Original Research Article

Study of sickle cell haemoglobinopathy effects over the course of pregnancy

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Abstract

Background: Sickle cell hemoglobinopathies are the most important disorders of hemoglobin structure associated with pregnancy. The effect of pregnancy on patients with sickle cell disease and the effects of maternal sickle cell disease on the outcome of pregnancy have been the subject of many discussions. **Aim:** To study the course of pregnancy in patients with sickle cell hemoglobinopathies. **Material and Methods:** A hospital based prospective study, where pregnant women having sickle cell hemoglobinopathies were studied and compared with that of pregnant women with normal HbAA pattern. Antenatal complications like anaemia, preeclampsia, urinary tract infections, crisis were documented **Results:** The mean Hb% in subjects was 8.357□1.371 g%, 0.932 g% less than that of controls. Among the subjects, mean Hb% in SS group was 7.083±1.0 g% and in AS group, 8.721±1.246 g%. Mean Hb% in controls (AA) was 9.289±1.217 g%. UTI were seen in 29.61% of subjects and 11.11% of controls. In subjects, UTI was statistically significant (p=0.0030) when compared to controls. 41.67% of SS patients (p=0.0220) and 26.2% of AS patients (p=0.0644) had UTI. Hypertensive disorders of pregnancy (HDP) was seen in 24.07% of subjects (p=0.4741) and 16.67% of controls. In SS patients, 33.33% had hypertensive disorders of pregnancy (p=0.2323).**Conclusion**: Sickle cell hemoglobinopathies put pregnant women into several complications. The course of pregnancy is also gloomy with high rates of pregnancy wastage and preterm deliveries. So, pregnancy in sickle cell hemoglobinopathies mandates vigilant multidisciplinary management, so as to reduce maternal and fetal morbidity.

Key Words: sickle cell hemoglobinopathies, pregnancy, anaemia, Hypertensive disorders of pregnancy

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INTRODUCTION

Pregnancy may be a blessing or a burden in a woman's life. One such burden is pregnancy in a woman with sickle cell hemoglobinopathy. Sickle cell hemoglobinopathies are inherited disorders characterized primarily by chronic anemia and periodic episodes of pain that result from structurally abnormal beta globin chain of the adult hemoglobin molecule. It is the result of a genetic mutation that causes hemoglobin to be defective.[1,2] Sickle cell hemoglobinopathies are the most important disorders of hemoglobin structure associated with pregnancy.[2] The effect of pregnancy on patients with sickle cell disease and the effects of maternal sickle cell disease on the outcome of pregnancy have been the subject of many discussions. Comprehensive care with counselling, aggressive surveillance and innovative treatment have led to dramatic decline in morbidity and mortality associated with the disease. Therefore, pregnancy can be successfully completed in most women with sickle cell hemoglobin disorders with an expectation of near normal outcome for the mother and infant. This study was conducted to study the course of pregnancy in patients with sickle cell hemoglobinopathies and its effects on maternal and fetal outcome.

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MATERIAL AND METHODS

This study was conducted in Department of Obstetrics and Gynaecology of a tertiary care hospital over a period of two years. The study was approved from Institutional Ethics Committee.

Study design

A hospital based prospective study, where pregnant women having sickle cell hemoglobinopathies were studied and compared with that of pregnant women with normal HbAA pattern.

Sample size

The study population consisted of pregnant women attending OPD services or admitted in the antenatal wards in the Department of Obstetrics and Gynaecology over a period of two years. During the study period, 108 pregnant women were studied, of whom, 54 women had sickle cell hemoglobinopathies (12 had homozygous sickle cell disease or HbSS and 42 had sickle cell trait or HbAS), taken as study subjects and remaining 54 women had normal haemoglobin HbAA pattern, taken as controls.

