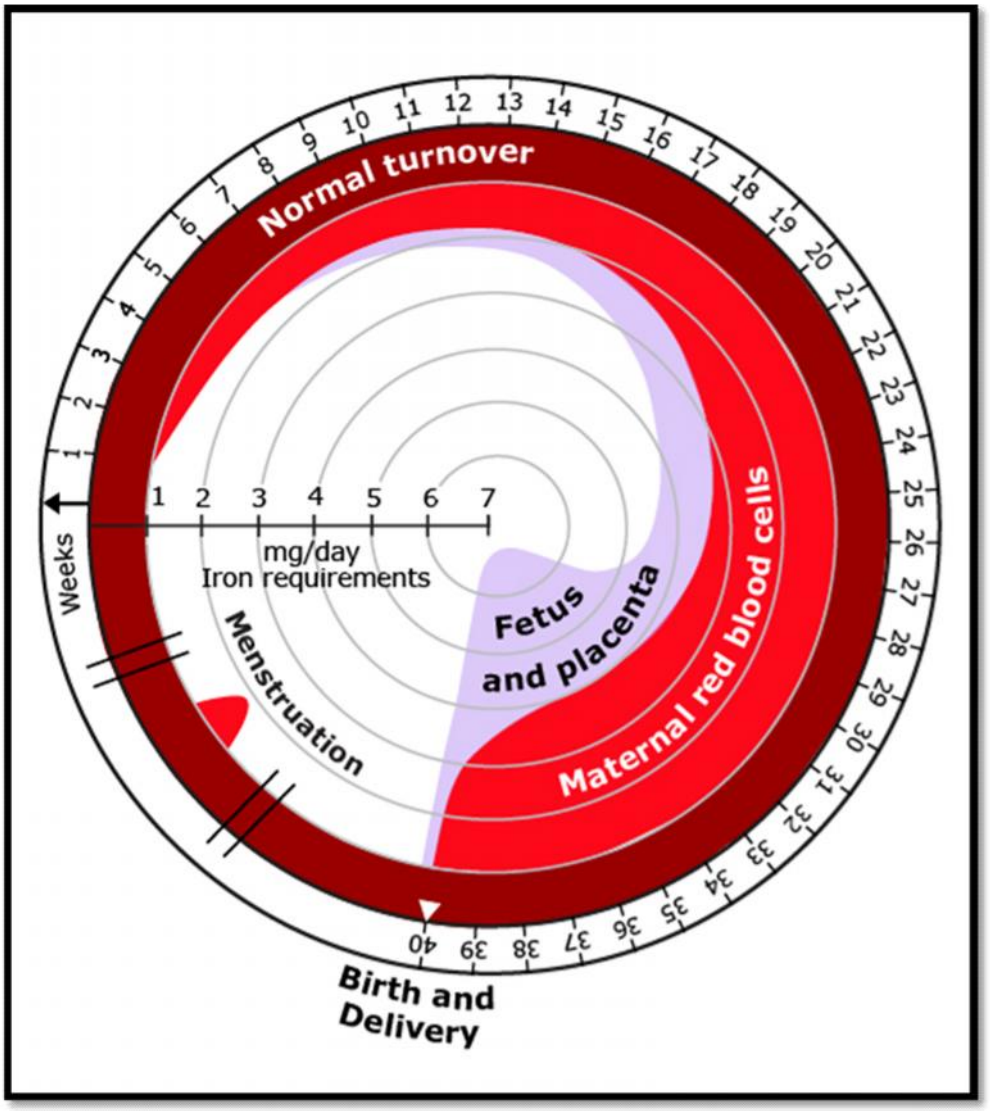
Nutritional deficiencies are the most important reason for anemia in developing nations. Various macro and micronutrient deficiencies play a role in development of anemia both in non-pregnant and pregnant women. Most common micronutrient deficiency leading to anemia worldwide is Iron deficiency.

Iron deficiency:

As per WHO estimates, Iron deficiency is by far the most significant nutrient deficiency resulting in anemia. Not only during pregnancy but Iron deficiency is prevalent extensively across all age groups. Reasons for this extensive prevalence of Iron deficiency are lesser pre-pregnant stores, which is predominantly due to inadequate dietary intake. A Prospective study done in Mysore by Shoberi et al showed that mean iron intake among women from middle and high income groups was 21.9±1.8 to 23.5±2.2 and 22.8±3.7 to 24.8±4.3mg/day respectively. This intake was far below the recommended daily intake for pregnant women[6]. As per NFHS-4 data, percentage of Women who consumed Iron folic acid tablets for complete 100days was only 30.3% (Urban- 40.8%; Rural- 25.9%). In Karnataka, though 84% of pregnant women have received Iron folic acid tablets at least once, only 45% of them have completed the total recommended course of 100days[3].

Adequate intake of Iron is required during antenatal period to meet the increasing requirements of both mother and the fetus. Iron is essential for the expansion of maternal RBC mass, fetal erythropoiesis, fetoplacental growth and to compensate the delivery losses. Totally ~500mg of Iron is required for maternal RBC expansion, 300-350mg is required for fetal erythropoiesis and 250mg is required for compensation of delivery losses. ~150mg of Iron is saved due to absence of menstrual losses. This takes us to the figure of 1000mg of Iron that is recommended during pregnancy. And moreover Iron requirements during various trimesters of pregnancy are not the same. In first trimester, ~1-2mg/day of Iron is enough to compensate the routine GI losses and early pregnancy related increase in RBC mass. During second trimester, 4-5mg/day of Iron is required for increase in maternal RBC production as well as fetal erythropoiesis and placental growth. It further increases to >6mg/day during the third trimester[14]. These daily requirements of Iron according to gestation and its purpose have been elaborated in Figure 2.

Figure 2: Iron requirement during various phases of pregnancy



Many studies have shown that iron deficiency anemia is associated with adverse maternal and fetal outcomes[15-16]. In India, iron deficiency is a widespread phenomenon and is very common in reproductive age women. Preexisting low Iron stores superimposed by inadequate dietary intake is the main reason for such high prevalence of Iron deficiency anemia during pregnancy.

Folic acid deficiency:

After Iron, folic acid deficiency is the most common nutritional cause of anemia. More than anemia Folic acid is known for its causal association with neural tube defects. Generally folic acid deficiency causing anemia is rare as routine diet has plenty of folic acid.

WHO recommends 800µg of folic acid intake during the antenatal period. But studies have shown that 500µg of folate that is contained in many iron preparations is also enough. In an established case of folic acid deficiency, 5mg OD folic acid is given for treatment. There are conflicting reports regarding the effect of folic acid deficiency on maternal and fetal outcomes. Nelen et al who studied relationship between serum levels of folate, homocysteine and risk of early pregnancy loss found that women with recurrent early pregnancy losses had significantly lower serum folate levels. Odds of having early pregnancy loss with folic acid deficiency were 2-3 times more when compared to controls[17]. Another study done by Nilsen et al evaluating the benefit of folic acid and multivitamin supplementation in preventing abruption showed that there was 26% of risk reduction with either folic acid or multivitamin intake[18]. But in contrary, study done by Hadavand et al showed that there was no significant correlation between Folic acid intake and pregnancy outcomes[19].

Vitamin B12 deficiency

Apart from folic acid deficiency, Vitamin B12 deficiency is also known to cause the macrocytic anemia. But vitamin B12 deficiency alone causing anemia in pregnancy is rare as daily requirement of vitamin B12 recommended during pregnancy is only 3µg, which can be easily met with a normal diet. But it poses problem particularly in pregnant women who are strict vegetarians. Along with folic acid, studies have also shown beneficial effect of Vitmain B12 in preventing neural tube defects[20].

Increasing RBC mass requires extra supplementation of Iron, folic acid, vitamin B12, but in women with already low stores, superadded decreased intake during pregnancy keeps them at a very high risk of developing anemia and its complications.

b) Hemorrhage

Apart from nutritional deficiencies, blood loss occurring during pregnancy- both acute and chronic, forms an important cause of anemia in pregnancy. Anemia could be because of acute blood loss occurring in cases of Antepartum hemorrhage or chronic losses occurring due to worm infestation. Among this acute blood loss has deleterious effects on

both maternal and fetal outcomes ranging from preterm labor to even maternal death. Study done by Lankoande et al found that 80.3% of cases with APH had complications.

c) Hemolytic anemia

Hemolytic anemia occurring during pregnancy can be because of disease process related or unrelated to pregnancy that exist since child hood and can be divided into hereditary and acquired as shown below

1. Hereditary:

a) Membrane defects- Sickle cell anemia

b) Hemoglobinopathies - Thalassemia

2. Acquired: TTP, Auto immune hemolytic anemia

In a known case of Thalassemia, pre-existing anemia could worsen due to the increasing demand of erythropoiesis. Sickle cell anemia can have other complications due to its vaso -occlusive effects on various organ systems apart form anemia related complications. It was shown that 14.2% of pregnancies in sickle cell patients end up in stillbirth. Similarly in acquired causes, thrombosis occurring in cases of TTP forms an independent risk factor for maternal and fetal morbidity and mortality[18].

d) Infections

Infections are also an important cause of anemia, especially in tropical areas. Malaria is one of the major infection that causes anemia during pregnancy and also has serious implications on both mother and fetus[21]. Other chronic smoldering infections like TB can also cause anemia in pregnancy.

e) Chronic diseases

Chronic diseases like chronic kidney disease, aplastic anemia also can cause anemia during pregnancy. These patients can go into failure and crisis situations during pregnancy because they cannot cope up with the increasing metabolic demands.

