Do gender differences influence the prevalence of sickle cell disorder and related morbidities among school children in rural central India?

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Abstract

Background and Objectives: Sickle cell disease (SCD) is a genetic disorder of great epidemiological, clinical and public health relevance in developing countries like India. It is irreversible, untreatable health problem responsible for increased morbidity and mortality of school children. With this background, the present study was undertaken to estimate the prevalence of sickle cell disorder and associated morbidities and also to assess the gender differences in rural school children of central India.

Methods: A cross-sectional study was carried out among 735 school going children studying in 5th to 10th standard of Sevanand High School, Mahadula village, Koradi road district Nagpur. Detailed information regarding socio-demographic profile was inquired. Each student was subjected to thorough general and systemic examination. Also, haemoglobin estimation and sickling test was performed. In addition, Haemoglobin electrophoresis was done in students with positive sickling test.

Results: Out of total 735 students, 56.2 % were male and 43.8% were female students belonging to different caste. 6.7% students showed sickling test positive with 30 (7.3%) males and 19 (5.9%) females. Majority of sickle positive students were males and belonged

to schedule caste (mahar). All sickling test positive children were found to be sickle cell trait on haemoglobin electrophoresis. Mean haemoglobin level and mean quetelet index was found to be significantly lower in sickle cell trait students ($p<0.001$). Related morbidities like lymphadenopathy, upper respiratory tract infection, joint pain and otitis media were found in Hb AS students with greater prevalence among male students as compared to female students.

Conclusions: The overall prevalence of sickle cell trait was found to be 6.7% in rural school children with higher prevalence among male students and preponderance in schedule (mahar) caste. Also, high prevalence of anaemia and morbidities (lymphadenopathy, upper respiratory tract infection, joint pain and otitis media) were found in sickle cell trait male students.

Key words: Sickle cell disorder, haemoglobinopathy, school children, rural.

Running title: *Sickle cell disorder in rural school children*

Introduction

Sickle cell disorder has remained a neglected field of research in developing countries like India and magnitude of problem has never been appreciated in spite of the fact that the sickled RBCs were detected in the blood of Indian patients as early as 1952. Sickle cell disorders are a group of autosomal recessive disorders, caused by point mutation at the sixth position in beta globin chain, valine substituting glutamic acid.[1] The resultant HbS has poor solubility in the deoxygenated state and can polymerize within the red cells. The red cell shows a characteristic shape change because of polymer formation and becomes distorted and rigid, the so-called sickle cell.[2]

Because of its prevalence and wide-spread consequences, sickle cell disease is an important public health problem in India. Sickle cell disease is an autosomal recessive genetically transmitted hemoglobinopathy responsible for considerable morbidity and mortality. It is one of the most common hereditary diseases occurring worldwide, which may affect any organ or system of human body.[3] In India, sickle cell disorder is more common in central and southern parts of the country. It is the second most common haemoglobinopathy, next to thalassemia in India.[4] School age children forms 25% of the world's population, approximately one-fifth of Indian population comprises of school age children. The school going age is a dynamic period of physical growth and development, when children undergo mental, emotional and social changes. The health status of school children varies from one place to another also varies in urban, rural and tribal areas. The health of school children is influenced by complex of genetic, environmental, social and economic factors.[5] It was proposed that distribution of sickle cell disorder in India has an ethnic and racial basis. Sickle cell trait in India, contrary to view once held that it was found only in the isolated pocket, has systematic and widespread distribution between the various tribal, rural and few other related population. Very few studies have been conducted in school children in rural areas of Nagpur city where sickle cell disorders are very rampant. Therefore the present study was conducted to estimate the prevalence of sickle cell haemoglobinopathy with associated morbidities and also to assess the gender differences in rural school children of central India.

Methodology

A Cross sectional study was carried out among the rural school children of Sevanand High School, Mahadula village, Koradi road district Nagpur. The school is situated 16 km away from Indira Gandhi Government Medical College, Nagpur.

