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PREVALENCE OF SICKLE CELL ANAEMIA IN PREGNANT WOMEN ADMITTED IN TERTIARY HEALTHCARE CENTRE OF CENTRAL INDIA

Obstetrics & Gynaecology

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ABSTRACT

Introduction: Sickle cell disease (SCD) is a disease caused by inheritance of a defective hemoglobin gene resulting in red blood cells changing shape in hypoxic conditions and subsequent chronic hemolysis. **Methodology:** The present Prospective observational study was conducted in a Tertiary Care Institution, Central India from January 2021 to December 2022 among 2500 Pregnant patients admitted in the Department of Obstetrics and Gynaecology. **Results:** In this cross-sectional study 256 patients had sickle cell anemia (prevalence 10.2%). The mean age of patients was 26.6±4.2 years. Majority of the women 205(80.1%) were newly diagnosed cases and about 64 (25%)women had consanguineous marriage. Most of the women 184(71.9%) had the sickle cell trait "AS", while (sickle cell disease) "SS" was seen in 72(28.1%) of the pregnant women. About 148 (57.8%) women had moderate anaemia followed by severe anaemia 62(24.2%) and mild anaemia 46(18%). Preeclampsia was seen in 41(16%), while IUGR/oligohydramnios in 37(14.4%) cases. About 31(12.1%) women had hemolytic crisis, 20(7.8%) had vaso-occlusive crisis and 13(5.1%) had acute chest syndrome. These complications were significantly more among sickle cell disease patients [38.9%,27.8%,16.7%] than sickle cell trait patients [1.6%,0%,0.5%] respectively. Intensive care unit stay was needed for 9(3.5%) women and maternal mortality was 4(1.6%). **CONCLUSION** There is a high prevalence (10.2%) of Sickle Cell Disease among pregnant women in this region necessitating more efforts to increase awareness in highrisk communities regarding sickle cell anemia and to institutionalize appropriate health interventions for early detection and treatment of SCD in India.

KEYWORDS

sickle cell anaemia, high risk pregnancy, vaso-occlusive crisis, hemolytic crisis

INTRODUCTION

Sickle cell disease is the most common inherited genetic blood disorder worldwide[1] . The blood cells contain abnormal hemoglobin (Hb S) called sickle hemoglobin which causes the red blood cells to become sickle shaped that were normally discoid , when exposed to low oxygen levels. This leads to impaired microcirculation resulting in local hypoxia.[2]

Sickle-cell anemia is predominant in countries like Nigeria, India and Democratic Republic of Congo. The prevalence of sickle cell in India varies between 1-44% because of consanguinity, caste and area endogamy.[3] It is extremely common in the tribal belt of Southern and Central India which includes the states of Gujarat, Madhya Pradesh, Maharashtra, Chhattisgarh, Orissa, Tamil Nadu and Kerala.[1,4]

Sickle cell trait individuals usually are asymptomatic and appear healthy. However pregnancy in a sickle cell disease is associated with higher clinical and obstetric complications[5] that include increased risk of pre-eclampsia ,maternal death, stillbirths, preterm deliveries, and small-for-gestational-age newborns.[2]

The physiological changes of pregnancy like increased metabolic demand, increased blood viscosity and hyper-coagulability gets aggravated in SCD patients leading to increased incidence of complications like a Vaso-occlusive crisis, acute chest syndrome, osteonecrosis, hepatic necrosis, leg ulcers, thromboembolic events, renal medullary damage, cerebrovascular accidents etc. There is also hepatomegaly,spleenomegaly and an increased predisposition to infection and sepsis.[6,7] Vaso-occlusion also occurs in placenta leading to villous fibrosis, necrosis and infarction, thereby causing impaired uteroplacental circulation resulting in chronic fetal hypoxia and adverse fetal outcomes.[8] HbS is injurious to the erythrocyte membrane resulting into cellular dehydration, oxidative damage and increased adherence to endothelial cells thereby causing a chronic state of inflammation, irreversible sickling and hemolysis. This state of chronic hemolytic anemia accompanied with decreased hemoglobin levels in pregnancy becomes more pronounced requiring blood transfusion more so in HbSS patients.