IV. MATERNAL AND FETAL OUTCOME

On reviewing the literature, over past decades many authors studied the effect of anemia on maternal and fetal outcomes, but results of all these studies are not totally in concurrence. According to WHO 2011 estimate, maternal anemia is associated with LBW, increased risk of maternal and perinatal mortality[13].

Multiple observational studies have shown that anemia has its maximum effect on maternal and fetal outcomes if it is present in first trimester rather than in second and third trimesters[3,16,22,23]. Recently a meta-analysis was done by Rahmati et al in 2016 and included 30 studies spanning over nearly two decades (1990 to 2016) with an overall sample size of 11,94,746 pregnant women. She showed that maternal anemia in first trimester had a significant relationship with low birth weight (RR: 1.28, 95% CI, 1.10-1.50; $p<0.01$), pre-term birth (RR: 1.26, 95% CI, 1.11-1.44; $p<0.01$) and small for gestational age (RR: 1.12, 95% CI, 1.05-1.19; $p<0.01$), indicating that maternal anemia in first trimester increases the risk of these outcomes. Anemia in second and third trimesters had no significant relationship with LBW, pre-term birth ($p>0.05$)[6]. The meta-analysis by Xiong et al in 2000 also showed similar findings[24].

Contrary to these results, some cross-sectional studies that estimated the effects of anemia during late pregnancy or in labour showed significant relationship between anemia and LBW, preterm birth, APGAR score.[10,13,15,25,26].In 2010, Elhasan et al, in a study to find out risk factors for LBW, showed that lack of antenatal care (OR-5.9, 95% CI-1.4-24.4; $p<0.01$) and maternal anemia (OR-9.0, 95% CI-3.4-23.8; $p<0.001$) were the main risk factors for LBW[25].

In a recent meta-analysis published in 2018 by Figueiredo et al analyzing data of 9,16,990 pregnant women showed that maternal anemia is associated with LBW (OR: 1.23; 95%CI: 1.06-1.43)[24].

In another meta-analysis done by Rahman et al in 2016, analyzing 26 studies done exclusively in middle and low income countries found that maternal anemia was associated with increased risk of LBW, pre-term birth, perinatal mortality and neonatal mortality. Prevalence of anemia was 42.7% (95% CI: 37%- 48.4%), pooled relative risk for LBW was 1.31 (95%CI: 1.13-1.51), for pre-term birth was 1.63 (95% CI: 1.33-2.01), for perinatal mortality was 1.51 (95% CI: 1.30-1.76) and for neonatal mortality was 2.72 (95% CI: 1.19-6.25). They also found that 12% of LBW, 19%of pre-term birth and 18% of perinatal mortality was attributable to maternal anemia[25].

Some studies also have shown that, mild anemia could be beneficial in late pregnancy[15]. Various studies also showed that there is a U-shaped relationship between maternal anemia and incidence of preterm birth, LBW status[10,16,27-29].The postulated pathophysiology behind this is the increasing viscosity occurring with increasing Hb hindering the placental circulation[16].

Not only the fetal outcomes but also anemia has a significant effect on maternal outcomes. In a secondary analysis of the WHO Multi-country Survey on Maternal and Newborn Health done by Lumbiganon et al, it was found that Anemia was the most common indirect cause for higher obstetric complications[30]. Recently a multilevel analysis was done by Daru et al in 2018 and estimated the risk of maternal mortality in women with severe anemia during pregnancy. They found that the adjusted odds ratio for maternal death in women with severe anemia was 2.36 (95% CI 1.6-3.48) compared with those without severe anemia.[5] In the propensity score analysis, they also found that severe anemia was also associated with maternal death {adjusted odds ratio 1.8(95% CI 1.39-2.49)}[29]. Similarly many of the other studies have shown increased risk of maternal mortality, preterm birth and increased risk of sepsis[4,31].

Out of all these studies, there are few studies that found no relationship with maternal anemia and perinatal outcomes. In a recent study published by de Sá et al, it was found that Anemia was positively correlated to umbilical cord ferritin (r= 0.3889, p-0.01) but had no significant relation with birth weight and head circumference (Birth weight- 3.37±.51 Kg vs 3.3±0.45 Kg; p>0.05)[31].

Salient features of various recent studies on maternal anemia and pregnancy outcomes are tabulated in Table 1

Table 1: Overview of studies on Anemia during pregnancy, its maternal and fetal outcomes

Sl.no	Author	Year	Type of study	Sample size (n)	Results
1	Daru et al[29]	2018	Secondary analysis of cross sectional study	12,470	• Odds ratio for maternal death in women with severe anemia- 2.36 (95% CI 1.60-3.48) • Odds ratio for association of severe anemia with death- 1.86 (95% CI 1.39-2.49)
2	Figueiredo et al [24]	2018	Meta analysis	9,16,990	• Maternal anemia was associated with LBW; OR: 1.23
3	Suryanaryana et al[32]	2017	Prospective observational study	446	• Prevalence of anemia- 62.3% • Anemia increases the maternal and fetal risks
4	Rahman et al [25]	2016	Meta analysis	7,20,000	• Prevalence of anemia- 42.7% • Maternal anemia was associated with increased risk of LBW (RR- 1.31), pre-term birth (RR-1.63), perinatal mortality (RR-1.51) and neonatal mortality (RR-2.72) • 12% of LBW, 19%of pre-term birth and 18% of perinatal mortality were attributable to maternal anemia
5	Rahmati et al[6]	2016	Meta- analysis	11,94,746	• Maternal anemia in first trimester increases the risk of LBW (RR- 1.28), Preterm birth (RR-1.26), SGA (RR- 1.12); $p<0.05$ • Second and third trimester anemia had no correlation to LBW or Preterm birth or SGA

6	Mangla and singla et al[12]	2016	Prospective observational study		• Prevalence of anemia- 98% Mild- 41.7%; Moderate- 37.05%; severe- 3.2% • Number of ANC visits and duration of IFA tablet intake determine severity of anemia
7	de Sá et al[31]	2015	Cross-sectional observational study	54	• Frequency of maternal anemia- 53.7% • Maternal iron and umbilical cord ferritin were positively correlated (r = 0.3889; p- 0.01) • No correlation between birth weight, OFC and maternal anemia
8	Hadavand et al[19]	2013	Cohort study	191	• No correlation between folic acid intake and pregnancy outcomes
9	Akhter et al [15]	2010	Cross-sectional study	50	• Prevalence of anemia- 36% • Iron deficiency anemia was the most common reason • Maternal anemia has significant correlation with placental weight (r=0.4), birth weight (r=0.35), APGAR score (r=0.52), gestational age (r=0.61) and birth asphyxia. • Maternal ferritin also has correlation with cord ferritin, placental weight and birth weight, indicating that IDA has significant adverse effect on fetal outcome.
10	Elhassan et al [25]	2010	Case control study	1224	• Maternal anemia (OR- 9.0) and lack of antenatal care (OR-5.9) were the main risk factors for LBW.

11	Kalaivani et al [4]	2009	Review article	-	• Directly or indirectly 40% of maternal deaths are due to anemia. • Hb <5 gm/dl is associated with 8-10 fold increase in maternal mortality rate. • Hb <8 gm/dl is associated with 2 times more risk of LBW and 2-3 times increase in perinatal mortality.
12	Nilsen et al [18]	2008	Retrospective study	2,80,127	• Folic acid and multivitamin supplementation is associated with reduced incidence of placental abruption. (OR- 0.68)
13	Shoberi et al [6]	2006	Cohort study	500	• Prevalence of anemia was 45-49%in first and second trimesters and 16% in third trimester. • Mothers having normal Hb value were associated with decreased risk of LBW. • Mean daily iron intake in both middle and high income groups were far below the recommended range.

PURPOSE OF THE STUDY

Anemia is one of the most prevalent medical disorders seen in pregnancy. It seems to be associated with adverse perinatal outcomes. However, the literature regarding the association of maternal anemia and perinatal outcomes is conflicting and there is no single stand on the effects of anemia during pregnancy. Some of the studies show that only early trimester anemia has deleterious effects on fetus[3,6,16,24]and some reported that anemia detected at delivery also has adverse outcomes[13,15,26], where as some studies completely negate the effects of maternal anemia on fetal outcomes[31]. Because anemia is so prevalent in pregnant women, any adverse effect it bears on perinatal outcomes will have a significant impact on overall maternal and neonatal health. In light of these facts; this observational study was conceptualized to better understand the effect of anemia on maternal and fetal outcomes.

