Prevalence of anemia in pregnancy at booking visit

Dissertation submitted in partial fulfillment of the requirements of TamilNadu Dr. M.G.R. Medical university for the degree of M.S. branch II (Obstetrics and Gynecology) examination to be held in April 2014.
Certificate

This is to certify that the dissertation entitled “Prevalence of anemia in pregnancy at booking visit” is the original work of Dr. Madhu Priya N, done under my guidance towards the M.S Branch II (Obstetrics and Gynecology) Degree Examination of the Tamil Nadu Dr.M.G.R. Medical University, Chennai to be held in April 2015.

Dr. Ruby Jose,
Professor and Head,
Obstetrics and Gynecology Unit IV,
Christian Medical College, Vellore,
Tamil Nadu, 632004.
Certificate

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August 18, 2014

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Sub: Fluid Research Grant Project:
Detecting low haemoglobin (BLOOD) levels in pregnant women at their first visit to CMC, Vellore.
Dr. Madhu Priya, Obstetrics and Gynaecology Unit IV, Dr. Ruby Jose, Dr. Reeta Vijaya Selvi, Obstetrics and Gynaecology, Dr. L. Jeyaseelan, Biostatistics, CMC, Vellore.


Dear Dr. Madhu Priya,

I enclose the following documents:

1. Institutional Review Board approval

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

C.C. Dr. Ruby Jose, Obstetrics and Gynaecology, CMC, Vellore.
August 18, 2014

Dr. Madhu Priya
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Ref: IRB Min No. 8943 [OBSE INE] dated 07/07/2014

Dear Dr. Madhu Priya,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled “Detecting low haemoglobin (BLOOD) levels in pregnant women at their first visit to CMC, Vellore.” on June 07th 2014.

The Committees reviewed the following documents:

1. IRB Application format
2. Curriculum Vitae of Drs. Madhu Priya, Ruby Jose, Reeta Vijaya Selvi, L. Jeyaseelan.
3. Informed Consent form (English, Tamil & Telugu)
4. Information Sheet (English, Tamil & Telugu)
5. No of documents 1-4

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on June 07th 2014 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

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<td>Professor, Colorectal Surgery, CMC, Vellore</td>
<td>Internal, Clinician</td>
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<td>MD, Ph D.</td>
<td>Professor &amp; In-charge Retrovirus Laboratory</td>
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<td>Dr. Denise H. Fleming</td>
<td>B. Sc (Hons), PhD</td>
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<td>Internal, Scientist &amp; Pharmacologist</td>
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<td>Rev. Joseph Devaraj</td>
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<td>Legal Expert, Vellore</td>
<td>External, Legal Expert</td>
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OFFICE OF RESEARCH  
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Chairperson, Research Committee & Principal

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| Dr. Anuradha Rose  | MBBS, MD  | Assistant Professor,  
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<tr>
<th>Community Health, CMC, Vellore</th>
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| Dr. Nihal Thomas,  | MD, MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin) FRCP(Glasg)  | Professor & Head,  
Endocrinology. Additional  
Vice Principal (Research),  
Deputy Chairperson, IRB,  
Member Secretary (Ethics Committee), IRB, CMC, Vellore  |  | Internal, Clinician |

We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any adverse events occurring in the course of the project, any amendments in the protocol and the patient information / informed consent. On completion of the study you are expected to submit a copy of the final report. Further information can be obtained from the following link:  
http://172.16.11.136/Research/IRB.Policies.html in the CMC Intranet and in the CMC website link address:  
http://www.cmcvellore.edu/Static/Research/Index.html

Fluid Grant Allocations:

A sum of 13,200/- INR (Rupees Thirteen Thousand Two Hundred only) will be granted for 3 months.

Yours sincerely

Dr. Nihal Thomas  
Secretary (Ethics Committee)  
Institutional Review Board

Cc: Dr. Ruby Jose, Obstetrics and Gynaecology, CMC, Vellore

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Aims and Objective

Aims of the study:
1. This study aims at finding out the prevalence of anaemia and correlate with risk factors for its occurrence.
2. Make recommendations for prevention and correction of anaemia in pregnant women.
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Acknowledgements

I am deeply grateful to Dr. Ruby Jose, my guide, who had spent so much of her valuable time in guiding me and correcting me, both in Obstetrics and English grammar. Actually I took it as a great honor when I had the opportunity to do my thesis under Dr. Ruby’s guidance in Unit IV. Mam I thank you so much for your patience with me. I have always admired you throughout my stay in CMC & H for your clinical skills and strong evidence based teaching, now after being with you during this thesis period I really want to learn more research from you. Thank you mam for taking those extra steps for me in this thesis (I am sure I would have made you to take a thousand miles of extra steps). I will try and reach your expectations mam.

I acknowledge with gratitude all the patients who agreed to take part in my study. Next I want to thank OPD staffs- MROs and USG room people, Ms .Sheeba who helped me in recruiting patients.

I thank Dr. Thambu David, who took those Epidemiology classes and took so much pain in making us understand what we are supposed to do.

I extend my sincere thanks to Dr. JeyaSeelan from Dept. of Bio statistics for being in my thesis as a co-investigator. Without your help I would not have achieved those magic numbers and tables on the very last day before submission.

I also thank Mr. Alphonse and Mr. Madhan from CEU for their timely helps.
I am deeply grateful Dr. Aruna N. Kekre for allowing me to take leave and finish this work in time. I thank Dr. Lilly Varghese for her timely advice. I thank Dr. Jessie Lionel for allowing me to take Ms. Sheeba’s help in collecting patients in my absence during the OPD timings.

I sincerely thank all my friends who squeezed their time to fill in the proforma and to recruit patients in my study.

I realized that writing thesis is like running a long and lonely marathon, but whenever I turned around I had my friend Dr. Jeyasheela with her suggestions as glucose packets during marathon.

Finally I thank my family for providing me such an environment, where I can concentrate on my study. Although they hardly understand what writing thesis is and what I research on, they usually support any decision I make.

Ultimately Prayer changes things.

MadhuPriya N
Aims and Objective

Aims of the study:

1. This study aims at finding out the prevalence of anemia and correlate with risk factors for its occurrence.

2. Make recommendations for prevention and correction of anemia in pregnant Women

Objective of the study:

To find out the prevalence of anemia in Obstetrics OPD patients during their first antenatal visit to CMCH, Vellore.
Material and methods
This study, the prevalence of anemia in pregnant mothers during their first visit to the Obstetric outpatient department, Christian Medical College & Hospital, was approved by the Research Committee and the Institutional Review Board (Ethics committee) of Christian Medical College, Vellore. The study was reviewed in detail and then was accepted and approved.

**Study Design:** Observational study with sample size of 600 patients.

Fund from fluid research, Rs.13, 200 was granted for the study.

**Sampling Procedures:**

<table>
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<td>Expected Proportion</td>
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<tr>
<td>Precision (%)</td>
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<tr>
<td>Desired confidence level (1- alpha) %</td>
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<td>Required sample size</td>
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The prevalence of anaemia has been reported to be ranging from 33% to 89% (38). However, we have considered that this prevalence would be at the worst 33%. In order to estimate this with the precision of 5%, 4% and 10% of 33% (3.3%), with 95% CI, the sample size needed ranged from 340 to 780 respectively. And, it was decided to study 600 pregnant mothers.
Study Setting:

- All eligible pregnant women attending their first visit in the Outpatient department of Obstetrics and Gynaecology in Christian Medical College, Vellore.

Inclusion Criteria:

- All pregnant women attending the OPD for the first visit, on all days, irrespective of their gestational age and obstetric risk factors.
- Both private and general patients.

Exclusion Criteria:

- Patients already diagnosed with haematological disorders

Primary Outcome:

- Prevalence of anemia in pregnant women at booking visit

Secondary Outcomes:

- Grading the severity of anemia
- Factors associated with anemia
**Recruitment of Patients:**

Recruitment of patients was done in the OPD on all days after getting informed written consent from the patients. A proforma containing demographic details, financial status, educational qualification, present occupation, family type, dietary patterns and obstetric history details was filled by the care provider usually a registrar who provided the ante natal care on that day. They were asked to give blood sample on the same day if possible or with in a week’s time for their haemoglobin estimation.

**Haemoglobin Estimation:**

According to WHO, haemoglobin estimation is the most important test for detection of anaemia in the community level (1).

Method of assessment: In our institution haemoglobin estimation is done in clinical Pathology laboratory using Cyan methemoglobin method (39).

The method for hemoglobin determination is the cyan meth hemoglobin method (This is a type of colorimetric method). The principle of this method is that when blood is mixed with a solution containing potassium ferri cyanide and potassium cyanide, the potassium ferri cyanide oxidizes iron to form meth hemoglobin. The potassium cyanide then combines with meth hemoglobin to form cyan meth hemoglobin, which is a stable color pigment read photo metrically at a wave length of 540nm following Lambert-Beer’s Law and is directly proportionate to the hemoglobin levels in the blood.
Three advantages of the cyan meth hemoglobin method are:

1. Measures all forms of hemoglobin except sulfa hemoglobin
2. Can be easily standardized
3. Cyan meth hemoglobin reagent (also called Drabkin's solution) is very stable

**Primi and Multigravida Definitions:**

Primi gravida: A woman who is pregnant for the first time

Multi gravida: A pregnant woman who has been pregnant earlier

**Family types Definitions:**

Nuclear Family / Elementary Family: Married couple and their children while they are still considered as dependants.

Joint Family / Extended Family: A number of married couples and their children who live together in the same household.

Third generation Family: Household where there are representatives of three generations. Usually occurs when young couples are unable to find separate housing accommodation and continue to live with their parents and have their own children. Thus representatives of three generations related to each other by direct descent live together.(40)
**Modified Kuppuswamy’s Scale** is used for Socio Economic Status (41)

(A) Education Score

1. Profession or Honors 7
2. Graduate or post graduate 6
3. Intermediate or post high school diploma 5
4. High school certificate 4
5. Middle school certificate 3
6. Primary school certificate 2
7. Illiterate 1

(B) Occupation Score

1. Profession 10
2. Semi-Profession 6
3. Clerical, Shop-owner, Farmer 5
4. Skilled worker 4
5. Semi-skilled worker 3
6. Unskilled worker 2
7. Unemployed 1
(C) Monthly family income (in Rs Score Modified for 2012)

1. $\geq 2000$ $12 \geq 13500 \geq 32050$

2. 1000-1999 $10 \ 6750 - 13499$ 16020 – 32049

3. 750-999 $6 \ 5050 - 6749$ 12020 – 16019

4. 500-749 $4 \ 3375 - 5049$ 8010 – 12019

5. 300-499 $3 \ 2025 - 3374$ 4810 – 8009

6. 101-299 $2 \ 676 - 2024$ 1601 – 4809

7. $\leq 100$ $1 \leq 675 \leq 1600$

Total Score Socioeconomic class

26-29 Upper (I)

16-25 Upper Middle (II)

11-15 Middle/Lower middle (III)

5-10 Lower/Upper lower (IV)

<5 Lower (V)
**Statistical Methods:**

**Data Entry:**

Data entry was done using Epidata software with quality checks such as range and consistency.

