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Maternal and Neonatal Outcomes with Sickle Cell Disease (SCD) in a Tertiary Health Care Hospital in a South Indian Population

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Keywords: Sickle cell disease; Sickling; Anaemia in pregnancy; Oxygen; LSCS.

Key message: Newer approach of treatment with better pregnancy outcomes in mothers with SCD.

Abstract

Introduction: Sickle Cell Disease (SCD) is a major risk factor contributing to obstetric complications and perinatal mortality in addition to sickle cell related complication. The management of SCD requires a multidisciplinary approach by teams of obstetricians, anesthesiologists, hematologists, neonatologist and intensive care setups who are capable of managing SCD. The recommendations for several decades have been prophylactic transfusion for treatment of pregnant women with SCD.

Objectives: To assess the pregnancy outcomes of mothers with SCD in a South Indian population.

Study design: Our study was a retrospective record study, which looked into various aspects of obstetrical outcomes and complications in sickle cell disease mothers. Records of the In-Patient Medical Record Department (MRD) folders of patients with Immune thrombocytopenia who delivered at St. Johns Medical College Hospital, Bangalore were studied.

Results: Out of eight pregnant women, four women were diagnosed (50%) with established Sickle cell disease while three (37.5) had been diagnosed with sickle-thalassemia hemoglobinopathy and one patient (12.5%) had a sickle cell trait. The most common obstetric complication encountered in women with SCD was grade II MSL (25%). PGE2 (25%) was the preferred mode of induction in two patients followed by PGE1+PGE2 in 12.5% of the study subjects. Higher chance of LSCS rates (75%) were seen when compared with normal deliveries.

Conclusion: SCD when managed vigilantly in the antenatal period poses minimal risks to mother and foetus. Mothers with SCD should be screened antenatal to look for features of hydrops or bleeding manifestations such as intraventricular haemorrhage in foetus.

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Introduction

Sickle Cell disease (SCD) is a major risk factor contributing to obstetric complications and perinatal mortality in addition to sickle cell related complication [1,2]. The most common haemoglobinopathy reported in the United States was SCD, in 8% of African Americans [3,4].

In 1972 Hendricks et al reported maternal mortality as high as 11.5% in women with SCD [3]. Recent advances in medicine have caused a decline in such cases of maternal mortality from 4.1% to 1.7% after 1972, as reported by Powars et al. [3]. Ghana reported 2% of neonates to be affected by SCD leading to 14,000 new cases annually [5].

Mutations that give rise to variation in the β chain are seen in Africa, Saudi Arabia and India [6]. Pregnant women of African descent have higher risk of adverse pregnancy outcomes compared to European women with SCD [7]. Prevalence of sickle cell anemia in the Saudi population was estimated to be 26 % [8]. Gayatri et al stated that India accounted for 14.5% of the total newborns with SCD [9].

SCD occurs in homozygous individuals for the SS gene (β^s), heterozygous individuals for the β^s allele and different abnormal β globin gene allele like β^c , $S\beta^0$ thal or $S\beta^+$thal [1]. The disease results from the abnormal pairing of hemoglobin S (HbS) with other abnormal hemoglobin, the most severe being HbSS and HbSC [3].

The management of SCD requires a multidisciplinary approach by teams of obstetricians, anesthesiologists, hematologists, neonatologist and intensive care setups who are capable of managing SCD [1,8]. The recommendations for several decades has been prophylactic transfusion for treatment of pregnant women with SCD [6].

The disease causes anemia, acute vaso-occlusion affecting organ systems like the heart, lungs, kidneys, intestines, brain and long bones causing patients to undergo recurrent hospitalization and prolonged hospital stay for these problems [7].

Sickling crisis in SCD pregnant women can occur in cases of extreme anemia, dehydration, acidosis, vigorous exertions and high altitude [8]. Sickle cell crisis, Urinary Tract Infections (UTI's), anemia, gestational diabetes, pneumonia are other complications encountered in patients with SCD [5].

Abortions, preeclampsia, Intrauterine Growth Restriction (IUGR), preterm labour, premature delivery, perinatal mortality, abnormal placentation, infertility, have been common complications encountered in pregnant women with SCD [6,10]. Neonatal complications like low birth weight, fetal distress, were reported by Boafor et al [2].

Some clinicians would advice their patients with SCD to avoid pregnancy and undergo primary sterilization, elective abortions and post partum sterilization to avoid further obstetric complications [3].

Hence the disease varies in clinical severity and potential serious complications and high maternal morbidity and mortality and adverse perinatal outcomes [10].

With few studies on SCD in the Indian sub continent on obstetric and medical complications in women with SCD we undertook a study to look into the outcomes of pregnancy in women with SCD.