MATERIALS AND METHODS

Study design:

Cross sectional, observational study

Study setting:

KLE Dr Prabhakar Kore Charitable Hospital and Medical Research Centre, Belagavi

Study period:

January 2017 to December 2017

Selection criteria

Inclusion criteria:

1. Antenatal women with Hb less than 9 gm/dl

Exclusion criteria

1. Multiple pregnancies
2. Known cases of Hemoglobinopathies, Hemorrhagic disorders
3. Known cases of Bone marrow disorders

Sample size:

All the antenatal pregnant women getting admitted in labour room with Hb less than 9 gm/dl during the study period.

Methodology:

- All the antenatal pregnant women presenting to labour room were screened for inclusion in the study.
- Waver of consent was taken from the institutional ethics committee.

- Detailed information of each patient including symptomatology, examination findings and laboratory reports were recorded in a predesigned proforma **(Annexure 1)**.
- Demographic details like age, residence etc., were recorded. Along with these, details of educational status, occupation and monthly income were also noted and patients were classified into various socioeconomic classes based on Modified Kuppuswamy scale 2016[33].
- Detailed obstetric history, presenting complaints, past history of various medical disorders along with examination findings like pallor, edema, any signs of nutrient deficiencies were recorded.
- Systemic examination was also done and any abnormalities in cardiovascular and respiratory system examination were also noted.
- Peripartum details including type of delivery, need for blood transfusion, parenteral iron, any peri -partum complications like pre-eclampsia, eclampsia, PPH, death etc., were noted.
- Venepuncture was done under strict aseptic precautions and 2ml of EDTA blood was taken for the assessment of Hb and smear. Sampling was done along with routine sampling done as a part of investigative workup.
- Hemoglobin was assessed using Sodium Lauryl Sulphate method in automated cell analyzer –SysmexXN350 and they were divided into two sub groups based on their hemoglobin level.
- Patients were classified into two groups based on the Hb level according to WHO classification. Patients with Hb level between 7.1-9 gm/dl were

classified into moderate anemia and patients with Hb level ≤ 7gm/dl were classified as severe anemia.

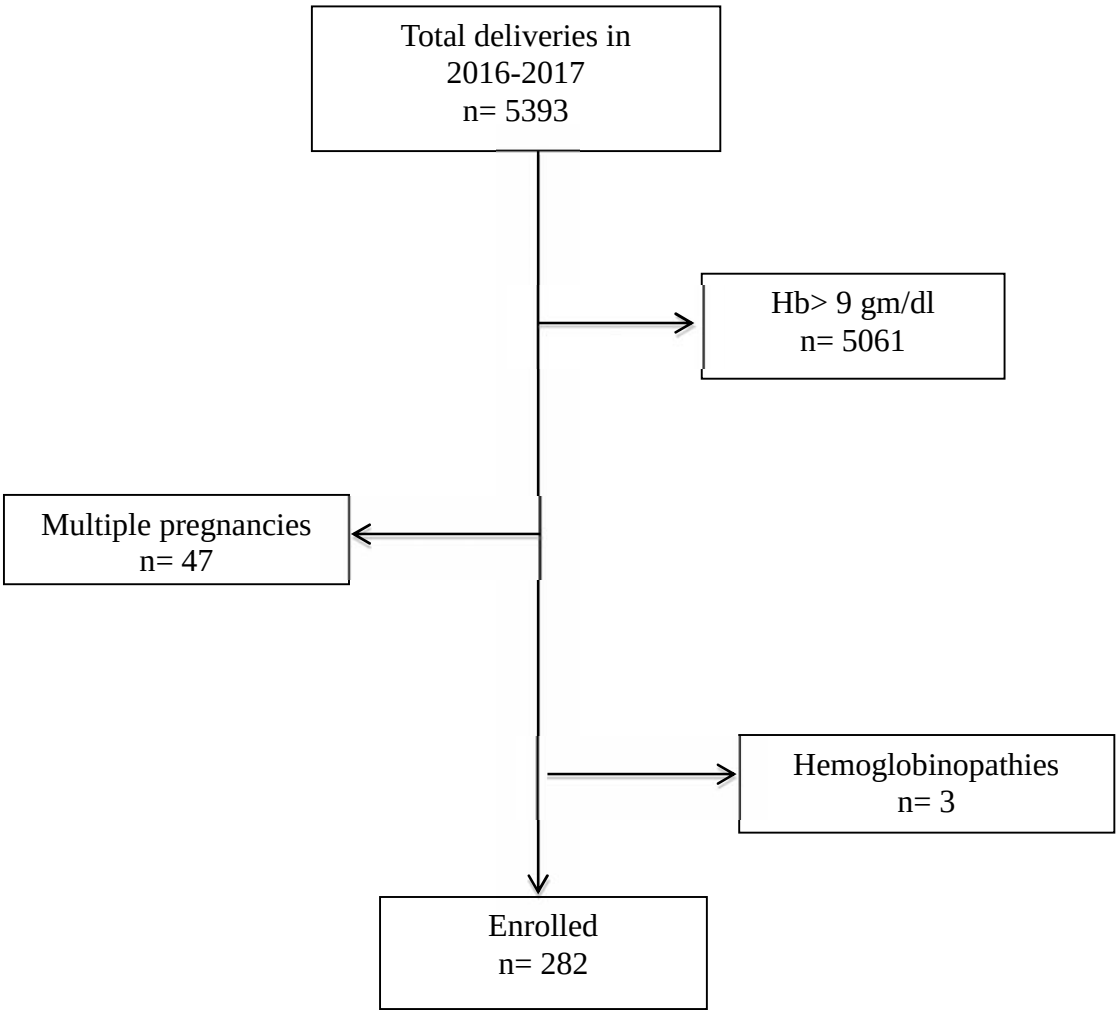
- Fetal outcome was assessed using parameters like birth weight, APGAR score at 0, 5 and 10 minutes, appropriateness for gestation, IUD etc.,
- All the data was recorded in the proforma was entered in Microsoft excel and was analyzed using SPSS (Statistical Package for Social Sciences) software version 21.0 (SPSS Inc, Chicago).

STATISTICAL ANALYSIS

- Statistical analysis was done using SPSS (Statistical Package for Social Sciences) software version 21.0 (SPSS Inc, Chicago). Normality of the data was tested using one-sample Kolmogorov -Smirnov test. Categorical variables were denoted in proportions and continuous variables were denoted as Mean ± SD (for normal distribution), Median, IQR (for skewed distribution). Quantitative values of Birth weight, Gestational age were compared between moderate and severe anemia groups by Mann-Whitney U test. Categorical variables like number of pregnant women having low preterm labour etc., were compared using Chi-square test. All tests were two-tailed and level of significance was taken as less than 5% i.e., p-value<0.05.

RESULTS

This prospective observational study was conducted in the Department of Obstetrics and Gynaecology, KLE Dr.Prabhakar Kore Charitable Hospital and Medical Research Centre, from January 2017 to December 2017, to study the maternal and fetal outcomes in pregnant women with anemia. Total of 5393 pregnant mothers presenting to labour room were screened to meet the inclusion criteria. Out of which, 5061 had Hb >9, 47 were multiple pregnancies and 3 women had some form of hemoglobinopathy. Finally 282 mothers satisfying the inclusion criteria were enrolled in the study.



a) Socio-demographic characteristics:

Median age of the study population was 24 (22.26%) yrs. 164(58.2%) of pregnant women were in the age group of 21-25yrs and 5 women (1.8%) were more than 35yrs of age. Distribution of patients according to age groups is as tabulated in Table 2.

Table 2: Distribution of patients according to age

AGE GROUPS (years)	n (%)
<20 yrs	33 (11.7%)
21-25 yrs	164 (58.2%)
26-30 yrs	69 (24.5%)
31-35 yrs	11 (3.9%)
>35 yrs	5 (1.8%)