**Data processing and analysis:**

Data were analyzed using SPSS version 16.0 software. Data was further screened with Box-cloxplot and histograms. Description of means, proportions, frequencies and rates of the given data for each variable were calculated. The prevalence was presented as point estimate with 95% CI. The statistics were presented separately for different age groups and risk groups. Presence of anemia (yes / no) had been taken as an independent variable.

Bivariate analysis was done to compare each independent variable with the outcome variable and presented as OR and 95 % CI.

Logistic regression analysis was done as the prevalence was more than 10% with log link.

For the Multiple logistic regression analysis we took all variables.
Consort Algorithm

All pregnant women at booking visit are recruited after informed consent

Collection of demographic variables and blood sample given for Haemoglobin estimation

Follow up of Haemoglobin report

Analysis of demographic data and risk factors
Introduction
Anemia literally means without blood, a word from the Greek language, denoting deficiency of red blood cells and/or hemoglobin. Anemia is the most common deficiency disease in the world, affecting 1.62 billion people globally corresponding to 24.68% of the world population (1).

According to the WHO (World Health Organization), anemia is taken as a disease of low public health importance when the prevalence is less than 20%, of medium public health importance, when it is between 20 to 39.9% and severe when the prevalence is 40% and more in the population (1). Among developing countries, India has the highest prevalence of anemia (2) evidently linked to poverty.

The recent NHFS (National Health Family Survey) III by the International Institute of Population Sciences, India, says that adolescence in girls in India goes hand in hand with anemia. The percentage of children with anemia has increased from 74.3% from NHFS II to 78.9% in NHFS III (1). These children undergo the most vulnerable period of adolescence with anemia and as a tradition in India, the girls get married early and become pregnant adding to the damage. So every second Indian woman in India is anemic and one in every five maternal deaths is directly due to anemia. Most women are anemic prior to their first pregnancy itself and others become so during pregnancy progressively (3).

Even though the National Nutritional Anemia Prophylaxis Programme (NNAPP) had been started in 1973, during the fourth 5 year plan with the aim of reducing the prevalence of anemia to 25%, the latest statistics show a rising trend of this disease which is alarming and a cause of great concern. The WHO/World Bank has ranked iron deficiency anemia as the third leading cause of disability-adjusted life years (DALYs) lost for females 15–44 years of age (4). Anemia
contributes to 1, 20,000 deaths globally. In low and middle income countries like India 18% of maternal mortality has been attributed to anemia(5). In addition, anemia causes several adverse effects on health including maternal mortality and morbidity, neonatal and perinatal morbidity and mortality, low birth weight, poor immunity, poor cognitive development in children and decreased work productivity in adults.

Taking into consideration of all these facts, the UNDP (United Nations Development Programme) has adopted reducing the maternal mortality rates as one of the three health related goals, Goal No. 5 in the Millennium Development Goals by the end of 2015 (6).

Prevalence of anemia is an important indicator of health because it affects the most vulnerable group of people, mainly the pregnant women and the children. The two most common causes for anemia in pregnancy is due to nutrition and acute blood loss during delivery. Nowadays lot of attention is being focused on the post-partum anemia as it has alarming increase with little
recognition from health care settings. Even in good centers the post-partum follow ups are disappointing. Recent study from CMC &H has highlighted this issue (7).

At the national level it reflects the impact of the widespread interventions to prevent anemia in the country. So studies about the prevalence of anemia help us to track towards the goal of reducing anemia and to monitor the progress of reproductive health.

Women of reproductive age group are physiologically more vulnerable to pregnancy due to repeated blood loss during menstruation, demands of pregnancy and repeated conceptions with other social and cultural factors aggravating the disease.

Anemia combines with hypertension and sepsis forming the deadly triad, the common cause for maternal mortality in India, even in tertiary centers (8). Anemia is the cause for 20% of direct maternal mortality and 20% of indirect maternal mortality. With only 16% of world’s area India contributes to 20% of maternal mortality.
Definition of Anemia

There are many definitions for anemia in the general population. During pregnancy, the standards are different from the non-pregnant definitions.

- Anemia, in general, is defined as low hemoglobin (Hb) concentration resulting in decrease in oxygen carrying capacity of the blood.
- Statistical definition: Hemoglobin less than 2 standard deviations below the mean for a healthy matched population.

In pregnancy, there are physiological variations in normal values.

- According to the WHO, anemia in pregnancy is defined as a hemoglobin value of less than 11gms/dl. Anemia is further graded as mild, moderate or severe as given below.

  Mild anemia : 10.0 - 10.9 g/dl
  Moderate anemia: 7.0 - 7.9 g/dl
  Severe anemia : < 7.0 g/dl

- WHO further defines post-partum anemia as hemoglobin less than 10.0gms%(9)
- According to Centre for Diseases Control and Prevention (CDC- USA) 1998, anemia in pregnancy is defined as a hemoglobin value less than the fifth percentile of the distribution of hemoglobin in a healthy reference population based on the stage of pregnancy.
First and third trimester Hb<11.0gms/dl
Second trimester Hb<10.5gms/dl

- The Federation of Obstetric and Gynecological Societies of India accepted this as the standard to be followed in India (10)

- The Indian Council of Medical Research (ICMR) defines anemia as follows:

  Mild  9.0 – 10.9 grams/dl
  Moderate 7.0 – 8.9 grams/dl
  Severe <7.0 grams/dl
  Very severe <4.0 grams/dl

- The National Academy of Sciences Panel on Nutrition and Pregnancy defines anemia as serum ferritin level less than 12 micro gram/L (12)
Global and Indian scenario

WHO has estimated the prevalence of anemia as 14% in developed countries, 51% in developing countries and 65 to 75% in India (13).

South East Asian countries have the highest prevalence of anemia in world. WHO has noted that India has the highest prevalence among the South East Asian countries. More important fact is that India contributes up to 80% of the maternal deaths in South East Asia.

According to WHO (World Health Organization), anemia is taken as low public health importance when the prevalence is less than 20%, moderate when it is between 20 to 39.9% and severe when the prevalence is 40% and more of the population.

- Classification of anemia as a problem of public health significance

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<th>Prevalence of Anemia</th>
<th>Category of Public health significance</th>
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<td>&lt;4.9 %</td>
<td>No public health problem</td>
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<tr>
<td>5.0 to 19.90%</td>
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<tr>
<td>20.00 to 39.9 %</td>
<td>Moderate public health problem</td>
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<tr>
<td>&gt;40.0%</td>
<td>Severe public health problem</td>
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</table>
Worldwide Prevalence of Anemia, by severity

Severity of Anemia
- Normal (<5.0%)
- Mild (5.0-19.9%)
- Moderate (20.0-39.9%)
- Severe (≥40.0%)
- No data
Global Prevalence of anemia is 40%, mainly affecting the vulnerable group of the population, the women (35% non-pregnant, 51% pregnant) and children.
Worldwide the prevalence is 20% in Western Europe, 29% in North America, 44% in Africa and 79% in South East Asia. Among south east Asian countries 74% in Bangladesh, 68.5% in Bhutan, 51% in Indonesia, 68% in Maldives, 52% in Myanmar, 40% in Nepal and Srilanka, 13.4% in Thailand and 87.5% in India.

Among this 13% belong to mild and 57% to moderate and 12% to severe anemia according to ICMR in India.

According to NFHS III, the prevalence of anemia has increased from 52.0% (NFHS II) to 57.9% and there has been no decline in this disease over the past 3 decades.
In 2001, Government of India had grouped eight Indian states into one group known as Empowered Action Group (EAG) states. They are Bihar, Jharkhand, Uttar Pradesh, Rajasthan, Orissa, Assam, Madhya Pradesh, and Chhattisgarh. These states have 45% of the Indian population in them but they lag behind so much in their socio demographic, economic and health dimensions when compared to other states. So the Government of India focuses on improving the anemia status in these states as a marker of their health status improvement. (14)

Among the EAG states Assam is the worst affected with 72% followed by Haryana (69.7%) and Jharkhand (68.4%). An important point to be noted is that the available evidence suggests that in nineties in India the magnitude of reduction in anemia cases is less than other South East Asian countries.

The prevalence has been estimated by 5 major surveys in India

1. National Family Health Survey (NFHS) 2
2. National Family Health Survey (NFHS) 3
3. District Level Household Survey (DLHS)
4. Indian Council of Medical Research (ICMR) Micro nutrient survey
5. National Nutrient Monitoring Bureau (NNMB) Survey
Causes of high prevalence of Anemia in India

1. Dietary Habits: Consumption of lower bio availability foods like rice, maize, wheat, beans compared to high bio availability foods like meat, fish poultry and ascorbic acid.

Avoidance of certain foods during pregnancy - Food faddism, may be due to dislike or cultural beliefs. E.g.Papaya is not allowed in pregnancy.

Ingestion of soil or other non-edible substances – Pica

2. Socio-cultural factors: Due to patriarchal nature of our society women are discriminated from birth. This results in an attitude of neglect resulting in inadequate nutrition right from childhood. This results in anemia in female children and adolescence and womanhood. After marriage a woman’s status in the family and society is determined by her reproductive performance, especially in giving birth to male children. Women are supposed to offer their husbands the best of everything in the household including the food they have. So most of the time woman eats the left-over food after everyone had finished their food.

3. Defective absorption : Helminthiasis (hook worm),amebiasis, giardiasis, celiac disease and tropical sprue

4. Low iron stores and iron loss: Low iron stores as baseline, multiple pregnancies at short intervals (lack of contraceptive knowledge, want of many children or trying for male child), prolonged breast feeding without iron supplementation especially in case of a boy child.
5. Chronic diseases like malaria, Tuberculosis, schistosomiasis and hookworm infestation (average blood loss of 0.02 to 0.3 ml/day), HIV infection.

6. Menorrhagia not treated.

7. Abundance of other vitamins and trace metals deficiency: Vitamin B12, A, folic acid.

General classification of anemia

According to Etiology:

1. Physiological                 Pregnancy


                              Chronic - Hemorrhoids, hook worm infestations.

4. Acute on chronic infections   Malaria, TB, UTI etc.

                              Acquired - Microangiopathic hemolytic anemia, immune hemolytic anemia

6. Hemoglobinopathies           Sickle cell disease, sickle cell trait, beta thalassemia
According to Morphology:

1. Microcytic Hypochromic anemia (MCV < 80 fl) Iron deficiency, thalassemia

2. Normocytic Normochromic anemia (MCV 80 – 100 fl) Acute and chronic blood loss

3. Macrocytic anemia (MCV >100 fl) Folate, Vit B12 deficiency

**Erythropoiesis:**

Formation of blood in bone marrow is known as erythropoiesis and in an adult it passes through the steps shown in the following diagram originating from the pluripotent stem cells.

