Anemia in pregnancy

Definition: - WHO defines anemia as Hb conc. is <11.0g/dL.

Types:-

1. Physiological: - caused by increase plasma volume by (40%) while red cell mass increase by (18%), this cause dilution of blood with decrease in Hb level which reach greatest at 32 weeks.

2 .Pathological:- caused by deficient essential hematinics (**iron, folic acid,Vit.B12**) arise from increased requirement & inadequate intake. This include:-

A. Iron deficiency:-

1.Daily iron requirement during pregnancy is 4mg (**2.5mg** early in pregnancy increase to **6-8mg** from 32 weeks onward).
2. Total iron requirement is **900mg**; **500-600mg** is to meet demand for increase in red cell mass & **300mg** is for fetus & placenta.
3. This requirement can achieved by increase dietary iron absorption & mobilizing from stores.
4. If women enter pregnancy with deficient iron store; iron deficiency anemia will occur & clinically presented as: -

Symptoms:-

1. Easy fatigue.
2. Intolerance to exercise.
3. Palpation.
4. Shortness of breath.
5. Generalized bone pain.
6. Headache.
7. Blurred vision.
8. fainting in sever cases.
9. Easy to get infection.

Signs:-

1. Pallor discoloration of skin, mucous membranes in conjunctiva, mouth.
2. Tachycardia.
3. Low B.P.
4. Systolic cardiac murmur.

Diagnosis:-

1. Decrease serum ferritin level is the first abnormal laboratory test. Its level reflect iron stores accurately & quantitively.
2. Decrease serum iron level.
3. Increase total iron binding capacity (TIBC).Both serum iron level & TIBC provide an estimate of transfferin saturation. Transfferin is carrier proteins secreted in liver which bind iron in circulation so reduced transfferin saturation indicate deficient iron supply to tissues so develop iron deficiency anemia.

4. Increase zinc protoporphyrin as there is defective iron supply to red cells.
5. Decrease Hb level is a late manifestation.
6. Blood film show microcytic (decrease MCV) hypo chromic (decrease MCHC).
7. Bone marrow stainable sample show no stainable iron (hemosidrine) once serum ferritin is <40mg/L,

Fetal risk:-

1.Preterm labor.
2. IUGR.
3. I.U.D.
4.Neonatal anemia in first year of life consequent to decrease fetal iron store, such anemia cause behavioral changes due to change in conc. of chemical mediators in brain.

Treatment:-

A. Prophylactic Iron:-

Aim:-

To maintain maternal iron store during increase in physiological demand, prevent anemia in infancy, prevent reduced or absent iron store after pregnancy so reduce risk of iron deficiency in subsequent pregnancy.

Disadvantages:-

1. GIT effect as nausea, vomiting.
2. Interfere with absorption of other trace element as zinc causing IUGR.
3. Excess iron produces free radicals & oxidative damage so implicated in C.V. disease & cancers.

Methods of supply:-

1. Selective: - Indicated in those with serum ferritin level <50ug/L in early pregnancy.

2. Routine:- WHO recommended universal oral iron with **60mg** elemental iron daily for 6 months in areas where prevalence of iron deficiency is **<40%** & continue 3months postpartum if prevalence is **>40%.**Various iron salts are available as **(fume rate, gluconate, sulphate, succinate)**used either intermittent weekly or twice weekly dosing which is effective as daily dosing. Iron rich natural mineral H2O may be acceptable alternative as oral iron prophylaxis.

B. Therapeutic iron: -

1.By oral dose of elemental iron of **(100-200mg)** daily. Ferrous sulphate **200mg/three times** daily are equivalent to **(195mg)** elemental iron daily. Other types of oral iron are ferrous gluconate or fumerate.
2. Rx should continue until Hb level is normalize & followed by prophylaxis or maintaince dose until 3 months postpartum to ensure that iron stores are replenished.
3. Reticulocytes count increase within **5-10 day**s & Hb level increase by **0.8g/L within week**. If no response within **3-4weeks**; re-evaluation of diagnosis for: -

1. Ongoing blood loss.
2. Infection.
3. Non compliance to Rx.
4. Additional hematinics deficiency.
4. Parental iron can be given by I.M., I.V.or infusion. It has no advantages over oral therapy if oral iron is well tolerated. The response rate to both parental & oral iron is same.