Figure 3: Distribution of patients according to age

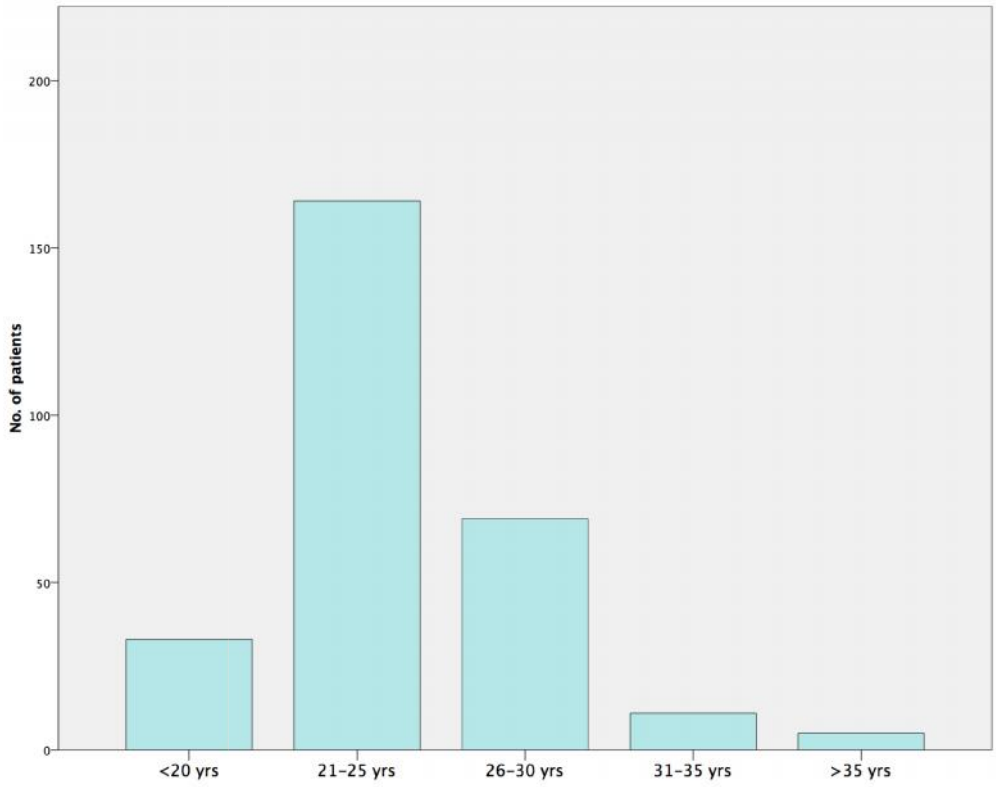


Table 3: Distribution of patients according to socioeconomic status

Socioeconomic status	n (%)
Upper	0 (0%)
Upper middle	8 (2.85%)
Lower middle	23 (8.2%)
Upper lower	239 (84.8%)
Lower	12 (4.3%)

239(84.8 %) women belonged to upper lower socioeconomic class according to modified Kuppuswamy scale 2016. Distribution of patients according to socioeconomic status has been depicted in Table 3.

Table 4: Distribution of patients according to status of registration

Sl no.	Status of Registration	n (%)
1	Registered in KLE	173 (61.3%)
2	Registered at outside hospital	82 (29.1%)
3	Unregistered	26 (9.2%)

Among the study population 256 (90.8%) cases were antenatally registered at some or the other hospital, whereas 26 (9.2%) cases were unregistered. Of the 256 registered cases 173 (61.3%) were registered in KLE and the other 83 (29.5%) were primarily registered in other hospitals as shown in Table 4.

96(34%) women were primi-gravida and the rest 186(64%) were multigravida.

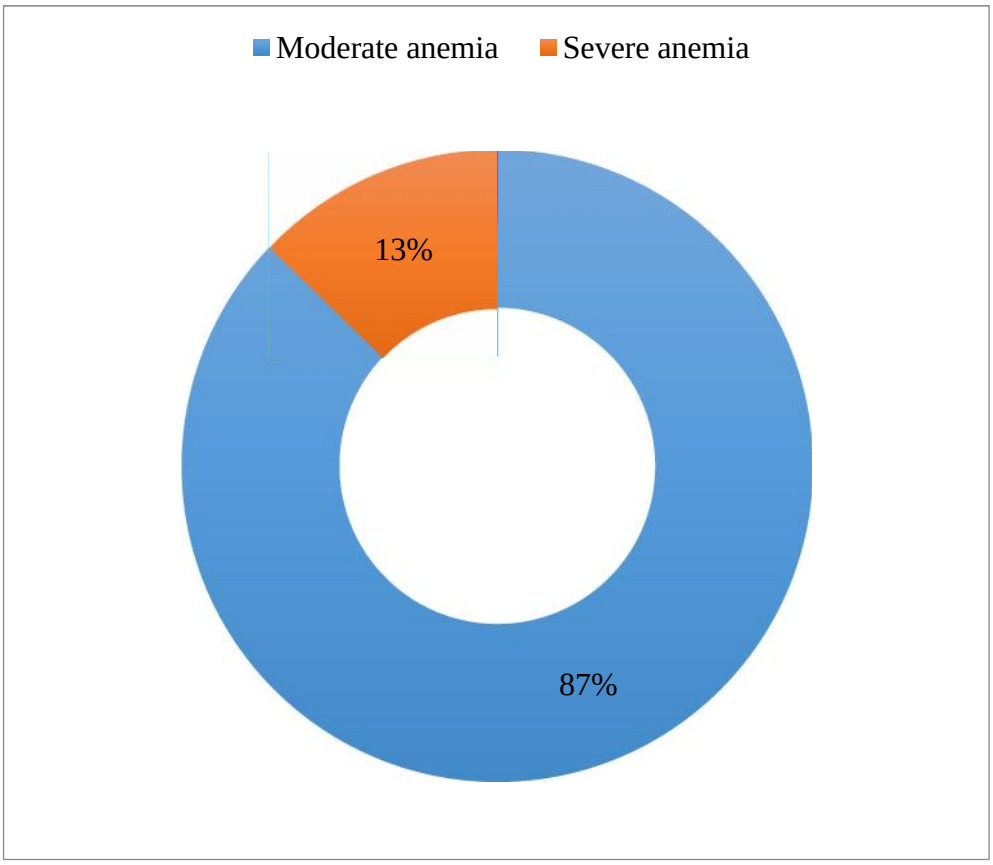
b) Severity of anemia

282 pregnant women enrolled were further divided into two sub groups, moderate (Hb: 7.1-9gm/dl) and severe (Hb≤7) anemia based on the WHO criteria as shown in Table 5. Prevalence of Moderate anemia in our study population was 246 out of 5393 i.e., 4.56%, whereas prevalence of severe anemia was 36 out of 5393 i.e., 0.66%. Out of 282 women enrolled, 246 (87.2%) classified for moderate anemia where as 36 (12.8%) classified for severe anemia as depicted in Table 5.

Table 5: Distribution of patients based on severity of anemia

Sl no.	Severity of anemia	n (%)
1	Moderate anemia	246 (87.2%)
2	Severe anemia	36 (12.8%)

Figure 4: Distribution of patients based on severity of anemia

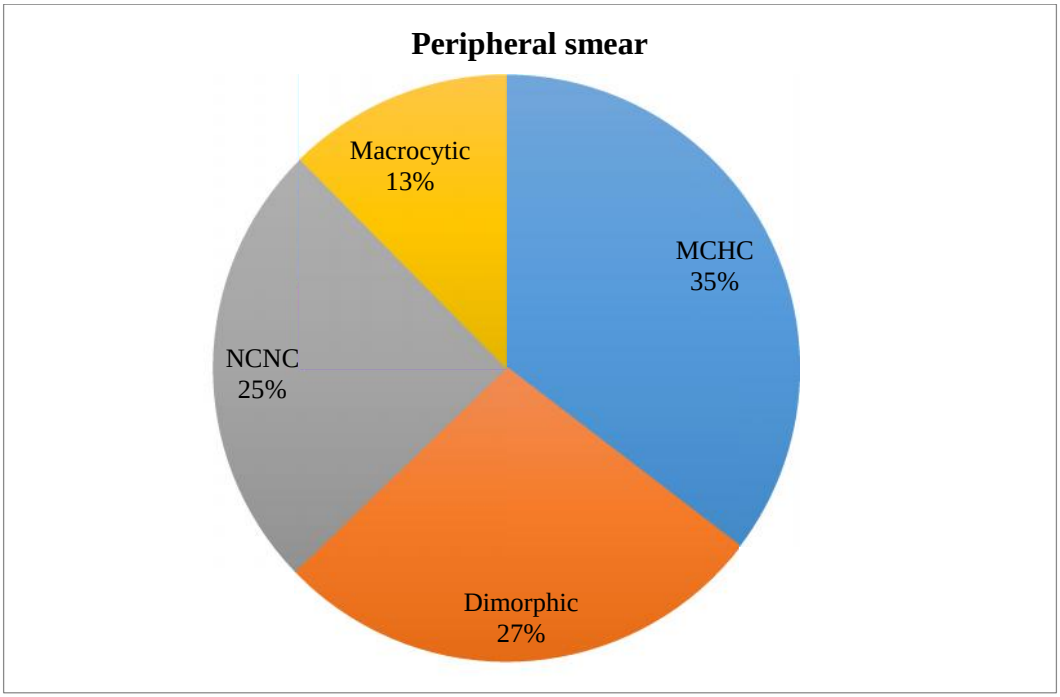


Peripheral smear of patients was also examined to give an idea about the cause of the anemia. Most common smear finding was microcytic hypochromic anemia, which was found in 100 (35.4%) patients. Next to microcytic hypochromic anemia was Dimorphic anemia in 77 women (27.4%) followed by normochromic normocytic in 70(25%) and macrocytic anemia in 35(12.4%) as tabulated in Table 6.