![Red Blood Cell Maturation Diagram](image-url)
After their average life span of 120 days the red blood cells degenerate by breaking down into hemosiderin and bile pigments.

**Factors required for erythropoiesis:**

1. **Proteins**: For synthesis of globin in hemoglobin

2. **Hormones**: Erythropoietin from kidneys plays a major role. In pregnancy, human placental lactogen and progesterone stimulate erythropoietin secretion enhancing the erythropoiesis. Thyroxine, androgens also help to some extent.
3. Minerals and trace elements:
   - Iron is the most important mineral required for the synthesis of hemoglobin. Other trace elements like zinc, cobalt and copper are also required for the synthesis of hemoglobin. Zinc is particularly useful in nucleic acid metabolism.

4. Vitamins:
   - Folic acid and Vitamin B 12 are very important for the nucleic acids synthesis in the erythro poietic cells. Vitamin B 12 is required for the early stages of synthesis of RNA and folic acid for the later stages of synthesis of DNA.
   - Vitamin C is useful for conversion of folic acid to folinic acid, which is vital for cell growth and division.
   - Vitamin A is required for immune functions, cell growth and differentiation and maintenance of integrity of epithelium.
**Hematological changes in pregnancy: Physiological anemia**

There is 40 to 45% increase in maternal blood volume as early as 6 weeks of gestation which reaches a maximum at 32 weeks of pregnancy. The increase in blood volume is mainly affected by an increase in plasma volume (40%) much more than the red cell volume (20%) resulting in the physiological anemia of pregnancy.

Physiological anemia has the following criteria:

1. Hemoglobin 10.0 grams/dl or PCV 30%
2. RBC 3.2 million/cubic mm
3. Peripheral blood smear examination: RBC morphology: Normocytic normochromic anemia
As seen in the diagram the physiological anemia is more pronounced in the second trimester of pregnancy.

Plasma Volume: Both fetal and maternal production of estrogen and progesterone contribute to the increase in plasma volume. Production of aldosterone is enhanced by progesterone. Both estrogen and aldosterone increase plasma renin activity resulting in increased sodium absorption and water retention through the renin-angiotensin aldosterone system. Also there is increase in potent vasodilator peptide plasma adrenomedullin in pregnancy significantly correlating with the increased blood volume.

RBC Volume: During the first eight weeks of pregnancy there is a decrease in RBC volume which slowly increases to pre pregnancy levels by 16 weeks. Increase in RBC volume is due to elevated erythropoietin levels and the erythropoietin effects of progesterone, prolactin and human placental lactogen.
As the increase in plasma volume exceeds the RBC volume increase it results in hemo
dilution resulting in decrease in blood viscosity resulting in reduced resistance to blood flow. In spite of
increased red cell mass this dilution brings down the hemoglobin by 2 grams%. Late in
pregnancy plasma expansion essentially ceases while red cell mass continues to increase.
Maternal blood volume returns to normalcy by 10 to 14 days post-partum.

**Advantages of Hemodilution and Hypervolemia:**

1. Demands of enlarged uterus and its hypertrophied vascular system are met
2. Nutrition to fetus and placenta
3. Protection of mother and the fetus from supine hypotension due to impaired venous return in
   supine position.
4. Protection of the mother from adverse effects of blood loss during delivery
5. Decreased blood viscosity helps in optimum gaseous exchange in maternal and fetal
circulation.
Pathophysiology of anemia:

To understand the pathophysiology of anemia, let us look into the normal and the compensatory delivery mechanisms of oxygen in anemia. In blood oxygen is carried in two forms:

1. Dissolved form in plasma as a physical solution
2. As oxyhemoglobin (chemical combination with Hb)

Hemoglobin is iron containing oxygen carrying metallo protein in the red blood cells. It contains two alpha and two beta chains. In normal people when the beta chains come closer together, oxygen gets bound to hemoglobin. When the oxygen is released the beta chains move apart allowing the 2, 3 Di PhosphoGlycerate molecules resulting in lowered affinity of hemoglobin for oxygen and improved delivery of oxygen to the tissues. These mechanisms result in sigmoid shape of the Oxygen Dissociation Curve.

Oxygen - Hemoglobin Dissociation curve (ODC):

The percent saturation is the number of sites in the hemoglobin molecule occupied by the oxygen (%) and it forms the Y axis. The small amount of dissolved oxygen is measured by the partial pressure of oxygen (PO2 in mmHg) and it forms the X axis. The relationship between the partial pressure of oxygen and the hemoglobin saturation is the oxygen hemoglobin dissociation curve.
1. Under normal conditions there is 100% saturation of hemoglobin in maternal arteries.

2. At all partial pressures fetal hemoglobin has increased affinities towards oxygen.

3. Steep portion of the curve represents unloading of oxygen in peripheral tissues like placenta.

- Upper oxygen association curve (alveolar capillary environment) and the lower oxygen dissociation curve (tissue capillary environment). Shifts of the curve at the steep portion have greatest impact because they affect oxygen delivery.
- The curve is shifted to left by increase in pH, decrease in 2,3 DPG in RBCs, decrease in temperature leading to a lower than normal O2 tension saturates Hb in the lung and subsequent release of O2 to the tissues occur at lower than normal capillary O2 tension (Haldane Effect).

- The curve is shifted to right by decrease in pH, increase in 2,3 DPG, increase in temperature reduce the affinity of hemoglobin to oxygen leading to increase in P50 facilitating the unloading of oxygen in peripheral tissues (Bohr Effect)(16)
In anemia there are other compensatory mechanisms come into play to maintain the oxygenation as follows:

1. Increase in CO and shift in ODC.
2. Increase in 2,3 DPG concentration in RBC.
3. Increase in temperature will shift the curve to left.
4. Increase in pH will shift the curve towards left.
5. Release of renal erythropoietin and decrease in blood viscosity
6. Redistribution of blood flow: To allow continuous blood flow to vital organs there is selective vaso constriction of some non vital organs blood flow. There is shunting of blood flow away from skin results in pallor, the cardinal sign of anemia.
7. Increased Cardiac Output and heart rate.

**Iron deficiency anemia**

Iron deficiency anemia is considered as prototype of anemia and the health burden of anemia can be extrapolated from the global prevalence of anemia. We will concentrate mainly on iron deficiency anemia in our study.
Iron metabolism

Iron comprises 5% of the earth’s crust. Because of its redox potential it is useful in evolving biological processes (17). The most abundant iron containing protein in humans is hemoglobin.

Three variables predominantly reflect the balance of iron metabolism in healthy individual:

1. Nutritional intake
2. Iron loss
3. Current demand

- Nutritional Intake: Daily iron requirement on an average is 4 mgs/day (ranging from 2.5 mgs per day in early pregnancy, 5.5 mgs per day in mid pregnancy to 6.6 mgs per day from 32 weeks onwards). Iron absorption increases during pregnancy from normal 10% to 20 to 30%. Iron is present in diet as heme iron and non heme iron from non-vegetarian and vegetarian diets respectively.

Dietary sources rich in Iron:

1. Vegetarian:
   - Green leafy vegetables – Spinach, mustard, fenugreek, drumstick leaves
   - Cereals – Whole wheat, bajra, jowar
   - Pulses – Green peas, beans, ground nuts
   - Fruits – Apple, banana
   - Others – Dates, jiggery
2. Non Vegetarian :

   Liver, meat – Good sources

   Fish, egg – Medium sources

**Factors enhancing iron absorption from the diet:**

1. Heme iron, proteins, meat
2. Ascorbic acid, fermentation, gastric acidity
3. Ferrous iron, alcohol, low iron stores
4. Increased erythropoietin activity like high altitude, hemolysis, bleeding

**Factors inhibiting iron absorption from the diet:**

1. Phytates in cereals
2. Oxalates in vegetables
3. Tannins in tea, poly phenols in coffee
4. Calcium, alkalies, antacids
5. Decreased erythropoiesis
6. Infections, iron excess.
7. Drugs like alpha dopa, ciprofloxacin, cimetidine
Iron Absorption:

Iron absorption mainly occurs from the duodenum and the proximal jejunum. Non heme iron is mostly in ferric (Fe 3+) form and it has to be reduced to ferrous (Fe 2+) form to get absorbed. After absorption it is again oxidized to ferric form in the cell.

Mucosal block theory: Ferric iron combines with Apo ferritin to form ferritin. Once Apo ferritin is saturated with ferric iron it acts as a mucosal blocker and further iron absorption is prevented. But recent isotopes study challenge this theory and now it is said that the iron combines with Apo ferritin to form ferritin which gets deposited in the intestinal wall cells and later gets desquamated. The iron which does not combine with Apo ferritin is absorbed and circulated in the plasma as ferric form combined with transferrin.

Iron Uptake into the Blood

[Diagram showing the process of iron uptake into the blood]
Absorption from heme iron is 2 to 3 times more from non heme iron. Heme iron is present in ferrous form and it is absorbed through heme receptors. Iron is subsequently released from the heme molecule by hemeoxygenase.

Transport of iron is by transferrin, a beta globulin present in blood.

- **Storage of iron:**

  Stored in the reticulo endothelial cells in liver, spleen, bone marrow as,

  1. Ferritin – Major source
  2. Hemosiderin

- **Distribution of body iron:**

  1. Hemoglobin 65 to 70 %
  2. Stores (ferritin, hemosiderin) 20 to 25 %
  3. Myoglobin, enzymes (e.g. Cytochromes) 5 to 10 %
  4. Plasma iron (bound to transferrin) 0.1 to 0.2 %

- **Excretion of iron:**

  1. Daily loss is up to 0.8 to 1.0 mg, in exfoliated GI mucosal cells, sweat, stool and urine.
  2. Menstruation causes 1.0 mg /day extra loss.
- **Iron deficiency:**

  Occurs in three stages:

  1. Depletion of iron stores - low serum ferritin levels
  2. Decrease in serum iron and increase in TIBC - normal hemoglobin levels
  3. Iron deficient anemia - low hemoglobin levels

  So, decrease in hemoglobin estimation represents the very last stage of iron deficiency anemia.

  According to WHO, hemoglobin estimation and serum ferritin level measurement are considered as the best markers of anemia prevalence in a community level.

**Iron homeostasis in Humans:**

Each day roughly 20 mgs of iron is recycled between erythrocytes and circulating transferrin.

