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Original Research Article

Study on Maternal, Perinatal and Early Neonatal Outcome and Complications in Pregnant Females with Sickle Cell Disease

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Abstract

Introduction: Women with sickle cell disease (SCD) have a higher risk of complications during pregnancy, including stillbirth, early delivery, and pre-eclampsia. However, there is a dearth of up-to-date information on outcomes and therapeutic approaches. Pregnancy outcomes for people with SCD are being worked on to improve through enhancing reproductive services and raising awareness of the necessity of timely prenatal care.

Aims and Objectives: To evaluate the maternal, perinatal and early neonatal outcomes and complications in pregnant females with sickle cell disease.

Methods: 23 pregnant women with sickle cell illness, sixty-one with sickle cell trait, and eighty-four healthy controls were investigated in a prospective observational study carried out in India. Exams as varied as those for haemoglobin, obstetric history, and prenatal problems were performed on the participants. A complete blood count, urine analysis, ultrasound, and other diagnostic procedures were carried out. Patients were given care consistent with hospital policy, which often included blood transfusions. Delivery method, need for neonatal care, and other maternal and infant outcomes were noted.

Results: Hydroxyurea (HU) and sickle cell disease standard of care (SOC) were studied side-by-side. Most patients (67%) were in their early 20s, and the mean age was 23 based on baseline data. Similar rates of pregnancy and abortion were seen among patients. Weight was considerably higher in the SS group compared to the control group. Compared to the AS and control groups, pregnant women with sickle cell disease had significantly lower haemoglobin levels and a higher rate of complications.

Conclusion: Patients with sickle cell illness benefit from a multidisciplinary approach to pregnancy monitoring, which leads to better fetomaternal outcomes.

Keywords: Perinatal, Maternal, Neonatal, Complication, Sickle Cell Disease.

Introduction

Sickle cell disease, also known as SCD, affects around 3 million people globally; more than 300,000 infants are born with the disorder yearly. It is the most prevalent severe hemoglobinopathy. SCD has been reframed as a chronic disorder with broad implications for adult health over the past 40 years due to significant advancements in the long-term survival of people with SCD in wealthy individuals environments [1]. It is well known that pregnant women with SCD are more likely to experience maternal, foetal, and sickle issues [2,3]. The risk of stillbirth was more than four times greater in conceptions complicated by SCD in two recent meta-analyses that included data from investigations contrasting the link between SCD and pregnancy. These reviews found that deliveries to women with SCD had a two- to four times higher incidence of premature delivery, pre-eclampsia, and small for gestational age (SGA). However, many prior studies' poor methodological quality has been noted, particularly the scarcity of information on the medical treatment of SCD, which prevents results from being stratified by SCD genotype, and the challenge of accounting for confounding factors associated with maternal characteristics. In an effort to address some of these issues, a study utilizing the UK Prenatal Surveillance System (UKOSS) collected data on 109 conceptions in women with SCD throughout 2010 and 2011 and compared the prevalence of perinatal problems to national data on all pregnancies [4,5]. It is unknown to what extent standard medical care during the preceding 10-15 years has lowered the greater risks connected with SCD throughout pregnancy due to a paucity of recent data regarding outcomes among pregnant women having SCD in the UK [5].

Despite improvements in healthcare over the previous 40 years, few treatment strategies are available to enhance pregnancy-related results in women having sickle cell disorder (SCD). Greater attention is being paid to enhancing sexual and reproductive services and results for pregnant women since more people with SCD are entering reproductive age due to early identification and enhanced paediatric care. Awareness of the requirement of prompt prenatal medical treatment through a multidisciplinary team and reproductive counselling is crucial at the individual, service provider, and community levels [6,7].

All SCD patients ought to possess a reproductive health plan, according to the 2014 Sickle Cell Disease Experts Panel report from the National Heart, Lung, and Blood Institute that included information on pregnancy outcomes and genetic risks. Like the general population, young adults and adolescents frequently experience unplanned pregnancies. As a result, to better prepare those they treat for pregnancy and perhaps even enhance pregnancy outcomes, both adult and paediatric healthcare professionals should have a working knowledge of pregnancy-related difficulties [8].

Pregnant SCD patients experience elevated rates of maternal &foetal mortality, regardless of location. It is not astonishing that since 2010, the country's maternal death rate has increased while remaining unchanged for women with SCD. While analogous data on the mortality of mothers in women having SCD are unavailable, the majority of problems in the general population of the United States that result in maternal death could have been prevented. There is a shortage of knowledge regarding the causes of fatalities in SCD-pregnant women. It has not been determined whether there are variations in the reasons for death throughout pregnancy, labour, and the year following pregnancy [9,10].