Table 6: Distribution of patients based on morphological subtype of anemia

Morphological subtype of anemia	n (%)
Microcytic hypochromic anemia	100 (35.4%)
Dimorphic anemia	77 (27.4%)
Normocytic normochromic anemia	70 (24.8%)
Macrocytic anemia	35 (12.4%)

Figure 5: Distribution of patients according to peripheral smear



c) Clinical symptoms

Most common symptoms that the pregnant women complained of were Fatigue in 111(39.4%), followed by Giddiness in 51(18.1%), Headache in 24(8.5%), Palpitations in 22(7.8%), Breathlessness in 5(1.8%) and burning micturition in 3(1.1%) in decreasing order of frequency as shown in Table 7.

Table 7: Distribution of patients based on Symptoms

Sl no.	Symptoms	n (%)
1	Fatigue	111 (39.4%)
2	Giddiness	51 (18.1%)
3	Headache	24 (8.5%)
4	Palpitations	22 (7.8%)
5	Breathlessness	5 (1.8%)
6	Burning micturition	3 (1.1%)

On examination pallor was detected in 260 (92.2%) and 18 (6.3%) had ejection systolic murmur. Features of micronutrient deficiencies like glossitis, angular stomatitis was found in 4 (1.4%) and 2 (0.7%) women respectively.

Table 8: Frequency of clinical signs

Sl no.	Clinical signs	n (%)
1	Pallor	260 (92.2%)
2	Edema	35 (12.4%)
3	Glossitis	4 (1.4%)
4	Angular stomatitis	2 (0.7%)
5	Ejection systolic murmur	18 (6.3%)

Comparison of clinical features between Moderate and severe anemia groups

When we compared various clinical features between moderate and severe anemia groups, we found out that all clinical features were more frequently seen in case of severe anemia group, which was statistically significant ($p<0.05$).

Table 9: Comparison of clinical features between moderate and severe anemia groups

Sl.no	Clinical Feature	Moderate anemia (n= 246)	Severe anemia (n= 36)	p value
1	Fatigue	85(35.55%)	26(72.22%)	**0.000**
2	Giddiness	35(14.22%)	16(44.44%)	**0.000**
3	Headache	16(6.5%)	8(22.22%)	**0.000**
4	Palpitations	6(2.43%)	16(44.44%)	**0.000**
5	Breathlessness	2(0.81%)	3(8.33%)	**0.016**
6	Systolic murmur	2(0.81%)	17(47.22%)	**0.000**
7	Glossitis	2(0.81%)	2(5.55%)	0.08
8	Stomatitis	1(0.41%)	1(2.77%)	0.23

a) Adequacy of Iron intake

Adequacy of iron intake was assessed by history and it was considered adequate if they had taken at least 100 tablets of Iron and Folic acid during the pregnancy. In our study group, out of 282, 62 (21.9%) women did not meet the criteria for adequate iron intake.

Associated comorbidities

Patients were assessed for associated comorbidities and Hypothyroidism was found to be most common 16(5.7%). Other comorbidities in our study group were chronic hypertension in 12(4.3%), Type 2 diabetes in 1(0.4%) and Tuberculosis in 1(0.4%) as shown in Table 10.

Table 10: Frequency of co-morbidities

Sl no.	Prior Co-morbidity	n (%)
1	Hypothyroidism	16 (5.7%)
2	Chronic hypertension	12 (4.3%)
3	Diabetes	1 (0.4%)
4	TB	1 (0.4%)

b) Intra-partum events

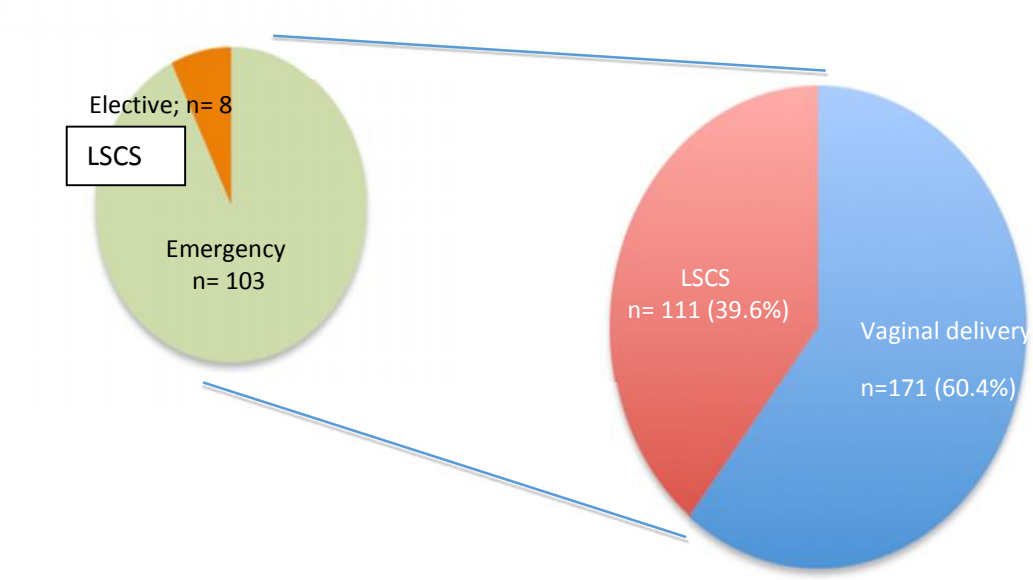
Among the study group, Median gestation at delivery was 38 weeks + 2days (36+2, 39+6). Of the 282 deliveries, 171 (60.4%) were vaginal deliveries and the rest 111 (39.6%) were C-section as tabulated in Table 11.

Table 11: Frequency of various modes of delivery in cases

Sl no.	Mode of delivery	n (%)
1	Vaginal delivery	171 (60.4%)
2	LSCS	111 (39.6%)
2a.	Emergency LSCS	103(92.7%)
2b.	Elective LSCS	08 (7.2%)
3	Instrumental delivery	
3a.	Forceps assisted delivery	4 (2.34%)
3b.	Vacuum assisted delivery	33 (19.3%)

Among the vaginal deliveries 4 (2.34%) were forceps assisted and 33 (19.3%) was vacuum assisted delivery. Among the LSCS, majority of sections 103(92.7%) were done due to emergency indications, only 8(7.2%) C-sections were done electively as depicted in Figure 6.

Figure 6: Frequency Of Mode Of Delivery



Among the various indications of emergency C-section, we found that previous LSCS was found in almost 41.4% of cases. Other indications included Abruption in 12(10.8%); Eclampsia and pre-eclampsia in 11(9.9%); Deep transverse arrest and non-progression of labour in 9(8.1%); Mal-presentation and malposition in 9(8.1%); Fetal distress in 5(4.5%); severe oligohydramnios in 4(3.6%); Doppler abnormalities in 3(2.7%); Placenta previa in 3(2.7%); Thick MSL in 2(1.8%) and scar rupture in 1(0.9%). These indications are not mutually exclusive as some patients had more than one of the above-mentioned indications.

Table12: **Frequencies of various indications requiring Emergency LSCS are tabulated in**

Sl no.	Indication	n (%)
1	Prev. LSCS	46 (41.4%)
2	Abruption	12 (10.8%)
3	Eclampsia and Pre-eclampsia	11 (9.9%)
4	Arrest/ Non progression of labour	9 (8.1%)
5	Mal-presentation/ Malposition	9 (8.1%)
6	HELLP	6 (5.4%)
7	Fetal distress	5 (4.5%)
8	Severe oligohydramnios	4 (3.6%)
9	Abnormal Doppler	3 (2.7%)
10	Placenta previa	3 (2.7%)
11	Thick MSL	2 (1.8%)
12	Scar rupture	1 (0.9%)

When modes of delivery were compared between moderate and severe anemia groups, 33.3% (12 out of 36) women in severe anemia group and 40.4% (99 out of 245) women in moderate anemia group underwent C-section, however this difference was not statistically significant (p value- 0.46).

Maternal Complications

Most common complication overall was pre term delivery, occurring in 30.6% (86) of pregnant women, of which 16.7% delivered between 34 – 36+6 weeks, where as 4.3% delivered before 28 weeks. Pre eclampsia was found to be the second most common maternal complication, affecting 21.3% (60) of women. Other complications included Abruption in 26(9.2%), Eclampsia in 6(2.1%), PPH in 6(2.1%), HELLP in 6(2.1%), Congestive cardiac failure in 3(1.1%), AKI in 1(0.4%) and Puerperal sepsis in 1(0.4%). In our study, 2 women (0.7%) had mortality. One patient expired due to Disseminated Intravascular Coagulation, where as the other expired due to ante partum hemorrhage and acute renal failure and cardiac arrest postoperatively. Various maternal complications and their frequencies are tabulated in Table 13.