This recycling pathway is supported by iron absorption, erythrophagocytosis, hepatic iron stores and iron incorporation into hemoglobin.
The diagrammatic representation is:

Note about the key iron regulatory protein, Hepcidin (18) secreted by the liver, negatively impacts the iron metabolism. It blocks both non heme iron absorption from the diet and iron mobilization from macrophages and hepatocytes. Hepcidin production is induced by iron stores and inflammation and is suppressed by erythropoietin activity and hypoxia. As few studies are only available more studies are needed to assess the diagnostic utility of hepcidin in pregnancy.
Iron transport across the placenta:

Placenta transports all the iron required for the baby’s growth and development from the mother by active transport. The iron is obtained from three primary sources (18):

A. Dietary sources of Iron (Fe)

Approximately 13 mgs of Fe is consumed by pregnant woman per day (12 mgs of heme iron and 1 mg of non heme iron). Of this 25% (3-4 mgs) is absorbed as transferrin bound iron into the Fe pool

B. Catabolism of senescent RBCs produce 10 times (20mgs) more Fe into the system.

C. Intravascular RBC breakdown and body iron stores contribute to additional 1-2mgs of Fe.

Oxygen transport across the placenta:

Gases cross plasma membranes by simple diffusion (Fick’s law). Diffusion of oxygen occurs in several steps. 100 ml of maternal arterial blood contains 0.3 ml of dissolved oxygen and 20ml of oxygen bound to the hemoglobin under normal conditions. The oxygen carrying capacity of 1 gm. of hemoglobin is 1.34 ml. So for an average adult with 15 grams of hemoglobin, the amount of oxygen bound to hemoglobin will be 20.1 vol % O2.

Always the dissolved oxygen and the hemoglobin bound oxygen are in equilibrium. Only the dissolved oxygen can cross the syncytiotrophoblast. So most of the oxygen transported to the fetus has to dissociate first to get absorbed and travel through the erythrocyte membrane (18).
Transport of Oxygen across the placenta occurs as follows (19):

a. Hemoglobin – oxygen dissociation in erythrocytes
b. Diffusion through the RBC membrane
c. Diffusion across syncytiotrophoblast
d. Diffusion across basement membrane and villous stroma
e. Diffusion across fetal endothelial blood vessel
f. Diffusion through fetal erythrocyte membrane
g. Fetal hemoglobin oxygen binding
**Predisposing Factors for anemia in Pregnancy:**

1. Pre pregnant anemic status as in Indian population

2. Physiologically increased demands of iron, folic acid, vitamin B12

3. Decreased intake (Hyperemesis, poor diet, irregular meals)

4. Multiple gestation

5. Molar pregnancy

6. Infection (Malaria, asymptomatic bacteriuria, Tuberculosis, HIV)

7. Hemorrhoids, worms’ infestation

8. Drugs induced (Anti folate drugs – Anti convulsants)

**Effects of anemia on Mother**

Ante partum:

1. Preeclampsia, folate deficiency (31.2%)

2. Infection through effects on immune function

3. Cardiac Failure

4. Preterm labor (28.2%)
5. Inadequate weight gain during pregnancy
6. Poor work capacity and performance (9)

Intra partum:

1. Uterine dysfunction
2. Postpartum hemorrhage
3. Cardiac failure
4. Shock
5. Abruptio placentae (20)

Post-partum:

1. Post-partum hemorrhage and shock
2. Sub involution
3. Failing lactation
4. Puerperal sepsis
5. Thromboembolism
6. Cardiac failure
7. Poor working capacity and general well being
8. Depression, disturbances of post-partum emotions and cognition (21)
Effects of anemia on fetus:

1. Fetal growth restriction (22)
2. Increased perinatal mortality and morbidity
3. Preterm birth
4. Intra uterine death
5. Early infantile anemia
6. Behavioral abnormalities
7. Cognitive skills impairment and affective disorders

Clinical Features of Anemia in Pregnancy

Symptoms:

1. Mild anemia:
   Asymptomatic usually
2. Moderate anemia:
   Weakness, fatigue, lassitude, exhaustion, giddiness, breathlessness, indigestion
3. Severe anemia: Three distinct stages are described as follows:
   Compensated, decompensated and in failure. Patient presents with worsening of palpitations, breathlessness, pedal edema at times even with anasarca. At presentation to the hospital one third of them are in failure. A blood loss of even 200 ml at this stage produces shock and death in these patients.
Signs:

1. Mild anemia may not have signs, moderate and severe anemia will have,
2. Pallor, nail changes (koilonychia)
3. Cheilosis, glossitis, stomatitis
4. Pedal edema
5. Signs of hyper dynamic circulation
6. Signs of congestive heart failure
7. Plummer-Vinson syndrome- Rare condition with IDA, nail changes and dysphagia.

- **Mechanism of development of Pallor:** Pallor develops due to reduced amount of oxygenated hemoglobin in the blood leading to decreased oxygen carrying capacity of the blood and also due to reduced peripheral perfusion resulting in decreased oxyhemoglobin in the tissues.

- **Studies have suggested correlations between iron deficiency and chronic mental disorders in women (CMD).** The reasons suggested are that anaemia contributes to alteration in the myelination and neuro transmitter metabolism and function which in turn leads to fatigue, irritability, apathy, inability to concentrate and finally depression. Beard et al showed a significant correlation between iron deficiency anaemia and increased Edinburgh post natal depression scale score in South Africa. In Iran, USA postpartum depression symptoms had been correlated to severity of iron deficiency anaemia. As these studies were cross sectional, the investigators conclude that IDA proceeded and contributed to CMD in post-partum women (21)
Diagnosis of iron deficiency anemia

1. **Hemoglobin Estimation**:

   The most practical method of diagnosis. There are many methods available for hemoglobin estimation. But cyanmethemoglobin method is the most accurate. Because of its simplicity, Sahli’s method (acid hematin method) is widely used. The other methods like HomoCue can be used in the field as a screening method.

   Anemia is graded according to the WHO classification(1):
   - **Mild**: 10.0 to 11.0 grams%
   - **Moderate**: 9.9 to 7.0 grams%
   - **Severe**: < 7.0 grams%

   There are so many methods used for the estimation of hemoglobin levels in blood depending upon the place, facilities and the available finances. The methods commonly used are:

   a. **Visual color comparison method**
      
      E.g. Sahli’s acid hematin method: Hemoglobin is converted into acid hematin by the addition of hydrochloric acid. Then its color change is calibrated against the comparator block.

   b. **Spectrophotometric method**: Reference Method

   The method for hemoglobin determination is the cyanmethemoglobin method (This is a type of colorimetric method). The principle of this method is that when blood is mixed with a solution containing potassium ferricyanide and potassium cyanide, the potassium ferricyanide oxidizes
iron to form met hemoglobin. The potassium cyanide then combines with met hemoglobin to form cyanmethemoglobin, which is a stable color pigment read photo metrically at a wave length of 540nm following Lambert-Beer’s Law and is directly proportionate to the hemoglobin levels in the blood.

Three advantages of the cyanmethemoglobin method are:

1. Measures all forms of hemoglobin except sulfhemoglobin
2. Can be easily standardized
3. Cyanmethemoglobin reagent (also called Drabkin's solution) is very stable

· Hemo Cue photometer Method:
  
  In resource poor settings where automated machines are not available, or unable to reach health care facility immediately like in remote areas the Hemo cue system can be very useful. The advantages being simple to use, portable, requires only small amount of capillary or venous blood, inexpensive, does not require refrigerator or even electricity and gives immediate digitally displayed results. Do not require special training to promote its use by field workers. Results are comparable to the routine tests (23).
Peripheral blood smear stained with Leishman stain is very useful in studying the morphology of red blood cell and to find out the type of anemia.

**Normal:** Normocytic (normal sized RBCs), normochromic (normal colored RBCs) cells

**Iron Deficiency Anemia:** Hypochromic (paler RBCs), microcytic (smaller RBCs) picture with anisocytosis (variation in the size of the cells) and poikilocytosis (variation in the shape of the cells) with or without target cells. E.g. Tear drop cells, pencil shaped cells.
3. **Reticulocyte Count:**

Reticulocytes appear slightly bluer than other red cells when looked at with Romanowsky’ stain. Reticulocytes are relatively larger. Normal range is 0.5 to 2.5% and it’s a good indicator of bone marrow activity.

Increased number of reticulocytes known as reticulocytosis and it reflects an increased production of red blood cells in order to overcome severe or chronic loss of blood e.g. Hemolytic anemia.

Abnormally low reticulocyte count will be seen in iron deficiency anemia, vitamin B12 anemia, pernicious anemia, problems with renal erythropoietin.
4. **Hematocrit estimation:**

Reflects the percentage of RBCs in specific volume of blood. Low hematocrit indicates decrease in number or decrease in size of RBCs or an increase in plasma volume.

Normal is 32 to 36 %. It is less than 30 % in iron deficiency anemia.

5. **Blood Indices :**

**MCV:** Mean Corpuscular Volume is the average volume of the red blood cell. Normally it is 80 to 100 femtoliters.

It is increased in macrocytic anemia, can go up to 150 flits. It is decreased in microcytic anemia, upto 60 to 70 flits. In thalassemia it is lower even though the hemoglobin is normal.

**MCH:** Mean Corpuscular Hemoglobin is the average mass of hemoglobin per red blood cell. Normally it is 27 to 31 Pico grams. Calculated by dividing the total mass of hemoglobin by the number of red blood cells in a given volume of blood. It is reduced in hypochromic anemia.
**MCHC:** Mean Corpuscular Hemoglobin Concentration is the single most sensitive index of iron deficient anemia as it is independent of RBC count. It is a measure of concentration of hemoglobin in a given volume of packed red cells. Calculated by dividing the hemoglobin by the hematocrit. Normal is 32 to 35 grams /dl. It is decreased in microcytic anemia, normal in macrocytic anemia, increased in hereditary spherocytosis.

6. **Serum Iron:**

   Normal is 40 to 175 micro grams / dL(15). It is below 30 in IDA.

7. **Total Iron Binding Capacity:**

   TIBC – Normal is 216 to 400 micro grams /dL(15). It is elevated beyond 400 in IDA.

8. **Serum Ferritin:**

   High molecular weight glyco protein in plasma giving a picture about the iron stores.

   Normal level is 50 to 145 Nano grams/ml. First test to go abnormal in IDA, not affected by recent iron intake. Levels less than 15 Nano grams is diagnostic of IDA.
9. **Serum Transferrin Saturation:**

Ratio of serum iron and total iron binding capacity multiplied by 100. Normally it is 16 to 60 % (15). Less than 15 percent is taken as IDA. It is the second parameter to become abnormal in IDA after serum ferritin (24).

10. **Free erythrocyte Protoporphyrin level (FEP):**

The third estimation of iron status, measures non complexed, non hemeproporphyrin concentration in the blood. Normally it is 40 micro grams /dL(25). The test becomes abnormal after 2 to 3 weeks of depletion of iron stores.

From the above serum iron studies,

- Reduced stores : Decreased ferritin only
- Iron Deficiency without Anemia : Decreased ferritin, decreased transferrin saturation, increased FEP
- Iron Deficiency Anemia: Decreased ferritin and transferrin saturation with increased TIBC and FEP.

11. **Serum Transferrin Receptors:**

Specific and sensitive marker and best indicator for IDA in pregnancy. Normal level is 4 to 9 mg/ L. But the disadvantage is being very costly.
12. Bone Marrow Examination:

In IDA without stain for iron it is seen as below

Special staining with potassium ferrocyanate
Special staining with potassium ferrocyanate as shown in the above picture will show blue granules of iron inside the erythroblasts is the most accurate method for iron stores.