5. Types of parental iron: -
a. Iron dextran.
b. Iron sucrose.
c. Iron sorbitol.

6. Dosage is calculated by (**0.3 multiply by B.W. multiply by HB deficit**).
Iron dextran is given as complex of ferric hydroxide that contains **50gm/ml** iron.
Total dose is given as: -
1. I.V. infusion in 0.9% normal saline fluid over several hours.
2. I.M. as series of undiluted injection up to 100mg each.
Iron sucrose contains **20mg/ml** iron used as **5-10ml I.V.** up **to 3times/week** in second & third trimester.
7. Indications: -
a .Patient intolerance to oral preparations.
b. Malabsorption.
c. Non compliance.
8. Blood transfusion is rarely indicated if women has severe anemia (Hb level is less than 8gm/dl) beyond 36 weeks gestation & no time to achieve reasonable Hb before delivery.

B. Megaloblastic Anemia:-

1. Plasma level of folate decrease as pregnancy advance reaching half of non pregnant values at term. This caused by: -
a. Decrease dietary intake because of loss of appetite.
b. Increase plasma clearance of folate by kidneys.
c. Transfer of folate to fetus **(800Ug)** at term.
d. Uterine hypertrophy & increase red cell mass.
2. Incidence is **(0.2-5.0%)**; it is higher in multiple pregnancy & closely successive gestation.
3. Folate body store is predominantly in liver & the total is **(10 mg).** If body reserves are low; stores last for **4-5** months before symptomatic anemia develop.
4. Clinically it present as in iron deficiency in addition to angular stomatitis, loss of papillae of tongue, tongue ulcers, repeated vomiting, diarrhea.
5. Fetal risk of folate deficiency is **harelip, cleft palate, neural tubal defect**.
6. Diagnosed by: - a. Macrocytosis; blood film show oval macrocyte, hyper segmented nuclei of neutrophil.
b. Decrease reticulocytes.
c. Decrease red cell folate.
d. Serum folate level fluctuates from day to day & increase postprandial so it is of

limiting use in diagnosis.
e. In absence of above changes; megaloplastic is suspected when the expected response to adequate iron is not achieved.
7. **Rx: -**

A. prophylaxis: -
Given as **(200-300Ug)** daily in combination of iron supplement. It indicated in countries where nutritional & megaloplastic anemia is common.
B. Therapeutic: - as **5mg** daily continue through whole pregnancy & several weeks postpartum.

C. Pernicious Anemia: -
Caused by B12 deficiency, rare in pregnancy as patients are commonly old aged or infertile.

D. Hemoglobinpathies: -
These are inherited disorders in which there is qualitative or quantitative abnormality in synthesis of globins chain of Hb molecule. It include: -

1. Sickle cell syndrome:-
These are qualitative defect caused by single A.A. substitution in an alpha or beta chain result synthesis of abnormal Hb. It is divided into: -

A. Sickle cell disease :-(HbSS).

B. Sickle cell trait: - (HbAS). Clinical consequences of sickling include: -

1. Vaso-occlusive crises (micro & macro- infarcts) leading to painful crises & organ damage.
2. Anemic crises as result of sever hemolysis, red cell aplasia or splenic sequestration.
3. Chest & girdle syndrome.
4. Neurological events. (C.V.A.).

Maternal & fetal risks: - Heterozygous (HbAS) is benign with no particular antenatal squeal. Those patients are slightly more prone to renal papillary necrosis & U.T.I. Recently there is increased incidence of pre- eclampsia. Those with homozygous (HbSS) are more serious. Maternal risk include: -
1. Chest infection.
2. Hypertensive disorders.
3. Thromboembolic complication.
4. U.T.I.
Fetal risks are: - 1. Abortion. 2. Preterm labor. 3. IUGR.

Management:-

A. Prepregnancy:-
1. Crises outside pregnancy indicate likelihood of crises throughout pregnancy.
2. The use of (**hydroxyurea**) which is a disease modifying drug that increase HbF, improve red cell hydration, decrease rate of polymerization of HbS so its use decrease frequency of crises. This drug should discontinue in those who plan to conceive since it is teratogenic.
3. Discussion of contraception & pregnancy planning is useful in those with chronic

debilitating disease. None of contraception choices are excluded in sickle cell disease & the risk of pregnancy outweigh those of contraception.

