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Fetomaternal Outcome in Patients with Sickle Cell Disease in Southern Odisha, India

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ABSTRACT

Hemoglobinopathy is a diverse group of inherited single gene disorder of haemoglobin production and function; they are inherited as autosomal co-dominant traits. Each year about 0.3 million infants are born with a major hemoglobinopathy. Sickle cell hemoglobinopathy is the most common hemolobinopathy encountered during pregnancy. (a) To find out the prevalence of sickling positive cases in pregnant women admitted to department of O and G, MKCG Medical College, Berhampur (b) To study the feto-maternal complications and outcome in sickling positive pregnant women. The study was a prospective observational study conducted in the department of O and G of MKCG Medical College, Berhampur, Odisha; India, leading medical college of southern Odisha from December 2016 to October 2018. Those pregnant women having sickling positive were subjected for detailed history taking followed by clinical examination. Routine examination covering hemoglobin, TLC, CPS, VDRL, HIV, HbsAg, TFT, urine (R and M) and obstetric ultrasound were done for all selected cases followed by electrophoresis and HPLC. They were promptly treated for any sickle cell crisis or other complications. Information on mode of delivery, indications of caesarean section, maternal and fetal complications was noted. Fetal outcome like live born or still born, birth weight, babies requiring neonatal intensive care monitoring were also noted. Incidence of the diseases was 0.54 % including 23 cases (0.14%) of sickle cell disease (SS or homozygous) and 61 cases (0.37%) of sickle cell trait (AS or heterozygous). When the normal hemoglobin concentration was taken as 11 g%, 23 cases (100%) of SS women, 59 cases (96.7%) of AS women and 78 cases (92.8%) of control women were anemic. In SS group 9 cases (39.1%) of women were severely anemic whereas in AS and control group 5 cases (8.1%) and 3 cases (3.5%) women were severely anemic. Out of 23 SS women, 8 cases (34.8%) were having UTI whereas 9 cases (14.7%) and 11 cases (13.1%) of AS and control group have UTI respectively. Women who had suffered from painful crisis were 7 cases (30.4%) of SS, 3 cases (4.9%) of AS group respectively. Painful crisis of SS group were more compared to control group which is statistically significant. Out of all, 9 cases (39.1%), 7 cases (11.5%) and 4 cases (4.8%) of SS, AS and control group women presented with pregnancy induced hypertension(PIH) and incidence of PIH is high in case of SS women as compared to control group. Post-partum hemorrhage(PPH) was seen in 8 cases (34.8%), 2 cases (3.2%) and 3 cases (3.5%) of SS, AS and control group respectively and incidence of PPH is more in SS group as compared to control group. Maternal mortality was seen in 3 cases (13.0%) of SS women and 2 cases (3.2%) of AS women i.e incidence of maternal death is high among SS group as compared to control group. PIH was indication in 2 cases (18.1%), 1 case (8.3%) and 2 cases (10.0%) of SS, AS and control group respectively. Previous C.S was indication in 4 cases (36.3%), 5 cases (41.6%) and 8 cases (40.0%) of SS, AS and control group respectively. Hypoxic ischemic encephalopathy (HIE) was seen in 2 babies (3.2%), 3 babies (3.5%) of AS and control group respectively. Anemia in newborn was seen in 1 case (4.3%), 1 case (1.6%) and 1 case (1.2%) of babies of SS, AS and control group respectively. The total perinatal death included 3 cases (13.0%), 8 cases (13.1%) and 8 cases (9.5%) of SS, AS and control group respectively. Premarital counseling and testing for the sickle cell gene with close antenatal check-up, identification of antenatal complications and good intranatal management in a well-equipped hospital will help in achieving the improvement of fetal outcomes and also prevent the maternal complications.

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Key Words
Sickle cell anemia, hypoxic ischemic encephalopathy, preterm labor, perinatal death