Aims and objective(s) of the Study

1. To assess the pregnancy outcomes of mothers with SCD in a Tertiary Health care hospital in a South Indian population.

Methodology

The study was a retrospective record review carried over 6 years. Records of all the patients with SCD diagnosed by clinical signs, symptoms, deranged blood investigation, peripheral smear with sickle cells etc. were studied. The other hemoglobinopathies like hereditary spherocytosis, G6PD deficiency, thalassemia, protein S and C deficiency were excluded, although co existing illnesses were considered (eg. SCD and thalassemia). The study population included patients who were admitted and evaluated for SCD, in the past five years (1stJanuary 2014-30thApril 2020) at a tertiary care hospital. Ethical approval was obtained from the Institutional Ethics Committee prior to the start of the study (IEC Ref No: 319/2020).The number of antenatal visits, fetal growth assessment, and development of any new vaso-occlusive symptoms were recorded. Initial diagnosis and treatment medications used were recorded. Perinatal outcomes like mode of delivery, APGAR, complications at birth, NICU admission were studied.

Maternal variables

Development of any new symptoms like fatigue, jaundice, decreased fetal movements, pain abdomen, bleeding or leaking per vagina were noted. Blood parameters like complete haemogram, liver function test levels, and renal function tests of the mother at admission were documented. Pregnancy outcomes like need for induction of labor, mode of delivery was recorded. Complications like severe preeclampsia, PPH (post partum hemorrhage), need for admission into Intensive Care Unit (ICU) and need for blood transfusions was documented. Monitoring of blood loss during vaginal delivery or LSCS was studied.Treatment of patients during the antenatal, intrapartum and postnatal period was also studied.

Fetal variables

Neonatal outcomes like complications at birth, preterm births, intra uterine fetal demise, APGAR scores, and birth weight were reviewed.

Analysis

Data was analysed using the SPSS version 16 after it was manually entered in Micro Soft Excel. Description of variables such as gestational age, gestational age of diagnosis and obstetric outcomes for analysis of pregnancy outcomes in SCD was done.

Results

General population characteristics

We detected 8 pregnant women (with a total of 9 pregnancies: one mother had both deliveries at the same hospital) with SCD over a period of 5 years with a mean age of 26.25 years and mean gestational age of 37 weeks at the time of delivery.

Obstetric outcomes

Out of 8 women patients 2 were prim gravidae (25%) and 6 were multigravida (75%). All pregnant mothers with SCD were booked patients with regular antenatal check-ups. Four women were diagnosed (50%) with established Sickle cell disease while 3(37.5) had been diagnosed with sickle-thalassemia

hemoglobinopathy and 1 patient (12.5%) had a sickle cell trait.

The most common obstetric complication encountered in women with SCD was grade II MSL (25%). All patients spontaneously conceived. PGE2 (25%) was the preferred mode of induction in 2 patients followed by PGE1+PGE2 in 12.5% of the study subjects. The most common indication for induction was decreased foetal movements. Six patients underwent LSCS of which 50% were taken up for emergency LSCS while 25% underwent elective LSCS. The indications for LSCS were previous LSCS (25%), grade II MSL (12.5%), fetal distress(12.5%), severe oligohydramnios(12.5%) and failed induction (12.5%).

Table 1: Demographic details of women with SCD in pregnancy.

Variables	N=8(100%)	Frequency	Percent(%)
Booked patients		8	100.0
Age	<20 years	1	12.5
	21-30 years	5	62.5
	>31 years	2	25.0
Obstetric Score	Primigravidae	3	37.5
	Multigravidae	5	62.5
Gestational Age	<37 weeks	2	25.0
	>37 weeks	6	75.0
Type of hemoglobinopathy	Sickle cell disease	4	50.0
	Sickle Thallesemia	3	37.5
	Sickle cell trait	1	12.5
Mode of induction	PGE2	2	25.0
	PGE2 + PGE1	1	12.5
Mode of Delivery	FTVD	2	25.0
	EMERGENCY LSCS	4	50.0
	ELECTIVE LSCS	2	25.0
Antenatal transfusions	Present	5	62.5
	Absent	3	37.5
History of abortions/Intra uterine death	1 abortion	1	12.5
	2 abortion	1	12.5
	>3 abortions	1	12.5
	IUD	1	12.5

Table 2: Neonatal outcomes in women with SCD complicating pregnancy.

Variables	N=8(100%)	Frequency	Percent(%)
Birth Weight	<2.5kgs	5	62.5
	>2.5kgs	3	37.5
Gender	Boy	4	50.5
	Girl	4	50.5
Placenta Weight	<500g	7	87.5
	>500g	1	12.5
APGAR 1 minute	<7	0	0
	>7	8	100
APGAR 5 minute	<7	0	0
	>7	8	100

Out of a total of 8 neonates born, 50% were male and 50% were female babies. Most babies born had a birth weight of <2.5Kgs (62.5%) when compared to the 3 babies(37.5%) who were of a normal birth weight of >2.5Kgs. Good APGAR scores at 1min and 5min being >8 and 9 respectively.

