University Of Fallujah
College Of Medicine

Hematological disease in pregnancy

Lecture: 6
Stage: 4th
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Learning objectives

1. Review types of types and treatments of anemia in pregnancy.

2. Know the main type of Haemoglobinopathies in pregnancy and their effect on pregnancy and fetus.

3. Approach to thrombocytopenia in pregnancy.

4. The managements of clotting disorder in pregnancy.

5. Understanding the effect of epilepsy in pregnancy.

Haematological abnormalities:

Anaemia in pregnancy:

Physiological anaemia is common in pregnancy due to increase in plasma volume greater than the increase in red cell mass. However, the haemoglobin (Hb) should not fall to <11 g/dl in the first, or <10 g/dl in the second and third trimesters. Anaemia in pregnancy may be due to iron, folate, or rarely, vitamin B12 deficiency.

Iron and folate requirements in pregnancy

- The maternal need for iron averages close to 1000 mg. Of this, 300 mg is for the fetus and placenta; 500 mg for maternal hemoglobin mass expansion; and 200 mg that is shed normally through the gut, urine, and skin.
- The total amount of 1000 mg considerably exceeds the iron stores of most women and results in iron deficiency anemia unless iron supplementation is given.
- Folate, requirements increase to around 400 µg/day during pregnancy. Folate deficiency is more common in multiple pregnancy, frequent childbirth, and adolescent mothers.
- The body stores around 3 mg of B12, with a daily dietary requirement of 3µ g/day. The only B12 source is animal foodstuffs; thus, vegetarians are at risk of dietary deficiency.

- Aside from anaemia, folate and B12 deficiency are linked to neural tube defects. B12 deficiency can also result in a demyelinating neuropathy.

Diagnosis of anaemia of pregnancy:

The initial evaluation of a pregnant woman with moderate anemia should include measurements of hemoglobin, however, normal pregnancy leads to a progressive fall in serum iron, ferritin and an increase in TIBC, a markedly reduced serum ferritin (<12 µg/l) remains diagnostic.

Prophylaxis:

- The Hb concentration is often used to screen for anaemia, with an assessment at presentation and again in the early third trimester.
- Supplementation can be achieved with 30–60 mg of elemental iron/day, which produces few side effects.
- To prevent neural tube defects, folic acid supplementation (at 400µ g/day) is routinely given in the first trimester. It should also be taken for 3 months prior to conception in those planning pregnancies
- Higher dose of folic acid (5 mg) is needed if there is:
  - ❖ a previous child with a neural tube defect
  - ❖ women with chronic red cell disorder.
  - ❖ in women on anti-epileptic drugs that antagonize folate metabolism
  - ❖ in those with likely dietary deficiency.

Treatment:

- The treatment of established iron deficiency is with oral iron compounds ferrous sulfate, fumarate, or gluconate that provide about 200 mg/day of elemental iron. This may lead to gastrointestinal up set. Iron absorption is maximized when combined with ascorbic acid such as taking the iron supplements with fresh orange juice or a vitamin C preparation.
- Parenteral iron therapy is useful in malabsorption and failed compliance, but otherwise does not produce a faster response than oral iron and side effects are common.
- Proven folate deficiency anaemia should be treated with folic acid (5 mg/day).
- In B12 deficiency, a single dose of 1000 µg of intramuscular B12 weekly injections should be employed until anaemia resolves

Haemoglobinopathies:

Sickle cell anaemia:

Sickle cell disease is an autosomal recessive condition, where abnormal haemoglobin (HbS) contains beta-globin chains with an amino acid substitution that results in it precipitating when in its reduced state. The red blood cells become sickle shaped and occlude small blood vessels. There is severe anaemia, chronic hyperbilirubinaemia, a predisposition to infection.

