TNFOG

Tamil Nadu Federation of Obstetricians & Gynaecologists

“Anemia in Pregnancy”

e News Letter

9th March 2023

PRESIDENT'S MESSAGE

Dear friends,

Warm Greetings to all.

In this MARATHON CME, we have taken up the topic of Anemia in pregnancy, which is the most common preventable cause of maternal mortality as well as morbidity. Various topics right from iron metabolism to management of Anemia in pregnancy are going to be discussed.

Let us take a step forward to reduce MMR by way of eradicating anemia.

Welcoming you all to this CME to enjoy the scientific feast.

Thank you.

Dr. Revathy Janakiraman

President: TNFOG

SECRETARY'S MESSAGE

Happy to release the E Newsletter on Anaemia in Pregnancy in connection with International Womens day.

Anaemis is prevlent in 60 - 70 % of population from Adolescent - pregnancy- perimenopause.

Iron rich diet with regular timing of diet is very important at all stages.

When a girl 12 years her Hb should be 12gms.unless corrected in adolescent- MMR cannot be reduced, since 60% mmr are due to anemia.

Inspire of Many govt projects as Anaemia mukth bharat still anaemi incidence are increasing.

Lifestyle changes can alone avoid all complications at all stages of life.

Hope this E Newsletter with basic physiology to management will be useful to junors' seniors & pgs. Make use of it.

Thanks to all contributors.

Jai Hind.

Dr. S. Sampathkumari

Secretary: TNFOG

Tamil Nadu Federation of Obstetricians & Gynaecologists

IRON METABOLISM IN PREGNANCY

Dr. Monika. R

Iron is an essential micronutrient that plays a critical role in dioxygen transport, storage, and delivery through hemoglobin and myoglobin. Iron is required for cellular respiration, energy production, DNA synthesis, and cell proliferation. However, excess iron generates reactive oxygen species, leading to cellular and tissue injury. This can lead to cell death by ferroptosis or iron-dependent apoptosis. Both excess iron and iron deficiency can be observed. Women are at high risk of developing iron deficiency, particularly during pregnancy, and iron supplementation is almost universally recommended. Aron deficiency is the most common nutritional deficiency worldwide. Iron deficiency will lead to feto-maternal morbidity and mortality. Moreover iron plays a important role in the long-term neurodevelopment of newborns and infants. In iron overload, like hemoglobin diseases such as sickle-cell disease, thalassemia, and hereditary hemochromatosis, excess iron can be toxic.

The Enterocytes absorb 15% of heme iron and 85% of non-heme iron, non-heme iron source mainly from plant-based food. Iron absorption can be modified by dietary components, such as ascorbic acid and polyphenols.

Iron rich food include liver, meat, egg yolk, green leafy vegetables, dates, jaggery, whole grain and cereals. In a typical Indian diet, the major quantity of iron is received from cereals, although they contain iron only in moderate amount. Jaggery is a good source of iron and milk is poor source of iron, which contains less than 0.1mWml. recommended dietary allowance of iron in pregnant women is about 30-60mg.

IRON REQUIREMENT IN PREGNANCY:

Average iron requirement during pregnancy is 4-	
First trimester	1-2 mg/day
Second trimester	4-5 mg/day
Third trimester	6 mg/day

Total iron requirement during pregnancy is 1000mg	
Fetus and Placenta	300 mg
Mother	500 mg
Basal loss	200 mg
No menstrual blood loss	300 mg
Maternal blood loss at delivery	200 mg

HAEMATOLOGICAL CHANGES IN PREGNANCY

Haematological component	Changes
Plasma volume	Increases by 30-50%
RBC mass	Increases by 20-30%
Haemo lobin concentration	Decreased
Erythropoietin	Increased

Physiologic anemia of pregnancy occurs as a consequence of a greater increase in the plasma volume relative to the increase in RBC mass. The MCV (mean corpuscular volume) mildly decreases between 26 and 38 weeks, because the placental iron transfer is most intense uring this period, decreasing the iron availability for maternal erythropoiesis.

ABSORPTION OF IRON

Only 10 % of iron in dietary form is absorbed. So pregnant female requires 4-6mg of iron she needs to take 40-60 mg of iron. Everyday taking 40-60mg in diet is practically not possible and therefore iron supplements are mandatory during pregnancy.

Iron is called as one way substance, as it is absorbed and excreted from small intestine. Iron absorbed in duodenum and upper part of jejunum in three forms as ferrous iron, ferric iron, heme iron. It is mostly absorbed in the ferrous form. The transporter protein DMT1 (divalent metal transporter 1) located in the apical surface of enterocytes, which facilitates the uptake of non heme ferrous iron (Fe') from intestinal lumen. Ferric iron (Fe') in intestinal lumen must be reduced to ferrous ion (Fe") by DcytB (duodenal cytochrome B reductase) before DMT1 uptake.

After taken up by the intestinal mucosa, iron is either stored in the form of ferritin in the mucosal cells or transferred into bloodstream via protein ferroprotein. Once it enters blood, iron binds to the transport protein transferrin and transported mostly to bone marrow for erythropoiesis. Some of the irons are taken up by macrophages in the reticuloendothelial system as a storage pool.

Factors affecting non heme iron absorption:

Improve absorption	**Inhibit absorption**
Meat, fish and poultry	Tannis in tea, coffee and cocoa
Citrus fruits (vitamin C)	Phytates in wholegrains
Kiwi fruit	Soy protein
Tomatoes	Dietary fibres
Capsicum	Calcium
Broccoli, cauliflower	Oxalate

REGULATION OF IRON

Absorption of the iron is regulated primarily by a peptide called hepcidin, expressed in the liver. It functions by directly binding to ferroportin , resulting in its degradation and preventing iron from leaving the cell. It also functions by inhibiting transcription of DMTlgene, which future leads to reducing the iron absorption.