Inclusion criteria

- Subjects - pregnant women attending OPD services or admitted in the antenatal wards with sickle cell hemoglobinopathies diagnosed by Hb electrophoresis
- Controls - pregnant women with normal haemoglobin HbAA pattern

Exclusion criteria

- Pregnancies which terminated in abortions during the study period
- Women not willing to participate in the study or not providing written informed consent

Sampling technique

Pregnant women visiting OPD or admitted in antenatal ward who were screened for sickle cell disorders and found to be positive were subjected to Hb electrophoresis to confirm the diagnosis. Those who were diagnosed to be having a sickle cell disorders were included in the study as subjects after taking their informed written consent. Once a subject of sickle cell hemoglobinopathies was chosen, the next pregnant women of same age and gravida, found to be negative during the screening test, was taken as potential 'control'. Her Hb pattern was confirmed by Hb electrophoresis. If the Hb pattern was found to be normal (Hb AA pattern) and if the woman was willing to participate in the study, then she was taken as a definite 'control'. If the electrophoresis showed abnormal Hb pattern e.g., thalassemia, then that potential control was dropped from the study and the procedure was repeated for the next pregnant woman with the same age and gravida and negative screening test. To avoid bias, only the gravida status of the control was considered, irrespective of the previous pregnancy outcomes.

Solubility test and sickling test were used as screening tests whereas Hb electrophoresis (Agarose gel electrophoresis, pH 8.5) was used as confirmatory test.

Data collection

A detailed history was taken with special emphasis on obstetric history with previous pregnancy outcomes and antenatal events. Detailed examination including systemic examination and obstetric examination was done.

Necessary investigations at the start of the study were done which included complete blood count, blood grouping, peripheral smear, liver function test, renal function test, blood sugar level, urine routine and microscopy and culture, ultrasonography and colour Doppler. The subjects and controls were followed once in every 2 months (apart from their routine antenatal follow up in OPD). During follow up, history regarding any complaints were asked, examination and relevant investigations were done. Antenatal complications like anaemia, preeclampsia, urinary tract infections, crisis were documented and treated. Hospitalization was done whenever indicated. Fetal growth monitoring was done by clinical examination and serial ultrasound, colour Doppler was done in all high risk patients.

Statistical analysis

The data of all variables of interest was entered in excel sheet and analyzed. The statistical difference of complications between the two groups of patients was calculated by the Fisher Exact Test. A p value of <0.05 was considered significant.

RESULTS

The subjects consisted of 54 pregnant women with sickle cell haemoglobinopathy, of which 12 had homozygous sickle cell disease or Hb SS and 42 had sickle cell trait or Hb AS, taken as study subjects and remaining 54 women had normal haemoglobin Hb AA pattern, taken as controls. The subjects and controls were in the age ranging from 19 years to 35 years. The average age of all the subjects and controls was 23.96□3.80 years. The controls were age matched with subjects. In SS group, youngest was 19 years and oldest 27 years, and the average age was 22.75±2.05 years. There was no SS patient aged above 30 years in this study. In AS group, youngest was 19 years and oldest 35 years, and the average age was 24.31±4.12 years.

Table 1: Gravida wise distribution of subjects and controls

Group	Primigravida		Second gravida		Third gravida		Fourth gravida or above	
	No.	%	No.	%	No.	%	No.	%
SS (n=12)	6	50%	4	33.33%	2	16.67%	0	0%
AS (n=42)	18	42.86%	15	35.72%	5	11.90%	4	9.52%
AA (n=54)	24	44.44%	19	35.19%	7	12.96%	4	7.41%

Among the subjects and controls, 44.44% were primigravidae, 35.19% were second gravida, 12.96% third gravida and 7.41% were fourth gravida or above. The controls were gravida matched with subjects. Previous spontaneous abortions were seen in 14.81% of subjects and 9.26% of controls. 33.33% patients in SS group (p=0.0497) and 9.52% patients in AS group (p=1.000) had spontaneous abortions in the previous pregnancies. Thus, spontaneous abortions were statistically significant (p<0.05) in SS group when compared to controls but no significant in AS group. Previous perinatal loss was seen in 9.26% of subjects and 5.56% of controls. 6.67% patients in SS group (p=0.2215) and 7.14% patients in AS group (p=1.000) had perinatal loss in previous pregnancies. Thus, previous perinatal loss was not statistically significant in either SS or AS patients (p>0.05) when compared to controls. Thus, past pregnancy wastage was seen in 24.07% of subjects and 14.81% of controls. Past pregnancy wastage in SS group was 50% (p=0.0144) and in AS group was 16.67% (p=1.000). Thus, past pregnancy wastage was statistically significant in SS group (p<0.05) when compared to controls, but not significant in AS group.