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INTRODUCTION

Hemoglobinopathy is a diverse group of inherited single gene disorder of haemoglobin production and function; they are inherited as autosomal co-dominant traits. According to WHO, approximately 250 million people constituting 4.5% of the world population carry a potentially pathological hemoglobinopathy gene. Each year about 0.3 million infants are born with a major hemoglobinopathy[1]. Sickle cell hemoglobinopathy is the most common hemolobinopathy encountered during pregnancy. The sickle cell syndromes are caused by a mutation in the -chain of globin gene that changes the sixth amino-acid from glutamic acid to valine. It is classified as sickle cell anemia (SCA), sickle cell trait (SCT) and other variants. These abnormalities provoke unpredictable episodes of microvascular vaso oclusion and premature RBC destruction (hemolytic anemia)[2]. Pregnancy in patient with sickle cell disease has always been a challenge for obstetrician, hematologist and neonatologist. Maternal mortality in SCD has decreased dramatically over 40 years from 11.5% to less than 1% in recent years[3,4]. With advances in medical and neonatal care and transfusion medicine, the perinantal mortality has also significantly decreased. Increased risk of delivery complications in sickle cell anemia include gestational hypertension, pre-eclampsia, eclampsia, placental abruption, preterm delivery, IUGR and aggravation of pre-existing medical disorders like cardiomyopathy, pulmonary hypertension, renal failure[5]. This study was undertaken to observe the complications of pregnancy in sickle cell disease and its outcome in Southern Odisha.

MATERIALS AND METHODS

The study was a prospective observational study conducted in the department of O and G of MKCG Medical College, Berhampur, Odisha; India, leading medical college of southern Odisha from December 2016 to October 2018. Cases were selected in accordance to following criteria:

Inclusion criteria: All cases admitted in dept. for known sickling positive pregnancy

Exclusion criteria: All sickling negative and other hemolobinopathy pregnant women.

Those pregnant women having sickling positive were subjected for detailed history taking followed by clinical examination. Routine examination covering hemoglobin, TLC, CPS, VDRL, HIV, HbsAg, TFT, urine (R and M) and obstetric ultrasound were done for all selected cases followed by electrophoresis and HPLC. Blood transfusions were carried out for patients with hemoglobin less than 7.4 g (%). They were promptly treated for any sickle cell crisis or other complications. Information on mode of delivery, indications of caesarean section, maternal and fetal complications was noted. Fetal outcome like live born or still born, birth weight, babies requiring neonatal intensive care monitoring were also noted. Total 84 sickling positive cases were studied and the parameters were compared with 84 control cases having no sickling positive status.

Statistical analysis carried out in SPSS-1.7 version software. Chi square test were applied whenever applicable.

RESULTS

Out of 15440 pregnant mothers, 84 cases were found to have sickle cell anemia (sickle cell disease and sickle cell trait) giving rise to incidence of 0.54%. After electrophoresis and HPLC 23 cases (0.14%) were of sickle cell disease (SS or homozygous) whereas 61 cases (0.37%) were of sickle cell trait (AS or heterozygous). Maximum numbers of cases were of 21-25 years. Among SS group, 15 cases (65.2%) were primigravida, 7 cases (30.4%) were second gravida and 1 case (4.3%) was third gravida and among AS group, 43 cases (70.5%) were primigravida, 11 cases (18.0%) were second gravida, 6 cases (9.8%) were third gravida and 1 case (1.6%) were 4th gravida. In the control group, 53 cases (63.1%) were primigravida, 14 cases (16.7%) were second gravida, 12 cases (14.3%) were 3rd gravida, 3 cases (3.6%) were 4th gravida and 2 cases (2.4%) were 5th gravida (Table 1).

The average height of the pregnant mothers with SS, AS and control group was 59.48 inch, 60.28 inch and 60.30 inch respectively. The height of SS mothers is statistically significantly low as compared to control group (p = 0.0001). When the normal hemoglobin concentration was taken as 11 g (%), 23 cases (100%) of SS women, 59 case (96.7%) of AS women and 78 cases (92.8%) of control women were anemic (normocytic normochromic). In SS group 9 cases (39.1%) of women were severely anemic whereas in AS and control group 5 cases (8.1%) and 3 cases (3.5%) women were severely anemic. The mean hemoglobin of SS women was low as compared to control women (p<0.0001) (Fig. 1).

Table 1: Distribution of study and control group according to gravida

	SS (23)		AS (61)		Control group (84)	
Gravida	No	%	No	%	No	%
G1	15	65.2	43	70.5	53	63.1
G2	7	30.4	11	18.0	14	16.7
G3	1	4.3	6	9.8	12	14.3
G4	0	0	1	1.6	3	3.6
G5 or more	0	0	0	0	2	2.4
Mean	1.2		1.4		1.6	