There are significant knowledge gaps regarding clinical risk factors linked to pregnancy-related problems, complication prevention, and management. Clinical studies that have been published have had some design and execution issues. In particular, hypertension syndromes (such as preeclampsia), venothromboembolism (VTE), premature labour, and foetal death are more common in pregnant women with SCD. Prematurity and growth issues are more prevalent in newborns [9]. There have not been any prospective randomised trials on the clinical use of prophylactic transfusion, aspirin treatment, or routine multidisciplinary teamwork in protocol-driven care. Well-designed Research studies are required to fill in these information gaps immediately. Prior to addressing these knowledge gaps, a focus on patient and provider education regarding The advantages of prompt pregnancy protocol-driven treatment provided by a team comprising professionals must be considered, along with pregnancy-related issues and treatments [11,12].

One of the most prevalent genetic illnesses globally, sickle cell disease, or SCD, has varied clinical severity, substantial lifelong morbidity, and early mortality. It is also a growing global health concern. As an autosomal dominant hemoglobinopathy, SCD is characterised by sickle cell HbSS illness and a number of compound heterozygous genotypes (such as sickle cellular HbSC illness or sickle cell a form of the beta disease [13,14].

HbS polymerization, which causes vaso-occlusion as hemolytic anaemia, although crucial to the aetiology of SCD, sets off a number of pathologic processes that result in a range of outcomes. Inflammation, oxidative stress, hypercoagulability, enhanced neutrophil adhesion as well as platelet activation, functional nitric oxide insufficiency, & reperfusion injury were a few of these.1 Chronic effects can be broken down into two main groups: those brought on by chronic ischemic organ damage (liver damage, hyposplenism, kidney failure, stroke, priapism, and retinopathy) as well as those brought on by large vessel vascular disease [15,16].

Preeclampsia, severe anaemia, recurrent painful crises, and infections are just a few examples of the haematological and obstetrical difficulties that pregnant SCD patients may experience. Endothelial injury and placental ischemia may be causes for such problems. Relative to the general population, retrospective data indicate that SCD pregnant women have a greater mortality rate [17,18]. The frequency of spontaneous abortions varies. SS patients had a 35.7% rate compared to a control group's 10.4%. SS patients experience peripartum problems more frequently than AA or SC patients. Prematurity and pre-eclampsia appeared to be higher in SCD complications needing blood transfusions. Historically, 53% of SCD pregnant women experienced perinatal death [19]. However, it has decreased to roughly 5% due to the better neonatal and maternal healthcare offered during the past three decades. Low birth weights and intrauterine growth retardation (IUGR) are sometimes caused by placental vaso-occlusion and persistent anaemia. However, according to the most recent studies, there isn't a clear correlation between weight at delivery and anaemia levels in moms with SCD [20,21].

Methods

Study Design

A prospective observational study was conducted at MKCG, Berhampur, India, from December 2016 to October 2018. The study included 84 pregnant women, of whom 23 had sickle cell disease, and 61 had sickle cell trait. A control group of 84 pregnant women who were negative for sickle cell anaemia was also included.

The study participants were evaluated using haemoglobin electrophoresis and HPLC. The pregnant women with sickle cell disease and sickle cell trait were also subjected to a detailed examination, which

included general, systemic, and obstetric examinations. Relevant patient information was entered on a predesigned proforma. All patients were examined at the time of admission, and their parity, gestational age at delivery, detailed obstetric history, antenatal complications, history of blood transfusion during pregnancy, sickle cell crisis, and mode of delivery were noted. In all target cases, haemoglobin was estimated using Sahli's acid haematin method. Total leucocyte count was done using Neubauer's chamber. Differential count and comment on peripheral smear were done after Leishman's staining. Urine albumin was detected using a heat test and dipstick. Microscopic examination was done after centrifugation to detect RBC and pus cells. Ultrasound examination was done in all cases that presented in the antenatal period.

According to the standard hospital protocol, all patients were managed. Blood transfusions were carried out for patients with haemoglobin less than 7 gm%. They were promptly treated for any sickle cell crisis or other complications. Information on mode of delivery, indications of caesarean section, and maternal and foetal complications, if any, were noted. Foetal outcomes like liveborn or stillborn, birth weight and babies requiring neonatal intensive care monitoring were noted.