Study area

There are 6 census town in the Nagpur district (census town is that town where ¾ of the male working population was engaged in non agriculture pursuits, if the density of population is expected to reach the figure of 400 sq. km and minimum population for that area is 5000). Out of which Mahadula has maximum population of schedule caste and schedule tribe as per census (2001). There were three schools in the Mahadula village, out of which one was selected randomly i.e. Sevanand High School, Mahadula, Nagpur.

Permission was obtained from headmaster of the school. A meeting was held before the start of the study by calling the teachers and parents of the children. The purpose of the study in detail was explained to them and also assured co-operation to conduct the study. There were 739 students in 5^{th} to 10^{th} class. There were 4 students who were absent since long period, they were excluded from study. Hence 735 students were included in the study.

Data collection

School was visited thrice a week. During each visit near about 7 to 8 students were covered. A rapport was established with the students and teachers. For each student detail information regarding socio-demographic factors was obtained as per the predesigned proforma. Students who were not present during the first visit were covered in subsequent visit. After obtaining general information every student was subjected to thorough clinical examination and investigation. Every student was enquired about presenting complaints as well as complaints related to sickle cell disorder. Also, detail clinical and systemic examination was done. Anthropometric measurements like weight and height were taken as per standard technique.[6]

Every student was subjected to haemoglobin estimation and sickling test. Haemoglobin electrophoresis was done in students with positive sickling test. For this purpose, 2 ml of venous blood was taken from every study subject by taking all aseptic precaution. This blood sample was collected in EDTA bulb. The bulb was then labeled and packed properly and was brought to Indira Gandhi Government Medical College, Nagpur. Haemoglobin was estimated by Sahli's Haemoglobinimeter method [7, 8] and sickling test was also performed.[9] Sickling positive samples were subjected to haemoglobin electrophoresis using cellulose acetate method.[9]

Statistical analysis

Percentages mean and standard deviation was calculated. For statistical analysis, between-group comparisons were conducted using chi-square tests, Fisher's exact test and student t

test. Epi Info statistical package programme version 6.0. updated 2009 was used to analyse the data. Statistical significance was assessed at a type I error rate of 0.05.

Results

Total numbers of screened students were 735, out which 413 (56.2%) were males and 322 (43.8%) were females. The demographic and other characteristics of study subjects are shown in Table 1. Most number of students was found in the age group of 13-14 years i.e. 127 (17.3%) while least number of students found in the age group 17-18 years i.e. 33 (4.5%) with male (17.4%) as well as female (17.1%) preponderance in the age group of 13-14 years.

As far as caste distribution of students is concerned, more students belonged to schedule caste (mahar) i.e. 265 (36.1%), out of which 106 (32.9%) were females and 159 (38.5%) were males; followed by other backward community, out of which 10.1% were teli, 8.7% were Kunbi and 8.2% belonged to Mali caste. Students of other caste and sub-caste found were scheduled tribe, nomadic tribe and vimukta jamati.

When the habits like tobacco/ghutka chewing and smoking were compared in male and female students, it was observed that more proportion of male students (31.2%) had the habit of tobacco/ghutka chewing and smoking (1.9%) as compared with female students (18.3%).

It was observed that out of 735 students, 49 (6.7%) showed sickling test positive out of which 30 (7.3%) boys were positive for sickling test while 19 (5.9%) girls were positive for sickling test. However the difference between male and female students was not found to be statistically significant ($p>0.05$). Moreover, the various grades of anaemia (mild, moderate and severe) in male students were found to be statistically significant with female students ($p<0.01$) as shown in Table 2.

When caste wise distribution of sickle positivity in male and female students were compared (Table 3), it was observed that out of total 49 sickle positive students, preponderance of male students from mahar (60%) and Teli caste (13.3%) was found as compared with female students. Although the difference between them was not found to be statistically significant ($p>0.05$). The findings are summarized in Table 3.

Haemoglobin electrophoresis of 49 sickling test positive results was found to be sickle cell trait i.e. Hb AS. It was found that mean haemoglobin level among the sickle cell trait students was less as compared to mean haemoglobin level among the normal students. The difference was found to be statistically significant ($p<0.001$). Also, the mean Quetlet index between the normal students (HbAA) and sickle cell trait students (HbAS) was found to be statistically significant ($p<0.001$) as evident from Table 4.

