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Prevalence of Sickle Cell Anemia in Pregnancy: A Prospective Study in Tertiary Health Center

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ABSTRACT

Background: Sickle cell disease comprises a group of diseases characterized by the presence of HbS. It is classified as sickle cell anemia (Hb SS), hemoglobinopathy SC, hemoglobinopathy SD, S-beta thalassemia (Hb S-beta) and other associations of mutant hemoglobin with Hb S. Sickle cell disease is the most common inherited disorder worldwide. Pregnancy in sickle cell disease is at high risk.

Methods: This prospective study was conducted on pregnant females OPD in DGH from 1st January to 1st April 2017. Consenting participants were interviewed using a pre-structured questionnaire. All the data were tabulated according to parameters: age, literacy, anemia, gestational age, parity and HPLC findings.

Result: The total numbers of pregnant women screened for hemoglobinopathy were 2500. 6.4 % had positive sickle solubility tests. Further HPLC analysis was done in the second group and 5.8 % showed hemoglobinopathies. 44.13% were in 1st trimester, 28.96 % were in 2nd trimester and 26.89 % were in last trimester. Majority of the female (57.24%) attended ANC OPD for the first time, out of which 22 (26.50 %) were in first trimester, 41 (49.39%) were in 2nd trimester and the rest of 20 (24.09%) were in last trimester. And there were 62 women visited OPD as followup checkup.

Conclusion: In present study, gravid population has higher prevalence of hemoglobinopathy (5.8 %), mainly SCT (94.48 %). More efforts are required to increase awareness in high risk populations concerning sickle cell anemia before the dream to control hemoglobinopathy in India.

Keywords: Hemoglobinopathy, Sickle cell anemia, Sickle cell trait, Sickle cell Disease, Thalassemia trait

INTRODUCTION

A group of genetic disorders of hemoglobin are termed as Hemoglobinopathies. They affect 4.5% of the world population. [1] The prevalence of β- thalassemia trait and sickle cell in India varies between 3-17% and 1-44% respectively because of consanguinity and caste and area endogamy. [2] Every year, ten thousand children with β- thalassemia major are born in India, which constitutes 10% of the total number in the world. [3] Inherited hemoglobin disorders are an important cause of morbidity and mortality. The curative treatment like bone marrow transplantation is costly and so prevention is the cost effective strategy, which includes population screening, genetic counseling and prenatal diagnosis. [4-6]

Sickle-cell anaemia (also known as sickle-cell disorder or sickle-cell disease) is a genetic blood disorder, where the blood cells contain abnormal hemoglobin (Hb S) called sickle hemoglobin. As a result Red Blood Cells which are normally discoid in shape, become sickle shaped when they are exposed to low oxygen levels.

Sickle cell disease (SCD) comprises a group of diseases characterized by the presence of sickle hemoglobin (Hb S). It is classified as sickle cell anemia (Hb SS), hemoglobinopathy SC, hemoglobinopathy SD, S-beta thalassemia (Hb S-beta) and other associations of mutant hemoglobin

with Hb S. Sickle cell disease is the most common inherited disorder worldwide with varying clinical severity and potentially serious complications.

Pregnancy in sickle cell disease is at very high risk. Many reports have documented a substantial maternal risk of morbidity and mortality and high perinatal adverse consequences. Women with SCD have an increased risk of pre-eclampsia and maternal death, stillbirths, preterm deliveries, and small-for-gestational-age newborns. The prevalence of sickle-cell anaemia is extremely common in the tribal belt of Southern and Central parts of India which includes tribal in the states of Gujarat, Madhya Pradesh, Maharashtra, Chhattisgarh, Orissa, Tamil Nadu and Kerala. [7-9]

Sickle cell trait individuals are absolutely normal and healthy, unless they have a special blood test investigation for Hb S electrophoresis or HPLC. Confirmation of patient suffering from sickle cell disease is carried out only by laboratory investigations only. Therefore blood examination in antenatal cases at large is needed to estimate the load of cases and carriers of sickle cell haemoglobin-opathies.

The present study was an effort which had been made to assess and identify the pregnant women with sickle cell disease or the carriers of sickle cell disease and look for the prevalence in the selected group.

