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"ADVERSE MATERNAL AND PERINATAL OUTCOMES IN SICKLE CELL DISEASE (Hb-SS) AND SICKLE CELL TRAIT (Hb-AS) COMPARED TO NORMAL PREGNANCIES (Hb-AA) : A RETROSPECTIVE STUDY FROM RURAL INDIA"

Obstetrics & Gynaecology

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ABSTRACT

Background: Sickle cell disease (SCD) poses significant maternal and perinatal risks, particularly in rural areas. This study compares adverse outcomes in pregnancies with SCD (SS), sickle cell trait (AS), and non-SCD controls (AA) in a tertiary care hospital. **Objectives:** To evaluate and compare maternal and perinatal outcomes among mothers with hemoglobin SS, AS, and AA , focusing on complications like anemia, preterm labor, and neonatal morbidity. **Methodology:** A retrospective study of 145 pregnant women (123 AS, 22 SS) and 200 AA controls was conducted at VNGMC, Yavatmal, Maharshtra. Data on demographics, obstetric history, and complications were analyzed using logistic regression. Outcomes included anemia, preterm labor, preeclampsia, neonatal weight, and mortality. Statistical analysis was performed using SPSS version 26. **Results:** The SS group exhibited severe anemia (59.1% vs. 31.7% AS, 6.5% AA), higher transfusion needs (50% vs. 10.6% AS, 6% AA), and increased sickle cell crises (45.5%). Maternal mortality was 4.5% in SS vs. 1.6% AS and 0% AA. Preterm labor (18.2% SS, 7.3% AS, 4% AA), UTI (27.3% SS), and puerperal sepsis (13.6% SS) were more prevalent in SS. Neonatal outcomes showed lower mean birth weight (1.9 kg SS vs. 2.1 kg AS, 2.4 kg AA), higher IUGR (59.1% SS), and perinatal mortality (13.6% SS) in SS. PIH incidence was comparable (18.2% SS, 17.9% AS, 12.5% AA). **Conclusion:** SCD pregnancies (SS) face elevated risks of maternal and perinatal complications, necessitating targeted interventions for improved outcomes.

KEYWORDS

Sickle cell disease, pregnancy, maternal outcomes, perinatal outcomes, anemia, rural health.

INTRODUCTION:

An estimated 30 million people worldwide suffer with sickle cell disease (SCD), a prevalent monogenetic hematological illness that is a serious health issue linked to high rates of morbidity and death [(1)]. 14.5% of all babies in India have sickle cell disease [(2)]. People who are homozygous for the βS globin gene (SS) or heterozygous for the βS allele and other aberrant β globin gene alleles, including βC (SC), Sβ0 thalassemia, or Sβ+ thalassemia, are at risk for SCD [(3)]. In addition to sickle-related difficulties, pregnant women with sickle cell disease are more likely to have perinatal mortality and obstetrical complications [(4)]. Anemia, prepartum and postpartum painful crises, preeclampsia, eclampsia, pulmonary difficulties, preterm delivery and other related hazards, and intrauterine growth restriction (IUGR) are among the issues that can affect both the mother and the fetus [(5)]. Numerous studies have demonstrated a detrimental correlation between SCD and perinatal outcomes and mother health [(6)]. The risk of unfavorable pregnancy outcomes with SCD has not been well studied in India [(7)]. Tribal people in Gujarat, Madhya Pradesh, Odisha, and Chhattisgarh are prone to SCD.

The sickle gene is primarily present in Maharashtra's eastern districts, including the Vidarbha area, and in certain areas of Marathawada. In various tribes, the percentage of sickle cell carriers ranges from 0% to 35%. In the Indian state of Maharashtra, tribes including the Bhils, Madias, Pawaras, Pardhans, and Otkars have a high frequency of HbS (20–35%), according to Kate and Lingojwar [(8)]. Additionally, it is believed that there are about 5000 instances of sickle cell anemia in the districts of Gadchiroli, Chandrapur, Nagpur, Bhandara, Yavatmal, and Nandurbar [(20)]. In a rural tertiary care hospital, this retrospective study compared the effects of sickle cell trait and sickle cell disease on pregnancy, labor, puerperium, and fetal outcome with non-SCD pregnancy as a control.

This retrospective study aimed to compare the outcomes among SCD and sickle cell trait on pregnancy, labor, puerperium, and fetal outcome and non-SCD pregnancy as control in tertiary care hospital in rural setting.