TRANSPORT OF IRON

The iron (Fe') entering the mucosal cells by absorption is oxidized to ferric form (Fe') by the enzyme ferroxidase (ferroxidase activity of ceruloplasmin). Major source of iron in plasma is from degraded erythrocytes. Fe' combines with apoferritin to form ferritin, which is the temporary storage form of iron. From the mucosal cells, iron enter the blood stream.

Transport of iron in the plasma

- Iron enters the plasma in ferrous form.
- It is oxidized to ferric form by a copper containing protein, ceruloplasmin —ferroxidase activity.
- Ferric iron binds with a specific iron binding protein transferrin or siderophilin.

Transport form of iron is transferrin

- It is a glycoprotein, synthesized in liver.
- Normal plasma level of transferrin is 250 mg/dl
- One molecule of transferrin can transport 2 ferric atoms and the half life of transferrin is 7-10 days

Serum iron and serum iron binding capacity

- Total iron binding capacity (TIBC) of transferrin is 250-450 gg/d1
- In iron deficiency anemia, serum iron level is decreased and TIBC is increased.

STORAGE OF IRON

It is stored in the liver, spleen and bone marrow in two forms, ferritin and its insoluble derivative haemosiderin. In the mucosal cells, ferritin is the temporary storage form of iron. Ferritin contains about 23% of iron. Ferritin in plasma level is elevated in iron overload. Ferritin level in blood is an index of body iron stores, it is an acute phase reactant, elevated in the inflammatory diseases. Hemosiderin is another iron storage protein, accumulates when iron levels are increased.

EXCRETION OF IRON

It is important to know that there is no specific mechanism for iron excretion. About 1-2 mg of iron are lost from the body everyday from the skin and gastrointestinal mucosa. Iron is not excreted in urine but in nephrotic syndrome loss of transferrin may lead to increased loss of iron in urine.

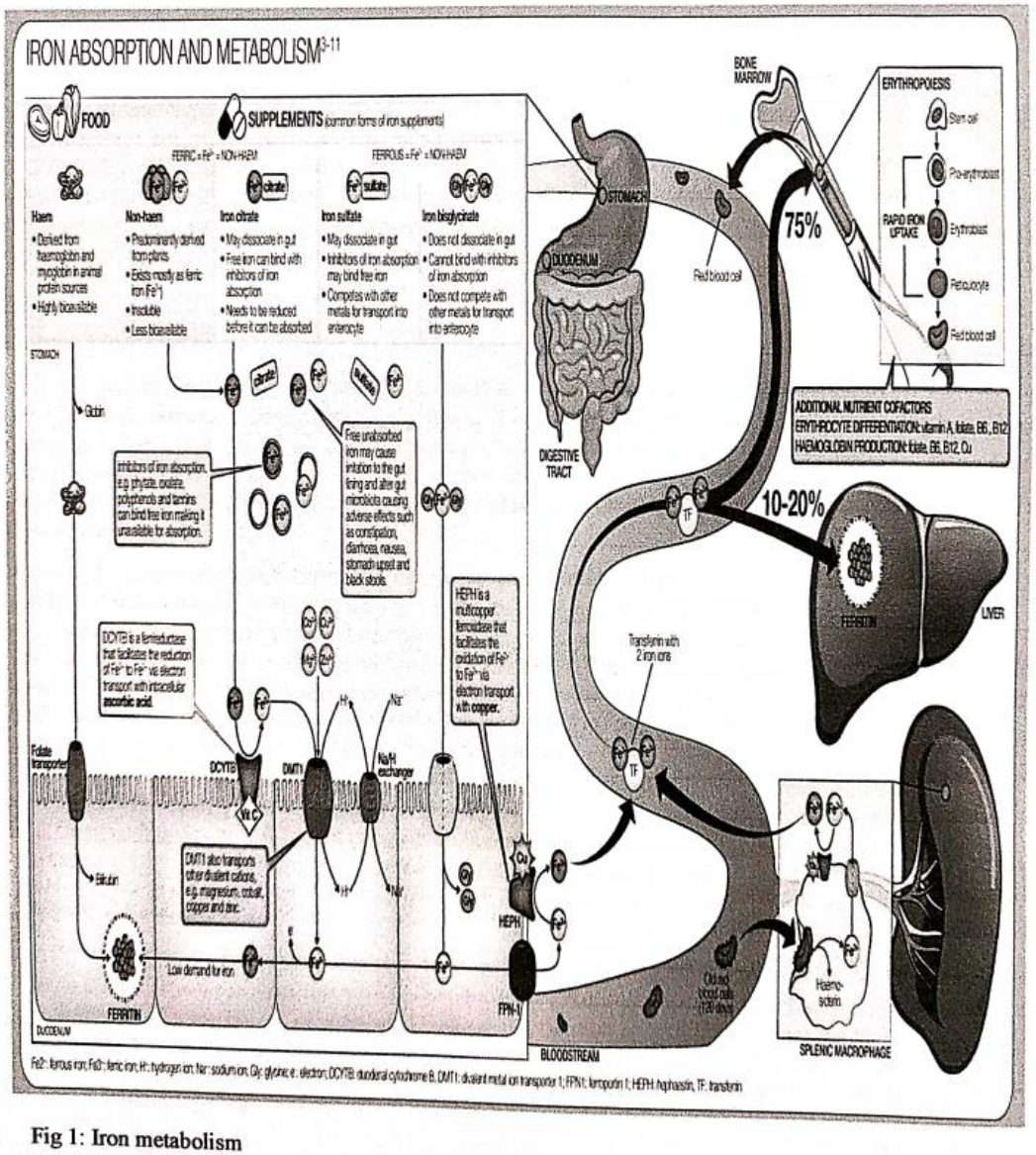

Fig 1: Iron metabolism

CHANGES IN THE IRON VARIABLES DURING PREGNANCY

Serum Ferritin (SF) concentration is the most frequently used marker of iron stores. Ferritin is secreted by macrophages and to a lesser extent by hepatocytes, SF is proportional to body iron stores. As ferritin production is also regulated by inflammatory cytokines, SF may not reflect accurately on iron stores in the presence of inflammation.