Table 5 shows the various morbidities observed in HbAS male and female students. It was seen that lymphadenopathy18 (36.8%), upper respiratory infection 9 (18.4%), joint pain 8 (16.4%), otitis media 6 (12.2%), and epistaxis 02 (4.1%) formed common morbidity in sickle cell trait students. Although the prevalence of these morbidities were higher in male students, the differences in morbidities between male and female students were not found to be statistically significant ($p>0.05$).

Discussion

The present study emphasized the comparative assessment of the hematological and morbidity pattern of male and female sickle cell disease (SCD) children belonging to rural areas. The SCD male children exhibited statistically significant ($p < 0.05$) lower values for all the measurements.

As per census 2001 Mahadula and other villages have the highest population of scheduled caste in Nagpur district. The present study reported quite high prevalence of sickle cell trait (6.7%) with preponderance in male school students when compared with female students. Although SCD, a genetic disorder, is prevalent in many areas of India.[10] However, the reported prevalence estimates show an enormous variation (i.e., 0–40%).[11-13] Kamble M et al [11], reported incidence of sickle cell trait to be 2.17%. Sahu T et al,[14] reported 16.55% prevalence of sickle cell disorder in below fifteen years children in tribal areas of Gajapati district of Orissa. Balgir R S et al,[15] observed sickle cell disease in Bhuyan and Kharia tribes of north-western Orissa and reported 25.5% prevalence of sickle cell disease in school adolescents. The highest frequency of sickle cell gene in India is reported in Orissa followed by Assam, Madhya Pradesh, Utter Pradesh, Tamilnadu and Gujarat.[16] Patel A B et al,[17] reported older age of presentation, absence of severe anemia, male preponderance in their study. It indicates limited availability of health services, education and counseling available to susceptible populations,[18] which was also observed in present study.

Caste wise, the prevalence of sickle cell trait in our study was found to be highest in Mahar i.e.36.1% followed by Teli (10.1%), Kunbi (8.7%) and Mali (8.2%). These findings are consistent with the findings of other investigators. The study carried out by Bhobate SK et al (1983)[19] in Chandrapur district of Maharashtra in their study found sickle cell trait, 9.42% i.e. maximum in Mahar caste and 5.06% in Teli. Kar BC (1983)[20] also reported high prevalence of sickle cell trait in Mahar (19.8%). Another study carried out by Shukla RN et al (1958)[21] among 1010 subjects in Nagpur found the prevalence of sickle cell trait about 22.2% in Mahar and 11.3% in Teli caste. These observations support the hypothesis that the sickle cell disorders are present in scheduled castes, tribals and few communities of OBCs and not found in so called higher castes; though the review of literature says it is present invariably in all castes8.

Our study also reported higher non-significant prevalence of various sickle cell related morbidities like lymphadenopathy, upper respiratory infection, joint pain, otitis media, and epistaxis in male SCD children. However, Bhobate SK et al in their study,[19] found joint pain to be the most prevalent morbidity.

In the present study, anemia was found to be very common morbid condition in SCD children (Hb AS trait) as compared to normal children (Hb AA pattern) with mean hemoglobin of 7.9 ± 0.635 and 10.83 ± 1.254 respectively. Kamble M. et al (2000)[11] and Carol K et al (1984)[22] had obtained similar findings in their study. It is believed that anemia plays a role in the pathophysiology of SCD; however, it is not very clear whether anemia affects either specific organ function or over-all cellular metabolism sufficiently to result in growth retardation. Anemia can be corrected by giving multiple blood transfusions which will ultimately help to reduce the number of cells capable of sickling to clinically insignificant levels. The steady-state hemoglobin level may have a potential impact on growth of the school children because of its direct relationship with oxygen delivery to the tissues.[23] Therefore, this study,

specifically highlights the need of a multidimensional approach for understanding the hematological and anthropometric variations seen among the Indian SCD rural children.