AIM AND OBJECTIVE

AIM

- To screen samples of ANC women and then to find prevalence of sickle cell anemia

OBJECTIVES

- To create awareness about genetic inheritance of SCD amongst entire community.
- To survey the common perinatal problems of future mother having sickle cell anemia. Prevention of spread of sickle cell disease by reducing sickle cell births through screening and referring her for genetic counseling.

REVIEW OF LITERATURE

James Herrick, a physician first described the characteristic sickle shaped red cells in a medical student from Grenada in 1910. [10-11]

Linus Pauling and his colleagues presented that sickle haemoglobin (HbS) had an altered electrophoretic mobility and they were the first to define it as a molecular disease in 1949. [10]

The first report of sickle hemoglobin (Hb S) in India was by Lehman and Cut bush in 1952 in the tribal populations in the Nilgiri hills in south India (hills of Tamilnadu) and later discovered in other states. [3] The incidence varies from 5 % to 34 % and it is mainly restricted to the tribal [12]

A few years later in 1957, Vernon Ingram discovered that sickle hemoglobin resulted from a single amino acid substitution in the hemoglobin molecule. [13-14]

In the same year, Dunlop and Mazumderlike wise reported the occurrence of sickle hemoglobin in the tea garden workers of Upper Assam who were migrant labourers from tribal groups in Bihar and Odisha. [21] Since then, many population groups have been screened and the sickle cell gene has been shown to be prevalent among three socio-economically disadvantaged ethnic groups, the scheduled tribes, scheduled castes and other backward classes in India. [14-20]

The prevalence of sickle cell carriers among different tribal groups varies from 1 to 40 percent. [10] Madhya Pradesh has the highest load with an estimated number of 9,61,492 sickle heterozygotes and 67,861sickle homozygotes. [14] Further, 27 of the 45 districts in Madhya Pradesh fall under the sickle cell belt and the prevalence of HbS varies from 10 to 33 percent. [10] It has also been estimated that 13,432 pregnancies would be at risk of having a child with sickle cell disease in this state and the

expected annual births of sickle homozygotes would be 3358. [22]

High prevalence of sickle gene has been established in various tribal communities of Gujarat including Bhils and Dhodias of Panchmahal, Dhanka, Gamit, Vasava, Bariya, Varli, Vaghari, Kukna, Halpati,Dublas, Naikas, Koli, Chaudhari etc. [23]

Tribal accounts 15 % of the total population of Gujarat and distributed in various districts of the state such as Sabarkantha, Banaskantha, Panchmahal, Vadodara, Narmada, Bharuch, Surat, Valsad, Dang and Div-Daman [23-24]

MATERIALS & METHODS

This prospective cross-sectional study was conducted on pregnant females attending ANC (Anti Natal Care) OPD in Dhiraj General Hospital, Piparia, for a period of three months from 1st January 2017 to 1st April 2017. Most of patients were from tribal background and lower socioeconomic status.

Before conducting the study, permission was obtained from the Human Research Review Penal (HRRP) of SBKS MIRC and Institutional Ethics Committee (SVIEC) of Sumandeep Vidyapeeth for consideration of ethical aspects and final approval.

Women included in this study were in their steady state for a long period of time without any chronic systemic illness or other diseases which could affect the hematological parameters. Subjects who have been transfused in the last 3 months were excluded from the study and those who are not willing to participate.

Consenting participants were interviewed using a pre-structured questionnaire. The information like name, age, sex, address, education, socio-economic status, previous transfusion history, sibling history, consanguinity any family history of blood disorders, etc., were filled in according the proforma. Data were collected accordingly and recorded in Microsoft Excel.

For this study, collection of Blood samples were done according to practical manual of Dacie. [23] The blood samples were mixed on electric blood mixture for 8 to 10 minutes and subsequently analyzed on the coulter LH750. All EDTA samples will be screened for PBS(Peripheral blood smear) examination and Sickling solubility test.

The positive solubility test samples were further screened for subtyping of Hemoglobinopathy. These samples were analyzed on the Bio-Rad Variant I HPLC system to check for the quantification of variants of hemoglobin. The raw data were integrated and chromatograms were generated. All the data had been collected and evaluated.

