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Case Report

# Leucoerythroblastosis in pregnancy: Can it be sickle cell disease? - A rare case report

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ABSTRACT

Sickle cell disease is the most common inherited hemoglobinopathy associated with adverse maternal and fetal outcomes. It is often diagnosed at an early age. Presentation for the first time in pregnancy as leucoerythroblastosis is rare. Diagnosis requires a strong suspicion with the demonstration of hemoglobin S in blood.



## 1. Introduction

Sickle cell disease (SCD) is the most common inherited hemoglobinopathy occurring with high incidence in countries like Africa, India, and the Middle East countries. Among these countries, Africa has the highest prevalence of sickle cell disease in pregnancy, with a maternal mortality of 0.38 - 1.29/per 100,000 births.[1] It is a debilitating systemic disease that usually presents in the first two decades of life and is characterized by chronic hemolytic anemia, a vaso-occlusive crisis caused by obstruction of microcirculation with sickled red blood cells and multiple organ dysfunction. These symptoms are aggravated during pregnancy due to various physiological changes that occur during pregnancy, resulting in adverse maternal outcomes like preeclampsia, eclampsia, preterm labor, and increased risk of a cesarean section along with adverse fetal outcomes like intrauterine growth restriction due to placental insufficiency, intrauterine fetal death, and stillbirth.[2] A prompt diagnosis is essential for management and a favorable outcome in this scenario.[1] However, the presentation of sickle cell disease during pregnancy for the first time has rarely been seen.[3] Herein, we report a case of sickle cell disease in a twenty-three-year-old pregnant female, presenting for the first time in pregnancy.

## 2. Case Report

A 23-year-old pregnant female ($G_1P_1L_0A_0$) presented to a tertiary care hospital in Delhi for the first time with labor pains at 38 weeks of gestation. Informed consent was taken from the patient as per protocol. On examination, vitals were within normal limits. Patients did not have any antenatal checkups; however, the past history and antenatal history were insignificant. A TORCH screen and triple marker test (HIV, Hepatitis C, and Hepatitis B) were also negative. Complete blood counts (CBC) revealed hemoglobin(Hb)- 74 g/l, RBC count- 2.47 $x10^{12}$/l, hematocrit (Hct)- 0.24 l/l, mean corpuscular volume (MCV)- 100 fl, mean corpuscular hemoglobin (MCH)- 29.8 pg, mean corpuscular hemoglobin concentration (MCHC)-297 g/l, total leucocyte count (TLC)- 97.4 $x10^9$/l, and platelet count (P/C)- 255 $x10^9$/l. A CBC was repeated the next day which revealed similar findings- Hb- 70g/l, TLC- 100 $x10^9$/l and P/C- 261 $x10^9$/l. A possibility of leukemia was thought of with such high TLC. However, peripheral blood smear examination

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(Figure 1 A) revealed a leucoerythroblastic blood picture with no atypical cells. There were 508 nucleated red blood cells (NRBCs) per 100 WBCs showing megaloblastic and dyserythropoietic features with a dual population of normocytic normochromic and microcytic hypochromic RBCs.