So, with the overall prevalence of sickle cell trait of 6.7% found in rural school children in our study with higher prevalence among male students and preponderance in schedule caste (mahar); spreading high awareness about sickle cell disease in the community becomes a prerequisite for early detection and management of SCD particularly in school age children. Also, since high prevalence of anaemia and related morbidities like lymphadenopathy, upper respiratory tract infection, joint pain and otitis media found in sickle cell trait male students in our study, efforts should be taken to reach community through school adolescents by imparting health education to them. After completion of study, we imparted health education to the students of each class separately regarding the sickle cell disorder using posters and flip charts. The parents of sickle positive students were called at school and were given health education regarding the various morbidities related to sickle cell disorder. Also they were given the genetic counselling regarding this disorder so as to prevent the carrier state or sickle cell disease in future generation.

Conclusions

The overall prevalence of sickle cell trait was found to be 6.7% in rural school children with higher prevalence among male students and preponderance in schedule (mahar) caste. Also, high prevalence of anaemia and morbidities (lymphadenopathy, upper respiratory tract infection, joint pain and otitis media) were found in sickle cell trait male students. In conclusion, this study highlights the need for conducting a more comprehensive study by integrating the clinical, nutritional, and social aspects associated with SCD. Besides, a dedicated monitoring programme for assessing hematological parameters of SCD-SS needs to be initiated for effective management. Education for patients with SCD should focus on specific food intake which can increase the nutritional value through various foods and can effectively alleviate anaemia or other symptoms. Also, there is an urgent need to improve primary health care professional training in the care of children with sickle cell disease in areas where children with sickle cell disease are more vulnerable than adults. In this context, it is necessary to investigate whether doctors and nurses who serve in these areas are adequately trained and prepared to assist these children and their families. So far, the initiatives of Indian Government have not shown great results of improving the quality of life of SCD sufferers. Many non-governmental and voluntary organizations working for sickle cell anemia and identification work are doing camps, where large number of people gathers, and their blood samples are collected to carry out laboratory investigation but that`s all on temporary basis. Unfortunately neither the diagnostic nor the treatment facilities are available in tribal area and all this are beyond their reach. Without diagnosis and comprehensive care, children suffer crippling medical problem leading to lack of education, employment opportunities and integration into the society. Therefore the limited availability of medical and health care in rural areas, as well as other support systems calls for an increase in community based healthcare services.

List of abbreviations:
SCD: Sickle cell disease
OBC: other backward community
Hb AA: Haemoglobin AA (normal adult pattern)
Hb AS: Haemoglobin AS (sickle cell) trait

IRB permissions
The project has been approved by Clinical ethics Committee, Indira Gandhi Government Medical College, Nagpur
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Table 1: Demographic and other characteristics of study subjects

Characteristic		Male students 413 (56.2%)	Female students 322 (43.8%)	Total (N = 735)
Age (years)				
10-11		61 (14.8)	50 (15.5)	111 (15.1)
11-12		60 (14.5)	53 (16.5)	113 (15.4)
12-13		58 (14.0)	49 (15.2)	107 (14.6)
13-14		72 (17.4)	55 (17.1)	127 (17.3)
14-15		52 (12.6)	48 (14.9)	100 (13.6)
15-16		46 (11.1)	32 (9.9)	78 (10.6)
16-17		44 (10.7)	22 (6.8)	66 (9.0)
17-18		20 (4.8)	13 (4.0)	33 (4.5)
Caste				
Schedule caste: Mahar		159 (38.5)	106 (32.9)	265 (36.1)
Other backward community:		38 (9.2)	36 (11.2)	74 (10.1)
	Teli			
	Kunbi	36 (8.7)	28 (8.7)	64 (8.7)
	Mali	36 (8.7)	24 (7.5)	60 (8.2)
	Sonar	10 (2.4)	08 (2.5)	18 (2.5)
	other OBC	12 (2.9)	09 (2.8)	21 (2.9)
Schedule tribe:	Gond	24(5.8)	26 (8.1)	50 (6.8)
	Gowari	14 (3.4)	14 (4.3)	28 (3.9)
	Lohar	16 (3.9)	10 (3.1)	26 (3.5)
	Thakur	09 (2.2)	02 (0.6)	11 (1.5)
Nomadic tribe:	Dhivar	05 (1.2)	03 (0.9)	08 (1.1)
	Kirat	12 (2.9)	07 (2.2)	19 (2.6)
	Ahir	06 (1.5)	06 (1.9)	12 (1.6)
	Beldar	04 (1.0)	04 (1.2)	08 (1.1)
Vimukta jamati:	Rajput	06 (1.5)	09 (2.8)	15 (2.1)
	Lodhi	03 (0.7)	04 (1.2)	07 (1.0)
Other caste		23 (5.6)	26 (8.1)	49 (6.7)
Habits: 1.Tobacco/Ghutka chewing		129 (31.2)	59 (18.3)	188 (25.6)
2. Smoking		8 (2.0)	0	8 (1.1)
3. Multiple habits		14 (3.4)	0	14 (1.9)
4. No habits		262 (63.4)	263 (81.7)	525 (71.4)