Clinically significant variants of haemoglobin:

- ❖ Sickle cell trait (Hb AS)
- ❖ Sickle cell disease (Hb SS)
- ❖ Sickle cell/haemoglobin C disease (Hb SC)
- ❖ Sickle cell/beta thalassaemia

Complication of Sickle cell anaemia in pregnancy:

- Pregnancy associated with an increased incidence of sickle cell crises that may result in episodes of severe pain, typically affecting the bones or chest. Crises in pregnancy may be precipitated by hypoxia, stress, infection and haemorrhage.
- Mothers are also at increased risk of miscarriage, pre-eclampsia, fetal growth restriction (FGR) and premature labour, with three times the risk of eclampsia compared to women without SCD.
- Thromboembolic events including cerebral vein thrombosis and deep venous thrombosis are implicated in the higher rates of maternal deaths.
- Carriers are usually fit and well, but are at increased risk of urinary tract infection, and rarely suffer from crises.
- Carriers (Hb AS) have a 1:4 risk of having a baby with SCD if their partner also has sickle cell trait. Screening for abnormal hemoglobin antenatally is important in the population at risk.

Management of Sickle cell anaemia during pregnancy:

- pre-pregnancy optimization of maternal health and education about the risks in pregnancy.
- High-dose folate supplements (5 mg daily) are recommended
- the following vaccines are recommending for sickle-cell disease pneumococcal, Haemophilus influenzae type B, and meningococcal vaccines.
- managed from early pregnancy on low-dose aspirin (75 mg daily).
- Oxygen, Analgesia, adequate hydration
- Screen for infection (urinary, respiratory) and treat immediately by antibiotics

- Blood transfusion
- Prophylaxis against thrombosis (heparin)
- Fetal monitoring

Thalassaemia:

The thalassaemia syndromes are autosomal recessive disorder. It is divided into:

- **Alpha-thalassaemia:** result from defects in the normal production of the alpha chains. Two types:
  - **Alpha-thalassaemia major:** there is a deletion of the two normal alpha genes for haemoglobin production, the condition is lethal and the effected fetus usually die in utero.
  - **Alpha-thalassaemia minor:** there is a deletion of only one of the two normal alpha genes for haemoglobin production Although the affected individual is chronically anaemic, this condition rarely produces obstetric complications except in cases of severe blood loss. It is important to screen the woman's partner for thalassaemia if he is also affected, there is a 1:4 chance of the fetus having alpha-thalassaemia major, which is lethal, and to consider prenatal diagnosis.

- **The beta-thalassaemia:** result from defects in the normal production of the beta chains. Two types:

1. Beta Thalassemia major: were uncommonly encountered during Pregnancy. Transfusions are given throughout pregnancy to maintain the hemoglobin concentration at 10 g/dL. This is coupled with surveillance of fetal growth

2. Beta thalassaemia minor: is not a problem antenatally, although women tend to be mildly anaemic. Iron and folate supplements should be given and partners should also be screened. However, if both partners have beta-thalassaemia minor, there is a 1:4 chance that the fetus could have beta-thalassaemia major, which is associated with profound anaemia in post-natal life, and to consider prenatal diagnosis.

Thrombocytopenia in pregnancy:

Thrombocytopenia is defined as a platelet count <150× 10^9/L. Incidental thrombocytopenia is common and is found in 7–8 per cent of pregnant women. Mild falls in platelet counts to between 100 and 150× 10^9/L are only very rarely associated with poor maternal outcome. Bleeding is rarely a complication unless the count is <50 ×10^9/L. However, the diagnosis of gestational thrombocytopenia is a diagnosis of exclusion and can only be made when autoimmune and other causes have been excluded.

Causes of thrombocytopenia in pregnancy:

- Idiopathic (gestational thrombocytopenia)

- Increased consumption or destruction

❖ autoimmune (ITP).
❖ antiphospholipid syndrome.
❖ pre-eclampsia.
❖ HELLP syndrome (haemolysis, elevation of liver enzymes and low platelets).
❖ disseminated intravascular coagulation.

Bleeding disorders in pregnancy

Autoimmune thrombocytopenia

In immune thrombocytopenic purpura, autoantibodies are produced against platelet surface anti gens, leading to platelet destruction.

The incidence in pregnancy is around 1 in 5,000.

The maternal platelet count may fall at any stage of pregnancy and can reach levels of 50 × 109/L. but maternal bleeding during pregnancy or at birth is unlikely if the platelet count is >50 × 10(9/L.

There is a 5–10% chance of associated fetal thrombocytopenia (<50 × 109/L), which cannot be predicted using maternal counts or antibody tests.

