



# **Maternal and Fetal Outcome in Pregnancy with Sickle Cell Disease in the Third Trimester in Central India: A Retrospective Study**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## **ABSTRACT**

**Introduction:** Sickle cell disease is an uncommon cause of anemia and jaundice during pregnancy. However, SCD is expected in Maharashtra, especially the Vidarbha region. SCD in pregnancy can cause various maternal and fetal complications. This study was conducted to know maternal and fetal outcomes in pregnancy with sickle cell disease in the third trimester.

**Methodology:** This retrospective data were collected from hospital records of medical colleges located in central India for one and a half years, from November 2019 to January 2021. Forty-two women were admitted with pregnancy with sickle cell disease in the third trimester during the study period. The baseline characteristics, frequency of sickle hemoglobin variants, and maternal and fetal pregnancy outcomes were collected.

**Results:** Compiled data were analyzed by simple descriptive statistics and frequency tables. Majority were primigravida (59.52%). Type of sickle cell was determined based on HB

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electrophoresis; out of 42 patients, 36 had AS pattern, 5 had SS pattern SCD, and 1 had As+b thal minor. The most common medical complication was anemia [73.80%] and UTI 26.19%. The most common adverse obstetric outcomes observed were IUGR/Oligohydramnios 42.85% and pre-eclampsia 21.42%. Majority of patients delivered by LSCS 42.85%. An adverse outcome in the fetus was fetal distress 45.23% and meconium-stained amniotic fluid 42.86%.

**Discussion:** Due to hematological changes, extra demands, and sickle crisis, complications in both mother and fetus are more common in sickle cell anemia.

**Conclusions:** Early detection and management of sickle cell anemia during pregnancy can reduce the adverse outcome in both mother and baby.

*Keywords: Fetal outcome; pregnancy; sickle cell disease; anemia.*

## 1. INTRODUCTION

Sickle cell disease (SCD) is a group of inherited single-gene autosomal recessive disorders caused by the 'sickle' gene, affecting hemoglobin structure (Hb S) [1-5]. Sickle cell disease (SCD) is globally the most typical inherited single-gene autosomal recessive disorder [6]. The disease results from a single base A>T mutation in the triplet encoding the sixth residue of the  $\beta$ -globin chain, leading to a substitution of valine for glutamic acid and the abnormal hemoglobin S (HbS) [3,7-9]. The abnormal hemoglobin polymerizes under hypoxic conditions to form rigid and fragile, sickle-shaped red cells leading to hemolysis and vas occlusion in microvasculature Hb S occurs commonly in populations previously exposed to falciparum malaria, i.e., Africa, India, and Saudi Arabia. In India, in the tribal belts of Madhya Pradesh, Chhattisgarh, Odisha, Andhra Pradesh, and Maharashtra. In Maharashtra, the sickle gene is widespread in all the eastern districts, also known as the Vidarbha region, in the Satpura ranges in the north and some parts of Marathawada. The prevalence of sickle cell carriers in different tribes varies from 0 to 35 percent. The tribal groups with a high prevalence of HbS (20-35%) include the *Bhils*, *Madias*, *Pawaras*, *Pradhans*, and *Oskars*. It has also been estimated that Gadchiroli, Chandrapur, Nagpur, Bhandara, Yoetmal, and Nandurbar districts would have more than 5000 cases of sickle cell anaemia [10]. There are little data on the maternal and perinatal outcomes of women with sickle cell disease in India, particularly in Maharashtra. A prospective study from Orissa showed that neonatal outcomes such as low birth weight, perinatal mortality rate, admissions to the neonatal care unit, intrauterine growth retardation, and preterm births were significantly higher in sickle cell anemia mothers with successful pregnancies being achieved in 84.44 percent of the case [11]. Maternal and perinatal outcomes were also evaluated retrospectively from patients' case files in women with sickle cell

disease in a tribal population in Madhya Pradesh. There were 25 deliveries to women with sickle cell disease and preeclampsia, and disseminated intravascular coagulation was standard. There was no maternal mortality; however, there were five intrauterine fetal deaths and one early neonatal death [12]. SCD is standard, and our center receives many referrals. Maternal and fetal outcomes in pregnant patients with sickle cell disease in third-trimester pregnancies in women with sickle cell anemia and its complications were studied.

## 2. PATIENT AND METHODS

The case records of all 42 patients were studied retrospectively. All case papers were from November 2019 to January 2021. type of sickle cell was determined based on hemoglobin electrophoresis. The outcome of both mother and fetus/newborn in the third trimester was studied in detail. The maternal outcome was studied from both medical and obstetric points of view. Data obtained was compiled and analyzed by simple descriptive methods like frequency and percentage.