In pregnancy, SF concentrations gradually decrease to reach the lowest concentrations in the third trimester. In hemodilution, this decrease likely reflects efficient iron mobilization from stores with the progressive hepcidin decrease during pregnancy. lion supplementation will have a lesser SF decrease in the third trimester. Higher SF concentrations in the second or third trimester are associated with less favourable pregnancy outcomes (increased risk of preterm delivery). Therefore, apart from reflecting higher iron stores in the mother, higher SF would also reflect the presence of inflammation in complicated pregnancies or the failure of the plasma volume to expand. Whether maternal iron excess by itself, contributes to adverse outcomes is less clear and is an important research question.

PLACENTAL IRON TRANSPORT

During pregnancy, the placenta retains 90 mg of iron for its own function and transports, on average, 270 mg of iron to the fetus. Most of the iron transfer to the fetus occurs during the 3th trimester , and this transfer coincides with lowest maternal hepcidin expression, which allows for a maximal rate of iron supply into the maternal circulation. Maternal transferrin production increases during pregnancy, which functions to increase iron delivery to the placenta.

The transport of non heme iron across the placenta to the fetus is unidirectional. The uptake of iron transferrin from maternal circulation is mediated by TfR1 on placental syncytiotrophoblast. TfR1 is located on the apical membrane of syncytiotrophoblast and the TfR1-transferrin complex was internalized via clathrin-coated vesicles, similar to iron -transferrin endocytosis that occurs in the other epithelia. In the acidic environment of vesicle, iron dissociates from the transferrin and ferric iron is reduced to ferrous iron by ferrireductases, possibly 6-transmembrane epithelial antigen of the prostate 3 and 4 (STEAD 3 and 4). After iron was released from transferrin, TfR1—apotransferrin complex recycles back to the membrane, apotransferrin was released and the cycle repeats. Maternal has been associated with increased placental TfR1 expression in the humans and in the animal models. The likely mechanism is the development of placental when mother was iron deficient whereby a low

intracellular iron concentration in the trophoblast cells may increase TfR1 expression via IRP1 and IRP2 regulators.

On apical side of the syncytiotrophoblast, maternal iron Tf binds to the TfRl. After internalization, iron dissociates from the Tf, is reduced by a ferrireductase and is exported from endosome into the cytoplasm, possibly via DMTI or another transporter. Iron is exported from syncytiotrophoblast by the iron exporter Fpn and eventually oxidized by ferroxidase to be loaded onto fetal Tf or possibly transferred into the fetal circulation as NTBI. How the iron is transported across the fetal endothelium is unclear.

How iron was transported from vesicle into cytoplasm is not fully understood, but iron transporters DMT1, Zrt/Irt-like protein (ZIP) 8, and Z1P14 have been identified as potential candidates. DMT1 which plays a critical role for the endosomal iron release in erythroid cells , strongly localizes to human placental syncytium . ZIP8 is also abundantly expressed in the placenta. ZIPS hypomorphic embryos are severely anemic in utero and do not survive >48 hours after birth; however, whether this outcome was related to ZIP8 function in placental iron transport or also in fetal RBCs needs to be clarified.

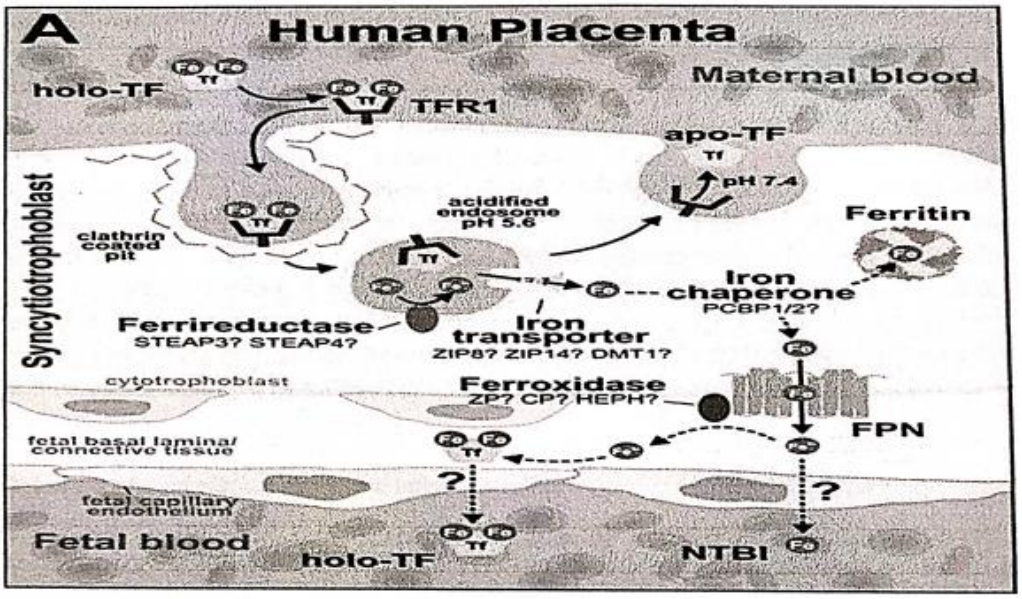

Fig 2 : Placental iron transport

[Cp, ceruloplasmin; DMT1, divalent metal transporter 1; Fpn, ferroportin; Heph, hephaestin; NTBI, non-transferrin-bound iron; STEAP, 6-transmembrane epithelial antigen of prostate; Tf, transferrin; TfR1, transferrin receptor 1; Zip, Zrt/Irt-like protein; Zp, zyklopen]

