

## RECURRENT PREGNANCY LOSS DUE TO HAEMOGLOBINOPATHY (THALASSEMIA)

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### Abstract:

*Thalassemia disorder is a heterogenous disorder of alpha and beta globin chain production. It results in destruction of red blood cells leading to hemolytic anemia. Pregnancy complicated by thalassemia is rare to occur. It can result in pregnancy wastage when uncared for. Pregnant woman with thalassemia are prone for pre-eclampsia, intra uterine growth restriction, preterm labour and poor reproductive outcome. A case of pregnancy complicated by beta thalassemia is presented here. She was third gravida with full term pregnancy with severe anemia with signs of cardiac failure, severe hepatosplenomegaly, severe intrauterine growth restriction resulting in fetal death. She was treated with urgent blood transfusion and delivered a fresh still born baby. Her haemoglobin was 4.2 gm%. Her haematological profile showed reduction in mean corpuscular volume and mean corpuscular haemoglobin.. Although her Hb electrophoresis showed thalassemia minor trait, there were features in favour of thalassemia intermedia. Post natal counselling was done to prevent recurrence of intrauterine death due to severe anaemia in future pregnancies.*

**Key words:** Haemoglobinopathy, Recurrent fetal loss, Thalassemia.

### Introduction:

Haemoglobinopathies are the most common genetic diseases of human race. According to WHO, the world wide carrier frequency is 4.5% and the affected birth rate is 2 in 1000 live births<sup>[1]</sup>.

Thalassemia disorders are a diverse group of microcytic hemolytic anaemias that have deficient synthesis of alpha or beta globin chains. They occur in individuals of Mediterranean, Middle Eastern, South East Asian, African and Asian Indian descent.

### Clinical Summary:

A 25 years old 3<sup>rd</sup> gravida presented with 39 weeks of gestation with intrauterine fetal demise with severe anaemia. She was a known case of beta Thalassemia minor with recurrent fetal wastage.



Figure 1: A Case of beta Thalassemia with Chipmunk facies.

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On general examination, there was typical Chipmunk (Thalassemic) facies, which include depressed nasal bridge, prominent malar and parietal prominence, flat forehead and protruding jaw. She had tachycardia with severe degree of pallor and no icterus. Per abdominal examination revealed 30 wks gestation with intra uterine fetal death with good uterine contractions. Severe hepatosplenomegaly was present. On per vaginal examination, cervix was fully dilated.

Patient was diagnosed as Gravida 3, Abortion 2 with full term gestation with intrauterine fetal death with severe anaemia with known case of thalassemia trait in second stage of labour. She delivered a severely growth restricted dead baby of 1.3 kg. There were no obvious congenital anomalies in fetus. Placental weight was 300 gms. Patient received three units of blood transfusion. Postnatal period was uneventful. Her haemoglobin on discharge was 6.3 gm%.

### Investigations:

Haemoglobin-4.2 gm%, Blood group-A positive, Total leucocyte count-4,600 cells/mm<sup>3</sup>, Differential leucocyte count-Polymorphs-62%, Lymphocytes-34%, Eosinophils-1%, Monocytes-3%, Platelet count-58,000 cells/cubic mm, Reticulocyte count-2.5%, Prothrombin time-12 seconds, Mean corpuscular volume-79 fl, Mean corpuscular haemoglobin-24.9 pg, Mean corpuscular haemoglobin concentration-31.2%, Liver function tests-within normal limits, Renal function tests-within normal limits, Serum proteins-within normal limits, Serum iron-86 microgm/dl, Total iron binding capacity-321 microgram/dl, Sickling test-negative, Haemoglobin electrophoresis-Fetal haemoglobin-8.7%, Hemoglobin A2-4.30%, Ultrasonography abdo-pelvis revealed massive splenomegaly and moderate hepatomegaly.

### Discussion:

Beta thalassemia is a heterogenous disorder of the beta globin chain. Most cases are autosomal recessive, but dominant pattern of inheritance exist. Beta thalassemia major is also known as Cooley's anaemia. There is absence of beta globin chain production whereas alpha

chain synthesis is maintained. There is erythrocyte hemolysis and ineffective erythropoiesis. If untreated, life expectancy of an individual is approximately six years. If these individuals survive, they are prone for iron toxicity like cardiac and hepatic dysfunction and endocrinopathies like diabetes mellitus, hypothyroidism, hypoparathyroidism, and women are likely to be infertile due to gonadal dysfunction.<sup>[2]</sup>

With improved facilities and treatment, many women are reaching to child bearing age. These women are prone for pregnancy complications like pre-eclampsia, preterm labour, fetal growth restriction and open neural tube defects.

Worsening of anaemia occurs during gestation and requires intensification of the transfusion and surveillance regimen. Once or twice weekly antepartum testing can be initiated at 28-32 weeks of gestation depending on maternal and fetal status. Pre-conceptual or early prenatal care should include a thorough physical assessment of cardiac, liver and splenic abnormalities. Laboratory studies including evaluation of complete blood count, platelets, ferritin, electrolytes, calcium, partial thromboplastin time, total protein, albumin, liver function and renal function should be done. Repeat complete blood count every two weekly and ferritin monthly is suggested. Liver function, renal function, thyroid function and electrolytes should be repeated in each trimester. Cases of beta-thalassemia major should receive 5 mg folic acid per day. Iron supplementation should be avoided.

Most patients with transfusion dependant beta-thalassemia major are on a regimen of iron chelation therapy with a goal to maintain serum ferritin levels below 1300ng/ml. Chelation therapy is often discontinued before or during early pregnancy due to unknown teratogenic risks in pregnancy.<sup>[3]</sup>

Women with beta-thalassemia major often have skeletal abnormalities and small stature due to marrow expansion and hypermetabolism. There is increased risk of cephalopelvic disproportion requiring elective caesarean section.

Thalassemia trait patients do well, and generally have no greater maternal and fetal mortality though they

sometimes require blood transfusion to relieve symptoms or when the Hb appears to drop down below 8 gm%.<sup>[4]</sup>

As transfusion and chelation improves the physical condition of these women, vaginal delivery becomes more likely to be successful. Regional epidural anesthesia is preferred during vaginal delivery for pain relief.

During postpartum period, birth control needs should be addressed and unplanned pregnancies should be discouraged. Estrogen containing oral pills are contraindicated for fear of thrombo embolism in women who have undergone splenectomy.

Successful pregnancies are reported in women after bone marrow transplantation. Stem cells derived from fetal cord blood or fetal liver have been successfully used for transplantation.

**Pre-conceptual counselling:** Father of the fetus is advised hemoglobin electrophoresis (if Mean corpuscular volume is low). When father is having normal hemoglobin, fetus has a 50% chance of beta-thalassemia minor and 25% chance of normal hemoglobin. When father is beta-thalassemia minor, the risk of fetus being beta-thalassemia major is 50%. Prenatal diagnosis can be made with chorion villous sampling<sup>[5,6]</sup>. Pre-implantation blastomere biopsy and DNA study is possible to select unaffected embryos during in-vitro fertilization<sup>[7]</sup>.

Elegance of molecular biology and modern concepts of management of these high risk pregnancies have

considerably brightened the prognosis over the last two decades.<sup>[8]</sup>

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