Figures in parentheses indicate percentage.

Table 2: Distribution of subjects according to sickling positivity and grades of anaemia

Characteristic	Male students (N = 413)	Female students (N = 322)	Total (N = 735)	χ^2	df 1	p value
Sickling test positive	30 (7.3)	19 (5.9)	49 (6.7)	0.54		0.46
Grades of anaemia:						
Normal	96 (23.2)	45 (14.0)	141 (19.2)	Normal Vs other grades		
Mild	199 (48.2)	186 (57.8)	385 (52.4)	10.03		0.001
Moderate	114 (27.6)	88 (27.3)	202 (27.7)			
Severe	4 (1.0)	03 (0.9)	7 (0.9)			

Figures in parentheses indicate percentage.

Table 3: Caste – wise distribution of sickle positive students

Caste	Male students (N = 30)	Female Students (N = 19)	Total sickle positive students (N = 49)	χ^2	df 1	p value
Mahar	18 (60)	11(57.9)	29 (59.2)	0.42		0.51
Teli	4 (13.3)	2 (10.5)	06 (12.2)	0.26		0.60
Gond	2 (6.7)	2 (10.5)	04 (8.2)	-		
Mali	1(3.3)	2 (10.5)	03 (6.1)	-		
Kirat	1(3.3)	1(5.3)	02 (4.1)	-		
Thakur	0	2 (10.5)	02 (4.1)	-		
Sheikh	1(3.3)	0	01 (2.0)	-		
Kunbi	1(3.3)	0	01 (2.0)	-		
Gowari	0	1(5.3)	01 (2.0)	-		

Figures in parentheses indicate percentage.

Table 4: Mean Haemoglobin level and Mean Quetelet index in Hb AA and Hb AS students

Electrophoretic pattern	No. of students (N = 735)	Mean haemoglobin level ± S.D.	Z test P value	Mean Quetelet index ± S.D.	Z test P value
Hb AA	686 (93.3)	10.83 ±1.254	28.08	0.148 ± 0.0089	6.23
Hb AS	49 (6.7)	7.95 ± 0.635	<0.001	0.141 ± 0.0075	<0.001

Figures in parentheses indicate percentage.

Table 5: Distribution of subjects according to morbidities in HbAS students

Morbid condition	Male (N = 29)	Female (N = 14)	Total (N = 43)	χ^2 df 1	p value
Lymphadenopathy	12 (40)	6 (31.6)	18 (36.8)	0.008	0.92
Upper respiratory tract infection	6 (20)	3 (15.8)	09 (18.4)	0.003	0.95
Joint pain	5 (16.7)	3 (15.8)	08 (16.4)	0.10	0.74
Otitis media	5 (16.7)	1 (5.3)	06 (12.2)	0.80	0.37
Epistaxis	1(3.3)	1 (5.3)	02 (4.1)	0.29	0.58

Figures in parentheses indicate percentage.