Iron is transported out of the syncytiotrophoblast by ferroportin. The complete knockout of ferroportin is embryonic lethal, whereas the conditional knockout of ferroportin that preserves its expression in the placenta results in normal embryonic development and birth , thus confirming the essential role of ferroportin in placental iron export. Ferroportin likely to export iron into the fetal stroma. As iron still needs to cross the endothelium to reach fetal circulation, With consideration, non—transferrin-bound iron is present in fetal circulation, it is possible that some form of non—transferrin-bound iron was transported across fetal endothelial cells. Alternatively, after being exported from syncytiotrophoblast by ferroportin, iron may be oxidized to the Fe. form before loading onto fetal transferrin. Once iron is loaded onto fetal transferrin, it may be transported to fetal circulation through endothelial cells although this mechanism is unclear. Whether the heme is transported across the placenta and the role heme transporters played in the placenta are much less understood. FLVCRI (Feline leukemia virus subgroup C receptor—related protein) is a heme exporter that is highly expressed in placenta. It has following 2 isoforms: FLVCRI a is expressed on the cell surface, and FLVCR1b is expressed on mitochondria, but role of each isoform and their localization and regulation remain to be determined. Maternal anemia is associated with lower placental FLVCRI expression, but biological implication of this observation is not yet understood. More research is needed to determine the specific roles of placental iron transporters and regulators, their interactions and control of the placental iron transport by maternal iron status and fetal iron status.

IRON METABOLISM IN PATHOLOGICAL PREGANANCIES

1. Pre-eclampsia

Pre-eclampsia defined by hypertension and proteinuria, associated with a pro-inflammatory state and hypoxia. It complicates about 2% to 5% of pregnancies and is one of the leading causes of maternal death in developed countries. With delivery before 34 weeks of gestation

(early-onset Pre-eclampsia) appears to be caused by abnormal trophoblastic invasion and remodelling of placental spiral arteries. And the late-onset Pre-eclampsia (with delivery after 34 weeks of gestation) is likely induced by fetal demands exceeding the placental capacity. Both situations result in the endothelial dysfunction, which leads to hypoxia. Iron metabolism is disturbed during Pre-eclampsia. Hepcidin levels are increased by inflammation and decreased by hypoxia, both occur during Pre-eclampsia.

2. Impact of Toxoplasma and Plasmodium Infections

Iron metabolism in the pregnant women is infected by Toxoplasma gondii or Plasmodium falciparum, two frequent parasites which are found worldwide, with which infections are associated with increased hemolysis.

HAEMOGLOBIN DISEASES AND PREGNANCY

1. Sickle-Cell Disease

Sickle-cell disease (SCD) is an autosomal recessive disease which is caused by mutations in the beta-globin genes. It increases the risk of adverse maternal and fetal outcomes during pregnancy, like Pre-eclampsia, maternal death, fetal growth restriction, and stillbirth. Anemia severity is based on the type of SCD (homozygous or compound heterozygous). SCD is associated with inflammation, with the high II-6 concentrations. As II-6 increases the hepcidin transcription via signal transducer and activator of transcription 3 (STAT3), this mechanism is likely responsible for the low iron concentrations and contributes to the anemia observed during SCD.

2. Thalassemia

Thalassemia is a total or partial lack of alpha or beta globin synthesis. On one hand, the majority of patients exhibit iron overload caused by hemolysis and transfusions, they can be

treated with iron chelation to decrease the impact of iron overload. On other hand, the patients with thalassemia can also exhibit iron deficiency, which lead to an increased risk of anemia in pregnancy. However, only fewer women with thalassemia have iron deficiencies than those without thalassemia. Fertility is affected in the thalassemia affects women. Iron overload impairs hypothalamic—pituitary—ovarian axis, which explains why the concentration of ferritin inversely correlates with reproductive hormone concentrations in the thalassemic women.

INVESTIGATIONS OF ANAEMIA IN PREGNANCY

Dr. Gayathri S

Considering the high prevalence of anaemia in pregnancy and its negative impact on maternal and fetal/neonatal morbidity and mortality, screening for anaemia, particularly Iron deficiency anaemia is recommended. The specific guidelines may vary in different countries, but routine Hemoglobin measurement at each trimester of pregnancy is generally recommended. According to the American College of Obstetrics and Gynecologists (ACOG), Centers for Disease Control and Prevention (CDC), and United Kingdom guidelines, every pregnant woman should receive a Complete blood count evaluation at the initial antenatal visit. Depending on the general population and the prevalence of Iron deficiency anaemia and other anemias, some countries recommend additional screening strategies for other hemoglobin disorders such as thalassemias or sickle cell trait/disease.

ICMR grading of anemia – Mild – 10 to 10.9g/dl

Moderate – 7 to 10g/dl

Severe – 4 to 7g/dl

Very severe - <4g/dl

PHYSIOLOGICAL ANEMIA IN PREGNANCY– The modest fall in hemoglobin and hematocrit values during pregnancy stems from a relatively greater expansion of plasma volume compared to red cell volume resulting in physiological anemia.

IRON DEFICIENCY ANEMIA – One of the most common causes of anemia during pregnancy. Maternal need for iron is nearly 1000mg which exceeds the iron stores of most women and results in anemia unless supplementation is provided.

The following characteristic are diagnostic of iron deficiency anemia

Hemoglobin - <11g/dl

RBC count - <4million/cu.mm

PCV<30%

Peripheral smear– Microcytic hypochromic anemia

Mean corpuscular volume - < 80fl

Mean corpuscular hemoglobin concentration - <30%

Mean corpuscular hemoglobin- <25pg/dl

Serum Ferritin - 10-15mg/L

Total iron binding capacity – High

Transferrin saturation – 15% OR LESS

Hepcidin level decreases – Hepcidin inhibits iron transport by binding to ferroportin (iron transport channel).

ANEMIA OF CHRONIC DISEASE – Diseases associated with chronic inflammation such as chronic renal insufficiency, inflammatory bowel disease and connective tissue disorders cause anemia by releasing cytokines that restrict erythropoiesis and shorten red cell lifespan which is characterized by

Rise in Hepcidin levels

Decreased Erythropoetin

Peripheral smear - Microcytic hypochromic anemia.

Low transferrin saturation, **High serum ferritin** level.