## 3. RESULTS

Out of 42 patients, 25 were primigravida; among these 25 patients, 4 had SS pattern sickle cell disease, 20 had AS pattern, and one had AS pattern plus beta-thalassemia trait. Seventeen patients were multigravida, with one patient having an SS pattern and the rest 16 had AS pattern.

73.80% (n=31) presented as anaemia of which (n=5) were SS pattern, (n=25) were AS pattern and (n=1) was AS pattern+ beta thalesemia minor, only one patient that is 2.38% (n=1) had sickle cell crisis. 26.19%(n=11) had urinary tract infection and 6.66% (n=3) had lower respiratory tract infection at the time of delivery.

Out of 42 patients 9.52%(n=4) had previous perinatal loss, previous abortion was seen in 19.04% (n=8), gestational diabetes in 9.52% (n=4), IUGR/Oligohydramnios was seen in 42.85% (n=18), pre-eclampsia in 21.42% (n=9), gestational hypertention was seen in 9.42% (n=4), eclampsia in 2.38% (n=1), abruption was seen in 9.52% (n=4), preterm labour in 16.66%

(n=7), LSCS was done in 42.85% (n=18), 57.14% (n=24) delivered vaginally.

Out of the 42 women, 41 had live births, and one patient had a stillbirth. The stillbirth was fresh and was associated with thick meconium and severe IUGR with a birth weight of 1.9 kg at term.

**Table 1. Distribution of type of sickle cell disease and parity**

Type of sickle cell	Primigravida	Multigravida	total
Ss pattern	4	1	5
As pattern	20	16	36
As+b thal minor	1	-	1
	25	17	42

**Table 2. Medical complications**

Complication	SS	AS	AS+ b thalassemia minor	total	percentage
Anemia	5	25	1	31	73.80%
Hemolytic crisis	1	-		1	2.38%
UTI	3	7	1	11	26.19%
LRTI	1	2		3	7.14%

**Table 3. Mode of delivery**

Mode of delivery	SS	AS	AS+b thalassemia minor	total	percentage
LSCS	1	16	1	18	42.85
Vaginal delivery	4	20	-	24	57.14

**Table 4. Obstetric outcome**

Outcome	SS	AS	AS+ b thalassemia minor	Total	Percentage
Previous perinatal loss	0	4	0	4	9.52%
Previous spontaneous abortion	1	7	0	8	19.04%
GDM	0	4	0	4	9.52%
IUGR/OLIGO	3	15	0	18	42.85%
Pre-eclampsia	2	6	1	9	21.42%
Gestational hypertention	1	3	-	4	9.52%
Eclampsia	0	1	-	1	2.38%
Abruption	1	3	-	4	9.52%
Preterm labor	2	5	-	7	16.66%

**Table 5. Fetal outcome**

Outcome	SS	AS	AS+b thal trait	Total	Percentage
Prematurity	2	7	0	9	21.42%
LBW < 2.5 kg	3	13	0	16	38.09%
FD	3	16	0	19	45.23%
Meconium	3	15	0	18	42.86%
Meconium aspiration syndrome	1	3	0	4	9.52%
NICU admission	3	6	0	9	21.42%
Perinatal death	0	1	0	1	2.38%

The most common adverse outcome was fetal distress 45.23%(n=19) and meconium-stained liquor 42.86%(n=18). Out of 18 newborns with meconium-stained liquor, four, i.e., 9.52%, developed meconium aspiration syndrome. Total nine newborns required NICU admission.

Prematurity was noted in 21.42%(n=9), and 38.09% (n=16) newborns had low birth weight. That is their birth weight was below 2.5 kg.

#### 4. DISCUSSION

Vidarbha region is one of the high prevalence regions for sickle cell disease. SCD varies indifferent tribes from 0-35% in Maharashtra. The screening test for sickle cell is done in all pregnant women irrespective of the hemoglobin level because if both mother and father are sickle cell traits, the baby may have sickle cell disease.

With proper medical care, more females with sickle cell disease are reaching childbearing age. Thus, more pregnant females with sickle cell disease or sickle cell trait are reporting to the hospital. In our institution, every pregnant female is screened for sickle cell disease. If screening is positive, hemoglobin electrophoresis is done to diagnose sickle cell disease. In SCD, at low-oxygen conditions, polymerization of the abnormal hemoglobin occurs, leading to rigid and fragile sickle-shaped red cells. This leads to increased episodes of vaso occlusive crisis, acute chest syndrome, and pregnancy-related complications [RCOG guideline 61]. According to Villers et al. [3], maternal morbidity was increased due to increased rates of cesarean section, Pregnancy-related events like pre-eclampsia, abruption, pulmonary complications, hypertension, and infection.