Indications for Bone marrow examination:

1. No response to iron therapy after 4 weeks

2. Sideroblastic anemia

3. Aplastic anemia

4. Kalaazar

5. To differentiate alpha thalassemia from chronic anemia
13. **Urine Examination:**

Routine and microscopy with culture at times for asymptomatic bacteriuria and hematuria (occult blood for schistosomiasis)

14. **Stool Examination:** Ova and cysts of hook worm and occult blood to be examined.

15. **Peripheral Smear for Malarial parasite where the disease is prevalent**

16. **Sputum examination and Chest X ray (with abdominal shield) where tuberculosis is suspected.**

**Treatment of iron deficiency anemia**

The two most common causes of anemia in pregnancy and puerperium are iron deficiency and acute blood loss. It is very clear that we have to treat even the milder forms of anemia in pregnancy as it is often impossible to predict the course of the condition. The factors to be considered are:

1. **The severity of anemia**
2. **Time present until delivery**
3. **Additional risks e.g. Pre-termlabor**
4. **Maternal co-morbidities**
5. **Patient’s own wishes e.g. Refusal to accept blood and blood products as Jehovah’s witness**
Main treatment Options:

1. Oral iron
2. Parenteral iron
3. Stimulation of erythropoiesis with growth factors
4. Heterologous blood transfusion

Oral Iron

- Gold standard for the treatment of mild to moderate iron deficiency anemia.
- It is cheap, effective and safe in most of the cases.
- It is not clear yet whether intermittent iron therapy like weekly once or twice is similar to or better than daily oral administration. Studies are currently underway\(^{(26)}\). The ideal dosage is also not clear.
- The absorption rate is inversely proportional to the administered dosage. The recommended dose is 80 to 160 mgs per day.
- Iron (II)Salts: Ferrous salts are readily absorbed than ferric salts, present in tablet or liquid forms. Liquid forms are used in intestinal achlorhydria, e.g. following gastro intestinal surgery since tablets show poor solubility. Iron salts e.g. Ferroussulphate (most commonly used), ferrous Gluconate, ferrous succinate, ferrous fume rate.
- Iron (III)Compounds: Have very low bio availability and so not suitable for oral administration. They form virtually non absorbable and insoluble complexes in the intestine.
• Combined preparations like inclusion of multi vitamins and trace elements do not offer any advantage(27). In fact the addition of magnesium, calcium and zinc can inhibit the absorption of iron. Adding different salts in one preparation also does not help.

• Special Preparations :
  1. Carbonyl iron: Obtained by thermal decomposition of iron penta carbonyl. The obtained iron has high purity (> 98%) and uniform particle size. Easily absorbed and less toxic than available ferrous salts. Has a high safety range. eg. Livogen
  2. Ferrous bisglycinatechelate: Chelated form of iron where 2 glycine molecules are added to 1 iron molecule. Does not cause gastric irritation and constipation.
  3. Ferrous Feredetate: Contains ferric sodium EDTA. Iron is present in an unionized form. Not an astringent and does not discolore teeth, available as chewing tablet.
  4. Ferrous ascorbate: Synthetic molecule of ascorbic acid and iron. Ascorbic acid enhances the absorption of iron and there is no action of food inhibitors.
  5. IPC (Iron Poly Maltose) complex: Class of slow-release iron preparations - dextriferron, poly maltose acts like a casing around the trivalent ion ensuing the slow release of the iron from the complex.

  The advantages are: Less side effects profile, can be taken along with meals, reduced formation of oxygen radicals and so reduced plasma lipid peroxidation.

• WHO recommendation: Universal iron supplementation for pregnant women (60 mgs of elemental iron with 250 micro grams of folic acid once daily for countries with a prevalence of anemia less than 40% and for an additional 3 months post-partum if the prevalence is more than 40%.
• Ministry of Health, Government of India recommendation: 100 mgs of elemental iron with 0.5mg of folic acid in the second half of pregnancy for 100 days for prevention of anemia.

• Routine supplementation is considered as cost effective in countries like India as most women have depleted iron stores and will not get iron over load. Estimation of serum ferritin is costly.

**Amount of elemental iron in different iron formulations:**

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Dose of the salt (mgs)</th>
<th>Elemental Iron mgs% per tab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe- Sulfate (hydrous)</td>
<td>300</td>
<td>60 (20%)</td>
</tr>
<tr>
<td>Fe- Sulfate (dried)</td>
<td>200</td>
<td>65 (32.5%)</td>
</tr>
<tr>
<td>Fe-Fumarate</td>
<td>200</td>
<td>66 (33%)</td>
</tr>
<tr>
<td>Fe-Gluconate</td>
<td>300</td>
<td>36 (12 %)</td>
</tr>
<tr>
<td>Fe-Bisglycinate</td>
<td>300</td>
<td>60 (20%)</td>
</tr>
<tr>
<td>Carbonyl iron</td>
<td>100</td>
<td>98(98 %)</td>
</tr>
<tr>
<td>Na - feredetate</td>
<td>231</td>
<td>33 (14 %)</td>
</tr>
</tbody>
</table>

• Side Effects of Oral Iron therapy (30%): Nausea, gastric discomfort, eructation

Diarrhea, constipation, flatulence
Indicators of response to therapy

1. Feeling of well being
2. Better appetite
3. Improved look of the patient
4. Hematological: Reticulocytosis – 0.5% rise within 7 to 10 days.\(^{28}\)

Increase in hemoglobin is delayed, 0.2 gm.% day or 0.7 gm.% per week or 2.0 gm.% in 3 weeks. If no improvement in 3 weeks with good patient compliance then the diagnosis should be reevaluated.

Reasons for non-response to Oral therapy:

1. Non compliance
2. Faulty absorption due to GIT disorders like celiac or crohn’s disease
3. Continuous blood loss like hook worm infestation
4. Additional complications like renal failure
5. Infections which suppress erythropoiesis
6. Drugs that inhibit erythropoiesis like cyto toxic agents
7. Drug interactions leading to reduced absorption like tetra cyclines, trimethoprim, antacids such as omeprazole and cholestyramine. Whereas the reverse occurs with gyrace inhibitors, l-thyroxin and penicillamine
8. Incorrect diagnosis of iron deficiency
9. Associated other deficiencies like Vitamin B 12
**Parenteral Iron Preparations: Indications**

1. Poor compliance
2. Severe anemia
3. Intolerance to oral iron
4. Insufficient or no response to oral iron
5. Insufficient absorption to oral iron due to intestinal disease
6. Need for rapid efficacy
7. Combination with recombinant human erythropoietin (rhEPO) for prevention of functional iron deficiency.

**Mechanism of parenteral Iron:**

The natural mechanisms of intestinal iron uptake and protein binding are bypassed by this route of administration. Because of this non protein bound iron circulates as free iron which is toxic as it leads to peroxidation. Free iron enhances the formation of oxygen and hydroxide radicals leading to cell and peroxidation. Free iron enhances the formation of oxygen and hydroxide radicals leading to cell and tissue damage by peroxidation. So parenteral iron should not be given without knowing the iron status in the body. Available forms:(29)

1. Type I complexes – Iron dextrin and iron dextran (Imferon)
2. Type II complexes – Iron hydroxide sucrose complex (Imax S, Orofer S)
3. Type III complexes – Iron hydroxide sorbitol complex (jectofer,jectocos), iron Gluconate, iron ammonium citrate
Type I complexes:

- Have high molecular weight ( >1,00,000 Daltons ) and high stability leading to slow release
- Half-life is 3 to 4 days, associated with severe allergic reactions, not excreted
- Can be given both IM ( intra muscular ) and IV ( intra venous )

Type II complexes:

- Molecular weight of 30,000 to 1,00,000 with medium stability
- Half-life is 5.5 hrs. And maximum plasma concentration reach in 10 minutes, 30% gets excreted in urine. Used as intra venous preparation only.
- Oldest IV preparation available and first line in patients with chronic kidney disease.
- Ferric car boxy maltose is designed for rapid IV infusions (15mins), single dose of 1000 mgs.

Type III complexes:

- Molecular weight of less than 50,000 Daltons and are low stability labile complexes
- Given as intra muscular only, 1 ml contains 50 mgs of elemental iron.
Complications associated with the use of parenteral iron

1. Local: Intra muscular injections are painful, local skin discoloration, abscess formation
2. CVS: Chest tightness with pain, hypotension, tachycardia, flushing, arrhythmias.
3. Dermatologic: Urticarial rashes, purpura, cyanosis
4. GIT: Abdominal pain, nausea, vomiting and diarrhea
5. Musculoskeletal: Arthralgia, arthritis, myalgia, cellulitis
6. Respiratory: Dyspnea, bronchospasm, wheeze, respiratory arrest
7. Hematologic: Lymphadenopathy, leukocytosis
8. CNS: Convulsions, seizures, syncope

Pre requisites for the Parenteral iron therapy in Pregnancy:

1. Anemia, Hb less than 10.0 grams%
2. Confirmation of iron deficiency (Serum Ferritin levels < 15 micro grams / L)
3. Completion of first trimester
4. Failure of a 14 day course of iron therapy
5. No Hemoglobinopathies or liver disease
6. No acute or chronic bacterial infection
7. No known iron overload
**Calculation of Total Dose Infusion (TDI):**

Required dose in mgs = \((2.4 \times (\text{target Hb} - \text{actual Hb}) \times \text{pre pregnancy weight in kgs} + 1000\) mgs for stores replenishment\(30\). Oral iron has to be stopped while parenteral route is on.

**Intra Muscular Route:**

Test dose of 0.5 ml (25mgs) should be given as IM over 30 seconds.

75 to 100 mgs per day is given on alternate days. Given as deep IM, in the buttock’s upper and outer quadrant by \(\square Z \square\) technique (displacement of the skin laterally prior to injection) to prevent skin staining using a 19 G or 20 G needle, 2 to 3 inches long.

**Intra Venous Route: Precautions**

1. Before therapeutic dose IV test dose, 0.5 ml intravenously over 1 minute should be given.
2. Inj. Adrenaline (0.5 ml of 1 in 1,000 solution SC or IM) and other emergency resuscitative measures should be ready in case of anaphylactic shock and anaphylactic reactions.
3. At least 1 hour after test dose is required before the full dose.
Role of Erythropoietin:

Stimulation of erythropoiesis by the growth factor recombinant erythropoietin (rhEPO), a glycoprotein of molecular weight 30,400Daltons identical to natural erythropoietin has been used clinically since 1986, especially in patients with renal disease who have deficiency of erythropoietin. Others can be patients with malignancy, HIV infection and peri operative treatment of anemia in Jehovah’s witness(29).

Concomitant iron availability should be sufficient to prevent functional iron deficiency. One single dose of 150 to 300 units per kg, intra venous is usually sufficient.