Transferrin levels are used to differentiate between iron deficiency anemia and anemia of chronic disease, since both are characterised by Microcytic hypochromic anemia.

Transferrin levels are **increased in iron deficiency anemia** and decreased or normal in anemia of chronic disease.

THALASSEMIA SYNDROMES – A heterogenous group of inherited disorders caused by genetic lesions leading to decreased synthesis of either the alpha or beta globin chain of HemoglobinA.

Beta-thalassemia is caused by deficient synthesis of beta chain whereas Alpha thalassemia is caused by deficient synthesis of the alpha chain.

Beta thalessemias

1. Thalassemia major - Severe, requires blood transfusion
2. Thalassemia intermediate – Severe, but does not require regular blood transfusions
3. Thalesssemia minor – Asymptomatic with mild or absent anemia, Red cell abnormalities seen

Alpha thalessemias

1. Hydrops fetalis – Lethal in utero without transfusions
2. HbH disease – Severe, resembles Beta thalassemia intermedia
3. Alpha thalassemia trait – Asymptomatic, like beta thalassemia minor
4. Silent carrier – Asymptomatic, no red cell abnormality

Diagnosed by **haemoglobin electrophoresis** – Increased HbA2, reduced HbA, and probably increased HbF

Peripheral smear – Marked Anisocytosis and Poikilocytosis, Microcytosis with hypochromia.Target cells, basophilic stippling, and fragmented red cells.

Reticulocyte count – elevated.

Microcytic hypochromic anemia is characteristic of both iron deficiency anemia and thalassemia. This can be differentiated by **Mentzer index** which is calculated by dividing the mean corpuscular volume by RBC count.

Mentzer index = Mean corpuscular volume (in fL) / RBC count (millions/cu.mm)

A value more than 13 is suggestive of Iron deficiency anemia and a value less than 13 is suggestive of thalassemia.

Hematologic Indices of Iron Deficiency and Alpha and Beta Thalassemia

Test	Iron deficiency	Beta thalassemia	Alpha thalassemia
MCV (abnormal if < 80 fl in adults; < 70 fl in children six months to six years of age; and < 76 fl in children seven to 12 years of age)	Low	Low	Low
Red blood cell distribution width	High	Normal; occasionally high	Normal
Ferritin	Low	Normal	Normal
Mentzer index for children (MCV/red blood cell count)	> 13	< 13	< 13
Hb electrophoresis	Normal (may have reduced HbA2)	Increased HbA2, reduced HbA, and probably increased HbF	Adults: normal Newborns: may have HbH or Hb Bart's

Hb = hemoglobin; HbF = fetal hemoglobin; MCV = mean corpuscular volume.

MEGALOBLASTIC ANEMIA – It comprises of folic acid and vitamin 12 deficiency. Megaloblastic anemia developing during pregnancy almost always results from folic acid deficiency. It was previously called pernicious anemia of pregnancy. During pregnancy, 400mcg of folic acid per day is recommended. The fetus and placenta extract folate from maternal circulation, hence the fetus is not anemic despite severe maternal anemia.

The following characteristics are diagnostic of megaloblastic anemia.

Peripheral smear – Macrocytic anemia with hypersegmented neutrophils.

Vitamin B12 deficiency – Levels are lower than non-pregnant values, due to decrease in transcobalamin level.

Megaloblastic anemia is caused by either vitamin B12 or folic acid deficiency, which can be differentiated by checking vitamin B12 levels.

HEMOLYIC ANEMIAS

Autoimmune hemolysis – It is caused by autoantibodies and is diagnosed by doingDirect and Indirect Coombs test which are positive

Hereditary spherocytosis – An inherited disorder is caused by intrinsic defects in the red cell membrane that render red cells spheroid and vulnerable to splenic sequestration and destruction.

Sickle cell anemia– Sickle cell anemia is an important hereditary hemoglobinopathy, a type of disease characterized by production of defective hemoglobins. Sickle cell anemia is an inherited blood disorder caused by a mutation in the sixth amino acid of the β-globin gene and is characterized by an abnormality in the oxygen-carrying protein hemoglobin, leading to a rigid sickle-like red blood cell shape. The diagnosis is based on the detection of low red blood cell count (anemia) and of hemoglobin S at hemoglobin electrophoresis.

Peripheral smear – Sickle cells, Howell jolly bodies and target cells.

Hemoglobin electrophoresis – Increase in HemoglobinS and HemoglobinF,Decrease in Hemoglobin

Parameter	Iron deficiency anemia	Megaloblastic anemia	Microangiopathic hemolyticanemias	Aplastic anemia	Sickle cell anemia
Hemoglobin	↓	↓	↓	↓	↓/↓↓
Hematocrit	↓	↓	↓	↓	↓
RBC count	↓	↓	↓	↓	↓
MCV	↓↓	↑↑	N	N/↑	N/↓
MCHC (mean cell hemoglobin concentration)	↓	↓	N	N	N/↓
RDW (red cell distribution width)	↑	↑	↑	↑	↑
Reticulocytes	↓/N	↓/N	↑↑	↓	↑
Ferritin	↓	N/↑	–	–	–
Transferrin	↑	–	–	–	–
Transferrin saturation	↓	–	–	–	–
TIBC (total iron binding capacity)	↑/N	–	–	–	–
Serum Iron	↓	N/↑	–	–	–
Serum B12	–	↓/N	–	N/↑	–
Serum Folate	–	↓/N	–	N/↑	–
Eritro-morphology	Hypochromic RBCs	Macrocytic RBCs, Howell-Jolly bodies	Schistocytes, RBCs fragmentation	Unremarkable	Sickle cells, target cells, Howell-Jolly bodies
White blood count	N/↓	↓/N	N/↓	↓	–
Platelet count	N/↓	↓/N	↓↓	↓	–
LDH	–	↑	↑↑	N/↑	↑/N
Bilirubin	–	N/↑	↑↑	–	↑/N
Haptoglobin	–	N/↑	↑↑	–	N/↑
Hemoglobin electrophoresis	–	–	–	–	↑HbS, ↓HbA, ↑HbF

References: Williams textbook of Obstetrics and Gynaecology

Robin's textbook of Pathology

MANAGEMENT OF IRON DEFICIENCY ANEMIA

Prof. Dr. Revathy Janakiram

President TNFOG

Anemia is a preventable Global disease. Iron deficiency is the commonest cause. Around 56 million women are affected globally and 2/3rd in Asia. In India 58 % of pregnant women are suffering from IDA. It is the commonest cause of maternal mortality as well as morbidity. In 20% it is the direct cause and in 50% indirect cause for maternal death.