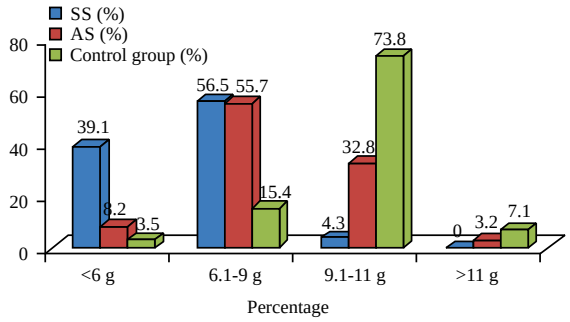

Fig. 1: Hemoglobin concentration in SS, AS and control group

Table 2: Maternal complication in SS, AS and Control group

	SS (23)		AS (61)		Control group (84)	
Complications	No	%	No	%	No	%
Crisis	7	30.4	3	4.9	0	0
PIH	9	39.1	7	11.5	4	4.8
PPH	8	34.8	2	3.2	3	3.5
IUGR	6	26.0	5	8.2	4	4.8
Mortality	3	13.0	2	3.2	0	0

Table 3: Indication of CS in study and control group

	SS (11)		AS (12)		Control group (20)	
Indication	No	%	No	%	No	%
Fetal distress	3	27.2	2	16.6	8	40.0
IUGR	2	18.1	4	33.3	2	10.0
PIH	2	18.1	1	8.3	2	10.0
Previous CS	4	36.3	5	41.6	8	40.0

The mean serum bilirubin concentration in SS, AS and control group was 1.99, 1.09 and 0.94 mg (%) respectively. The difference of mean serum bilirubin level between SS and control group is found to be statistically significant (p = 0.0001). Out of 23 SS women, 8 cases (34.8%) were having UTI whereas 9 cases (14.7%) and 11 cases (13.1%) of AS and control group have UTI respectively. UTI is highly seen in case of SS group as compared to control group (p = 0.0414). Urine albumin was present in 5 cases (21.7%), 7 cases (11.5%) and 6 cases (7.1%) of SS, AS and control group respectively i.e., presence of albumin in urine is not significant in case of SS women in comparison to control women (p = 0.130). Women who had suffered from painful crisis were 7 cases (30.4%) of SS, 3 cases (4.9%) of AS group respectively. Painful crisis of SS group were more compared to control group which is statistically significant (p = 0.0001). Out of all, 9 cases (39.1%), 7 cases (11.5%) and 4 cases (4.8%) of SS, AS and control group women presented with pregnancy induced hypertension(PIH) and incidence of PIH is high in case of SS women as compared to control group (p = 0.0001). Post partum hemorrhage (PPH) was seen in 8 cases (34.8%), 2 cases (3.2%) and 3 cases (3.5%) of SS, AS and control group respectively and incidence of PPH is more in SS group as compared to control group (p = 0.0001). IUGR was found in 6 cases (26.0%), 5 cases (8.2%) and 4 cases (4.8%) of SS, AS and control group i.e significant high incidence of IUGR seen in study group as compared to control group (p = 0.001). Blood transfusion required in 14 cases (60.8%), 7 cases (11.5%) 6 cases (7.1%) of SS, AS and control group i.e need for blood transfusion is higher in SS group as compared to control group (p<0.005). Maternal mortality was seen in 3 cases (13.0%) of SS women and 2 cases (3.2%) of AS women i.e., incidence of maternal death is high among SS group as compared to control group (Table 2).

Out of vaginal delivery cases 10 cases (43.5%), 48 cases (78.7%) and 56 cases (66.7%) belonged to SS, AS and control group respectively. Among instrumental delivery 1 case (4.3%), 3 cases (4.9%) and 8 cases (9.5%) belonged to SS, AS and control group respectively whereas among CS cases, 12 cases (52.1%), 10 cases (16.4%) and 20 cases (23.8%) belonged to SS, AS and control group respectively (Fig. 2). The number of preterm deliveries were in 9 cases (39.1%) of SS women, 18 cases (29.5%) of AS and 14 cases (16.6%) of control group respectively. Preterm labor was associated more with SS group as compared to control group (p = 0.043).

Fetal distress was indication for CS in 3 cases (27.2%), 2 cases (16.6%) and 8 cases (40.0%) of SS, AS and control group respectively. IUGR was the indication for CS in 2 cases (18.1%), 4 cases (33.3%) and 2 cases (10.0%) of SS, AS and control group respectively. PIH was indication in 2 cases (18.1%), 1 case (8.3%) and 2 cases (10.0%) of SS, AS and control group respectively. Previous C.S was indication in 4 cases (36.3%), 5 cases (41.6%) and 8 cases (40.0%) of SS, AS and control group respectively (Table 3).