Blood transfusion: Indications

1. Severe anemia near term or in labor
2. Not responding to oral or parenteral therapy
3. Associated infection
4. Thalassemia and sickling disorders in pregnancy
5. Anemia due to acute blood loss like APH and PPH (the primary principle is replacement therapy with fluids to maintain perfusion)

Packed cells transfusion is preferred than whole blood transfusion as the patient will have,

- Less volume over load
- Less transfusion reactions
• Separated components can be used for other patients

• One pint of packed cells transfusion increase the Hb by 0.8 to 1.0gms %

**Exchange Transfusion:** Particularly useful in patients with severe anemia in failure. Packed cells are given through ante cubital vein and whole blood is withdrawn from the femoral vein on the opposite side. To keep negative balance blood withdrawn should be 200 ml more than the transfused amount.

**Adverse Reactions to blood transfusion:**

• Transfusion Reactions :

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Risks per Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute fatal Hemolytic</td>
<td>1 : 1,00,000</td>
</tr>
<tr>
<td>Delayed Hemolytic</td>
<td>1 : 1,000</td>
</tr>
<tr>
<td>Febrile (no hemolytic)</td>
<td>1 to 4 : 100</td>
</tr>
<tr>
<td>Allergic (urticarial)</td>
<td>1 to 4 : 100</td>
</tr>
<tr>
<td>TRALI</td>
<td>1 : 5000</td>
</tr>
<tr>
<td>Anaphylactic Shock</td>
<td>1 : 1,50,000</td>
</tr>
</tbody>
</table>
• Infections:
  1. Viral: Hepatitis B, C, HIV, Cytomegalovirus
  2. Bacterial: Syphilis, gram negative bacteria
  3. Parasitic: Malaria

• Volume overload

• Others:
  1. Hypothermia
  2. Citrate toxicity
  3. Hyperkalemia (secondary to increased potassium in stored blood)
  4. Hypocalcaemia (secondary to binding of calcium by citrate based anti-coagulation)
  5. Iron overload (in thalassemia)
  6. DIC
  7. Rarely air embolism

**Key Principles for blood transfusion In Obstetrics:**

1. Even the mild forms of anemia need to be treated in order to avoid blood transfusions later
2. Blood losses should be minimized
3. Transfusion risks should be weighed up at decision of blood transfusion
4. Guidelines to be followed while making the decision of blood transfusion
5. If at all possible consider patient’s wishes
6. Trained staff should carry out and monitor the transfusion

7. Good record of indications, circumstances and complications should be maintained (29)

In modern Obstetrics blood transfusion should be the exception rather than the rule

Prevention of Iron Deficiency Anemia

1. Prevention should start from childhood with main emphasis to prevent anemia in adolescent females.

2. Prenatal checkup to prevent women entering pregnancy with anemia

3. Dietary modifications: Consumption of iron rich foods, cooking in iron utensils, avoidance of excessive coffee and tea, avoidance of over cooking.

4. Iron and folate supplementation of adolescent and non-pregnant women of child bearing age. E.g. Twelve by twelve initiative aims at reaching 12 grams of hemoglobin by the age of 12 years by prophylactic iron therapy and dietary advices.

5. Treatment of hook worm infestations by single dose of albendazole (400 mgs) or with mebendazole 100 mgs twice daily for 3 days either before pregnancy or after the first trimester, in the start of second trimester of pregnancy where the prevalence of infection is more than 20% as a routine part of ANC (31)
6. Iron supplementation in pregnant women: Routine supplementation is considered cost effective in India as estimation of serum iron is costly and also most of our women are in a state of having depleted iron stores so the concern of iron overload is hardly present. Two groups, INACG (The International Nutritional Anemia Consultative Group) (32) and WHO (World Health Organization) recommend universal iron supplementation. WHO recommends from booking whereas the other group recommends from second trimester with 60 mgs of elemental iron per day. Evidence for this came from Mother Care Project in 1993 (9). The Cochrane data base has confirmed this positive response by reviewing 49 trials (9). There is 30 to 50% relative risk reduction of anemia in term for those on iron supplementation.

- WHO recommendation: (33) In areas with prevalence of more than 40% the iron and folic acid supplementation is to be continued for an additional 3 months post-partum. In areas with prevalence rate of less than 40% the supplementation is given for 6 months during pregnancy in a dose of 60 mgs of elemental iron with 400 micro grams of folic acid once daily as universal iron supplementation.

- Note: If six months duration cannot be achieved in pregnancy then continue to supplement during post-partum period for 6 months or increase the dosage to 120 mgs per day.

- Note: Supplements with less folic acid to be used only when supplements with 400 micro grams are not available.
• The iron supplementation to the pregnant mother should target to cover the entire reproductive cycle rather than just the pregnancy alone. At least it should cover the pregnancy and the entire post-partum period or the end of lactation so that the iron stores are replenished. Entering pregnancy in an iron deficient status actually fails the supplementation. A good pre pregnancy reserves of iron status increases the effectiveness of iron supplementation.(34)

• Ministry of Health and Family Welfare (MoHFW): (1) Government of India recommends 100 mgs of iron with 500 micro grams of folic acid for 100 days in the second half of pregnancy for prevention to all women. This is followed by same dosage for 100 days post-partum.

• Food fortification: Fortification of common salt with iron (35) and other food stuff like cereals, sugar, curry powder, milk, fish sauce, noodles, rice with iron compounds are also useful(36).

• To improve the compliance twice weekly injections of 250 mgs at 4 weeks interval after 16 weeks have also been suggested with adequate results.(37)

• Intermittent supplementation of oral iron like weekly and bi weekly also have been suggested (1). Preventive supplementation based on weekly dosing has proven efficacious. This weekly supplements of proper iron and folate should be community based rather than health service based, whereas the health care facilities should supervise it. It is almost equal to targeted fortification (34).
Health programmes for anemia control:

1. National Nutritional Anemia Prophylaxis Programme: As the nutritional anemia is the major health problem in India with the prevalence of anemia more than 40% (1) according to WHO, India was the first country to start a health programme for the prevention and control of anemia almost four decades back, in 1970.

According to this 60 mgs of elemental iron with 500 micro grams of folic acid will be provided to all pregnant women, lactating women, family planning acceptor women and children from age 1 to 11 yrs.

Now the Ministry of Health and Family Welfare has recommended 100 mgs of elemental iron with 500 micro grams of folic acid for 100 days in the second half of pregnancy followed by 100 days post-partum.
2. **National anemia control programme:**

Launched in 1970 to prevent nutritional anemia in mothers and children. Programme is being taken up by Ministry of Health and Family Welfare, Maternal and Child Health Division. Now it is a part of RCH programme. It is basically implemented through primary health centers and sub centers in association with ICDS (Anganwadi workers, ANMs).

It takes care of pregnant and lactating women, children and IUD (Intra Uterine contraceptive Device) acceptors. It focuses on three vital strategies:

- Promotion of iron rich foods consumption regularly
- High risk groups receiving iron and folic acid tablets
- Identifying and treating patients with severe anemia

3. **Twelve - by - twelve initiative for anemia control:**

Launched on 23rd April 2007, with the aim of reducing the incidence of anemia in India in adolescents in order to ensure healthy parenthood, in association with,

a. World Health Organization (WHO)

b. United Nations International Children Education Fund (UNICEF)

c. Federation of Obstetrics and Gynecological Societies of India (FOGSI)

d. Government Of India
**Objectives:**

a. To determine anemia prevalence in children aged 10 to 14 years  
b. To give nutritional guidance and treatment for children with anemia  
c. To vaccinate all children against tetanus and all girl children against rubella  
d. To deworm all children and treat malaria if present.

**Megaloblastic anemia:**

Next common cause of anemia in pregnancy is megaloblastic anemia caused by folic acid deficiency, up to 3 to 4% of all anemia in pregnancy. Both folic acid and Vitamin B12 can cause this picture but the more common is folic acid deficiency.

Occurs in patients with multi parity (up to 5 times), multiple pregnancy (up to 8 times), excessive cooking of food, alcohol and drugs like phenytoin and phenobarbitone intake.

Diagnosis is made by macrocytic erythrocytes in peripheral smear with MCV more than 100 fl. Hyper segmented neutrophils will be present. Serum folate levels less than 3 micro grams/dL is the first sign with reduced red cell folate levels. Bone marrow will show megaloblastic erythropoiesis. Increased serum Lactate De Hydrogenase levels in blood will be present.

Treatment is by Inj.Cyanocobalamine 500 micro grams with folic acid 15 mgs intra muscularly once weekly.
Effects on Fetus: Neural tube defects can be prevented by taking periconception folic acid, 400 micro grams per day.

Megaloblastic anemia due to Vitamin B12 deficiency occurs in strict vegetarians. Vitamin B12 is produced by certain microorganisms and it is absent in plants and that’s why strict vegetarians suffer more from megaloblastic anemia due to Vitamin B12 deficiency than the non-vegetarians.

Found in good amounts in meat, egg, fish and milk, not destroyed by cooking.

Decreased Vitamin B12 levels and increased methyl malonic acid are diagnostic.

**Dimorphic Anemia**

Presence of both iron and folic acid with dominance of one type is usually seen in tropical countries. Treated with both iron and folic acid.

**Thalassemia**

Common in Asian women, the blood picture resembles that of IDA, but there is elevated HbA2 in beta thalassemia trait. Another screening test is NESTROFT test. (Naked Eye Single Tube Red cell Osmotic Fragility Test). The principle behind this test is that the normal red cells resist lysis but the thalassemia cells do lyse when exposed to hypertonic saline. Patients positive for this test will undergo electrophoresis.

Prenatal diagnosis should be offered to patients with thalassemia.
RESULTS
The prevalence of anaemia in the study population (600) was 23.16% (139) and the normal patients constituted 76.83% (461). The mean haemoglobin was 11.7% with SD of 1.29.

The grading of anaemia was 13.67% (82) of mild anaemia, 9.33% (56) of moderate anaemia and 0.17% (01) of severe anaemia. Thus the prevalence of mild anaemia was high in comparison to other degrees of anaemia.
Age groups in this study were classified into less than 20 years, 20 to 24 years, 25 to 29 years, and 30 years and above. Patients were 8.33% (50) in less than 20 years, 31.33% (188) in 20 to 24 years, 40.50% (243) in 25 to 29 years, 30 years and above in 19.83% (119) patients.

The mean age was 25.97% with SD of 4.16.
Most of the pregnant women were from rural area 54.17% (325) compared to urban area 45.83% (275). Among those from rural area 24% (78) had anaemia compared to 22.18% (61) from urban area.
Figure No.4: Distribution of patients according to Religion

Religion wise most of them 79.67% (478) were Hindu patients, 7.17 % (43) were Christians and 13.17 % (79) were Muslims.

Among Hindus, 23.01 % had anaemia out of 478 patients (79.67%) which is very high as most of them were vegetarians (non heme iron) or they avoided non veg due to cultural reasons during pregnancy or due to poor socio economic status or due to large joint families where women are usually left over with only rice to eat.
In Christian patients 23.25% had anaemia out of 43 patients (7.17%) and among Muslim patients 24.05% had anaemia out of 79 (13.17%) patients. This can be explained by heme iron in their non-vegetarian diet along with less customs compared to Hindu patients.