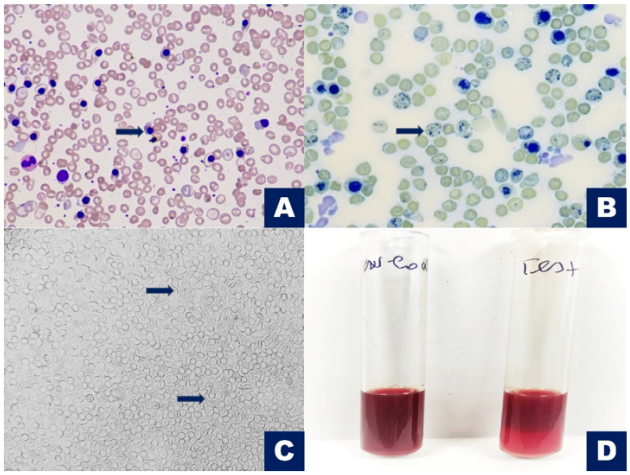


**Fig. 1: A:** Peripheral smear showing many NRBCs (arrow), 400X, Giemsa stain; **B:** Reticulocyte stain, 1% new methylene blue showing many reticulocytes (arrow), 400X; **C:** Sickling test with 1% Sodium Metabisulphite showing sickle cells (arrow), 400X; **D:** Positive solubility test showing a dark red precipitate at the top with reddish-pink color of subnatant

A fair number of poikilocytes, polychromatophils, and target cells were also seen with a mild left shift. Differential count (DLC)-Blast-0, myelocyte-04, metamyelocyte-06, neutrophils-66, monocyte-04, and lymphocyte-20. Platelets were adequate on smear. The corrected TLC was 22.1 $x10^9$/l. The reticulocyte count was 17.5% (Figure 1 B). A possibility of hemolytic anemia/ uteroplacental hemorrhage was considered. However, her Kleihauer-Bethke test, as well as direct antiglobulin test (DAT), were negative. The patient was transfused with two units of packed red cells, and an emergency LSCS was performed. Postpartum CBC (Hb- 93 g/l, RBC count-2.45 $x10^{12}$/l, Hct-0.25 l/l, MCV-102 fl, MCH- 29.9 pg, MCHC- 299 g/l, TLC- 19.3 $x10^9$/l and P/C- 288 $x10^9$/l) was similar to the previous one except with the presence of neutrophilia. A USG abdomen revealed a moderately enlarged spleen with possibly splenic abscess, for which the patient was managed conservatively on intravenous Piperacillin, Tazobactam, and Vancomycin. The blood cultures, malarial antigen test, and serum Widal test for Typhoid were also negative. To further investigate the cause of anemia, a sickling test was done, which showed the sickling of red cells within 2 hours of incubation with sodium metabisulphite (Figure 1 C). Subsequently, the sickle solubility tube test was also positive, showing a dark red precipitate at the top with reddish-pink color of subnatant solution (Figure 1 D). High performance liquid chromatography (HPLC) (performed on post-transfusion sample) revealed percentage of HbA- 35.3%, HbA2-4.5%, HbF-6.2% and a peak in S-window (HbS: 54%, Retention time: 4.41min) (Figure 2). Based on the findings of peripheral smear, sickling slide test, sickle solubility test, and HPLC, Sickle cell anemia was diagnosed. Since the peripheral smear revealed a microcytic hypochromic red blood picture, genotypic studies were advised to rule out compound heterozygosity with S/beta thalassemia. Still, the same could not be done as the patient was lost to follow-up.

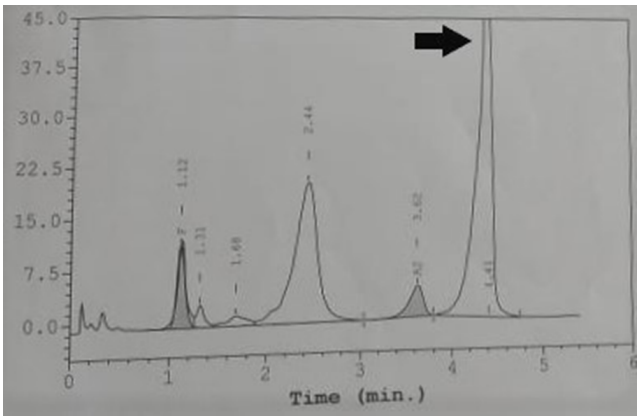


**Fig. 2:** HPLC showing a peakin the Hb S region (arrow)

## 3. Discussion

Sickle cell anemia is the most common single-gene disorder characterized by point mutation of a single nucleotide (GAG → GTG) in the 6th position of the beta chain of hemoglobin. It has an autosomal recessive inheritance pattern.[4] Sickle cell disease is defined as homozygous HbSS or heterozygous with HbS- βthalassemia or HbSC, while sickle cell trait is heterozygous for HbAS.[5]