The incidence of SCD SS pattern was 0.30%, and of AS pattern was 1.98% the low incidence recorded may be because of undiagnosed asymptomatic sickle cell patients delivering in other centers. 100% of patients with sickle cell disease SS pattern presented as Anaemia and the percentage reduced to 73.80% when AS pattern was included, which corroborated with other studies [2]. Other medical conditions complicating pregnancy were hemolytic crisis, UTI, and LRTI. Of the 5 patients of SS pattern, only one had a hemolytic crisis. UTI was observed to be the most common complication, i.e., 26.19% in contrast to a study by Afolabj et al. [12]. There was no significant difference between SCD and ordinary women. Common

organisms isolated from the urine culture samples were klebsiella and e-coli; no patient developed pyelonephritis. This observation was similar to Kavitha and Hota et al. [2]. LRTI was seen in 7.14% at the time of delivery.

SCD patients had a higher incidence of miscarriage, 19.04%, and perinatal loss, 9.52%. This incidence was comparable to other studies done by D'Couth S et al. In our study, the proportion of SA pattern is more than other studies [2,3]. The major obstetric complication was IUGR, with Oligohydramnios seen in 42.85%, comparable to other past studies in past [2].

More than half of the cases in this study were primigravida, i.e., 25 out of 42. All the women of SS pattern had received blood transfusions during pregnancy and anemia, and anaemia were corrected; they still had medical and obstetric complications during pregnancy; this was also seen in the study by NGO et al. [8]. In our study, only 5 patients were of SS pattern from whom only 1 had the hemolytic crisis. There was no maternal mortality in our study, similar to the study by sun et al. Apart from IUGR and oligo, other obstetrics complications were pre-eclampsia 21.42%, gestational hypertension 9.52%, and eclampsia 2.38%. This rate of pre-eclampsia was more than the study by Al Jama et al. [13]. This may be because of underlying renal disease, placental ischemia, endothelial damage, and hypertension. There was no increase in pre-eclampsia in SCD in studies by Afolabj et al. [14] and Serjeant et al. [15]. In this study, 9.52% had abruption, which was associated with pre-eclampsia. 16.66% had preterm labor which included the patients with pre-eclampsia.

Of all patients, LSCS was done in 42.85%, and 57.14% had a vaginal delivery. The indications for LSCS were mostly meconium-stained amniotic fluid, fetal distress, previous LSCS, CPD, and uteroplacental insufficiency. Higher rate of caesarean delivery 42.85 was seen in our study which was similar to other studies in past [2,16].

Mothers having sickle cell disease had adverse outcome in their newborns because of uteroplacental insufficiency, alloimmunization, and opioid exposure. In our study the most common adverse outcome seen was fetal distress 45.23% and meconium stained amniotic fluid 42.86% which was similar to other studies in past [2,3].

Several studies have been documented to have results showing increase in IUGR, preterm delivery and stillbirths [2,3,4]. In our study IUGR/oligo was seen in 42.85%, preterm delivery was seen in 21.42% and only one case of perinatal mortality was noted. Placental ischaemia because of pre-eclampsia may be an important factor resulting in IUGR and oligo. Perinatal mortality seen was less because of less number of SS pattern which have higher mortality rate [2,13,14].

Preterm deliveries were seen in 21.42% and low-birth weight was seen in 38.09% of newborn. The above findings were because of increased number of IUGR. Birth weight was <2.5 kg in 38.09% of newborns. Similar results were seen in studies done in past [2,17,13,16].

All the patients of SCD SS pattern had received blood transfusion during pregnancy for correction of anaemia. Routine blood transfusion are not recommended by the RCOG. Only indications for blood transfusion are aplastic crisis, bone crisis, hemolytic crisis (HbA1<20%, hematocrit< 25%0) and infection. All patients were given folic acid 5mg and tablet sodamint thrice daily. Patients in whom iron studies showed iron deficiency were given oral iron supplementation.

## 5. CONCLUSION

In our study we have observed increased morbidity in pregnancy in women with SCD because of increased number of medical and obstetric complications. There is need for screening for SCD in each and every pregnant women in the high prevalence area so that early detection and intervention could be done to improve the outcome of both mother and baby. Couples should be counselled to undergo preconceptional testing for sickle cell disease, so that measures can be taken to give the pregnant women better antenatal care right from first trimester. Preconceptional counselling and testing will lead to antenatal diagnosis of SCD in fetus and action can be taken accordingly.

## CONSENT AND ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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