Table 3: Characteristics of pregnancy complicated by SCD.

Variables	N=8(100%)	Frequency	Percent(%)
Family history of SCD	0	4	50.0
	1	3	37.5
Blood loss at delivery	<500ml	7	87.5
	>500ml	1	12.5
Clinical features			
a. Pallor	Present	8	100.0
b. Icterus	Present	3	37.5
Bishops Score	<6	2	25.0
	>6	3	37.5
	Information not available	3	37.5
Blood group	A positive	2	25.0
	B positive	3	37.5
	O positive	3	37.5
Peripheral smear	MCHC	5	62.5
	NCNC	1	12.5
Oxygen therapy		3	37.5
Antibiotics	Cephalexin	2	25.0
	Cefotaxim	3	37.5
	Metronidazole	1	12.5
Folic Acid		8	100

Case 1

25year old multigravida at 37+1weeks of gestation who was a diagnosed case of sickle-thalassemia with moderate anaemia (haemoglobin-7.8g %) was admitted for safe confinement. She was diagnosed during her first pregnancy at 37 weeks to have splenomegaly. Patients laboratory investigations showed features of haemolytic anaemia with HPLC: HbA1 1.4, HbF 34, HbS 56, Retic 22 and HbA2 4.4. She developed left pyelonephritis with splenic infarct following her delivery. She was treated for the same with antibiotics. During the current pregnancy she presented at 15 weeks of gestation with haemoglobin 8.3g% and was transfused 2 pint packed red blood cells. At 24 weeks patient received 3 doses of parenteral iron therapy in view of haemoglobin of 9.3g%. At 30 weeks she received 2 pints of packed red cells following which her haemoglobin increased from 8.4 to 9.2g%. Patient progressed spontaneously and underwent full term vaginal delivery with first degree perineal tear, grade 1 Meconium Stained Liquor (MSL) and delivered a baby boy with a birth weight of 2.7 kg with APGAR of 8/10,9/10. Patient was found to have a haemoglobin of 7.5g% at the time of delivery, and a haematologist advised to transfuse 2 pint packed red blood cells and she received uterotonics. Post transfusion she was stable and her haemoglobin increased to 10.1g%.

Case 2

19 year old prim gravidae at 36+3 weeks of gestation who was a diagnosed case sickle cell anaemia and thalassemia, post

splenectomy was admitted to the hospital with decreased foetal movements for 3 days presented with history of multiple joint pains. HPLC and the sickling test confirmed the diagnosis. She gave a history of splenectomy. During her pregnancy at 8weeks of gestation she was diagnosed with UTI, her urine culture was growing significant colonies of E.coli. At 36+4weeks of gestation she was induced in view of severe oligohydramnios (AFI:2.5cm). She underwent Emergency LSCS in view of severe oligohydramnios with severe IUGR and non-progression of labour and delivered a baby girl of 1.97Kg with APGAR 9/10,10/10. Haematology opinion was taken and advised to start folic acid and continue on O2 with mask at 4litre/min. Haematology further advised to give pneumovac vaccine of which one dose was given post operatively. Post operatively 1 pint PRBC was transfused. Post op Hb was 9.8g%. Patient was discharge and advised to receive pneumovac (pneumococcal) vaccination.

Discussion

There is an increased risk of adverse perinatal outcomes in pregnancy complicated with SCD [11]. SCD is associated with high levels of maternal and fetal morbidity and mortality reaching fetal death rates up to 20% during pregnancy. Maternal mortality in pregnancy of 14% was reported in pregnant woman with SCD by Can Boga et al [11]. Hence the disease in pregnancy demands a multidisciplinary team of experts in the field of hematology, general medicine, obstetrics, genetics, neonatology and intensive care specialists [11,12].

A Nagpur study by Dipty et al suggested vaccination against encapsulated organism like Neisseria meningitides, Streptococcus pneumonia and hemophilus influenza [13]. Out of eight pregnant women with SCD only one was found to be immunized for encapsulated organisms as per guidelines in our study.

A recommended daily dose of folic acid (5mg) and iron was recommended by Dipty et al [13]. Our study showed 100% of women had followed recommended guidelines and consumed iron and folic acid along with calcium. Drugs like hydroxyurea, angiotensin converting enzyme inhibitor, iron chelators were not recommended in pregnancy due to teratogenic effects on fetus [13]. No patients in our study received ACE inhibitors or hydroxyurea or other drugs.