Table 13: Frequency of maternal complications

S no.	Complication	n (%)
1	Pre term delivery a) Late pre-term b) Early pre-term c) Extremely pre-term	86 (30.6%) 47 (16.7%) 27 (9.6%) 12 (4.3%)
2	Pre-eclampsia	60 (21.3%)
3	Abruption	26 (9.2%)
4	Eclampsia	6 (2.1%)
5	Postpartum hemorrhage	6 (2.1%)
6	HELLP	6 (2.1%)
7	Congestive cardiac failure	3 (1.1%)
8	Maternal mortality	2 (0.7%)
9	AKI	1 (0.4%)
10	Puerperal sepsis	1 (0.4%)

Comparison of Maternal complications between moderate and severe anemia

Among the various maternal complications compared between the two groups, statistically significant difference was found only in the incidences of Pre term labour and HELLP, both of which were more in severe anemia group ($p<0.05$).

Table 14: Incidences of various maternal complications in both groups

S.no	Maternal complication	Moderate anemia (n= 246)	Severe anemia (n= 36)	p value
1	Preeclampsia	49(19.9%)	11(30.55%)	0.18
2	Eclampsia	6(2.43%)	0	0.59
3	Retained placenta	0	0	-
4	Abruption	19(7.72%)	7(19.44%)	0.057
5	Pre term labour	67(27.23%)	19(52.77%)	**0.003**
6	Dysfunctional labour	1(0.40%)	1(2.77%)	0.23
7	PPH	4(1.62%)	2(5.55%)	0.17
8	Puerperal sepsis	1(0.40%)	0	1.0
9	HELLP	2(0.81%)	4(11.11%)	0.000
10	Maternal mortality	1(0.04%)	1(2.77%)	0.23

Out of 282 women enrolled, 194 (68.8%) women treated with parenteral Iron therapy and 136 (48.2%) necessitated blood transfusion as depicted in Table 15.

Table 15: showing the type of support and frequency of patients requiring it

Sl no.	Type of support	n (%)
1	Parenteral iron	194 (68.8%)
2	Blood Transfusion	136 (48.2%)

Further when requirement of blood transfusion was compared between moderate and severe anemia groups, all the women in severe anemia group required blood transfusion, whereas 100 out of 245 women in moderate anemia group required blood transfusion ($p<0.001$) as depicted in Table 16.

Table 16: Comparison of requirement of blood transfusion among moderate and severe anemia groups

		Anemia		p value
		Moderate	Severe	
Blood transfusion	**Yes**	100	36	**<0.001**
	No	145	0	

c) Fetal complications

Most common fetal complication found in the study group was LBW, found in 160 (56.7%) women. 51.4% neonates were small for their gestation. Of these 26.6% of neonates were between 3rd to 10th centile and the rest 23.8% neonates were less than 3rd centile. 38 (13.5%) neonates had APGAR score<5 at 5minutes. Out of 282 women enrolled, 25 (8.9%) had IUD and 8 (2.8%) had FSB as depicted in Table 17.

Table 17: Frequency of Fetal complications

Sl no.	Complication	n (%)
1	LBW	160 (56.7%)
2	a) AGA b) 3^{rd} to 10^{th} centile c) 3^{rd} centile	140 (49.6%) 75 (26.6%) 67 (23.8%)
3	APGAR <5 at 5min	38 (13.5%)
4	Distress	29 (10.3%)
5	IUD	25 (8.9%)
6	FSB	8 (2.8%)

Comparison of Fetal complications between moderate and severe anemia

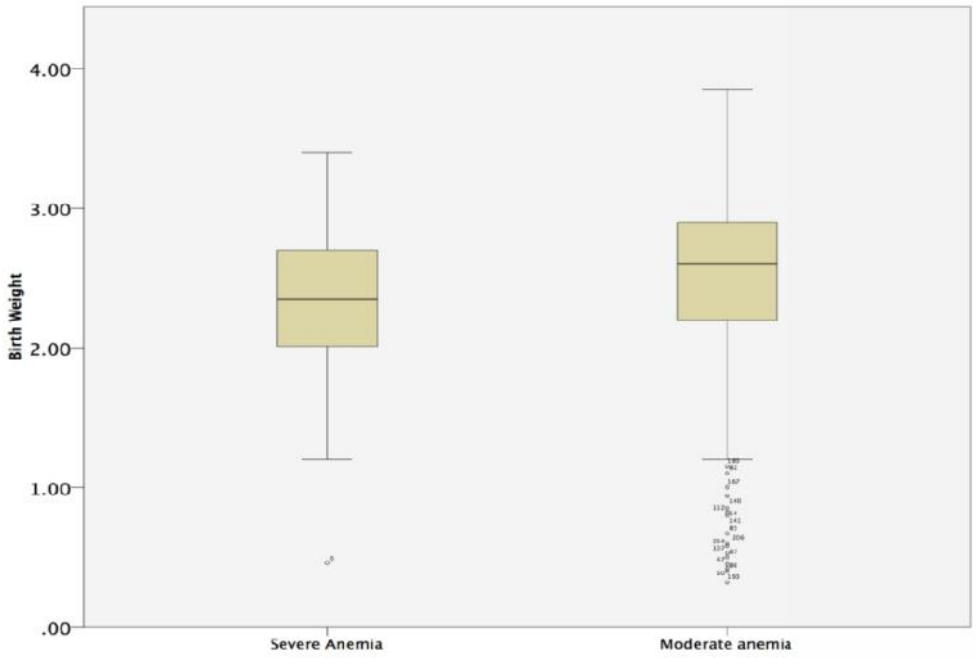
Among the fetal complications, statistically significant difference was found only in birth weight and median gestation age, both of which were lower in severe anemia group.

Table 18: Comparison of various fetal complications

Sl.no	Fetal complication	Moderate anemia (n= 246)	Severe anemia (n= 36)	p value
1	Pre term	67(27.23%)	19(52.77%)	**0.003**
2	LBW	99(40.24%)	23(63.88%)	**0.011**
3	APGAR<5 @5min	3(1.21%)	0	1.0
4	IUGR	126(51.21%)	14(38.88%)	0.21
5	IUD	19(7.72%)	6(16.66%)	0.10

Median birth weight in moderate anemia group was 2.6Kg (2.2, 2.9), where as in case of severe anemia it was 2.35Kg (2.0, 2.7) and this difference was statistically significant (p value <0.05). Difference in the birth weight between the two groups is depicted in the Box and Whisker plot as below.

Figure 7: Box and Whisker plot showing difference in the birth weight between both groups



When the Odds of having a LBW baby was calculated, women in severe anemia group has 2.62 times (95% CI: 1.2- 5.4) more chance of having a LBW baby compared to mothers with moderate anemia. In the similar way, Odds of having a pre term delivery was 2.98 times (95% CI: 1.46- 6.08) more as compared to moderate anemia.

DISCUSSION

Anemia is the most common haematological abnormality that occurs during pregnancy. The extent to which anemia during pregnancy affects maternal and fetal outcome is not yet clear. Hence this study was done, for better understanding of relationship between anemia and pregnancy outcomes. We enrolled pregnant women coming to labour room who were moderately or severely anemic.

Global prevalence of anemia during pregnancy is 38.9% to 48.7%[1]. In our study, prevalence of moderate anemia was 4.56% and of severe anemia was 0.66%. As per NFHS-4 survey, prevalence of moderate anemia among all the women in Karnataka was 11% and of severe anemia was 1%[3]. This difference could be because of different population sets as data of NFHS-4 survey was addressing all the women in Karnataka. We all know that prevalence of anemia in non-pregnant women is also high and probably that could have resulted in the increased prevalence of anemia as a whole. Mangla et al reported a prevalence of 37.05% for moderate anemia and 3.2% for severe anemia, which was more compared to our data. This could be because Mangla et al study was done among women from rural Haryana, where overall prevalence of anemia itself is high compared to our state and could also be because of high patriarchal nature of society that exists in Haryana[12].

In our study we found that 90.8% of women were registered at some or other hospital. This data was consistent with the Karnataka state fact sheet of NFHS-4, which stated that 91% of women had registered their last pregnancy[3]. This is important as effective antenatal care is of paramount importance in preventing all sorts of intra-partum and post-partum complications that can occur. Elhassanet al[25]

has shown that lack of antenatal care was associated with increased risk of LBW (OR- 5.9; 95% CI= 1.4- 24.4; p=0.01).

84.8% women in our study belonged to upper lower class of Kuppuswamy scale 2016, 12% belonged to lower class, 8.3%, 2.85% to lower middle and upper middle class respectively. This indicates that a high prevalence of anemia exists in poorer sections of the society. Many studies have shown association between socioeconomic status and Hb level during pregnancy[34,35]. This is because of poor nutritional status of women and low iron stores that exists among low socioeconomic class.

When peripheral blood smear was analyzed, we found that microcytic hypochromic picture was the most common among 100 (35.4%), indicating that iron deficiency anemia is the leading cause. This was followed by dimorphic anemia in 77 (27.4%), normocytic normochromic anemia in 70 (24.8%) and macrocytic anemia in 35 (12.4%). Worldwide reports state Iron deficiency as the leading cause of anemia during pregnancy. This is mainly due to inadequate daily intake of iron[6]. In our study group also, 21.9% of women did not take the recommended 100-day course of iron and folic acid tablets, indicating the need for adequate antenatal counselling regarding the importance of nutrition and compliance to medications. Studies have also shown association between maternal ferritin values and birth weight, gestational age and APGAR score[15,26]. Iron deficiency can exist even in the absence of anemia and the effect of such iron deficiency on pregnancy outcomes is not yet known and is an area that requires further exploration.