In relation to their consultation most of them had made general appointments 64.33% (386) compared to private consultations 35.67% (214).

Regarding the Socio Economic Status we followed Modified Kuppuswamy’s scale 2012. In reference to this, the monthly income was more than Rs. 32,050 for 17% (102), more than Rs. 16,020 for 18.33% (110), more than Rs. 12,020 for 15.17% (91), more than Rs. 8010 for 23% (138), more than Rs. 4810 for 17.83% (107), more than Rs. 1600 for 6.33% (38), less than Rs. 1600 for 2.33% (14) of patients.

Educational Status: Among the total patients in this study 1% (6) was illiterate, 0.8% (5) had done primary schooling, 9.5% (57) were in middle school grade, 32.33% (194) had done high school, 35% (210) had done college level of education, 12.50% (75) were post graduates and 8.83% (53) were professionals.

Occupational Status: Majority of the sample population were not working during pregnancy and most of them had come and stayed at their mother’s house till confinement. They were 88.50% (531), followed by 6.33% (38) of professionals, 2.50% (15) of skilled workers, 1.33% (8) of unskilled workers, 0.83% (5) of clerks, 0.33% (2) of semi-skilled workers and finally 0.17% (1) of semi-professional patient.
To get the Socio Economic Class, all the above three variables were added up and grouped patients into Class I, Upper SEC in 4.83% (29) of patients, Class II, Upper/ middle class in 27.17% (163) of patients, Class III, middle/ lower middle class in 20.50% (123) of patients, Class IV, lower / upper lower in 46.83% (281) of patients and 0.67 % (4) only in Class V, Lower SEC.

Considering the type of family, 62.83 % (377) patients were from joint family and 37.17% (233) were from nuclear family.

Regarding the dietary patterns, 11.17% (67) of patients were pure vegetarians and 88.83% (533) were non vegetarians.
Being a tertiary centre most of our patients come here either for safe confinement or at times due to associated risk factors. Out of these 600 patients, 52.83% (317) had already had ANC outside. 47.17% (283) had come to CMC&H for their first antenatal check-up. Out of this 283 patients 89.40% (253) had their haemoglobin done outside and 38.34% (97) had no anaemia and 30.04% (76) had mild anaemia, 31.23% (79) had moderate and 0.40% (1) had severe anaemia.
Regarding parity, primi gravid mothers were 51.83% (311) and multi gravid mothers were 48.17% (289). 47.50 % (285) were in their first trimester on their booking visit, 31.50% (189) in their second trimester and 21 % (126) in their third trimester.
As India is endemic for hook worm and other infestations, the habit of foot wear usage both indoors and outdoors was asked for. Even though most of the patients are from rural area where walking in the fields or outside the house with bare foot is expected to be a routine, only 1.50% (9) of people had the habit of not using foot wear outside their house. 98.50% (591) were using foot wear outside regularly. Indoor foot wear usage was present in 13.83% (83) of patients and
86.17% (517) did not use foot wear indoors. Only 1.67% (10) had history of passage of worms and the rest 98.33% (590) did not have the history of worms passage in stools.

In the study other etiological factors like bleeding per rectum, bleeding from gums and any proceeding history of menorrhagia were asked for. 3.17% (19) of patients had bleeding per rectum, 9.83% (59) of patients had bleeding per gums and only 0.67% (4) of patients had menorrhagia history six months prior to conception.

Associated risk factors for chronic anaemia like history of malaria, tuberculosis, bleeding disorders diagnosed previously (there were 2 patients who were excluded from the study) or other illnesses like diabetes, hypertension, SLE were enquired. Only 3% (18) had prior history of malaria or tuberculosis.

Childhood history of jaundice or anaemia was enquired and was present in only 2.5% (15) of patients.

The Body Mass Index of study patients were calculated from their first visit weight itself as most of them did not know the pre pregnancy and weight and majority were in first trimester is is decided to take first trimester weight for BMI. Among the total patients, 47.67% (284) were in first trimester. Among them 68.3% were underweight, 49.3% were having normal weight, 41.3% were overweight, 37.5% were obese.
On analyzing the data, initially the frequency distributions of the individual variables were calculated.

Age variable was taken as more than 25 years (48.7%0 and less than 25 years (51.3%) as the mean age at pregnancy was found to be 25.97 with SD of 4.16.

Occupation was made into 2 groups, one group with house wives (88.5%) and other group of working women (11.5%)
Education level was taken as primary (illiterate, primary school), high school (middle and high school) and third level as college and above. Similarly the income was also made into three categories. The other variables were taken as independent variables only.

Univariate Analysis was done for socio demographic factors and significant p (0.047) value was obtained for occupation only.

Multivariate analysis for socio demographic factors revealed the following results:

Working mothers had 1.99 times more chances to develop anemia than the non-working group.

Then the Obstetric variables were taken into the bivariate analysis which showed p value significant for ante natal checkups and gestational age. On calculating the multivariate analysis the association between second trimester and anemia only had significant p value with Odd’s ratio of 1.98.

None of the other variables showed significant p values both in univariate and multivariate analysis.
Table 1: Frequency Distribution

<table>
<thead>
<tr>
<th>Variables</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
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</tr>
<tr>
<td>&lt;=25</td>
<td>308</td>
<td>51.3</td>
</tr>
<tr>
<td>&gt;25</td>
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<td>1-Hindu</td>
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<td>3-Muslim</td>
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<td><strong>Ante Natal Care</strong></td>
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<tr>
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DISCUSSION

Iron deficiency is the most common cause of anaemia in pregnancy. It is not only the most prevalent but also the most neglected nutrient deficiency in the world. It is the late manifestation of the chronic iron deficiency state.

The prevalence of anaemia in this study is 23.16 % which according to WHO, gets classified as a disease of moderate public health significance (1).

According to WHO, a disease is taken as a disease with low, moderate and severe public health importance depending upon its prevalence. In our study the prevalence of anaemia is only 23% making it a disease with medium public health importance, the mild anaemia is present in 13.67%, moderate anaemia in 9.33% and severe anaemia in 0.17% of the study population.

Many studies that had been done earlier have shown decrease in prevalence in India and few studies show high prevalence. For e.g. the study done in All India Institute of Medical Sciences, New Delhi which is published in Tropical medicine and International Health, April 2014 which has shown the prevalence of mild and moderate to severe anaemia for the entire country as 24.1 % (95% CI 23.0 to 25.3%) and 30.5% (95 CI 29.3 % to 31.8%) respectively(42) which reflects India’s improvement in achieving the control of anaemia in reducing its prevalence and other major consequences of maternal anaemia as a cause of 20% direct causes and 20% indirect causes of maternal mortality.

Another study done in Madhya Pradesh, Bhopal, India published in Muller Journal of Medical Science and Research, June 2014, was done in general population. It has shown that the
prevalence of anemia is more among females in the reproductive age group and it is not changed much from the year 2012, around 26% (43).

A study done in Bhubaneswar, Orissa showed the prevalence of anemia among pregnant slum dwellers to be 60.8% over all, of which 39.6% mild, 20.0% moderate and 1.2% severe anemia (44). When we consider the NFHS III data, the prevalence of anemia in married women was 62.8% in Orissa and now showing the downward trend which is quite encouraging. That too the study population was very socially disadvantaged people living in slums where even though they have awareness it is very difficult to follow good hygiene and sanitation.

Study done in Aurangabad city, in India among pregnant women in 2012 and published in Annals of Nigerian Medicine gives prevalence of 87.2%. Of which the mild is 24.7%, moderate is 54.5% and severe is 7.9% (45). The reasons cited from the study could be the increased Hindu religious population in this region who consume only vegetarian diet during pregnancy due to social and cultural beliefs and compared to All India, Delhi study (April 2014) (42) the per capita income is low in this study patients leading to an increase in the prevalence of anemia in them.

The Task Force Multi-Center Study, the survey done in 16 districts of India revealed high prevalence rate of 84.9% of anemia. The study was approved by the ICMR (38) and was published in Food and Nutrition bulletin in 2006.

The study on prevalence of anemia in pregnant and lactating women in seven Indian states was done and was published in Indian Journal of Medical Research in 2006. This was done to confirm the findings of NHFS II which showed improvement in the prevalence of anemia. The states were Himachal Pradesh and Haryana in the North, Tamil Nadu and Kerala in south, Assam and Orissa in East and Madhya Pradesh in Central India. There were interstate differences as
expected, like lower literacy and nutritional status in Tamil Nadu compared to Kerala. While comparing the Himachal Pradesh with Haryana, the former had better literacy rate, lower fertility rate with better diet all leading to reduced prevalence in these particular states compared to our own other states (46).

Another factor to be considered is the more awareness about health for those living in urban areas when compared to rural areas. Also the increased intake of fast food and more of night working schedules especially in the Information Technology population lead to increasing anaemia in urban people in spite of health awareness. On the other hand the dramatic speed in urbanization of rural areas nowadays leading to avoidance of green leafy vegetables due to non-availability is also a concern. The present study does not show any difference in the prevalence of anaemia in these two groups.

The important thing considered in these studies is about the method of estimation of hemoglobin. The Hemo Cue method tends to show higher values than the standard methods (39).

A study done in adult population in Telungana region of South India, in a semi urban tertiary care teaching hospital found moderate prevalence of anemia 20.01% (47), published in International Journal of Advances in Medicine in May 2014. The study environment is similar to our study, semi urban tertiary care teaching institution.

All the studies definitely show that the prevalence of anemia changes in its severity from state to state and district to district. Individual consideration to be given as our country has different cultures and food habits in different states.

The previous study done in CMC&H in a peripheral rural centre in Tamil Nadu revealed a prevalence rate of 69.3% in 1996 (48), and it was published in National Medical Journal of India
in 2000. According to that study the prevalence in rural blocks of Gudiyatham and K.V.Kuppam was 69.3% with the mild, moderate and severe anaemiaas 30.2 %, 35.8 %, and 3.3% respectively with a mean haemoglobin value of 10.1 grams%.

The last study done in CMC& H is more than fourteen years back and we definitely expect the impact of the study in the community level with its recommendations being implemented and the ante natal care becoming more and more possible for all pregnant women leading to reduced anaemia prevalence.

But the overall improvements in the socio economic status of the people and very well increased awareness due to the media about health all lead to more and more health consciousness in the community about the diseases affecting them.

Finally a study done by our institution this year,(7) to know the determinants of post-partumanaemia shows the prevalence of anaemia in ante natal mothers as 26.8%, which reflects our study values. It definitely shows results on the lower side compared to national figures. This may be due to the fact that the study area has good ante natal coverage and maternal care being provided by multiple care providers both from private and government sectors. This is published in International Journal of Women’s Health in April 2014. This study has highlighted the alarming increase and serious neglect ion of post-partumanaemia which has risen from 26.8% to 47.3% six weeks post-partum. On the other hand this tells us about the good ante natal coverage of ante natal women.