Among still born babies, 2 cases (8.7%), 5 cases (8.2%) and 4 cases (4.7%) belonged to SS, AS and control group respectively. Low birth weight babies born to SS, AS and control group women includes 4 cases (17.4%), 8 cases (13.1%) and 6 cases (7.1%) respectively i.e LBW were seen more in study group as compared to control group. APGAR score at 5 minutes was low (<4) in 2 cases (8.6%) of SS women and 1 case (1.6%) of AS women. In SS women 4 babies (17.4%) required specialized newborn care whereas 7 babies (11.5%) of AS group and 9 babies (10.7%) of control group required the same. Rate of admission in SNCU of babies born to AS mothers were comparable to control group. Hypoxic ischemic encephalopathy (HIE) was seen in 2 babies (3.2%), 3 babies (3.5%) of AS and control group respectively. No HIE was seen in babies born to SS women. Neonatal septicemia was seen in 2 cases (2.4%) of control group only. No cases of septicemia were observed in SS and AS group. Anemia in newborn was seen in 1 case (4.3%), 1 case (1.6%) and 1 case (1.2%) of babies of SS, AS and control group

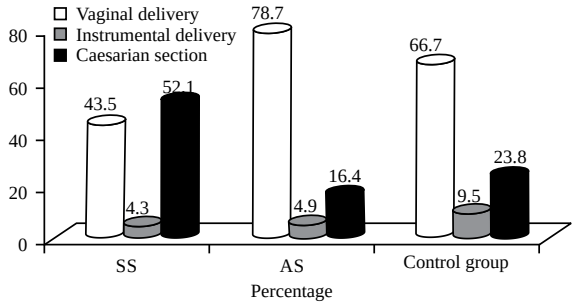

Fig. 2: Mode of delivery of SS, AS and Control group

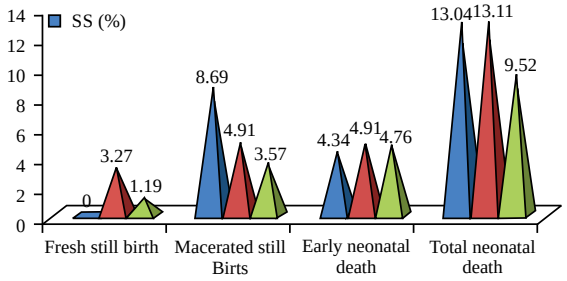

Fig. 3: Perinatal loss in SS, AS and control group

Table 4: Neonatal complications in SS, AS and control group

	SS (23)		AS (61)		Control group (84)	
Complications	No	%	No	%	No	%
HIE	0	0	2	3.2	3	3.5
Septicemia	0	0	0	0	2	2.4
Anemia	1	4.3	1	1.6	1	1.2
Jaundice	3	13.0	2	3.2	4	4.7

respectively. Jaundice develops in 3 cases (13.0%), 2 cases (3.2%) and 4 cases (4.7%) of babies of SS, AS and control group respectively. The jaundice was present in more number of babies born to SS women as compared to control group. The jaundice in AS group and control group were comparable (Table 4).

The total perinatal death included 3 cases (13.0%), 8 cases (13.1%) and 8 cases (9.5%) of SS, AS and control group respectively. Early neonatal death was found in 1 case (4.3%), 3 cases (4.9%) and 4 cases (4.7%) of SS, AS and control group respectively. The incidence of perinatal deaths of babies of SS mother is comparable to control group. Also incidence of total perinatal death of AS group and control group was comparable (Fig. 3).

DISCUSSION

The study was a prospective observational study conducted in the department of O and G of MKCG Medical College, Berhampur, Odisha; India, leading medical college of southern Odisha from December 2016 to October 2018.