Based on hemoglobin level, anemia was classified as per WHO severity grading criteria. Thus anemia in pregnancy ranges from mild (>10.0g/dl), moderate (7.0 - 9.9g/dl) to severe (<7.0 g/dl). The typing of anemia was done as per standard PBS examination method.

Statistical analyses were undertaken using Chi-square test, mean, percentages and proportions. P values less than 0.05 were considered significant.

RESULTS

The total number of pregnant women screened for hemoglobinopathy was 2500 from ANC OPD of Dhiraj General Hospital, Piparia, for a period of three months starting from 1st January 2017 to 1st April 2017.

160out of total screened women (6.4 %) had positive sickle solubility tests. The sickling test is dithionate qualitative solubility test, which is only for screening. Therefore there could be some chances of false positive results and that's why they must be confirmed with HPLC or Hb electrophoresis.

Further HPLC analysis was done in the second group and 145, showed hemoglobinopathies (5.8 %). We had evaluated 145 samples with positive HPLC results for further studies.

Additional findings apart from hemoglobinopathies, nutritional anemia was very much prevalent in and largely neglected due to lack of education amongst pregnant women. But those supplementary findings had not been evaluated further.

All the data were charted and tabulated according to mentioned parameters: age, literacy, anemia based on Hb level, gestational age, parity and HPLC findings. The demographic profile of the study population is shown in Table 1& 2.

Table: 1. A: Age of pregnant women in study population.

Age (years)	No. of females (Total-145)	Percentage (%)
<20	20	13.79
21-25	83	57.24
26-30	34	23.44
31-35	06	4.13
>35	02	1.37
Age (in years), Mean (SD)	23.8 (1.45)	-

Table: 1. B: Education of pregnant women in study population.

	No. of females (Total-145)	Percentage (%)
Illiterate	38	26.20
Left schooling midway	68	46.89
Finished schooling	36	24.82
Graduation	03	2.06

Table: 2: Distribution based on parity of the pregnant women

Parity	No. of female (Sample size- 145)	Percentage (%)
1	82	56.55
2	49	33.79
3	10	06.89
>3	04	02.75

Out of 145 women, 64 (44.13%) were in 1st trimester, 42 (28.96 %) were in 2nd trimester and 39 (26.89 %) were in last trimester.

Majority of the female (57.24%) attended ANC OPD for the first time, out of which 22 (26.50 %) were in first trimester, 41 (49.39%) were in 2nd trimester and the rest of 20 (24.09%) were in last trimester. And there were 62 women visited OPD as follow up check-up.

Following table 3 are showing the degree of anemia based on the hemoglobin level.

Table: 3: Degree of anemia in study group.

Degree of anemia (Hb level)	No. of women (Total -145)	Percentage (%)
Mild (>10.0g/dl)	65	44.82
Moderate (7.0 - 9.9g/dl)	73	50.34
Severe(<7.0 g/dl)	07	4.82

The following Table 4 is showing hemoglobinopathy based on HPLC finding.

Table: 4: Distribution of hemoglobinopathy based on HPLC finding.

Hemoglobinopathy	No. of Women (Sample size- 145)	Percentage (%)
SCT(Sickle cell trait)	137	94.48
SCD(Sickle cell Disease)	03	2.06
Thalassemia minor	05	3.44
Thalassemia major	00	00
Other	00	00

Out of 145 samples, 137 samples were having HbS level between 30%-45%, HbA between 50%-70% and HbF was <1%. This was confirmed by HPLC. The overall prevalence of hemoglobinopathies was 145 (5.8 %), comprised of 137 (94.48%) cases of SCT,3 cases (2.06%) of SCD and 5 cases (3.44%) of beta thalassemia minor.

DISCUSSION

Hemoglobinopathies though are common worldwide, but some geographic areas and some populations having higher prevalence of it comparatively.