Symptoms that we found in our study group were more of non-specific in nature and included fatigue (39.4%), giddiness (18.1%), headache (8.5%), palpitations

(7.8%) and breathlessness (1.8%). When we further analyzed the frequency of these symptoms between moderate and severe anemia groups, we found that all the symptoms were significantly higher in severe anemia group. Moreover 50% of women in severe anemia group had flow related murmur indicating that they are at a higher risk of landing in congestive cardiac failure.

On analyzing the intra-partum events, we found that the median gestation at delivery was 38 +2 weeks (36+2, 39+6). Out of 282, 171 (60.4%) women delivered vaginally and 111 (39.6%) women required C-section. Anemia did not have any association with the need of c-section as we found that there was no statistically significant difference between moderate and severe anemia groups. But some studies have shown that need of c-section was more in cases of anemia. We didn't find such difference probably because we analyzed among the subgroups of anemia rather than comparing with non-anemic women.

Most common maternal complication found in our study group was pre-term delivery occurring in about 30.6% of women. We also found that incidence of extreme pre-term delivery was higher (4.3%). 52.7% (19 of 36) women in severe anemia group had preterm labour, whereas only 27.2% (67 of 246) women had in moderate anemia group and it was statistically significant (p-0.003). Odds of having a pre-term delivery were 2.98 times (95% CI: 1.46- 6.08) more in severe anemia group as compared to moderate anemia. Our results concurred with the findings published in the meta-analysis done by Rahmanet al[25], who showed that pooled relative risk of having preterm delivery was 1.63(95% CI: 1.33-2.01). But conflicting results were shown in another meta-analysis done by Rahmatiet al[6], who found that only first trimester anemia is associated with pre-term delivery (RR-1.26; 95%CI- 1.11-1.44;

p<0.01). Some authors even found that increasing Hb is associated with increased incidences of preterm delivery[16]. As we know, preterm delivery is the leading cause of neonatal mortality; treating and preventing maternal anemia could be an important step in achieving the INAP goal of single digit NMR by 2030[36].

Pre-eclampsia was found to be the second most common maternal complication, affecting 21.3% (60) of women. Other complications included Abruption (9.2%), Eclampsia (2.1%), PPH (2.1%), HELLP (2.1%), Congestive cardiac failure (1.1%), AKI (0.4%), and Puerperal sepsis (0.4%). We did not find any difference in the incidence of maternal complications like PIH, sepsis between the two groups. But we found significant difference in the incidence of HELLP. 11% (4 of 36) women had HELLP in severe anemia group when compared to 0.8% (2 of 246) in moderate anemia group (p<0.001). This was probably because of the sicker and decompensated state of the women in severe anemia group. Reasons for mortality in our study population were DIC, Acute renal failure following APH. In our study 2 women had maternal mortality. The cause of death in one patient was antepartum hemorrhage and postoperatively cardiac arrest and acute renal failure. A G3P2L2 with 21 weeks period of gestation with previous LSCS had come with complaints of pain abdomen and pv bleeding on examination. There was scar tenderness noted hence patient was shifted into the OT. Intra-operatively uterine rupture, bilateral broad ligament hematoma extending to the retro-peritoneum was noted. Hysterectomy was done in view of uterine rupture and distorted anatomy. As the patient had continued to bleed, bilateral internal iliac artery ligation was done. Post-operatively, patient had acute renal failure followed by cardiac arrest. The cause of death in another patient was Disseminated Intravascular Coagulation. G3P2L2 with 38 weeks period of gestation with previous 2 LSCS had come with complaints of decreased fetal

moments, pain abdomen and per vaginal bleed. On examination uterus was tensed. Ultrasound showed Intra uterine death and abruptio placenta. Emergency LSCS was done intra-operatively ascites, couvelaire uterus and retroplacental clots were noted. Postoperatively patient was in disseminated intravascular coagulation, acute renal failure and thrombocytopenia. Studies also have shown that maternal mortality increases as Hb value decreases. On secondary analysis of WHO data, it was found that severe anemia had 2.36 (95%CI: 1.60-3.48) times more risk of developing maternal mortality. The maternal complications due to anemia in pregnancy were found to be statistically significant for pre-term labour and HELLP syndrome. Our study found very high proportions of women requiring parenteral iron (68.8%) and blood transfusions (48.2%). These high requirements of parenteral therapy increase the risk of transfusion related complications by many folds.

Among the fetal complications, Low birth weight was the most common (56.7%). 51.4% of neonates were small for gestation, 13.5% babies had APGAR score <5 at 5min and 11.7% had perinatal mortality. On subgroup analysis also we found that incidence of LBW was more in severe anemia group compared to moderate anemia ($p<0.05$). More than half (63.8%) of the babies born to women with severe anemia were LBW and in case of women with moderate anemia it was 40.2%. The fetal complications such as prematurity and LBW due to anemia in pregnancy was found to be statistically significant .These incidences were way more than those found in a normal population. The obvious factor that contributed to such high incidence was maternal anemia. Though some studies disagree the influence of maternal anemia on LBW, many studies, systematic reviews and meta-analyses showed a clear association between the two. Figueiredo et al(24) in their meta-analysis concluded that maternal anemia was associated with LBW with an adjusted odds ratio of 1.23

(95% CI: 1.06-1.43). Rahmanet al[25] also concluded the same (OR- 1.31; 95%CI: 1.13-1.51) in their meta-analysis. They found that 12% of LBW and 18% of perinatal mortality was attributable to maternal anemia.

Knitting all things together, we can see that maternal anemia increases the risk of maternal mortality, preterm birth and LBW by 1-2 times. In another perspective, it can be said that treating anemia could decrease the incidence of these complications by 50%. Any measure that helps in achieving this should be given a great importance. Hence, all pregnancies should be fully assessed as early as possible so that problems like anemia could be picked up and treated early. As many studies have shown anemia in early period of gestation has more adverse effects on perinatal outcomes, preventing this would be fruitful. Improving diet and Iron supplementation are the key steps in treating anemia. Iron supplementation should be continued during pregnancy and in post partum period so that anemia can be prevented in subsequent pregnancies.

CONCLUSION

The risk of pre-term delivery, pre-eclampsia, abruptio placenta, eclampsia, postpartum haemorrhage, HELLP syndrome, CCF and maternal mortality increases with anemia in pregnant women.

The risk of prematurity, LBW, less than 5 APGAR score, respiratory distress, IUD and FSB increases with anemia.

The risk blood transfusion increases with the severity of anemia. There by increases the risk of transfusion related complications.

Iron deficiency is the most common cause of anemia during pregnancy. Improving diet and Iron supplementation are the key steps in treating anemia. Iron supplementation should be continued during pregnancy and in post partum period so that anemia can be prevented in subsequent pregnancies. Early detection and effective treatment of anemia during pregnancy can improve both neonatal and maternal outcomes.

SUMMARY

1. 282 pregnant women with Hb value <9gm/dl were enrolled in the present cross-sectional study and they were grouped into 2 subgroups moderate and severe anemia.
2. Median age of the study population was 24 (22,26) yrs. 58.2%(164) of pregnant women were in the age group of 21-25yrs and 1.8%(5) were more than 35yrs of age.
3. 239 women(84.8%) belonged to upper lower socioeconomic class according to modified Kuppuswamy scale 2016.
4. Among the study population 256 (90.8%) cases were antenatally registered at some or the other hospital, whereas 26 (9.2%) cases were unregistered.
5. Prevalence of Moderate anemia in our study population was 4.56%, whereas that of severe anemia was 0.66%.
6. Out of 282 women enrolled, 246 women (87.2%) belonged to moderate anemia and 36 women (12.8%) belonged to severe anemia.
7. Iron deficiency anemia was the most common anemia in our group with Microcytic hypochromic smear accounting to 100 women (35.4%). Dimorphic anemia was next to Iron deficiency anemia accounting to 77 women (27.4%).
8. Fatigue was the most common symptom found in 111 (39.4%) of cases followed by Giddiness in 51 (18.1%), Headache in 24 (8.5%), Palpitations in 22 (7.8%) and Breathlessness 5 (1.8%).
9. All the clinical features were found more in severe anemia group compared to moderate anemia group.