Table 2: Distribution of subjects and controls depending on severity of anaemia

Group	Severe anaemia Hb<7 g%		Moderate anaemia Hb 7-<9.9 g%		Mild anaemia Hb10-<11 g%		No anaemia (WHO) Hb≥11 g%		No anaemia (Developing countries) Hb≥ 10 g%	
	No.	%	No.	%	No.	%	No.	%	No.	%
SS (n=12)	4	33.33%	8	66.67%	0	0%	0	0%	0	0%
AS (n=42)	3	7.14%	31	73.81%	7	16.67%	1	2.38%	8	19%
AA (n=54)	1	1.85%	35	64.81%	13	24.07%	5	9.26%	18	33.34%

In subjects, average Hb% in SS group was 7.083±1.0 g% and AS group was 8.72±1.246 g%. Average Hb% in controls (AA) was 9.29□1.217 g%. The prevalence of anemia (Hb <10 g%) was in SS group - 100% (p=0.0271), in AS group - 80.95% (p=0.1650) and in AA group - 66.67%. Thus, anaemia (Hb<10 g%) was statistically significant in SS patients (p<0.05) when compared to controls but was not significant in AS patients. Severe anaemia (Hb<7 g%) was seen in 33.33% of SS patients (p=0.0031), 7.14% of AS patients (p=0.3155) and 1.85% of controls. Thus, severe anaemia was statistically significant in SS patients (p<0.05) when compared to controls. Blood transfusion was given at some stage in the study to100% of SS patients (p=0.0001), 38.09% of AS patients (p=0.0209) and 16.67% of controls. Thus, blood transfusion was statistically significant in both SS and AS patients (p<0.05) when compared to controls.

Table 3: Antenatal complications in subjects and controls

Group	UTI		HDP		Jaundice		Crisis	
	No.	%	No.	%	No.	%	No.	%
SS (n=12)	5	41.67%	4	33.33%	3	25%	7	58.33%
AS (n=42)	11	26.2%	9	21.42%	1	2.38%	0	0%
AA (n=54)	6	11.11%	9	16.67%	0	0%	0	0%

(UTI= Urinary tract infections; HDP=Hypertensive disorders of pregnancy)

UTI were seen in 29.61% of subjects and 11.11% of controls. In subjects, UTI was statistically significant (p=0.0030) when compared to controls. 41.67% of SS patients (p=0.0220) and 26.2% of AS patients (p=0.0644) had UTI. In SS patients, UTI was statistically significant (p<0.05) compared to controls. In AS patients, though UTI was common (26.2% v/s 11.11%) compared to controls, it was not statistically significant (p>0.05). Hypertensive disorders of pregnancy (HDP) was seen in 24.07% of subjects (p=0.4741) and 16.67% of controls. In SS patients, 33.33% had hypertensive disorders of pregnancy (p=0.2323). Severe pre-eclampsia was seen in one patient (8.33%) and remaining three patients had mild pre-eclampsia. In AS patients, 21.42% had hypertensive disorders of pregnancy (p=0.6047). Severe pre-eclampsia was seen in two patients (4.76%) and eclampsia in one patient (2.38%). In AA group, severe pre-eclampsia was seen in two patients (3.7%) and eclampsia in one patient (1.85%). Though hypertensive disorders of pregnancy were more common in SS and AS group when compared to controls, they were not statistically significant in both the groups. Jaundice was seen in 25% of SS patients (p=0.0308 when compared to AS patients and p=0.0048 when compared to controls) and 2.38% of AS patients (p=0.4375) had jaundice. Jaundice was not seen in any of the controls.