Patients with sickle cell disease are at increased risk for maternal and fetal complication as they are more prone for hypoxia, vascular stasis and microvascular thrombi. The prevalence of sickle cell anemia was 0.53% which included both sickle cell diseases (0.14%) and sickle cell trait mother (0.39%). The prevalence of sickle cell disease was 1.48/1000 pregnancies is concurrent to Adam et al.[6] (0.4/1000 pregnancies). The prevalence of sickle cell trait was 3.95/1000 pregnancies. The mean height of SCD group (58.84 inch) was low as compared to control group (60.29 inch)(p = 0.0001). The mean Hb concentration in the SS group was 7.0 g (%) which was low as compared to control group (9.5 g (%)), similar to that of Tuck et al (65% of SS mother had hemoglobin <10 g (%)) and Sonawane et al (Hb=7.6 g (%) in SS women, 8.7 g (%) in AS women)[7,8]. Decrease in maternal and fetal mortality, decrease episodes of sickle cell crisis and preterm delivery in patients who has received prophylactic blood transfusion during pregnancy. So there is decrease in maternal and fetal mortality, decrease episode of sickle cell crisis and preterm delivery in patients who have received prophylactic blood transfusion is concurrent to Oteng-Ntim *et al.*[9]. The incidence of UTI was 34.8% in SS women and 14.7% in AS women, significantly high when compared to control group (13.1%) (p = 0.041) which is in accordance to Mc Curdy *et al*. (6.3%)[10]. Presence of albumin in urine; SS women: 21.7%, AS women: 11.5% and control group: 7.1% (p = 0.130) and presence of urine albumin in SS women is compared to control group and accordingly pre-eclampsia i.e no increased incidence of pre eclampsia in sickle cell anemia which is not similar to Villers *et al*.[11] (higher incidence of pre-eclampsia in case of SCD). Current study shows 13.0% of maternal mortality in case of SS mother, 3.2% of maternal mortality in case of AS group which is highly significant when compared to control group which is similar to Daivagane *et al*.[12] (10%). In SS group 3 maternal deaths occurred; 2 were due to acute chest syndrome and one was due to eclampsia with CVA. PIH was encountered in 39.1% of SS women, 30.7% of AS women and 4.9% of control group i.e incidence of PIH in SS women was significantly high in comparison to AS and control group, similar to Kobak *et al*.[13]. Painful crisis due to hemolysis and anemia observed in 30.4% of SS women, 4.9% of AS women and none from control group giving highly difference between study and control group (p<0.0001), similar to Alayed *et al*.[14] showing high incidence of painful crisis in SCD women. PPH due to anemia and toxemia occurred in 34.8% of SS women, 3.2% of AS women and 3.5% control group i.e significant high PPH in SS women in comparison to AS and control group. Among all cases, 26.0% of SS, 8.2% of AS and 4.8% of control group have IUGR babies i.e significant difference between study group and control group (p = 0.001). These findings is not consistent in between Desai et al (SS group: 2.3% and

control group were 39.1, 29.5 and 16.6%, respectively and was significant between study and control group which is similar to Seud *et al*.[16] (45%). Majority of babies i.e 43.5% of SS, 78.7% of AS and 66.7% of control group delivered vaginally. Instrumental deliveries were done in 4.3% of SS, 4.9% of AS and 9.5% of control group whereas caesarian section (CS) was done in 52.1% of SS, 16.4% of AS and 23.8% of control group which is similar to Boulet *et al*.[17] (CS rate of 43%). Previous C.S was most common indication: 42.85% in SS, 40% in AS and 31.03% in control group undergone CS. In case of AS and control group, fetal distress and previous C.S were common indication which is agreed with Couth *et al*.[18] (most common indication of CS was previous C.S (54.1%). Here 8.7% babies of SS mothers were stillborn as compared to 8.2% of AS and 4.7% of case of control group respectively, not concurring to Fort *et al*.[19] (30%). The perinatal death in case of SS group was 13.0%, comparatively high to that of control group (9.5%) which is not agreed to Blattner *et al*.[20] (No increase in the risk of still birth in women with sickle cell trait when compared with those of normal hemoglobin). Among SS women, 17.4% of babies were LBW (<2.5 kg) i.e. significantly high when compared to 7.1% of control group which is tallying to Daigavane *et al*.[12] (53%). In SS women, 8.6% babies have low APGAR score at 5 min (<4) as compared to 1.6% of AS group (p = 0.058) which is not similar to that of Kidanto *et al*.[21] (APGAR score at 5 min <7 in 34.5% cases). Among all cases, 17.4% of babies of SS women, 11.5% of AS women and 10.7% of control group were admitted to SNCU due to birth asphyxia, IUGR and prematurity which are more common in sickle cell disorder.

CONCLUSION

Adverse maternal outcome was more common as compared to fetal complications like neonatal anemia, jaundice and death. A multidisciplinary approach is required for comprehensive management of women with sickle cell disease so that complications to be dealt with appropriately. Premarital counseling and testing for the sickle cell gene with close antenatal check-up, identification of antenatal complications and good intranatal management in a well-equipped hospital will help in achieving the improvement of fetal outcomes and also prevent the maternal complications. There is also need for screening of this disease in all neonates.

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