Antepartum fetal surveillance such as 2D ECHO, ophthalmoscopy, renal and liver function tests was done to rule out sickle cell related end organ damage [13]. Women in our study were found to have normal LFT, RFT, and normal echo and were only done if the pregnancy was complicated by pre-eclampsia or vasospasm.

Kelly et al studied 344 cases of SCD and found significant results, where in 46.2% were nulliparous, 7.4% had <5 prenatal visits [14]. Severe preeclampsia (5.45%), preterm delivery <37weeks(25.9%), SGA<10th percentile(16.2%) were significantly high among pregnant women with SCD as compared with controlled subjects [14]. In comparison to our study, seven out of eight women delivered at term and preeclampsia was not prevalent as anticipated. C- section rates (46.2%) were higher in women with SCD compared to control group as discussed by Kelly et al [14]. Similar results were seen in a study done in Nigeria by Ugboma et al [15]. Women with SCD had a higher predilection to have pregnancies complicated by fetal anomalies (14%) (cardiac anomalies). Similar results were produced in a study undertaken in Tanzania [16]. In our study it was seen that no foetus had congenital anomalies and normal delivery is definitely a consideration.

Graham et al studied the outcomes of pregnancy in homozygous SCD and found that there was painful crisis in 13 subject, 5 had acute chest syndrome, 8 had UTI [17]. The study compared controls and subjects and found that spontaneous abortion (35.7%) and fewer live deliveries (7.1%) were significantly more common in women with SCD. The chance of vaginal delivery (84.1%) was more common than a caesarean delivery(15.9%) as studied in Jamaica [17]. A study done by Catherine et al showed that 18 of 31 women(58%) had painful crisis during pregnancy [18]. Our study showed crisis in possibly two women who recovered with oxygen therapy, in an attempt to prevent sickling.

Neonatal outcomes as predicted by APGAR score at 5min was >7(85%) with only 7.1% still births and 82.1% achieving a birth weight of >2.5Kgs [16]. In contrast to this study, women with SCD had higher rates of low birth weight, IUGR, still births and neonatal deaths in a study done in Saudi Arabia [19]. Our study showed 50% of the women to have low birth weight babies even at term, although the chance of preterm, IUD and neonatal death was not seen.

An observational study French Guiana found most women with SCD were primi parous (46.8%) with a mean age of 26.4years [20]. No maternal deaths were noted in the study [20].

A case report showed sickle nephropathy in a 40year old woman with SCD, previous C-section with sickle cell crisis was induced at 37weeks of gestation and delivered a baby of 2.78Kg by a repeat C-section in view of failed induction. She was also discharged on LMWH until 6wks postnatal [21]. Our study discharged women on folic acid and only in high-risk cases; anticoagulation therapy (12.5%) was administered.

Obstetric complications such as previous miscarriage (26.6%), and c-section deliveries(41%) were found to be present in a Brazilian study done on women with SCD [22]. Medical complications such as vaso-occlusive crisis (61.7%), acute chest syndrome(29.4%), UTI (23.5%), impaired cardiac function(14.7%) and maternal death (2.9%) were major non obstetrical complications seen in the study [22]. Our reports do not show any major medical complication encountered in pregnancy, but notice nearly half of our reports showed women to have a previous pregnancy resulting in a miscarriage or dead fetus.

Neonatal complications as detected by Rajab et al showed mean APGAR scores to significantly increase from 7.5 at 1min to 8.8 at 10mins in babies of mean birth weight of 2.9Kgs [23]. The hospital policy was to give blood transfusion to pregnant women with SCD if Hb dropped to <7g/dl or if the haemoglobin dropped more than 2g/dl from baseline [23]. Similar results were seen in our study.

Conclusion

SCD when managed vigilantly in the antenatal period poses minimal risks to mother and foetus as seen with the lower chance of NICU admission and early discharge of mother from the hospital after delivery. Mothers with SCD should be screened antenatal to look for features of hydrops or bleeding manifestations such as intraventricular haemorrhage in foetus. Prior bad obstetric history in SCD should predict and warrant strict antepartum foetal surveillance to determine the outcomes of the present pregnancy. LSCS may be more preferred to normal delivery due to obstetric complications in mothers with SCD. Pack red cell transfusion continues to still remain as

the gold standard for treatment of SCD in pregnancy. Although low birth weight is commonly encountered, most babies do well in tertiary care institutions with NICU care.

Limitations

Post intervention analysis could not be performed.

Importance

One among the first few papers where the outcomes of pregnancy in SCD mothers have been studied in detail and observed various treatment options in and Indian setting.

Scope for the Future: Maternal and Child Health Mission and NRHM+ A should anticipate the need for consideration of a separate scheme for SCD mothers, with schemes to help mothers and their families.

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