In India, According to hospital based study, average frequency of sickle cell gene is around 5%. The highest frequency of sickle cell gene in India is reported in Orissa (9%), followed by Assam (8.3%), Madhya Pradesh (7.4%), Uttar Pradesh (7.1%), Tamil Nadu (7.1%) and Gujarat (6.4%). [27-29]

The prevalence of sickle cell trait (5.8 %, n= 2500) in our study is in concordance with the reported prevalence of the study by P. Ashwin et al. [26]

The majority (50.34%) of anemic women demonstrated moderate anaemia while mild and severe anaemia were recorded in 65 (44.82%) and 07 (4.82%) pregnant women respectively. The severity of anaemia according to age groups is shown in Table 5.The results are concordant with the study by A. Nadeem et al. [30] according to which 50.86% of anemic women demonstrated moderate anaemia.

Table: 5: Anemia with its age wise distribution, in pregnant women

Sr. No.	Age (years)	Degree of anemia			
		Mild	Moderate	Severe	Total numbers of women (145)
		No. (%)	No. (%)	No. (%)	
1	<20	10 (6.89)	8 (5.51)	2 (1.37)	20
2	21-25	50 (34.48)	31 (21.37)	2 (1.37)	83
3	26-30	2 (1.37)	31 (21.37)	1 (0.68)	34
4	31-35	2 (1.37)	2 (1.37)	2 (1.37)	6
5	>35	1 (0.68)	1 (0.68)	0 (0)	2
Total		65 (44.82)	73 (50.34)	7 (4.82)	145

The peripheral smear acknowledged normocytic hypochromic and microcytic hypochromic blood picture to be most common morphological variant of anaemia. These two pictures of PBS are characteristic of iron deficiency anaemia. Underlying β thalassemia trait could have been missed in this group and investigations for iron deficiency followed by repeat HPLC after iron therapy is needed.

A highly significant association of anemia was found with the mother‘s age group (χ^2=28.38, p<0.001) and educational (χ^2=19.58, p<0.001). Other factors such as family structure (χ^2=1.46, p>0.05) and dietary habits (χ^2=2.37, p>0.05) were not significantly associated with anemia. All the women with multiple pregnancies were found to be anemic, though it was only moderate in nature.

Following table 6 is showing anemia with its correlation with educational status.

Table:6: Anemia with its correlation with educational status.

Educational status	Degree of anemia			Total (145)	
	Mild	Moderate	Severe		
	No. (%)	No. (%)	No. (%)		p<0.001
Illiterate	4 (2.75)	4 (2.75)	30 (20.68)	38	
Left schooling	27 (18.62)	33 (22.75)	8 (5.51)	68	
Finished schooling/Matrix finished	30 (20.68)	5 (3.44)	5 (3.44)	36	
Graduation finished	3 (2.06)	0 (0)	0 (0)	3	
Total (145)	64 (44.13)	42 (28.96)	39 (26.89)	145	P<0.001

In this study a high prevalence of anaemia among pregnant women was observed. The majority had moderate anaemia. Most of the anemic pregnant women were in the younger age group. This result was in concordant with the results obtained by similar study in the rural area of Delhi where patients in the age group (20-24 years) showed maximum prevalence of anaemia. [25]

The prevalence of anaemia was not significantly related with structure of family, birth interval and number of abortions. This result corresponds well with those of Bentley/Griffiths. [22] Women with first ever pregnancy more often had severe anaemia. The observed very high prevalence of anaemia and its severity in the current study is similar to earlier studies. [23,24]

As in other studies the severity of anaemia was inversely related to educational status and income. [25-26] These findings are significantly matching with the present study.

CONCLUSION

Studied gravid population has higher prevalence of hemoglobinopathy (5.8 %), mainly SCT (94.48 %).

One of the limitations of this study is small sample size, so that could affect the prevalence of hemoglobinopathy. There is also a need for screening of whole population by calculating sample size from the pilot study in high risk community in near future.

The most effective approach to minimize the problem of hemoglobinopathies in females in India is by increasing literacy rate, sensitization and screening of individual, genetic counseling, proper health education regarding the nature

of prenatal diagnosis and inheritance in a high-risk community. More efforts are needed to increase awareness in high‑risk communities regarding sickle cell anemia before the dream to control hemoglobinopathy in India.

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