Therefore, blood investigation in antenatal patients is needed to estimate the load of cases and carriers of sickle cell haemoglobinopathies. Sickle cell disease can be screened using the solubility test which shows typical sickling in HbSS, HbAS and HbSC patients. Hemoglobin Electrophoresis, High- performance liquid chromatography helps in confirmation. Although DNA analysis provides the most accurate diagnosis in patients of any age, it is relatively expensive.[9]

Nowadays, with improved health care facilities, antibiotic prophylaxis, vaccination, and availability of drugs like hydroxyurea, the life expectancy of SCD patients has improved. Adequate care throughout pregnancy ensures a better outcome. Also, recent advancements in the fields of prenatal diagnosis, preimplantation genetic diagnosis and genetic counselling help couples suffering from SCD to have a healthy baby.[10] Hence this study was conducted to know the prevalence of sickle cell anemia so that meaningful interventions or preventive measures could be developed.

AIMS AND OBJECTIVES

- To screen the women accessing antenatal care and to study the prevalence of sickle cell anemia in pregnant women.
- To study the socio-demographic profile of pregnant patients admitted with sickle cell anemia and sickle cell trait.

METHODOLOGY

The present Prospective observational study was conducted in a Tertiary Care Institution of Central India from January 2021 to December 2022 among Pregnant patients admitted in the Department of Obstetrics and Gynaecology. Ethical approval was obtained from the Institutional ethics committee. The required minimum sample size for the study was found to be 2500 which was determined using SAS 9.2 package by considering the anticipated prevalence of 6.4% [1] based on sickle cell disease in pregnancy from a review of literature and using the Formula $n = Z^2 \frac{pq}{d^2}$

Inclusion Criteria

Pregnant women aged >18 years getting admitted in the study duration

Exclusion Criteria Cases

1. Pregnant women affected with other haemolytic diseases, such as thalassemia and glucose-6-phosphate dehydrogenase (G6PD) deficiency
2. Patients with a history of blood transfusion (BT) within the last three months

3. Pre-existing liver disease / renal disease
4. Refusal of consent

Universal sampling was done and all women admitted in hospital for pregnancy were included in this study. Patients were briefed regarding the study and written informed consent was obtained. Enrolled pregnant patients were interviewed and their relevant clinical history was collected in accordance with the study proforma. A structured questionnaire was furnished to all cases regarding the demographic data, any painful crisis episodes, sickling status of previous child or MTP if done after prenatal diagnosis and prior complications. This was followed by clinical examination. Laboratory studies included complete blood count, reticulocyte count, sickling test etc. All EDTA samples was screened for peripheral blood smear examination and sickling solubility test. The sickling test used was dithionate qualitative solubility test, which was only for screening. Positive solubility test samples were further confirmed with HPLC or Hb electrophoresis. This provided the confirmation and also excluded false positive results if any. Patients were managed as per appropriate guidelines and pregnancy outcome was recorded.

Statistical analysis was carried out with the help of SPSS software. The description of the data was done in the form of arithmetic mean ± SD for quantitative data and frequency (%) for qualitative data. For comparison of categorical variables chi-square and Fisher's exact test was used.

OBSERVATIONS AND RESULTS

In this cross-sectional study about 272 (10.8%) out of 2500 screened patients had positive sickle solubility tests. Of which haemoglobin electrophoresis confirmed 256 patients to have sickle cell anaemia (prevalence 10.2%).

In the present study, all women were married. The mean age of patients was 26.6±4.2 years with a minimum of 19 and maximum of 37 years. When educational status of patients was studied, we found that majority 109 (46%) of the patients had completed secondary education, followed by primary education in 97 (37.9%) women . Majority of the women were residing in rural areas 184 (71.9%), while 72(28.1%) were residing in urban area. About 162(63.3%) were booked cases, while 94(36.7%) were un-booked cases. Sixty-four women (25%) had sharing of common ancestor(s), while no lineage was found in 192(75%) rest of the patients. Majority 107(41.8%) of the women were primigravida and most were in the gestational age of 37-40 weeks, followed by 28-36 weeks. (Table no.1)

Table 1: Distribution of pregnant women according to socio-demographic variables

Variables	No. of cases	Percentage (%)
Age groups (years)		
< 20	3	1.2
21-25	101	39.4
26-30	108	42.2
31-35	32	12.5
> 35	12	4.7
Education		
Primary	97	37.9
Secondary	109	42.6
Higher Secondary	41	16
Graduate and above	09	3.5
Place of residence		
Urban	72	28.1
Rural	184	71.9
Gestational age (weeks)		
<28	22	8.6
28-36	98	38.3
37-40	128	50
>40	8	3.1
Gravida		
1	107	41.8
2	87	34
3	40	15.6
>3	22	8.6
Booking status		
Booked	162	63.3
Un-booked	94	36.7
Consanguinity		
Yes	64	25
No	192	75
Maternal condition on admission		
Safe confinement	102	39.8
Preeclampsia	41	16
PROM	20	7.8
Preterm labour	21	8.2
IUGR/oligohydramnios	37	14.4
CRISIS	35	13.7

Most of the women 184(71.9%) had the sickle cell trait “AS”, while (sickle cell disease) “SS” was seen in 72(28.1%) of the pregnant women. Of the 184 AS patients, 82 got married to AS pattern husband and 11 got married to SS pattern husband, out of which 22 were found to be consanguineous marriage. And out of 72 SS pattern patients, 4 got married to SS pattern husband and 17 got married to AS pattern husband and 4 were consanguineous marriage. However in 35 (13.7%) husbands pattern was not known as they were not willing for the test.