MATERIALS AND METHODS:

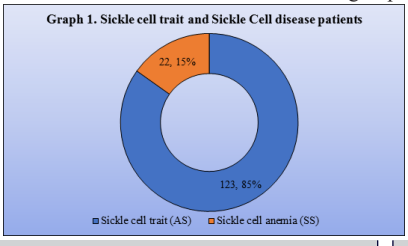
In a comparative retrospective study, a total of 145 pregnant women aged 19 to 40 years attending sickle OPD at VNGMC, Yavatmal, Maharashtra, between June 2024 to December 2024 were observed throughout pregnancy and delivery after acquiring consent from them. Their medical records were analyzed and compared with the result from 200 control pregnant women matched for age and gravida and of similar socioeconomic origin. A total of 145 SCD cases were studied compared with 200 pregnant age- and gravida-matched control with normal hemoglobin (genotype AA). Amongst the cases were sickle cell trait (AS; 123), and sickle cell anemia (SS; 22). During their visit to the prenatal clinic, women were included in the study based on their positive SCD status.

A thorough history was taken with special emphasis on the obstetric history and significant past history of symptomatology of underlying disease. Abortions were excluded from the study. Measurement and classification of the variables Preterm labor was defined as onset of labor before 37 completed weeks of gestation. Anemia was defined as hemoglobin concentration less than 10 gram%. Pregnancy-induced hypertension (PIH) was defined as blood pressure more than 140/90 mmHg on two occasions six hours apart with edema or proteinuria or both. Early neonatal death was defined as neonatal death within seven days of birth. Low birth weight (LBW) was defined as birth weight less than 2500 grams. IUGR was diagnosed when the birth weight was less than the 10th percentile of the average for gestational age. Delayed conception (primary infertility) was diagnosed if a couple failed to achieve pregnancy after one year of unprotected intercourse. Regarding onset of menarche, the first menstrual period usually occurs between the ages of 10-16 years, the average being 13.5 years in India, and an onset after 16 years is considered delayed menarche.

The complete proforma followed to study these cases has been given in the Appendix. Statistical analysis Cross tabulation method was used to estimate pregnancy outcomes, diagnosis morbidities and treatment received by SCD groups. We excluded the missing values from analysis. To evaluate the risk of these pregnancy outcomes logistic regression was performed. Outcome of each pregnancy and associated conditions were taken as a dependent variable and SCD status as an independent variable. Pregnant women with normal hemoglobin were compared to pregnant women with SCD and sickle cell traits. Odds ratios were calculated comparing sickle cell trait with SCD. We used SPSS version 26 (IBM Corp., Armonk, NY, USA) for statistical analysis.

RESULTS:

In the present study, of the 145 patients, 123 cases (84.8%) had sickle cell trait and 22 cases (15.2%) had sickle cell anemia. These instances were contrasted with 200 members of the AA control group.



In the AS group, age was ranging from 18 to 43 years, whereas the youngest was 18 and the oldest was 32 in the SS group. Since no one in the SS group was older than 32, it is likely that the majority of the patients in the SS group were younger due to their reduced life expectancy.

Table 1. Demographic Characteristics of the patients from 3 groups:

Characteristics		SS (n=22)	AS (n=123)	AA (n=200)	P value
Mean Age		22.6 years	29.3 years	31.7 years	>0.05 (NS)
Gravida Status	G1	10(45.5%)	62(50.4%)	102(51%)	>0.05 (NS)
	G2	6(27.3%)	38(30.9%)	73(35.5%)	
	G3	4(18.2%)	16(13.0%)	17(8.5%)	
	G4 or more	2(9.1%)	7(5.7%)	8(4%)	
Mean Age of Menarche		14.7 years	12.8 years	13.1 years	>0.05 (NS)
H/o Spontaneous Abortion		3(13.6%)	21(17.1%)	12(6%)	>0.05 (NS)

Majority, 50.4% of the AS patients had primi-gravidas and 30.9% had second gravidas. Majority, 45.5% of the SS patients had primi-gravidas, and 27.3% had second gravidas. They were contrasted with controls with normal hemoglobin. The mean age at menarche was comparable in all the groups (p value >0.05). History of Spontaneous Abortion was also similar in groups. (p value >0.05). Thirteen (6.5%) of the parous patients in the AA group, twenty-three (18.7%) in the AS group, and seven (31.8%) in the SS group had experienced a prior stillbirth.

Table 2. Blood Investigations and need of Blood Transfusion among 3 groups:

Characteristics		SS (n=22)	AS (n=123)	AA (n=200)	P value
Anaemia	Mild	1(4.5%)	22(17.8%)	39(19.5%)	**<0.05(S)**
	Moderate	8(38.4%)	62(50.4%)	148(74%)	
	Severe	13(59.1%)	39(31.7%)	13(6.5%)	
Blood Transfusion		11(50%)	13(10.6%)	12(6%)	**<0.05(S)**
Hb (gm%)		7.28	8.71	8.66	**<0.05(S)**
MCV		87.23	80.26	78.02	>0.05(NS)
MCHC		27.52	33.16	35.12	>0.05(NS)
RBC		2.18	2.9	3.35	>0.05(NS)
RC		2.97	2.38	1.20	>0.05(NS)

Maternal Complications:

The most frequent prenatal problem seen in both the control group and SCD patients was anemia. Normocytic normochromic anemia was quite severe in 97.5% of the SS group patients. These individuals reported feeling weak all over and being exhausted. History of blood transfusion was significantly high in SS groups compared (50%), compared to other groups (10.6% in AS and 6% in AA). The haematological characteristics of the AA and AS groups were similar (Table 2).

Table 3. Maternal Complications Among 3 Groups:

Maternal complications	SS (n=22)	AS (n=123)	AA (n=200)	P value
Sickle Cell Crisis	10(45.5%)	3(2.4%)	0(0%)	**<0.05(S)**
Pneumonia	1(4.5%)	0(0%)	0(0%)	**<0.05(S)**
PIH	4(18.2%)	22(17.9%)	25(12.5%)	>0.05(NS)
UTI	6(27.3%)	14(11.4%)	19(9.5%)	**<0.05(S)**
Pre-term Labour	4(18.2%)	9(7.3%)	8(4%)	**<0.05(S)**
Vaginal Delivery	13(59.1%)	48(39.0%)	63(31.5%)	>0.05(NS)
Maternal Mortality	1(4.5%)	2(1.6%)	0(0%)	**<0.05(S)**
Puerperal Sepsis	3(13.6%)	2(1.6%)	3(1.5%)	**<0.05(S)**

The incidence of sickle cell crisis in 19 (43.4%) of SS patients, who primarily presented with severe joint pain and dyspnoea, was the single most important factor contributing to maternal morbidity with sickle cell anemia. One patient from the SS group had pneumonia. As 22 (17.9%) in the AS group, 4 (18.2%) in the SS group, and 25 (12.5%) in the AA group, PIH was a prevalent prenatal complication in both groups.

Occurrence of urinary tract infections (UTIs), Pre-term Labour, Maternal Mortality and Puerperal Sepsis was also significantly higher in SS group. Impaired fetal well-being and PIH were the most frequent reasons for inducing labor at term in both the AS and SS groups. Need for Caesarean Section was highest in SS group but difference was not significant. The most frequent reason for emergency CS across all groups was fetal distress, which occurred in 143 (71.5%) AA cases, 96 (78.1%) AS cases, and 13 (50.1%) SS cases. In contrast to the control group, which saw no deaths, the research group experienced three maternal deaths—two in the AS group and one in the SS group.

Neonatal Complications:

SS individuals had a mean birth weight of 1.9 kg, whereas the AA and AS groups had mean birth weights of 2.2 kg and 2.1 kg, respectively. Only two infants in the SS group weighed more than 2.5 kg. IUGR and Perinatal mortality were significantly higher in SS group. The SS group experienced three stillbirths. Regarding stillbirth, we found no discernible difference between the groups.

Table 4. Neonatal Complications Among 3 Groups:

Neonatal complications	SS (n=22)	AS (n=123)	AA (n=200)	P value
Mean birth weight	1.9±0.92 Kg	2.1±0.81 Kg	2.4±0.76Kg	**<0.05(S)**
Low Birth Weight	20(90.9%)	78(63.4%)	76(38%)	**<0.05(S)**
IUGR	13(59.1%)	23(18.7%)	39(19.5%)	**<0.05(S)**
Still Birth	3(13.6%)	14(11.4%)	19(9.5%)	>0.05(S)
Perinatal mortality	3(13.6%)	6(4.9%)	4(2%)	**<0.05(S)**

DISCUSSION:

It is commonly recognized that pregnant women with sickle cell disease (SCD) are more likely than healthy women to experience maternal and fetal problems during pregnancy [4]. Due to inadequate prenatal treatment, particularly in rural areas, the death rate from SCD during pregnancy is 4–40% [10] in India and 7–12% in underdeveloped nations like those in Africa [11]. Our study's findings aligned with previously published information. Our findings are consistent with those of Hickman et al. [12] and Barfield et al. [13], who calculated that around 1% of all pregnancies had SCD. In India, anemia is quite common in pregnant women, and women with sickle cell disease (SCD) are more likely to have maternal and fetal health issues [14].