Another important cause noted for iron deficiency in pregnancy and puerperium, other than nutritional deficiency is the acute blood loss during delivery. So more vigilance in detecting excessive bleeding during delivery by following active management of third stage. Extra care
should be taken in the fourth stage of labour that is the first hour following delivery of the placenta as most of the bleeding problems occur in this one hour. The pulse rate, blood pressure need to be monitored at least once in fifteen minutes for this one hour. Any increased bleeding has to be controlled with uterine massage, oxytocics after excluding trauma and retained products. Patient should have health education about the normal bleeding after delivery and the dietary advice with iron and calcium tablets and extra calories for breast feeding. Patient and the relatives especially the husband and mother in law should know the need for post natal check-up and contraception. So efforts should be taken to maintain the normal haemoglobin levels even after delivery to prevent the patient entering next pregnancy with anaemia.

On analysis, significant correlation has been found with family’s income, patient’s education and occupation to maternal anaemia. Significant correlation is seen between Iron folic acid tablets ingestion and the absence of anaemia in pregnant mothers. Iron supplementation in pregnancy with or without folic acid had shown to improve the well-being of both the mother and foetus. So it plays a vital and significant role in reducing the maternal mortality and morbidity. The Cochrane data base of systemic Reviews, 2009, on effects and safety of preventive oral iron or iron and folic acid supplementation for women during pregnancy by Pena Rosas JP and Viteri FE, showed a significant reduction in Iron Deficiency anaemia at term (49). It was finally reported that routine supplementation reduces the maternal morbidity and mortality and improves the mean birth weight of the babies. This was published in Paediatric and Perinatal Epidemiology journal in 2012 (49).

It is also noted that patients who had not had antenatal check-up elsewhere also were on regular iron and folic acid tablets supplied by the health care workers. This reflects the awareness in the
population about the importance of prevention of anaemia in pregnancy and the effectiveness of ASHA in distributing the iron tablets by house visits in their areas.

Another important correlation between obesity and iron deficiency anaemia has to be mentioned. Iron haemostasis is affected by obesity and obesity related insulin resistance. Iron deficiency and anaemia are frequently found in obesity. Whereas hyperferritinemia with normal or mildly elevated transferrin levels are present in 33% of patients with metabolic syndrome. This condition is known as Dysmetabolic Iron Overload Syndrome (DIOS). In obesity associated inflammation, closely associated with iron deficiency there is impaired duodenal iron absorption and increased hepcidin concentrations. The present study showed 37.5% of patients with obesity in the first trimester associated with anaemia in 20.3% of patients.

An observation made by NHANES (National Health and Nutrition Examination Survey) say that low serum ferritin and low transferrin levels are two times higher in adolescents who are obese than normal adolescents.(50)
Limitations

1. Our study measured only the haemoglobin values and the type of anaemia was not confirmed. From the National and State wise statistics, it is presumed that common type of anaemia to be Iron Deficiency Anaemia.

2. As the serum Ferritin measurement is costlier it was not done for a sample size of 600 patients.

3. Follow up of these patients into labour and postpartum would have been ideal to get the full picture of the effects of anaemia.
Conclusions

1. Anaemia is prevalent in 23.16% of pregnant women who attended the Obstetric OPD for their booking visit in CMC & H.

2. In this 13.67 % had mild, 9.33 % had moderate and only 0.17 % had severe anaemia. In this study significant correlation was found between the socio economic status and anaemia and primi mothers had increased prevalence of anaemia.

3. The recommendations made for safe motherhood after this study is that all pregnant mothers should have antenatal check-ups and iron and folic acid supplementation prior to pregnancy in order to avoid anaemia in pregnancy.

4. The prevention of acute blood loss during delivery must be promoted to prevent anaemia and its adverse effects on mothers as most of the ante natal patients have normal haemoglobin levels in pregnancy when they reach labour.

5. The other recommendation would be to maintain the ante natal services to keep up the full coverage of ante natal mothers so that they get early ante natal booking visit, iron and folic acid supplementation throughout pregnancy followed by hospital delivery.

6. The important things to be reinforced are continuation of iron and folic acid in the post-partum period, having a post-partum check up to make sure that they do not enter next pregnancy with anaemia.

7. Promotion of weekly iron and folic acid supplementation (WHO)
**Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>ANCAnte Natal Care</td>
<td>Ante Natal Care</td>
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<tr>
<td>ASHA</td>
<td>Accredited Social Health Activist</td>
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<tr>
<td>CHETNA</td>
<td>Centre for Health Education and Training and Nutrition Awareness</td>
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<tr>
<td>CMC</td>
<td>Christian Medical College</td>
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<tr>
<td>CMC&amp;H</td>
<td>Christian Medical College and Hospital</td>
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<td>CDC</td>
<td>Centre for Diseases Control</td>
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<td>CMD</td>
<td>Chronic Mental Disorders</td>
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<td>DLHS</td>
<td>District Level Household and Facility Survey</td>
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<td>DPG</td>
<td>Di PhosphoGlycerate</td>
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<tr>
<td>FOGSI</td>
<td>Federation Of Obstetrics and Gynecological Societies in India</td>
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<tr>
<td>Hb</td>
<td>Hemoglobin</td>
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<tr>
<td>ICDS</td>
<td>Integrated Child Development Services</td>
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<td>ICMR</td>
<td>Indian Council of Medical Research</td>
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<tr>
<td>IDA</td>
<td>Iron deficiency Anemia</td>
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<td>IFA</td>
<td>Iron Folic Acid</td>
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<tr>
<td>INACG</td>
<td>International Nutritional Anemia Consultative Group</td>
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<tr>
<td>IUD</td>
<td>Intra Uterine contraceptive Device</td>
</tr>
<tr>
<td>MoHFW</td>
<td>Ministry of Health and Family Welfare</td>
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<tr>
<td>MDG</td>
<td>Millennium Development Goals</td>
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<tr>
<td>NHFS</td>
<td>National Family Health Survey</td>
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<td>NRHM</td>
<td>National Rural Health Mission</td>
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OPD  Out Patient Department
ODC  Oxygen Dissociation Curve
UNICEF  United Nations International Children’s Emergency Fund
WHO  World Health Organization
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Annexure
Dept. Of Obstetrics And Gynaecology
Christian Medical College, Vellore.
Proforma for patients participating in PAP study
in Obstetrics
(Prevalence of Anaemia in Pregnancy)

1. Name and Hosp. No:
2. Age:
3. Phone Number:
4. Rural/Urban:
5. Religion: Hindu/Christian/Muslim
6. Private/General:
7. Socio Economic Status: Income: >32,050/<16,020/16,020/>12,020/8,010/>4,810/>1,600/<1,600
   per month
   Education: Illiterate/Primary/Middle/High school/College/Post graduate/Professional
   Occupation: House wife/Unskilled/Semi skilled/Skilled/Clerical/Professional/Semi professional
8. Type of family: Nuclear/Joint family
9. Diet: Veg/Non veg: No. of non-veg meals per week/month:
10. Outside antenatal registration: Yes/No
    Hemoglobin result at booking visit:
    If severely anemic at first visit, other relevant results:
11. Received IFA tablets outside: Yes/No, if yes how many days:
12. Obstetric score and gestational age at booking:
13. Passage of worms: Yes/No
14. Deworming is done within prior 6 months of pregnancy: Yes/No
15. Footwear usage: Indoors-Yes/No, Outdoors-Yes/No
16. Bleeding P/R: Yes/No, Bleeding gums: Yes/No
17. H/O Menorrhagia 6 months prior to pregnancy: Yes/No
18. H/O Malaria/Tuberculosis/Other chronic illnesses: Yes/No
19. H/O Bleeding Disorders: Yes/No
20. H/O Anaemia, jaundice in childhood: Yes/No
21. Any other risk factors in pregnancy: 1. 2. 3. 4.
22. BMI at booking:

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சேலம் மாநில வுல்லூர் பஞ்சாயத்து, சேலம் மாநில வுல்லூர் மாவட்டம் பிள்ளை, தொழில் மற்றும் சங்க பிரிவு, தின்நாள்.

நூற்றாண்டு வருடாக விளங்கி வரும் காலத்தில் பார்வையில் ஆர்த்தோமம் பாதுகாப்பில் பார்வையில் அனுமதிக்கப்பட்ட பொருள் மற்றும் செயற்பாடுகளை எந்த வகையிலும் பாலிருந்து பிள்ளையாரில் பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் 

பொருள் நூற்றாண்டு வருடாக விளங்கி வரும் காலத்தில் பார்வையில் ஆர்த்தோமம் பாதுகாப்பில் பார்வையில் அனுமதிக்கப்பட்ட பொருள் மற்றும் செயற்பாடுகளை எந்த வகையிலும் பாலிருந்து பிள்ளையாரில் பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் பாலிருந்து பிள்ளை�ாரில் முடியும் பாலிருந்து பிள்ளையாரில் முடியும் 

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சேலம் மாநில வுல்லூர் பஞ்சாயத்து, சேலம் மாநில வுல்லூர் மாவட்டம் பிள்ளை, தொழில் மற்றும் சங்க 

பிரிவு, தின்நாள்.
பாதுகாப்பாளர் பாதுகாப்புள்ள நிலையைப் பெற்றது சரியான உயிரியல் கூட்டம் நிற்பெற்றுத் தக்கவர் தொடர்பில் கோட்டையில் முன்னேற்றம் செய்யவுடன் தொடர்பில் உள்நாட்டு உயிரியல் கூட்டம் நிற்பெற்றுத் தரும் வரை பேர்மாணை செய்யுள்ளோர்.
This sheet provides you the details about the research study in which you are requested to take part. The study is done on pregnant women when they come to our OPD, the first time for antenatal care. The study is done to find out the number of pregnant mothers with anemia, a condition which is diagnosed when the hemoglobin levels in the blood fall below 11 gms%. India is one of the countries with very high prevalence of anemia in the world. Almost 58% of pregnant women in India are anemic. Anemia is one of the common causes of many serious complications during pregnancy and delivery.

Taking cognizance of all these facts, in CMC, we have planned to do this study. Taking part in this study is purely voluntary. If you decide to take part in this study you will be asked to give your blood sample for estimation of hemoglobin levels and a proforma will be filled by collecting some details from you after signing the consent form.

Confidentiality will be maintained and you will not be referred to by name in any publication. This study does not require any additional test as your blood sample for Hemoglobin estimation will usually be requested by the doctor even if you are not in this study.
Consent Sheet

Title of the study: Prevalence of Anemia in Pregnancy (PAP)

Subject's Name:

Age:

- I confirm that I have read and understood the information sheet dated ____________ for the above study and have had the opportunity to ask questions.
- I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
- I understand that the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.

- I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

- I agree to take part in the above study.

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date:  
Signature:  
Signatory's Name:  
Signature:

Doctor taking consent: Name:  
Signature: