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STUDY ON THE FETO-MATERNAL OUTCOME IN SICKLE CELL HEMOGLOBINOPATHY AT A RURAL TERTIARY CARE CENTER IN KERALA

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ABSTRACT

Background: In India sickle cell disease is a genetic haematological condition that is common. Pregnancy outcomes can be adversely affected by sickle cell disease as it can exacerbate pregnancy difficulties. The present research was done to study the feto-maternal outcome in sickle cell hemoglobinopathy at a rural tertiary care center in Kerala.

Methods: The retrospective study was done among 28 pregnant women with sickle cell disease or trait who were seen in the department of OBG during the period of Dec 2017 – Nov 2019. Pregnancy outcomes, diagnostic morbidities, and treatments received were estimated using the cross-tabulation approach.For statistical analysis, we utilized SPSS version 25.0.

Results: Total patients suffering from sickle cell disease were 9 (32.1%) and those with sickle cell trait were 19 (67.8%). The commomcomplications seen during the pregnancy were pre-eclampsia (14.2%), postpartum eclampsia (3.5%), pre term labor (17.9%), hypertension (7.1%), IUGR (39.2%) and oligohydramnios (21.4%). Main SCD complication were Anemia (67.8%) blood transfusion (32.1%), UTI (28.5%), bone crisis (10.7%), and vaso-occlusive crisis (3.5%).Common mode of delivery was vaginal (53.5%) whereas 46.4% delivered through C-section. Perinatal outcome observed were postpartum depression and psychosis (7.12%), severe anemia and thrombocytopenia (3.5%), NICU admission (7.12%), shoulder dystocia (3.5%) and mortality (3.5%).

Conclusion: Due to obstetric and medical problems, pregnancy in individuals with sickle cell disease is linked to a higher risk of maternal morbidity and a higher risk of perinatal mortality.

Keywords: Maternal morbidity, Maternal mortality, Perinatal outcome, Perinatal mortality, Sickle cell disease, Vaso-occlusive crisis.

INTRODUCTION

The'sickle' gene, which modifies hemoglobin structure, is the cause of a set of hereditary singlegene autosomal recessive illnesses known as sickle cell disease (SCD). Sickle hemoglobin, also known as hemoglobin S, is produced when valine substitutes glutamic acid once in a single β chain. This process starts at codon 6 of the β gene, where an A-for-T substitution occurs. The term sickle cell disease (SCD) encompasses sickle cell anemia (HbSS) as well as combinations of HbS with aberrant hemoglobins such as hemoglobin C (resulting in HbSC), beta thalassemia (producing HbS-β thalassemia), and combinations with hemoglobin D, E, or O-Arab.[1] Known as sickle trait (AS), hemoglobin S coupled with normal hemoglobin (A) is generally asymptomatic with the exception of a potential increased risk of microscopic hematuria and urinary tract infections.

The main cause of sickle-shaped and fragile red blood cells (RBCs) in sickle-shaped disease (SCD) is the polymerization of hemoglobin under low oxygenation circumstances, which results in the creation of long fibers within the RBCs. The majority of the clinical manifestations of this multiorgan disease are caused by these cells' propensity for enhanced breakdown, which results in hemolytic anemia, and vaso-occlusion in the small blood arteries.A vasoocclusive event has been linked to red cell dehydration, aberrant RBC adherence to the vascular endothelium, inflammatory processes, activation of all vessel cells, and anomalies in nitric oxide metabolism.[2]

Pregnancy among women with sickle cell disease is associated with a multitude of obstetric, non-obstetric, and fetal problems. The concept of SCD has been put forth as a persistent state of inflammation. The microvascular damage may be attributed to the endothelial damage caused by sickled red blood cells and the subsequent production of proinflammatory cytokines. The physiological changes that occur in the vascular, endothelial, and inflammatory systems during pregnancy might potentially worsen these pathophysiological alterations, resulting in maternal problems such as preeclampsia and fetal growth limitation.[3] Maternal issues may emerge due to chronic underlying organ failure, such as renal illness or pulmonary hypertension, as well as acute complications associated with sickle cell disease (SCD), including vaso-occlusive crises and acute chest syndrome. Additionally, complications specific to pregnancy can also contribute to maternal problems. The primary maternal problems associated with pregnancies complicated by sickle cell disease include anemia, infection, vasoocclusive crisis, and preeclampsia. Fetal complications that impact perinatal outcomes encompass intrauterine growth restriction, preterm birth, aberrant fetal heart rate patterns, and intrauterine fetal demise.There are eight complications associated with sickle cell disease that can lead to preterm labor and an increased likelihood of requiring a caesarean section in order to enhance the overall outcome of the pregnancy.Pregnant women with sickle cell disease exhibit elevated rates of maternal and fetal mortality.[4]

In Gujarat, sickle cell disease is very common among the Dhodia, Dubla, Gamit, and Naika tribes.A number of south Gujarati tribal tribes, including the Chaudhary, Gamit, Rohit, Vasava, and Kukana, have demonstrated a high frequency of both the β-thalassaemia trait and HbS.[5]

In India, screening has been conducted across a wide range of population groups, and the results have indicated a high prevalence of the sickle cell gene among three socio-economically disadvantaged ethnic groups: the scheduled tribes, the scheduled castes, and other backward classes.[6]

The present research was done to study the feto-maternal outcome in sickle cell hemoglobinopathy at a rural tertiary care center in Kerala.

MATERIAL & METHODS

The retrospective study was done among pregnant women with sickle cell disease or trait who were seen in the department of OBG during the period of Dec 2017 – Nov 2019.Ethical clearance was taken from institutional ethical committee before commencement of study.

The total sample size came out to be of 28 patients. The patients were selected on the basis of inclusion and exclusion criteria as follows:

Inclusion Criteria
All pregnant women with sickle cell hemoglobinopathies.

Exclusion Criteria
Patients with previously diagnosed medical conditions in pregnancy such as C/C HTN, DM, cardiovascular diseases, autoimmune conditions
Data was collected from the medical records department. Demographic data included age, address, tribal background, BMI. The genotype of sickle cell disease, the blood hemoglobin levels and any h/o blood transfusion will be recorded. Maternal morbidity was assessed by analyzing both medical and obstetric complications such as anemia, infectious morbidity, sickle cell crises, IUGR, gestational hypertension, eclampsia, abruption, and preterm labor.
The mode of delivery, spontaneous or induced, gestation age at delivery and occurrence of intrapartum /postpartum complications was also noted.
Fetal outcomes were assessed by birth weight, NICU admission and mortality.
Pregnancy outcomes, diagnostic morbidities, and treatments received were estimated using the cross-tabulation approach. The missing values were not included in the analysis. Each pregnancy's outcome and any related conditions were considered dependent variables, while the presence of SCD was considered an independent variable. For statistical analysis, we utilized SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

RESULTS
Out of 18 patients 10.7 % were of less than 20 years of age group, 82.1% were of 20-30 years and 7.1% were of greater than 30 years as shown in table 1.

Age groups	**Frequency (%)**
<20 years	3(10.7)
20-30 years	23 (82.1)
>30 years	2 (7.1)
Table 1. Distribution of patients according to age	

Total patients suffering from sickle cell disease were 9 (32.1%) and those with sickle cell trait were 19 (67.8%) as shown in table 2.

Variable	**Frequency (%)**
Sickle cell disease	9 (32.1)
Sickle cell trait	19 (67.8)
Table 2.Division of patients	

The complications seen during the pregnancy and post pregnancy were pre-eclampsia (14.2%), postpartum eclampsia (3.5%), pre term labor (17.9%), hypertension (7.1%), IUGR (39.2%) and oligohydramnios (21.4%) as shown in table 2.

Complications	**Sickle cell disease**	**Sickle cell trait**	**Total**
Pre –eclampsia	2	2	4 (14.2)
Eclampsiapost-partum	1	0	1 (3.5)
Pre term labor	2	3	5 (17.9)
Hypertension	1	1	2 (7.1)
IUGR	2	9	11 (39.2)
Oligohyramnios	1	5	6 (21.4)
Table 3. obstetric complications			

Anemia (67.8%) was the most common complication in sickle cell disease . 32.1 % had blood transfusion, 28.5% had UTI, 3.5% bronchopneumonia, 10.7% had bone crisis, 14.2% had hemolytic crisis and 3.5% had vaso-occlusive crisis as shown in table 4.

Complications	**Sickle cell disease**	**Sickle cell trait**	**Frequency (%)**
Anemia	9	10	19 (67.8)
Blood transfusion	5	4	9 (32.1)
Urinary tract infection	4	4	8 (28.5)
Bronchopneumonia	1	0	1 (3.5)
Bone crisis	2	1	3 (10.7)
Hemolytic crisis	2	2	4 (14.2)
Vaso-occlusive crisis	1	0	1 (3.5)
Table 4. sickle cell disease related complications			

The common mode of delivery was vaginal (53.5%) whereas 46.4% delivered through C-section. Among those who delivered before 37 weeks were total 6 patients and 22 delivered between 37-40 weeks as shown in table 5.

Gestational age	**Vaginal**			**C-section**		
	Sickle cell disease	**Sickle cell trait**	**Total**	**Sickle cell disease**	**Sickle cell trait**	**Total**
<37 weeks	2	1	3 (20)	2	1	3 (23.1)
37-40 weeks	7	5	12 (80)	7	3	10 (76.9)
Total	15			13		
Table 5. Gestational age at delivery and mode of delivery						

The most common indications for C-section were fetal distress (38.4%), CPD-short primi (7.6%), previous C section (23.0%), breech, tachycardia (7.6%) and severe PE/ IUGR/ Abnormal Doppler/MSAF grade2 IUGR (23.0%) as shown in table 6.

Indications	**Sickle cell disease**	**Sickle cell trait**	**Frequency (%)**
Fetal distress	4	1	5 (38.4)
CPD-short primi	1	0	1 (7.6)
Previous C section	2	1	3 (23.0)
Breech , tachycardia	1	0	1 (7.6)
Severe PE/ IUGR/ Abnormal Doppler/MSAF grade2 IUGR	1	2	3 (23.0)
Table 6. Indications for C section			

The total babies having birth weight greater than 2.5 kg were 32.1%, those with birth weight between 1.5-2.5 kg were 64.2% and less than 1.5 kg were 3.5% as shown in table 7.

Birth weight	**Sickle cell disease**	**Sickle cell trait**	**Frequency (%)**
>2.5 kg	0	9	9 (32.1)
1.5-2.5 kg	8	10	18 (64.2)
<1.5 kg	1	0	1 (3.5)
Table 7. Baby birth weight distribution			

The perinatal outcome observed were severe anemia and thrombocytopenia (3.5%), NICU admission (7.12%), shoulder dystocia (3.5%) and mortality (3.5%) as shown in table 8.

Perinatal outcome	Sickle cell disease	Sickle cell trait	Frequency (%)
Severe anemia and thrombocytopenia	1	0	1 (3.5)
NICU admission	2	0	2 (7.12)
Shoulder dystocia	1	0	1 (3.5)
Mortality	1	0	1 (3.5)
Table 8. Perinatal outcome			

DISCUSSION

Sickle cell disease can complicate pregnancy since there is a higher chance of negative outcomes for both the expectant mother and the newborn. In patients with sickle cell disease, the physiological changes associated with pregnancy-such as elevated blood viscosity, increased metabolic demand, and hypercoagulability-are exacerbated. This increases the risk of complications like vaso-occlusive crisis, acute chest syndrome, osteonecrosis, hepatic necrosis, leg ulcers, and thromboembolic events. Additionally, vascular blockage in the placenta can result in villous fibrosis, necrosis, and infarction. This impairs uteroplacental circulation, which can cause long-term fetal hypoxia and unfavorable fetal outcomes.[7] A greater number of females are reaching childbearing age due to increased awareness of the condition and improved treatment choices and facilities. As a result, there are now more pregnant people with sickle cell disease.

Kerala is one of the states with a high rate of SCD prevalence, and scheduled tribes are frequently affected.[8]According to reports, the prevalence of sickle cell disease is 30% in North Kerala, particularly in the district of Wayanad's hilly areas.[9] More women are reaching childbearing age due to increased knowledge of the illness and improved treatment options and facilities in our area. Due to this, our center is now seeing a rise in the number of pregnant SCD patients-mostly from indigenous communities. Only 32.1% of the women giving birth in our institution had sickle cell disease in our study, while 67.8% had sickle cell trait which is dissimilar to study done by where to the 0.2% of women were suffering with SCD , the difference may be due to change in sample size number among two studies.[4]

Compared to the general population, sickle cell women are more likely to experience maternal and fetal problems during pregnancy.[10,11] In the current study out of total women (disease and trait), 3.5% of cases had eclampsia and 14.2% had pre-eclampsia. Wilson et al. found that women with sickle cell disease (HbSS) had a ten-fold increased risk of developing eclampsia, a potentially fatal consequence of preeclampsia.[12,13] Intrauterine growth restriction was observed in 39.2% of the patients in this investigation, compared to 20.1% in a study by Fatema et al[14] In32.1% of sickle cell births in the current study required blood transfusions; this is less than the 52.7% transfusions reported by Desai et al and comparable to the 32% transfusions reported by Yu et al[15,16] It has been demonstrated that pregnancy makes sickle cell crises worse. Approximately 3.5% of vaso occlusive crises in our research this is significantly less than the 61.7% of vaso-occlusive crisis cases found in a study by Pinto et al.[11]

The study found that the most common infectious complications among all women were urinary tract infections (28.5%) and pneumonia (3.5%). These findings are similar to those of a study by Yu et al., which found that the combined incidence of UTI, lobar pneumonia, and osteomyelitis was 19%, and a study by John et al., which found an extremely high incidence of 82.5%. In Muganyizi et al.'s Tanzanian study, 82% of sickle cell disease women died as a result of infections.[16,17,18]

In the current study the common mode of delivery was vaginal (53.5%) whereas 46.4% delivered through C-section. Among those who delivered before 37 weeks were total 6 patients and 22 delivered between 37-40 weeks. In a study done by Modi RS et al out of total 28 (65.11%) cases delivered vaginally, while 15 (34.88%) cases underwent caesarean section.[19]

The most common indications for C-section were fetal distress (38.4%), CPD-short primi(7.6%), previous C section (23.0%), breech, tachycardia (7.6%) and severe PE/ IUGR/ Abnormal Doppler/MSAF grade2 IUGR (23.0%). In a study done by D'Couth S et al themost common indication for caesarean section was previous caesarean (54.16%), followed by fetal distress and Doppler abnormalities associated with intrauterine growth restriction.[20]

The incidence of preterm birth in our study found in women suffering with sickle cell disease or trait was 24.1%, which was less than the 44–45% incidence found in studies by Desai et al and Ugobama et al.[4,15] Low birth weight has been linked to sickle cell disease in pregnancy; in our study, it was 64.2%. Ugboma et al reported that sickle cell disease was present in almost 50% of pregnancies, whereas Desai et al found it in 43% of cases.[4,15] This could be caused by intrauterine growth limitation, maternal anemia, hypertension, and reduced gestational age at birth.

In the current investigation, there was one maternal death overall (3.5%) in spite of numerous potentially fatal complications. This might be as a result of the primary healthcare services being improved and the early referral of cases of sickle cell disease from the isolated tribal communities to our facility. However, a small number of earlier investigations have found no rise in perinatal death.[6,13]

Kerala appears to have a greater rate of sickle cell anemia survival than other Indian states. When sickle cell disease complicates a pregnancy, there is a high risk of stillbirths and infant mortality in India and other nations. Due mostly to growth restriction, we also experienced a significant rate of perinatal mortality. However, a small number of earlier investigations have not found a rise in perinatal death.[20]

The current study has a few limitations. This study is retrospective and is based on patient data that was gathered and examined at a hospital. Women with SCD who gave birth at home were not included in our study.Consequently, it's possible that the study's findings cannot be applied to women who gave birth at home. The study only includes pregnant women who were admitted; however, it did not include pregnant women who were admitted for conditions unrelated to sickle cell disease.

CONCLUSION

Due to obstetric and medical problems, pregnant women with sickle cell disease have higher rates of maternal morbidity and neonatal mortality. Public health organizations must implement intensive screening programs to find sickle cell disease in women. Additionally, steps should be done to better care for patients, including early and better prenatal care, fast identification and treatment of problems, greater preconception awareness and counseling about the disease, and early referral to tertiary care facilities.

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