Thus, jaundice was statistically significant complication in SS patients (p<0.05) when compared to AS patients and controls. Sickle cell crisis were seen in 7 (58.33%) SS patients (p=0.0001 when compared to AS patients and p=0.0001 when compared to controls). 4 (33.33%) patients had painful crisis and 3 (25%) had hemolytic crisis. Thus, crisis was statistically significant (p<0.05) in SS patients when compared to AS patients and controls.

Table 4: Labour and mode of delivery in subjects and controls

Group	Preterm delivery		Full term normal delivery		Cesarean section	
	No.	%	No.	%	No.	%
SS (n=12)	3	25%	6	50%	3	25%
AS (n=42)	4	9.52%	27	64.29%	11	26.19%
AA (n=54)	5	9.26%	39	72.22%	10	18.52%

61.11% of subjects, and 72.22% of controls had full term normal delivery. Full term normal delivery was seen in 50% of SS and 64.29% of AS groups. Preterm delivery was seen in 12.96% of subjects and 9.26% of control. 25% of SS patients (p=0.1520) and 9.52% of AS patients (p=1.0000) had preterm delivery. 25.93% subjects and 18.52% of controls underwent cesarean section. 25% of SS patients (p=0.6910) and 26.19% AS patients (p=0.4573) had cesarean section. Thus, preterm delivery and cesarean section were not statistically significant either in SS patients or AS patients when compared to controls.

DISCUSSION

In this study, the mean age of all the subjects was 23.96±3.80 years. The mean age in subjects was 19-35 years. The mean age of the sickle cell anaemia patients (SS) in the study was 22.75±2.05 years. 16.67% patients were in the age group of 15-20 years and 83.33% patients were in the age group of 21-30 years. None of the SS mother was above 30 years of age. This may be explained by the fact that sickle cell anaemia patients have less life expectancy as has been shown in the literature.[3] The range of age in SS patients was 19-27 years. The mean age of SS patients in various studies, including our study, ranges from 22.75 years to 28 years.[4-7] The mean age in AS patients in our study is comparable to the mean age in other studies which ranges from 24.11 years to 27 years.[7-10] In the present study, maximum number of both subjects and controls were primigraviade. In SS patients, AS patients and controls there were 50%, 42.86% and 44.44% were primigravidae, respectively. In the study by Mohamed C *et al*,[5] 57.14% of SS patients were primigravidae, almost similar to that in our study. Omo-Aghoja *et al*,[11] reported 76.2% cases of sickle cell disease in his study to be either nulliparous or primiparous. In the study by Ilham M *et al*,[10] 51% of AS patients were primigraviade. In the study by Tan *et al*,[12] 44.1% of AS patients were nulliparous. In the present study, past pregnancy wastage was seen in 24.07% of subjects and 14.81% of controls. In SS group, 50% of patients had pregnancy wastage in the previous pregnancies (p=0.0144 when compared to controls). Freeman *et al* reported pregnancy wastage of 36.4% in SS patients in their study.[13] Mohamed *et al* reported previous unsuccessful pregnancies in 21.43% SS patients.[5] Thus, sickle cell anemia is a significant cause of pregnancy wastage. In AS group, 16.67% of patients had previous pregnancy wastage (p=1.0000 when compared to controls). In AS patients though past pregnancy wastage was more (16.67% vs 14.81%) as compared to controls, it was not statistically significant (p>0.05). In the study by Ilham *et al*,[10] 7.5% of AS patients had previous pregnancy wastage which was not statistically significant when compared to controls in the study. Previous spontaneous abortions were seen in 14.81% of subjects and 9.26% of controls. 33.33% spontaneous abortion were seen in SS patients (p=0.0497) in their previous pregnancies, which was statistically significant when compared to controls. Freeman *et al*,[13] reported 26.7% spontaneous abortions in SS patients in their study. Balgir *et al*,[14] reported that spontaneous statistically significant in SS patients in their study, similar to our study. Serjeant *et al*,[15] reported 36% of spontaneous abortions in their study, almost similar to our study. Thus, sickle cell anemia is a significant cause of spontaneous abortions. AS patients in our study had 9.52% of spontaneous abortions in their previous pregnancies (p=1.0000) which was not statistically significant when compared to controls. In the study by Ilham *et al*,[10] spontaneous abortions were 4.6% in AS patients. The mean Hb% in subjects was 8.357±1.371 g%, 0.932 g% less than that of controls. Among the subjects, mean Hb% in SS group was 7.083±1.0 g% and in AS group, 8.721±1.246 g%. Mean Hb% in controls (AA) was 9.289±1.217 g%. Thus, the mean Hb% in SS patients in our study is comparable to that of other studies that range from 7.0±1.3 g% to 7.8±1.68 g%.[5,16,17] The mean Hb% in AS patients in our study is also comparable to that of other studies and ranges from 7.8 g% to 8.721 g%.[6,16,17] The most common complication in the present study was seen in 85.19% of subjects and 66.67% of