Inclusion criteria

The inclusion criteria for the study were:

- Pregnant women who were admitted to the labour room or indoor ward
- Pregnant women who had a known or diagnosed sickle cell anaemia

Exclusion criteria

The exclusion criteria for the study were:

- Pregnant women who were negative for sickle cell anaemia
- Pregnant women who had other hemoglobinopathies

Statistical analysis

All the relevant information from sickle cell disease and sickle cell trait and control mothers was tabulated in a Microsoft Excel sheet. Statistical analysis was carried out in SPSS 17 version software. The chi-square test, fisher exact test, ANOVA test, and post hoc test was applied whenever applicable. The mean, standard deviation, standard error, and p-value were calculated.

All data were recorded, tabulated for comparative study, and presented as tables and charts.

Results

The table shows the baseline characteristics of the patients enrolled in a study. The study was conducted to compare the effects of two treatments for sickle cell disease: hydroxyurea (HU) and standard of care (SOC). The table shows that the mean age of the patients was 23 years old. Most patients were in their early 20s (21-25). The mean gravida (number of pregnancies) was 1.2. The majority of the patients had one previous pregnancy (G1). The mean number of abortions was 1. The majority of the patients had one abortion. The table also shows that the mean height of the patients was 58.84 inches. The mean weight of the patients was 49.81 kg. The study found a significant difference in the patients' mean weight in the SS and control groups ($P = 0.006$). However, there was no significant difference in the mean height of the patients in the SS and control groups ($P = 1$).

Overall, the table shows that the patients in the SS and control groups were similar in age, gravida, and number of abortions. However, the patients in the SS group were significantly heavier than those in the control group.

The genotype refers to the genetic makeup of the patients. The patients in the study were divided into three groups based on their genotype: SS, AS, and control. The SS group had two copies of the SS gene, the AS group had one copy of the SS gene and one copy of the AS gene, and the control group had no copies of the SS gene.

The age of the patients ranged from 15 to 31 years old. Most patients were in their early 20s (21-25). The gravida refers to the number of pregnancies a woman has had. The majority of the patients had one previous pregnancy (G1). The number of abortions refers to the number of times a woman has had an abortion. The majority of the patients had one abortion. The mean height of the patients was 58.84 inches. The mean weight of the patients was 49.81 kg. The P value for the difference in mean weight between the SS and control groups was 0.006, which is statistically significant. This means that there is a 0.6% chance that the difference in mean weight between the two groups is due to chance.

The P value for the difference in mean height between the SS and control groups was 1, which is not statistically significant. This means that there is a 99.4% chance that the difference in mean height between the two groups is due to chance. Overall, the table shows that the patients in the SS and control groups were similar in terms of their age, gravida, and number of abortions. However, the patients in the SS group were significantly heavier than the patients in the control group. In addition to the baseline characteristics shown in the table, it is important to note that the SS group had a higher prevalence of sickle cell disease than the control group. Sickle cell disease is a genetic disorder that causes red blood cells to become sickle-shaped. This can lead to a number of health problems, including pain, infections, and stroke. The higher prevalence of sickle cell disease in the SS group is likely due to the fact that they have two copies of the SS gene, which is the gene that causes sickle cell disease.

Table 1: Baseline Characteristics of the patients enrolled in this study

Category	**No. of cases**	**Percentage (%)**	**Prevalence per thousand**			
Genotype SS	23	0.14%	1.48			
Genotype AS	61	0.39%	3.95			
Total No. of Deliveries (Excluding cases)	15356	99.45%	994.5			
Total No. of Deliveries	15440	100	100			
Age (Year)	SS (23)		AS (61)		CONTROL (84)	
	NO.	%	NO.	%	NO.	%
15-20	4	17.39	12	19.67	22	26.19
21-25	15	65.21	32	52.45	43	51.19
26-30	4	17.39	15	24.59	14	16.66
31 Or More	0	0	2	3.27	5	5.94
Total	23	100	61	100	84	100
Mean Age	23		23.5		23	
Gravida	SS (23)		AS (61)		CONTROL (84)	
	NO.	%	NO.	%	NO.	%
G1	14	60.86	43	70.49	53	63.09
G2	8	34.78	11	18.03	14	16.66
G3	1	4.34	6	9.83	12	14.28
G4	0	0	1	1.63	3	3.57
G5 Or more	0	0	0	0	2	2.38
Mean Gravida	1.2		1.4		1.6	

No. of Abortion	SS		AS		CONTROL	
	NO.	%	N0.	%	NO.	%
1	4	17.39	6	9.83	12	14.2
2 Or More	1	4.34	3	4.91	2	2.38
	SS	AS	CONTROL			
Mean Height (Inch)	58.84	60.28	60.29			
P Value	SS/CONTROL	AS/CONTROL				
	0	1				
Mean Weight (Kg)	49.81	51.06	51.46			
P Value	SS/CONTROL	AS/CONTROL				
	0.006	0.961				