Managements

❖ Pregnant women with immune thrombocytopenic purpura who become pregnant should be cared for by a specialist obstetric/hematology team.
❖ If the platelet count is very low, treatment with corticosteroids or intravenous immunoglobulin (Ig)G may be considered.
❖ Vaginal delivery should be facilitated, and epidural/spinal anesthesia should be avoided if the platelet count <80 × 109/L.
❖ Fetal blood sampling in labour and instrumental delivery are best avoided because of the risk of fetal thrombocytopenia causing neonatal hemorrhage/hematomas.
❖ A cord blood sample must be collected to exclude neonatal thrombocytopenia.

Inherited coagulation disorders

Von Willebrand disease, carriers of haemophilia A and B, and factor XI deficiency account for over 90% of all women with inherited bleeding disorders. Hemophilia A (FVIII deficiency) and haemophilia B (FIX deficiency) are X-linked defects with prevalence's of 1 in 10,000 and 1 in 100,000, respectively, in the population.

Carriers of haemophilia A or B usually have clotting factor activity about 50% of normal, but while factor VIIIC levels increase in pregnancy, factor IXC levels increase only slightly.

Von Willebrand disease is the most common inherited bleeding disorder, with an estimated prevalence of 1%. It results from either a qualitative or quantitative defect in von Willebrand factor (VWF).

The inheritance of von Willebrand disease is usually autosomal dominant and, while increases in factor VIIIC and VWF antigen activity usually occur during normal pregnancy, they cannot be relied on to buffer the effects of the disease, particularly in severe cases.

Managements

Where possible, carriers of haemophilia and women with von Willebrand disease should be identified and counselled prior to pregnancy. Baseline coagulation factor assays should be performed as soon as pregnancy is confirmed and should be repeated in the third trimester. In haemophilia carriers, tests to confirm fetal sex should be offered, either by ultrasound or through sampling fetal DNA in maternal blood, as this influences the use of interventions in labour.

Individuals with bleeding disorders are at significant risk of primary and secondary post-partum haemorrhage, and this risk can be minimized by appropriate prophylactic treatment. Planning for delivery requires multidisciplinary input, including a specialist obstetric/haematology team, and is guided by the third-trimester clotting factor levels, taking into account the precise nature of the bleeding tendency. Those deemed to be at significant risk should have a care plan written that may include the use of factor concentrate, tranexamic acid or desmopressin (DDAVP) to cover labour and delivery.

In haemophilia carriers, epidurals may be permitted if the clotting factor is considered to be satisfactory.

Invasive fetal monitoring, ventouse and rotational forceps should be avoided if there is a possibility that the fetus may be affected, and cord blood samples should be collected for coagulation tests.

Epilepsy in pregnancy:

- Approximately 30 per cent of those with epilepsy are women in their childbearing years
- some women will have an increased in frequency of fits, others a decrease, and some no difference.
- the risks to pregnancy from seizures outweigh those from anticonvulsant medication, seizures should still be controlled with the minimum possible dose of the optimal drug.

Prepregnancy counselling:

- Alter medication according to seizure frequency
- Reduce to monotherapy where possible
- importance of compliance with medication
- Pre-conceptional folic acid 5 mg
- Explain risk of congenital malformation

Risk of epilepsy in pregnancy:

- The principal concern related to epilepsy in pregnancy is the increased risk of congenital abnormality caused by anticonvulsant medications. All of these drugs are associated with a two- to three-fold increased risk of fetal abnormality (5–6 per cent) compared to the general population. Polytherapy further increases the risk (15–25 per cent).
- The major fetal abnormalities associated with anticonvulsant drugs (including sodium valproate, carbamazepine, phenytoin, phenobarbitone) are neural tube defects, facial clefts and cardiac defects.
- Despite the risks of continuing anticonvulsants in pregnancy, failure to do so may lead to an increased frequency of epileptic seizures that may result in both maternal and fetal hypoxia. Therefore, women on multiple drug therapy should, wherever possible, be converted to monotherapy before pregnancy
- In women who have been free of seizures for two years, consideration may be given pre-pregnancy to discontinuing medication.