AETIOLOGY OF IDA

- ✓ Inadequate iron intake -poor iron content of food (20mg/day)
- ✓ Poor absorption
- ✓ Increased iron requirement
- ✓ Increased blood loss- worm infestation, menorrhagia
- ✓ Poor iron stores – frequent childbirth, inadequate spacing

MANAGEMENT INCLUDE THE FOLLOWING:-

- ➢ Prevention
- ➢ Iron – oral / parenteral
- ➢ Blood transfusion.

The choice of treatment depends on severity of anaemia, Gestational age and other associated risk factors.

PREVENTION OF IDA

Pre pregnancy counselling & Dietary advice.

- Rich sources include, Haem iron (meat, poultry, fish, egg yolk),dry fruit, dark green vegetables (Spinach, Legumes, beans, Lentils) .and iron fortified cereals.
- Using cast iron utensils for cooking and taking iron with vit c rich food (Orange juice) can improve its intake and absorption.
- Avoid foods which may inhibit iron absorption – polyphenols (coffee, certain vegetables). Tannins (tea),phytates(in bran) , calcium (dairy products)

Deworming

In a typical singleton gestation, the maternal need for iron averages close to 1000mg. It considerably exceeds the iron stores of most women and results in IDA, unless iron supplementation is given. Therefore, regardless of anemia status, daily oral supplementation with 30-60 mg of elemental iron with 400 mic. Gm of Folic acid is recommended in pregnancy

ORAL IRON THERAPY

Ferrous sulphate 200mg(containing 60 mg of elemental iron) is the most common preparation used. First week of response ,only reticulocytosis. Second week Hb starts raising 1Gm/dl per week. Ferrous ascorbate is also equally effective.

Conventional oral iron therapy is limited in many patients because of dose dependent side effects, insufficient absorption, lack of compliance and limitation in various inflammatory conditions. Liposomal iron is a technologically designed, innovative form of iron which due to its differential delivery system ensures higher absorption and bioavailability, greater tolerability, and least gastro-intestinal side effects unlike conventional oral iron preparations.

PARENTERAL IRON :-

Iron sucrose – 50 mg of elemental iron in one ampoule.. It may be administered undiluted by slow I/V 1ml/minute, not exceeding 100 mg per injection. or I/V infusion – 100 mg in 100 ml of normal saline over 15 minutes, 200 mg on alternate days. Unused diluted solution must be discarded.

Ferric hydroxide carboxy maltose , I/V single bolus of 1000 mg over 15 minutes can also be given.

ADVERSE EFFECTS OF IRON SUPPLEMENTATION

Oral :-

- Constipation (less often diarrhea)
- Metallic taste
- Nausea
- Gastric Cramping
- Thick, green, tenacious stool

Parenteral

Infusion Reactions (1-3%),Pressure in chest , Arthralgia or myalgia –,Headache , Flushing and Severe Hypersensitivity .

Blood Transfusion

Packed red cell transfusion is indicated for severe anemia, (<^gms) close to due date or < 8 gms, when there is risk of blood loss at delivery.

Intrapartum management

I V cannula, cross matched blood, AMTSL, strict asepsis to be followed.

Post partum management

Close monitoring should be done to look for signs of decompensation, infection or thrombosis. Appropriate thromboprophylaxis and contraceptive advice should be provided. Hematinic supplementation should continue.

OVERVIEW OF MANAGEMENT OF IDA

PRE-PREGNANCY	ANTENATAL	DELIVERY
Dietary advice and iron therapy	Iron supplementation	Cross matched blood
Folic acid supplementation	Oral 100-200 mg elemental iron with vit C , deworming , treatment of malaria. Intolerant to oral iron or noncompliance- parenteral iron	AMTSL
	If Hb < 6 gms blood transfusion	Continue iron for 6 months in P N period. Contraceptive advice

THALASSEMIA IN PREGNANCY

Dr. T K Shaanthy Gunasingh

Thalassemia is the most common monogenetic disease in the world with global prevalence due to migration. This is due to a quantitative defect in hemoglobin synthesis resulting from a reduced rate of production of one or more globin chains of the hemoglobin. The classification is based on the specific globin chain that is affected. Thalassemia is divided into α and β Thalassemia. β thalassemia is characterized by decreased production of β globin chains resulting in unmatched α globin chains to accumulate and aggregate and causes excessive hemolysis and impairs bone-marrow erythropoiesis. β-thal has three syndromes – 1. β-thal major – severe transfusion dependent disorder. 2. Thalassemia intermedia – anemia and splenomegaly with less frequent transfusions. 3. Thalassemia minor / β-Thal trait. Thalassemia is inherited in an autosomal recessive manner. It heavily burdens the families and the health sector. India has the dubious distinction of having the largest number of Thalassemia major children in the world.

Screening for Thalassemia is by examining the hematological indices and measurement of HbA2 levels. Thalassemia trait is associated with a reduced mean corpuscular volume (MCV), reduced mean corpuscular hemoglobin (MCH) and a normal to a near-normal mean corpuscular hemoglobin concentration (MCHC). The most accurate marker is MCH. βThalassemia in addition is associated with elevated HBA2 levels in hemoglobin electrophoresis. DNA analysis is required to confirm the diagnosis in Thalassemia. Iron

studies are indicated to rule out iron deficiency and also the degree of iron overload in thalassemic patients.