B .Antenatal: -

1. Male partner should screen for abnormal Hb.
2. Investigations:-

a. C.B.P.:- Hb level is typically between (6-10gm/dl), reticulocyte count is increased indicate rapid red cell turnover. Blood film show sickle shaped red cells. Platelets count & W.B.C. count is increased indicate hypo-splenism.
b. Red cell indices (MCV, MCHC, MCH) should be normal in sickle cell disease alone but low MCV, MCH may indicate iron deficiency or associated thalassemia trait.
c. serum ferritin level, serum folate level, blood urea & electrolytes.
d. Liver function tests; high bilirubin level indicates hemolysis, abnormal liver functions indicate cholelithiasis or acute cholycystitis
e. Sickling test is a quick screening test for sickling Hb only without detect type or quantity of sickling Hb.
f. Hb electrophoresis can separate various types of Hb. It allows detection of amount & character of variant Hbs.
g.. Blood test for hepatitis A, B&C, HIV, Rubella Abs.
i.. Urine dipstick & culture for asymptomatic bacteriurea.

3. Ante partum blood transfusion: -
The aim is to maintain **60%** of total Hb as normal **HbA.** Blood transfusion can be either: - 1**. Prophylactic** given in ante partum period.
2**. Selective** only if Hb level less than 8gm/dl.
Pregnancy outcome is similar in those who undergo prophylactic blood transfusion compared with those undergo selective transfusion. Because of development of atypical red cell Abs, there is no role of prophylactic transfusion.
4. Antenatal visits should be every 2-3weeks for early detection of complication.
5. Iron therapy is contraindicated in sickle cell disease since it can cause hemosiderosis but in sickle cell trait it can be given safely.

C. Labor & delivery:-

1.Crisis increased during labor if mother is dehydrated, or has hypoxia, acidosis or infection. Crises clinically characterized by severe chest pain, bone pain, hemoglobinurea, sever pallor.
2. Pain relief is mandatory since it reduce cardiac work, epidural is effective.
3. Patient should keep warm, well hydrated with adequate oxygen.
4. Blood transfusion if Hb is <8g/dl.
5. Thromboprophylaxis is given in those who are immobilized or experience crisis at time of delivery.
6. Avoid prolong labor.
7. Those that have C/S; start early mobilization & chest physiotherapy.
8. Risk of crisis persists in postpartum so maintain adequate hydration & oxygenation & monitor for infection.
9. Neonatal screening for hemoglobinpathies.

2. Thalassemia syndrome: -

Quantitative defect of globins chain production. It include:-

A. Alpha thalassemia:-

It can be:-

1. **Alpha thalassemia trait: -** there is missing of one or two gene of alpha globin chain which consists of four genes. This cannot detect by Hb electrophoresis.
2**. HbH disease: -** there is deletion of three genes characterized by chronic hemolytic anemia with normal life expectancy. This can be detected by Hb electrophoresis.
3**. Alpha thalassemia major:-**there is no alpha chain; in which there is no Hb A,A2,F but four Gamma chain form so called **(Hb Barts)** ; this type is incompatible with life since there is sever anemia, cardiac failure with abnormal organogenesis result **(Non immune hydrops).** This type is complicated with sever pre-eclampsia & difficult delivery. In first two types; there is no specific management in labor, delivery & postpartum.

B. Beta thalassemia: -

There is quantitative defect in beta chain of Hb molecule. It is of three types: -

1.Trait. 2. Intermediate. 3. Major.

a. In trait; it is indicated by hypo chromic microcytic red cells with increase HbA2 on Hb electrophoresis. Partner test is mandatory. Iron therapy can be given based on hematinics measurement. Racial groups at high risk include those of Mediterranean origin & some Asian population.
b. In major type; fertility is reduced in those with transfusion dependent type but pregnancy is possible if receive regular transfusion & iron chelation therapy.
c. During pregnancy iron chelating agent should discontinue & oral & I.V. iron are contraindicated because it causes hemosiderosis. Those with iron overload are at high risk of D.M. & birth defects.
d. Those with major type are short in stature so increase risk of C/S.
e. Fetal hypoxia, IUGR, IUD &preterm labor are common unless maternal anemia is managed well.
F. Medical assessment including evaluation of cardiac status, liver F.T., thyroid & parathyroid function & glucose testing.
g. No specific management in labor, delivery & postpartum.

E. Hemolytic anemia:-

1. Characterized by: -
a. Increase unconjugated bilirubin level.
b. Increase lactate dehydrogenase level.
c. Increase reticulocytes count.
d. Increase urobilinogen excretion.
2. Clinically presented as **anemia, jaundice, splenomegaly & pigmented gall stone**.
3. Intrinsic causes are: - a. Abnormal Hb structure or function (hemoglobinpathies).
b. Abnormal red cell membrane (hereditary spherocytosis).
c. Abnormal red cell metabolism (G6PD).
4. Extrinsic causes are: - a. Red cell directed Ab (autoimmune hemolytic anemia).
b. Altered intravascular circulation (DIC, Thrombocytopenic purpura).