10. 194 (68.8%) women required parenteral iron therapy and 136(48.2%) of women required blood transfusion. Requirement of blood transfusion was significantly higher in severe anemia group ($p<0.01$).
11. Median gestation at delivery was 38 weeks + 2days (36+2, 39+6). Of the 282 deliveries, 171 (60.4%) were vaginal deliveries and the rest 111 (39.6%) were C-section.
12. Among the LSCS, majority of sections 103 (92.7%) were done due to emergency indications, only 8(7.2%) C-sections were done electively.
13. Most common maternal complication was pre term delivery, occurring in 86 (30.6%)of pregnant women, of which 4.3% delivered before 28 weeks.
14. Pre-eclampsia was found to be the second most common maternal complication, affecting60(21.3%) of women. Other complications included Abruption 26(9.2%), Eclampsia 6 (2.1%), PPH 6 (2.1%), HELLP 6 (2.1%), Congestive cardiac failure 3 (1.1%), mortality 2 (0.7%), AKI 1 (0.4%), and Puerperal sepsis 1 (0.4%).
15. Among the various maternal complications compared between the two groups, statistically significant difference was found only in the incidences of Pre term labour and HELLP, both of which were more in severe anemia group ($p<0.05$).
16. Most common fetal complication found in the study group was LBW, found in 160 (56.7%) women.
17. 160 (51.4%) neonates were small for their gestation. 38 (13.5%) neonates had APGAR score<5 at 5minutes. 25 (8.9%) had IUD and 8 (2.8%) had FSB.
18. Among the fetal complications, statistically significant difference was found only in birth weight and median gestation age, both of which were lower in severe anemia group ($p<0.05$).

19. Median birth weight in moderate anemia group was 2.6Kg (2.2, 2.9), where as in case of severe anemia it was 2.35Kg (2.0, 2.7) and this difference was statistically significant (p value <0.05).
20. Women in severe anemia group had 2.62 times (95% CI: 1.2- 5.4) more chance of having a LBW baby compared to mothers with moderate anemia.
21. Odds of having a pre term delivery was 2.98 times (95% CI: 1.46- 6.08) more in severe anemia group as compared to moderate anemia.

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ANNEXURES

ANNEXURE I – ETHICAL CLEARANCE CERTIFICATE

K.L.E.UNIVERSITY'S
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
(Accredited 'A' Grade by NAAC)

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Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 52 **Date: 17/10/2016**

To,

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"ONE YEAR PROSPECTIVE OBSERVATIONAL STUDY ON MATERNAL AND FETAL OUTCOME WITH SEVERE ANAEMIA ADMITTED IN THE LABOUR ROOM AT KLE DR. PRABHAKAR KORE CHARITABLE HOSPITAL",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Ganga Pilli)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

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ANNEXURE-II

CONSENT FORM

From,

To,
DR. GANGA PILLI,
Chairman,
J.N.M.C Ethical Committee for Human Research,
KLE University,
Belgaum-590010.

(Through Proper Channel)

Subject :Waiver of consent for the study .

Respected Sir,

, Post Graduate in the Department of Obstetrics And Gynaecology, hereby inform you that I am submitting my dissertation synopsis.

My topic is **"ONE YEAR PROSPECTIVES OBSERVATIONAL STUDY ON MATERNAL AND FETAL OUTCOME WITH SEVERE ANAEMIA IN THE LABOUR ROOM AT KLE DR. PRABHAKAR KORE CHARITABLE HOSPITAL** a project wherein I am not going to come in direct contact with the patients as I am going to get all my study material from the Medical records. Hence , I am not going to need any consent form. Kindly grant me permission to do this study.

Thanking you,

Yours faithfully,
P. Divya
(Dr.P.DIVYA)

Guide :

ANNEXURE-III

PROFORM

I.P. Number: __/ __/ __/ __/ __/ __

Name of the Patient: _____

Age: ☐ Year:

Address: _____

Phone number: __/ __/ __/ __/ __/__/ __/ __/ __/ __

Date of admission: __/ __/ __

Socio-economic status:

Upper class (<5775) ☐ Upper middle class (2887-5774) ☐

Middle class (1733-2886) ☐ Lower middle class (866-1732) ☐

Lower class (<866) ☐

Occupation:

a. House wife ☐ b. laborer ☐

c. Agriculture ☐ d. Professional ☐

Education:

a. No formal schooling (Illiterate) ☐ b. No formal schooling (Literate) ☐

b. Formal schooling ☐ d. Graduate ☐

Whether the case is:

a. Registered in KLE ☐ b. Registered outside ☐ c.Unregistered ☐

Gravida: ☐ Para: ☐ Living ☐ Abortion ☐ Dead ☐ Still Birth ☐

LMP __/__/__

POG __weeks __days

EDD __/__/__

	YES	NO
Fatigue	☐	☐
Giddiness	☐	☐
Haedache	☐	☐
Breathlessness	☐	☐
Palpitations	☐	☐
Fever	☐	☐
Burning maturation	☐	☐
Consumption of: Tab Folic acid	☐	☐
: Tab Iron	☐	☐

Past History:	YES	NO		YES	NO
a.History of hypertension	☐	☐	b.history of diabetes mellitus	☐	☐
c.history of tb	☐	☐	d. history of asthma	☐	☐
e. History of hypothyroidism	☐	☐	F. History of transfusion	☐	☐
g. History of hemo-globinopathies	☐	☐	h. History of haemorrhagic disorders	☐	☐
i. History of renal diseases	☐	☐	j. History of hepatic diseases	☐	☐

1. History of bone marrow disorders ☐ ☐

1. any other specific medical History _____

General Physical examination

Pulse Rate:_____ bpm BP_____ mmhg

Pallor ☐ Edema ☐ Glossitis ☐ Angular stomatitis ☐

Cardiovascular system: Normal ☐ Any abnormality_____

Respiratory system : Normal ☐ Any abnormality _____

Fundal Height:

Appropriate for Gestational Age ☐

Not appropriate for gestational age: more I ☐ ☐

Progress of labour: Augmentation :yes /no:

ARM/ Oxytocin dose:

Date and time of delivery: Date ___/___/___ Time _____am/pm

OUTCOME:

Spontaneous Vaginal delivery: ☐ ☐

Instrumental delivery: Forceps: Indication:

Vaccum: Indication:

Complications if any:

Operative delivery:

Emergency LSCS ☐ ☐

Elective LSCS ☐ ☐

Indication : _____

Intraoperatively events if any : _____

Intraoperative transfusion if any ☐

Number of units of blood transfused ☐

Maternal outcome:

Pre-eclampsia	☐	Eclampsia	☐
Retained placenta	☐	Abruption Placenta	☐
Preterm labour:	☐	Dysfunctional labour:	☐
Anaesthesia risk :	☐	Postpartum haemorrhage	☐
Cardiac failure:	☐	Puerperal Sepsis	☐

Maternal mortality_____

Foetal outcome:

APGAR Score :1 min: ☐ 5 min: ☐ 10 min: ☐

APGAR Score less than 7 ☐

Birth weight:_____Kg Low birth weight, if any: ☐

Prematurity ☐	Intra uterine growth retardation: ☐
Foetal distress if any:	Resuscitation: ☐
Morbidity: ☐ _____	Intra uterine death: ☐
Birth asphyxia ☐	Neonatal distress: ☐
Neonatal anaemia ☐	Perinatal death ☐

Investigations:

Hb:_____ gm% Peripheral smear:_____

ANNEXURE-IV

KEY TO MASTER CHART

| Name | IP no. | Age | Income | Occupation | Education | Registered | Gravida | Gestation | Fatigue | Giddiness | Headache | Breathless | Palpitations | Fever | Burning micturitino | Iron | Folic acid | HTN | DM | TB | Hypothyroidism | Transfusion | Hbpathy | renal disease | liver disease | BM disorders | other | PR | BP | Pallor | Edema | Glossitis | Angular stomatitis | CVS | RS | Fundus | Fundus groups | Delivery | Augmentation | Forceps | Forceps indication | Vaccum | Vaccum indication | Complications | LSCS | LSCS Indication | Intraop complications | Bld transfusion | No. of units | IV iron | Pre-eclampsia | Eclampsia | Retained placenta | Abruption | Preterm labour | Dysfn labour | PPH | CCF | Puerperal sepsis | HELLP | Mat. mortality | APGAR 1 | APGAR 5 | APGAR 10 | B. Wt | Gender | IUGR | Distress | IUD | FSB | B asphyxia | Neonatal anemia | perinatal death | Hb | Smear | |
|---|---|---

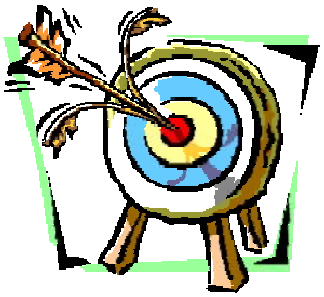
| | | |

| | | |

| | | |

| | | |

Introduction



Objectives

Review of Literature

Methodology

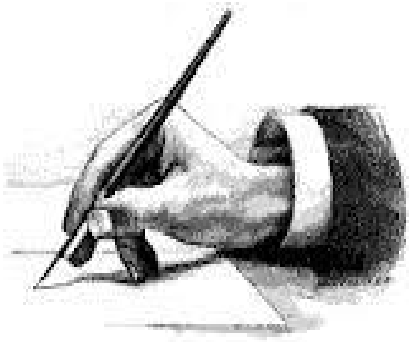
Results

Discussion

Conclusion

Summary

Bibliography



Annexures