controls. Anemia was seen in 100% of SS patients and was statistically significant (p=0.0271) when compared to controls. 80.95% of AS patients had anemia. It was not statistically significant (p=0.1650) when compared to controls. In the study by Ilham *et al*,[10] 41.4% of AS patients had anemia. Thus, the incidence of anemia in SS and AS patients is highest in our study. Anemia is high even in controls. This may be because of higher incidence of iron deficiency anemia in Indian women, which increases the overall incidence of anemia.[18] Urinary tract infections were seen in 29.61% of subjects and 11.11% of controls. In SS patients, 41.67% had UTI and was statistically significant (p=0.0220) when compared to controls. UTI is a statistically significant complication in the present study, similar to the study by Jama *et al*,[19] and other studies[5,13] who also showed that UTI is statistically significant in SS patients. In AS patients, though UTI was more common (26.2% v/s 11.11%) compared to controls, it was not statistically significant (p=0.0644). Incidence of UTI in pregnant sickle cell trait patients in various studies, including our study, varies from 6% to 26.2%.[8,10] Hypertensive disorders of pregnancy were seen in 24.07% of subjects and 16.67% of controls. In SS patients, 33.33% had hypertensive disorders of pregnancy (p=0.2323). Incidence of hypertensive disorders of pregnancy in SS patients varies from 5% to 33.33% as seen in various studies.[4,6,13,16,19] In AS patients, 21.42% had hypertensive disorders of pregnancy (p=0.6047). The incidence of hypertensive disorders of pregnancy in AS patients in our study is comparable to that of other studies that range from 6.5% to 40.85%.[9,10,16] Sickle crisis were seen in 7 (58.33%) SS patients, of which, 4 (33.33%) patients had hemolytic crisis. Crisis was statistically extremely significant (p=0.0001) in SS patients as compared to AS patients and controls. Incidence of crisis during pregnancy and puerperium in SS patients ranges from 23.81% to 58.33% in various studies.[4,5,16,11,19] Preterm deliveries were seen in 12.96% of subjects and 9.26% of controls. Among subjects, 25% of SS patients (p=0.1520) and 9.52% AS patients (p=1.0000) had preterm deliveries. Rate of preterm deliveries in our study in SS patients is comparable to that in other studies which ranges from 9% to 72%.[7,16,19] Rate of preterm deliveries in AS patients in our study is comparable to that in other studies which ranges from 7.8% to 30.1%.[7,10,16] 25.93% subjects and 18.52% of controls underwent cesarean section. Among subjects, 25% of SS patients (p=0.6910) and 26.19% AS patients (p=0.4573) had cesarean section. The rate of cesarean section in SS patients in our study is comparable to that in other studies which ranges from 12% to 73.6%.[5,16,11,6,7,19] Rate of cesarean section in AS patients in our study is comparable to that of other studies which ranges from 9.4% to 46.24%.[7,9,10,16]

CONCLUSION

Sickle cell hemoglobinopathies put pregnant women into several complications and the pregnancy outcome may not be fruitful always. The course of pregnancy is also gloomy with high rates of pregnancy wastage and preterm deliveries. So, pregnancy in sickle cell hemoglobinopathies mandates vigilant multidisciplinary management, so as to reduce maternal and fetal morbidity.

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