Most of the women had moderate anaemia 148 (57.8%), severe form of anaemia was noted in 62(24.2%) and mild anaemia was seen in 46(18%) of the pregnant women. The mean haemoglobin levels of patients were 8.6±1.4 g/dl with a minimum of 4 and maximum of 11 g/dl. There was a significant difference in numbers between anaemia type among sickle cell disease and sickle cell trait women; p<0.001 such that severe anaemia was more among SS pattern women . (Table no.2)

Table 2: Distribution of degree of anemia and its association with type of sickle cell disease

Anaemia Type	AS (n=184)	SS (n=72)	Total (%)	P value
Mild (>10.0g/dl)	39(21.2%)	7(9.7%)	46 (18)	<0.001
Moderate (7.0-9.9g/dl)	122(66.3%)	26(36.1%)	148 (57.8)	
Severe (<7.0g/dl)	23(12.5%)	39(54.2%)	62 (24.2)	

Table 3 Distribution according to time of diagnosis and complications

	No. of cases (n=184) AS	No. of cases (n=72) SS	Total
Time of diagnosis			
Known case of Sickle cell anaemia	44(23.9%)	7(9.7%)	51 (19.9)
Newly diagnosed	140(76.1%)	65(90.3%)	205 (80.07)
Blood transfusion	73(39.7%)	65(90.3%)	138(53.9%)
Haemolytic crisis	3(1.6%)	28(38.9%)	31(12.1%)
Vaso-occlusive crisis	0	20(27.8%)	20(7.8%)
Acute chest syndrome	1(0.5%)	12(16.7%)	13(5.1%)
ICU stay	1(0.5%)	8(11.1%)	9 (11.6%)

Majority of the women 205(80.1%) were newly diagnosed cases, while only 51(19.9%) were aware that they had Sickle cell anemia. Almost 138(53.9%) of them received blood transfusions, while 118(46.1%) did not receive it. This history of blood transfusion was significantly higher among SS (90.3%) patients than AS (39.7%)patients, p<0.001. About 31(12.1%) women had haemolytic crisis, 20(7.8%) of women had Vaso-occlusive crisis and 13(5.1%) had acute chest syndrome. These complications were significantly more among sickle cell disease patients [38.9%,27.8%,16.7%] than sickle cell trait patients [1.6%,0%,0.5%] respectively, p<0.001. About 9(3.5%) women needed intensive care unit stay, while the rest 247(96.5%) did not require it. ICU stay was significantly more among SS (11.1%) patients than AS (0.5%)Patients, p<0.001. Majority 102(39.8%) of the women were admitted for safe confinement. Preeclampsia was seen in 41(16%), while IUGR/oligohydramnios in 37(14.4%) cases (Table 3).

Majority of the pregnant women were discharged 246(96.1%).

Unfortunately, 4(1.6%) died and 6 (2.3%) women went Discharge against medical advice (DAMA). Among the deceased, three had sickle cell disease "SS" while 1 had sickle cell trait "AS". In cause of death was due to superimposed preeclampsia with pulmonary oedema.

DISCUSSION

Most pregnancies with sickle cell disease (SCD) result in live birth of a healthy baby. However, there are maternal and foetal risks of which clinicians and patients need to be aware. Vaso-occlusive phenomena and haemolysis are the clinical hallmarks of SCD. Access to a multidisciplinary care team knowledgeable about SCD and obstetric management of complicated pregnancies can significantly decrease morbidity and mortality. Due to relative paucity of data and to understand the profile of SCD patients, this study was carried out.

Hemoglobinopathies though common worldwide, some geographic areas have higher prevalence. In the present study the prevalence of sickle cell disease was 10.2%. Of which 71.9% were sickle cell trait and 28.1% were sickle cell disease. This was comparatively higher than the study conducted by Chandrayan P et al (2019) [11] which was 2.43%. However Desai G et al (2017)[12] found that 1.2% (131 out of 10519) of tribal delivery admissions was sickle cell disease and 15.6% (1645 out of 10519) of them had sickle cell trait which was more than our study.