PREVENTION:

1. It is important to offer genetic counseling in countries with high incidence of Thalassemia which is vital to warn carriers about consanguineous marriages.
2. Invasive prenatal diagnosis is the gold standard for establishing the diagnosis in high risk couples – chorionic villus sampling and amniocentesis. Preimplantation diagnosis can also be done.

MANAGEMENT:

Women with transfusion dependent thalassemias – major and intermedia are at increased risk of various maternal complications – cardiac failure, alloimmunisation, viral infections, thrombosis, osteoporosis, endocrinopathies like diabetes mellitus, hypothyroidism and hypoparathyroidism due to increasing iron burden. In Hb Barts, hydrops and consequent mirror syndrome in the mother with early onset preeclampsia and primary PPH is seen.

MANAGEMENT DURING PREGNANCY:

Preconceptional care: Screening should be done preconceptionally in individuals at increased risk of carriers for Thalassemia. If a pregnant woman is found to be a carrier, the partner needs to be screened as soon as possible. If positive, urgent expert genetic counseling is done to make prenatal diagnosis possible.

MEDICAL TREATMENT:

Patients with Thalassemia trait require no treatment or long-term monitoring. Iron supplements are unlikely to improve their anemia. Iron therapy needs to be administered if iron deficiency occurs. Treatment of β-thal major comprises of blood transfusion and iron chelation therapy. Desferrioxamane (DFO) is safe in second and third trimester. This

helps in reducing end organ damage. Diabetes and hypothyroidism should be looked for and corrected. A cardiologist should preferably assess the cardiac status in the periconceptional period. Bone density scan should be done and osteoporosis should be treated. Vitamin D supplements given. Vaccination against Hepatitis B, Pneumococcus and Hemophilus Influenza Type B must be given. Folic Acid 5mg per day prevents neural tube defects.

ANTENATAL CARE:

Multidisciplinary team consisting of an obstetrician, hematologist, endocrinologist and fetal medicine specialist is needed. Hp is done every 2 to 3 weeks. If Hp falls below 10gm/dL, a 2 unit blood transfusion is given. If Ferritin level is less than 30 mg/L, oral iron supplements are given. No role for parenteral iron. Folic acid to be continued at 5mg/day. Apart from routine scans, serial fetal biometry scans are offered every 4 weeks from 24 weeks to rule out fetal growth restriction.

INTRAPARTUM CARE:

Caesarean delivery is indicated only in obstetric indications. Crossmatched blood should be arranged prior to delivery. Intravenous DFO – 2gm over 24 hours should be administered. Continuous intrapartum electronic monitoring is done.

POSTPARTUM CARE:

Low molecular weight heparin is administered for a week following delivery and for 6 weeks following caesarean section. Breastfeeding is encouraged. DFO is restarted. No contraindication to hormonal methods of contraception.

In women with β-thal trait, pregnancy is generally uneventful. Inheritance of β-thal by the fetus is the problem and warrants prenatal testing.

CONCLUSION

Proper management of pregnant transfusion dependent thalassemia patient by appropriate monitoring during periconceptional, antenatal, intrapartum and postpartum periods and testing and monitoring of fetus will give a good outcome. Pregnancy outcome does not differ from the general population in β-thal carriers. But, prenatal testing is indicated.

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2. Thalassemia and its management in pregnancy – review article WJOA March 2017
3. Pregnancy in β-thalassemia trait carriers: An uneventful journey. Hemotology.
4. Management of β-thalassemia in pregnancy GTG 66.

NUTRITIONAL DEFICIENCY ANEMIA

Dr. Varshida

Anemia that occurs due to the deficiency of nutritive substances necessary for erythropoiesis is called nutritional deficiency anemia. The substances necessary for erythropoiesis are iron, proteins, vitamins like C, B12 and folic acid. The types of nutritional deficiency anemia are

1. Iron deficiency Anemia
2. Protein deficiency Anemia
3. Vitamin B12 or Folate deficiency Anemia

IRON DEFICIENCY ANEMIA:

This is the most common type of nutritional deficiency anemia. It is due to the deficiency of iron which leads to defective heme synthesis.

CAUSES OF IRON DEFICIENCY ANEMIA:

1. <u>Dietary lack</u> :

- Milk fed Infants, who are at high risk due to the very small amounts of iron in milk. Human breast milk provides only about 0.3 mg/L of iron.

- The impoverished, who can have suboptimal diets for socioeconomic reasons at any age.

- Older adults, who often have restricted diets with little meat because of limited income or poor dentition

- Teenagers, who subsist on junk food

2. Impaired absorption:

- Sprue

- Total or partial Gastrectomy (Billroth II surgery)

3. Increased requirement :

- Growing infants, children, and adolescents

- Premenopausal women, particularly during pregnancy and Lactating women

- Economically deprived women having multiple, closely spaced pregnancies are at exceptionally high risk.

4.Chronic blood loss :

- Menorrhagia

- Carcinoma of the cecum

- Hookworm infestation

PROTEIN DEFICIENCY ANEMIA :

Protein energy malnutrition stimulates an increased cytokines production with induction of inflammation, immunodeficiency and anemia. Deficiency of proteins also cause reduction in the synthesis of hemoglobin.

Vitamin B12 and Folate deficiency :

A lack of vitamin B12 or folate causes the body to produce abnormally large red blood cells that cannot function properly. Both vitamin B12 deficiency and folate deficiency are more common in older people, affecting around 1 in 10 people aged 75 or over and 1 in 20 people aged 65 to 74.

Causes of Vitamin B12 and B9 (Folate) deficiency :

1. Pernicious anaemia – The immune system attacks cells in the stomach, preventing the absorption of dietary vitamin B12 .