The current study shown that, in comparison to pregnancies with the SCD trait and those without, women with homozygous SCD are more likely to experience low birth weight, preterm birth, and stillbirth. Similar results have been observed by Smith-Whitley [15] and Muganyizi and Kidanto [16]; compared to normal births, SCD deliveries are more likely to result in lower baby weights, shorter gestational periods, and a greater stillbirth rate. Pregnancy has been linked to an increased risk of sickle cell crisis and hospitalization in women with sickle cell anemia. According to several publications, 50% of pregnant women with sickle cell disease experience sickle cell crisis, which can be fatal [17]. Nonetheless, we found that 45.5% of SCD patients experienced sickle cell crises in our research, which is comparable to another published study [18]. Abortion risk in women with sickle cell disease is significant, according to several studies.

The current study found that the maternal mortality rate for women with SCD was much greater than that of women without SCD, in contrast to studies conducted in industrialized nations (12,26,39). The sickle cell anemia (SS) group had a maternal death rate of 4.5%, which is comparable to other developing nations with subpar prenatal, perinatal, and postnatal care.

Although the exact cause of premature birth in women with sickle cell disease is still unknown, several published studies have indicated that these women are more likely to have preterm delivery [19]. However, in our study, the SS group experienced 18.2% of premature birth cases. Compared to women without SCD, more women with SCD had cesarean sections done. When choosing CS, surgeons may also benefit from ongoing fetal monitoring, such as fetal heart rate [4]. Fetal distress, unsuccessful labor progression, or a poor prior obstetrical history were the primary reasons for performing cesarean sections. Women with SCD are more likely to experience IUGR, according to several publications [20].

In our study, women with HbSS had a greater prevalence of IUGR than those with HbAS or the control group. Furthermore, compared to normal women, HbSS women had a higher risk of IUGR. Long-term maternal anemia, hypercoagulation during pregnancy, the degree of sickling, and vaso-occlusion, which impair placental circulation and

induce uterine growth limitation, may all contribute to this elevated risk [21]. IUGR is also caused by a decrease in blood oxygen levels, particularly in anemic women, which impacts or lowers placental perfusion. HbSS women were more likely to be anemic, according to Yu et al. Women with sickle cell disease had a significant frequency of anemia, which was caused by hemolysis or hypersplenism [22]. Numerous publications have documented additional problems in women with anemia, including spontaneous preterm labor, preterm birth, premature rupture of membrane (PROM), and LBW newborns. Both an elevated infant mortality rate (IMR) and a higher risk of perinatal morbidity and death are caused by these problems.

We found that women with HbSS had a higher risk of intrauterine fetal death (IUFD). IUFD and IUGR are caused by impaired metabolic exchange and decreased food availability, which are caused by placental vaso-occlusion, placental infarction, and placental insufficiency, according to a few studies [23]. Furthermore, persistent prenatal anemia in women with SCD has been linked to stillbirth and a high prevalence of PIH. 9.5% of the AA group, 11.4% of the AS group, and 27.3% of the SS group had UTIs in the current research. Similar findings were made by Thame et al. [24] and Seoud et al. [25], who noted that women with SCD are more likely to experience placenta previa and UTIs.

18.2% of PIH cases were found in the SS group, 17.9% in the AS group, and 12.5% in the AA group in the current study. Women with HbSS had a higher incidence of PIH, according to earlier published research. Preeclampsia is more common in women with HbSS than in healthy controls, according to several publications. Women with HbSS are more likely than those with HbAS to develop preeclampsia. While Cudihy and Lee [26] found that preeclampsia was up to 10 times more common in women with HbSS than in the control group, Larrabee and Monga [27] found that it was present in 24.7% of sickle-positive women.

CONCLUSION:

The study highlights significantly higher maternal and perinatal complications in pregnant women with sickle cell disease (SS) compared to those with sickle cell trait (AS) and controls (AA). Enhanced prenatal care, anemia management, and fetal monitoring are crucial to improving outcomes in SCD pregnancies, especially in rural settings. Identification of women at greater risk, routine screening for fetal development in the third trimester, women with sickle cell disease, and anemia care are critical to reducing unfavorable maternal and fetal outcomes.

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