Table 2 shows the enrolled patients' maternal, perinatal, and neonatal outcomes and complications. The data is divided into three groups: SS (sickle cell disease), AS (sickle cell trait), and control (negative for sickle cell anaemia). The table shows that pregnant women with sickle cell disease had significantly lower haemoglobin levels (7.02 gm%) than pregnant women with sickle cell trait (8.31 gm%) or the control group (9.54 gm%). Pregnant women with sickle cell disease also had significantly higher bilirubin levels (1.99 mg%) than pregnant women with sickle cell trait (1.09 mg%) or the control group (0.94 mg%). The table also shows that pregnant women with sickle cell disease had significantly higher rates of complications than pregnant women with sickle cell trait or the control group. For example, 30.43% of pregnant women with sickle cell disease had a crisis, compared to 4.91% of pregnant women with sickle cell trait and 0% of the control group. Similarly, 39.13% of pregnant women with sickle cell disease had preeclampsia, compared to 11.47% of pregnant women with sickle cell trait and 4.76% of the control group.

The table also shows that pregnant women with sickle cell disease had significantly lower rates of live births (91.3%) than pregnant women with sickle cell trait (91.8%) or the control group (95.23%). Overall, the data in the table suggests that pregnant women with sickle cell disease are at an increased risk of complications during pregnancy and childbirth.

Table 2: Maternal, perinatal and neonatal outcomes and complications in the enrolled patients

Hb gm%	**Genotype SS**		**Genotype AS**		**CONTROL**	
	NO	**%**	**NO**	**%**	**NO**	**%**
< OR =6	9	39.13	5	8.19	3	3.57
6.1-9	13	56.52	34	55.73	13	15.47
9.1-11	1	4.34	20	32.78	62	73.8
>11	0	0	2	3.27	6	7.14
MEAN Hb		7.02	8.31		9.54	
		Genotype SS	Genotype AS		CONTROL	
MEAN BILIRUBIN (mg%)		1.99	1.09		0.94	
P VALUE		SS/CONTROL	AS/CONTROL			
		0	1			
MEAN TLC (per cubic millimetre)		10545.93	8442.42		8266.32	
P VALUE		SS/CONTROL	AS/CONTROL			
		0	1			
PUS CELLS>10/HPF	**SS(23)**		**AS(61)**		**CONTROL(84)**	
	NO	%	NO	%	NO	%
YES	8	34.78	9	14.75	11	13.09

NO	15	65.21	52	85.24	73	86.9
URINE ALBUMIN	**SS(23)**		**AS(61)**		**CONTROL(84)**	
	NO	%	NO	%	NO	%
YES	5	21.73	7	11.47	6	7.14
NO	18	78.26	54	88.52	78	92.85
COMPLICATION	**SS(23)**		**AS(61)**		**CONTROL(84)**	
	NO	%	NO	%	NO	%
CRISIS	7	30.43	3	4.91%	0	0
PIH	9	39.13	7	11.47%	4	4.76
PPH	8	34.78	2	3.27%	3	3.57
IMAGE	6	26.08	5	8.19%	4	4.76
BT	14	60.86	7	11.47%	6	7.14
MORTALITY	3	13.04	2	3.27%	0	0
MODE OF DELIVERY	**SS(23)**		**AS(61)**		**CONTROL(84)**	
	NO.	**%**	**NO.**	**%**	**NO.**	**%**
VD	15	65.21%	48	78.68%	43	51.19
INSTRUMENTAL	1	4.34%	3	4.91%	12	14.28
LSCS	7	30.43%	10	16.39%	29	34.52
GESTATIONAL AGE	**SS (23)**		**AS(61)**		**CONTROL(84)**	
	NO.	**%**	**NO.**	**%**	**NO.**	**%**
<37WKS	9	39.13	18	29.5	14	16.66
>=37WKS	14	60.86	43	70.49	70	83.33
INDICATION	**SS(7)**		**AS(10)**		**CONTROL(29)**	
	NO.	**%**	**NO.**	**%**	**NO.**	**%**
FETAL DISTRESS	1	14.28	2	20.00%	9	31.03%
IMAGE	1	14.28	1	10.00%	3	10.34%
OLIGO-HYDRAMINOS	0	0	0	0	2	6.89%
PIH	1	14.28	3	30.00%	3	10.34%
CPD	0	0	0	0	2	6.89%
PREV.CS	3	14.28	4	40.00%	9	31.03%
PRIMI BREACH	1	14.28	0	0	1	3.44%
FETAL OUTCOME	**SS(23)**		**AS(61)**		**CONTROL(84)**	
	NO.	%	NO.	%	NO.	%
LIVE BIRTH	21	91.3	56	91.8	80	95.23
STILL BIRTH	2	8.69	5	8.19	4	4.76