About 94(36.7%) were un-booked cases.This was similar to the study done by Patel K.D et al.[1] where 57.24% were un-booked cases. Late booking status was also studied by Nwabuko et al.[13] where 83.1% of the pregnant women registered after the first trimester. Early antenatal booking is encouraged for better outcome of the mother having sickle cell disease. Majority of the women 205(80.1%) were newly diagnosed cases, while 51(19.9%) were known case of Sickle cell anaemia. Tutuba HJ et al (2022)[14] studied 600 pregnant women in Tanzania of which only 2 (0.3%) knew their SCD status while 7.7% declared having a family history of SCD. Lack of funds and publicity could be a major cause of unawareness.

In this study consanguineous marriages were noted in among Sixty-four women (25%), which thus emphasises on the need of sensitization and screening of individual, genetic counselling, proper health education regarding the nature of prenatal diagnosis and inheritance in a high-risk community. Though majority of the patients were booked at late gestation , but 15 cases out of those who presented early were advised for genetic counselling, and Amniocentesis or CVS; out of which 3 foetus came out to be SS positive and thus underwent MTP.

In this study majority of the pregnant women had moderate anaemia 148 (57.8%) followed by severe anaemia 62(24.2%) and mild anaemia 46(18%). The results were concordant with a study by Patel K.D et al,[1] where majority (50.34%) had moderate anaemia while mild and severe anaemia were noted in 44.82% and 4.82% pregnant women respectively. In this study more than half cases (53.9%) had received blood transfusion which was significantly more among the SS patients. Odum et al.[15] also found that antenatal and postpartum blood transfusion rates were 45.0% and 81.6%, respectively among the SCD patients.

We observed that along with maternal Anaemia, pregnant women also had preeclampsia 41(16%) and IUGR/oligohydramnios 37(14.4%). About 31(12.1%) women had haemolytic crisis, 20(7.8%) women had Vaso-occlusive crisis and 13(5.1%) had acute chest syndrome. All three complications were significantly more among SS group of patients than AS group. About 9(3.5%) women needed intensive care unit stay. While majority of the pregnant women were discharged 246(96.1%); unfortunately, 4(1.6%) died and 6 (2.3%) women went Discharge against medical advice. Similar complications were also noted in other studies.

A study by Silva-Pinto AC et al (2014)[16] found that 62% of patients had Vaso- occlusive crises, 29% had acute chest syndrome, 23% had urinary tract infection, 15% had impaired cardiac function and 6% developed pulmonary hypertension. Only one patient died in the postnatal period due to acute chest syndrome. There were seven foetal losses, including three stillbirths and four miscarriages.

Elenga N et al (2016)[17] noted that the main complications of pregnancies were anaemia (36.5%), infection (31.7%), Vaso occlusive crisis (20.6%), preeclampsia (17.5%), premature birth (11.1%), intrauterine growth retardation (15.9%), abnormal foetal heart rate (14.3%) and intrauterine foetal death (4.8%).

Dora SK et al (2019)[18] found that in a total of 59 patients with SCD and 119 patients with SCT; about 17 (28.8%) SCD and 5 (4.2%) SCT patients presented with painful crisis. Acute chest syndrome developed in 9 (15.3%) of SCD and 1 (0.8%) of SCT cases. Haemolytic crisis was seen in 4 (6.8%) of SCD patients. Ten (16.9%) of SCD and one (0.8%) of SCT patients had intrauterine death.

Unlike several studies that have reported increased incidence of spontaneous miscarriages, still birth and ectopic pregnancy in HbSS pregnant women, our study did not record any of these complications. This is probably because the women studied booked after the first trimester above 16 weeks, when the risk of spontaneous miscarriages and ectopic pregnancies are less.

Based on the study it implies that the prevalence of SCD and its complications is increasing thereby necessitating higher levels of awareness among the pregnant women.

CONCLUSION

There is a high prevalence (10.2%) of Sickle Cell Disease among pregnant women in this region. Late antenatal booking, anemia, consanguinity and poor education are the predictive markers of poor pregnancy outcome in this region. Therefore, there is a need to create awareness through media networking, involving the government and other donor agencies to institutionalize appropriate health interventions aimed at early detection and treatment of SCD in India.

The most effective preventive approach is by increasing literacy rate, sensitization and screening of individual, genetic counseling, health education regarding the nature of prenatal diagnosis and inheritance in a high-risk community. Hence more efforts are needed to increase awareness, especially in high-risk communities regarding sickle cell anemia in order to control hemoglobinopathy in India.

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