Pregnant patients with sickle cell trait seldom have symptoms, barring mild anemia, while sickle cell disease is associated with an increase in the risk of maternal mortality by nine folds compared to the general population.[6] This is because of the higher risk of developing maternal and fetal complications like preeclampsia, eclampsia, preterm labor, venous thromboembolism, acute chest syndrome, cardiomyopathy, and intrauterine growth restriction due to placental insufficiency, intrauterine fetal death, and increased risk of cesarean section & associated complications. Thus, pregnant patients with SCD requires close monitoring during the antepartum, intrapartum, and postpartum period.[1,2]

SCD presenting in pregnancy for the first time is rare, with only a few documented cases.[3] Although the presence of NRBCs in peripheral blood of SCD patients has been documented before,[7] presentation of SCD in pregnancy

as a leukemia-like blood picture with marked elevation in the number of NRBCs is rare. To the best of our knowledge, this is the first documented case report. The presence of NRBCs in term pregnancy suggests acute fetal hypoxia, possibly due to uteroplacental hemorrhage, maternal TORCH infections, maternal diabetes, chronic hypoxia due to preeclampsia, and rarely leukemia.[8,9] In the absence of these causes, this marked elevation in NRBCs in peripheral blood of a pregnant female with SCD can be explained by the fact that pregnancy is associated with increased blood viscosity, increased vascular stasis, and hypercoagulability, and increased metabolic demand inducing sickling of the RBC. The sickled RBCs cause vaso-occlusion of microcirculation, especially that of the placenta leading to hypoperfusion and villous infarction, causing impaired uteroplacental circulation. This leads to fetal hypoxia, stimulating erythropoietin's release, leading to accelerated erythropoiesis and premature release of immature RBC/nucleated RBC into circulation. Sequestration of damaged sickled RBC by spleen also has a contributory effect followed by occlusion of splenic sinusoids by sickled RBC, leading to autosplenectomy.[2,10]

As it might be difficult to find characteristic sickle cells on the peripheral blood smear, which usually shows variable degrees of anisopoikilocytosis, normocytic normochromic to microcytic hypochromic RBC, presence of target cells, Howell jolly bodies, and NRBCs, therefore, a diagnosis of SCD as a cause of anemia requires a high index of suspicion, ruling out other causes of hemolytic anemia along with the performance of sickling test, solubility test, and Hb electrophoresis or HPLC.

A patient presenting with sickle cell anemia can have a possible genotype of HbS homozygous or compound heterozygosity with HbS/beta-thalassemia. Both of these present with normal to reduced indices. However, the presence of microcytic hypochromic RBC in PS favors a diagnosis of compound heterozygosity with HbS/Beta-Thalassemia, as seen in our patient. Further, HPLC aids in differentiating between the two. In HbS Homozygous, HbA2 will be normal while HbF & HbS will be elevated. While in HbS/Beta-Thalassemia, HbA2 will be elevated (as seen in this case) along with elevated HbF & HbS. Thus, our case report considers a presumptive diagnosis of HbS/Beta-Thalassemia.

This is a rare case report where sickle cell disease presents itself for the first time in pregnancy with accompanying leucocytosis. However, the patient could not be followed up, and genetic and molecular studies could not be done to confirm the exact genotype.

## 4. Conclusions

Leucocytosis with nucleated RBC in blood film can be suggestive of sickle cell disease in pregnant females. Since sickle cells are rarely observed in the peripheral smear, a high index of suspicion with the demonstration of HbS helps clinch the diagnosis. Early diagnosis is critical for effective management in such patients to ensure favorable maternal and fetal outcomes.

## 5. Source of Funding

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## 6. Conflict of Interest

None.

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