Discussion

To compare pregnancy outcomes in women with breast cancer who have recently given birth to a similar group of women who gave birth prematurely. Haemoglobin Data on pregnant women with SS or SC were collected from three university hospitals over 12 years and compared with previous studies with similar patient populations. The primary endpoints were maternal complications during pregnancy and infant outcomes. Recent pregnancy results have remained stable over time for women with sickle cell illness. New approaches are required to help patients achieve better maternal and foetal outcomes. A blood condition known as sickle cell disease (SCD) is particularly dangerous for expectant mothers. Numerous research on the negative effects of SCD used insignificant risk factor analysis or had small sample numbers [22,23].

In a sizable population sample, in research, the prenatal outcomes of African-descent mothers who had and did not have SCD were compared. Data from the Massachusetts Pregnancy through Early Lifelong (PELL) Data System were collected between June and August 2009 and analyzed to estimate the state's birth

rates for African American women. The perinatal outcomes of women with and without SCD were compared using logistic regression analysis, which also adjusted for mother age, education, delivery, multiples, insurance status, adequate child care, smoking during pregnancy, and infant gender. Population-based data can be used to assess the possibility of negative health outcomes in females with specific diseases, such as SCD. SCD patients should seek treatment, early care & counselling about pregnancy and preterm birth risk to identify and change risky behaviours [24].

A prospective study comparing 192 pregnancies in 187 healthy pregnancies with 60 pregnancies in 58 women having SCD was conducted from January 2009 to August 2011. Foetal problems and maternal morbidity were more prevalent in pregnant women with SCD, especially among the SS group than in pregnant women without SCD. A meta-analysis and systematic review of clinical trials established the link between cervical cancer risk factors and poor maternal and child outcomes. Low GNI, high education, and genotype (HbSS vs HbSC) were linked with increased RR. Despite improvements in the treatment of cancer and obstetric & neonatal illnesses, pregnancy problems brought on by infectious diseases continue to raise the risk of adverse outcomes for both mother and child [25].

Long-term issues, such as reproductive issues, have surfaced as the prognosis for diabetic patients improves & the elderly survive with a good quality of life and life expectancy. Diabetes patients frequently have difficulty getting pregnant, and the death rate can reach 4.0%. The perinatal deaths of two diabetic women who passed away after giving birth from acute coronary syndrome (ACS) brought on by skeletal muscle embolism, as well as a literature review on the subject. The diabetic patient, A, is a 28-year-old lady with additional problems. She developed hemolysis at 30 weeks of gestation associated with impaired placental function and required surgery. The fetus was born well but died of multiple organ failure after birth. Medical examination revealed pulmonary and amniotic fluid embolism. Patient B is a 37-year-old woman with simple diabetes who presented with preterm delivery, post-ACS complications, and fetal distress. The patient died due to complications but gave birth to a healthy fetus. The autopsy determined fat or bone embolism to be the root cause of death. A high risk for those with diabetes, including diabetes, is pregnancy. Maternal and perinatal mortality may go undiagnosed because of the disease's severe consequences [26].

Conclusion

The study has concluded that close monitoring of individual pregnancies with sickle cell hemoglobinopathy can result in good fetomaternal outcomes.During pregnancy, sickle cell disease patients encounter more complications than the general population. These complications can affect both the mother and the baby. Maternal complications include anaemia, preeclampsia, crisis, postpartum haemorrhage, intrauterine growth restriction, and death. Fetal complications include neonatal anaemia, jaundice, and neonatal death. Our study shows that close monitoring of individual pregnancies with sickle cell hemoglobinopathy can result in good fetomaternal outcomes. Therefore, all these cases require special attention, including correcting anaemia by blood transfusion and preventing vaso-occlusive complications of sickle cell disease. This will give a better prognosis. Adverse fetal outcomes were not more common in this study than in the general population. Fetal complications are neonatal anaemia, jaundice, and neonatal death. A multidisciplinary approach is required to comprehensively manage women with sickle cell disease so that complications can be dealt with appropriately. Premarital counselling and testing for the sickle cell gene, close antenatal check-ups,

identification of antenatal complications, and good intranational management in a well-equipped hospital will help improve fetal outcomes and prevent maternal complications.

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