2. Vegan or a strict vegetarian diet - lack of these vitamins

3. Certain medications including anticonvulsants and proton pump inhibitors (PPIs), can interfere with the absorption of these vitamins

SYMPTOMS OF NUTRITIONAL DEFICIENCY ANEMIA:

*General Fatigue

*Weakness

*Pale Skin

*Shortness Of Breath

*Dizziness

*Strange Cravings (For Dirt, Clay, Ice Etc.,)

*Tingling In Legs

*Tongue Swelling

*Cold Hands and Feet

*Fast Or Irregular Heart Beat

*Brittle Nails

*Headaches

MANAGEMENT OF NUTRITIONAL DEFICIENCY ANEMIA :

Prevention:

1. **Iron rich foods** : Foods rich in iron include:

Red meat, pork and poultry

- Seafood
- Beans
- Dark green leafy vegetables, such as spinach
- Dried fruit, such as raisins and apricots
- Iron-fortified cereals, breads and pastas
- Peas

Citrus juice and ascorbic acid enhance iron absorption and hence fruits like Kiwi, Melons, Oranges, Strawberries, Tangerines and Tomatoes should also be added to the diet

2. **Vitamin B12 and Folate rich foods** :

Vitamin B12 is found in meat, fish, eggs, dairy products, yeast extract (such as Marmite) and specially fortified foods.

Good sources of folate include green vegetables, such as broccoli, brussels sprouts and peas.

PROPHYLACTIC IRON AND FOLIC ACID

SUPPLEMENTATION

Anemia Mukt Bharat programme :

1. **Children between 6 – 59 months of age :**

   Dose - 1 mL iron and folic acid syrup. Each mL contains 20 mg elemental iron + 100 mcg of folic acid

   Frequency -Biweekly

2. **Children 5-9 years of age :**

   Dose - 1 Iron and folic acid tablet.

   45 mg elemental iron + 400 mcg folic acid,

   Sugar-coated

   Frequency - Weekly

   Tablet colour – Pink

3. **Adolescent girls and boys of 10 – 19 years of age:**

   Dose - 1 iron and folic acid tablet

   60 mg elemental iron + 500 mcg folic acid,

   Sugar-coated

   Frequency - Weekly

   Tablet colour – Blue

4. **Women of reproductive age pregnant, non- lactating) 20-49 years : (under Mission Parivar Vikas)**

   Dose - 1 iron and folic acid tablet

   60 mg elemental iron + 500 mcg folic acid,

   Sugar-coated

   Frequency - Weekly

   Tablet colour - Red

5. **Pregnant Women and Lactating Mothers of 0-6 months child :**

   Dose - 1 iron and folic acid tablet starting from the fourth month of pregnancy is continued throughout pregnancy (minimum 180 days). It should also be continued for 180 days post- partum

   Daily 60 mg elemental iron + 500 mcg folic acid,

   Sugar-coated

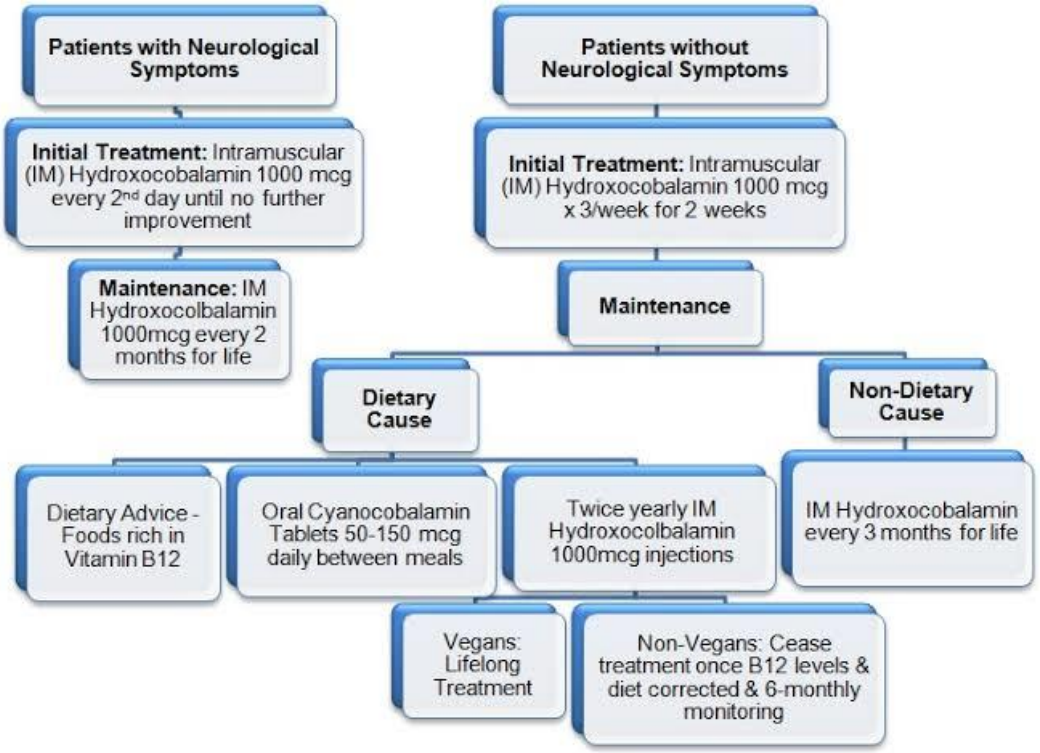
   Frequency – Daily

   Tablet colour – Red

- Prophylaxis with iron should be withheld in case of acute illness (fever, diarrhoea, pneumonia, etc.) and in a known case of thalassemia major/ history of repeated blood transfusion. In cases of children with severe acute malnutrition (SAM), IFA supplementation should be continued as per the SAM management protocol.

- All women in the reproductive age group in the pre- conception period and up to the first trimester of the pregnancy are advised to have 400 mcg of folic acid. Tablets, daily, to reduce the incidence of neural tube defects in the foetus.

TREATMENT OF VITAMIN B12 DEFICIENCY



Upcoming Events

TNFOG Bhodhana

Infertility

PGs from Kancheepuram GH


Shield
CONNECT