Original Research Paper

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Paediatrics

LOOKING BEYOND THE DISEASE HORIZON: IMPACT OF SICKLE CELL DISEASE ON PEDIATRIC QUALITY OF LIFE

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ABSTRACT **Introduction:** Sickle Cell Disease (SCD) is a progressively debilitating genetic disease, impacts the millions of children worldwide. India is estimated to have the second-highest burden of SCD after Nigeria, accounting for 14.5% of total newborn with SCD. In Madhya Pradesh about 27 districts fall under sickle cell belt. According to International Sickle Cell World Assessment Survey SCD has significant negative impact on Health-related Quality of Life (HRQOL) of children. The objective of the study was to evaluate the HRQOL of pediatric population suffering with SCD and compare it with other anemias (Nutritional, ACD, G6PD, haemophilia etc). A Generic measure Medical Outcome Study-36-items health survey (RAND) was used to evaluate the HRQOL. **Methods:** An observational, cross-sectional, comparative study was conducted in a tertiary care hospital of central India for period of 1year. The study enrolled 68 paediatric patients with SCD and 51 with other anemias between 5-18 years age. **Results:** The haemoglobin was 6.55(2.45) gm/dl & 7.79(0.75) gm/dl in SCD and control. 72% population were classified as HbSS; 28% as HbAS and HbS beta-thalassemia genotype. The SCD patients scored minimum in Role Physical 47.41(14.58); maximum score in Social Functioning 62.02(18.15). While, control scored minimum in Bodily Pain 54.25(10.59); maximum in Social Functioning 73.43(12.6). Thus, patients with SCD had significantly lower HRQOL as compared with control in both physical and mental health components of SF-36(p-value<0.001). **Conclusion:** The SCD is a chronic disease. It comes with financial, emotional and social burden on family. Hence, their counselling, frequent follow-up, screening, dietary advice, vaccinations are important to improve HRQOL and reducing morbidity and complications.

KEYWORDS : sickle cell disease, health-related quality of life, children.

INTRODUCTION

Hereditary hemoglobinopathies are the most common group of monogenic disorders in the world. Among them, Sickle Cell Disease (SCD), a progressively debilitating genetic disease, impacts the significant amount of the population worldwide. It is resulted by a single nucleotide substitution, converting a glutamic acid codon to a valine codon at position 6 of the beta-globin subunit. This amino acid substitution causes changes in the physical properties of the globin chain, leading to haemoglobin S (HbS) polymerisation during physiological stress causing erythrocytes to take on a sickle shape. This intracellular event also induces the expression of several cell adhesion molecules that facilitate the physical interaction of sickle-shaped erythrocytes with leukocytes and endothelium, leading to vaso-occlusive events and haemolytic anemia, which play a central role in the clinical complications associated with SCD (1).

According to WHO, SCD accounts for 200,000 newborn cases globally (2,3) and India is estimated to have the second-highest burden of SCD after Nigeria (4). India accounts for 14.5% of the total new-borns with SCD worldwide (5). In India, the sickle cell gene has been shown to be prevalent among socioeconomically disadvantaged ethnic groups; scheduled tribe, scheduled caste and backwards castes (6) (Figure1). According to ICMR, before reaching the age of two, 20% of tribal children with SCD die and 30% of children die before reaching adulthood (7).

Figure 1. Prevalence Of SCD in India

In India, Madhya Pradesh has the highest prevalence of SCD; about 27 districts fall under sickle cell belt and prevalence of HbS varies from 10-33%. (Figure2) According to the international Sickle Cell World Assessment Survey (SWAY) SCD has significant negative impact on Quality of Life (QOL) (8).

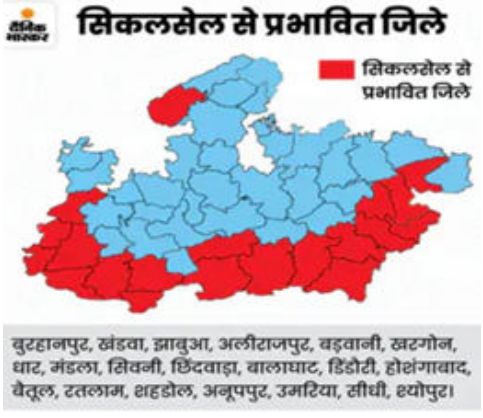


Figure 2. Prevalence of SCD in Madhya Pradesh

The objective of the study was to evaluate the health-Related Quality of Life (HRQOL) in children and adolescents with sickle cell disease and to compare them with HRQOL of patients with other anemia (nutritional, ACD, G6PD, haemophilia etc).

MATERIAL & METHOD

An observational and cross-sectional study was conducted in the Paediatrics department of a tertiary care hospital during the period of one year from September 2022 to August 2023. The enrolled paediatric population was consisted of male and female children and adolescents between 5 to 18 years of age group with confirmed clinical and laboratory diagnosis of SCD. The control group included paediatric patients of the same age group suffering from other anemia (nutritional, ACD, G6PD, haemophilia etc) attending OPD, IPD and PICU.

Inclusion Criteria:

1. Known cases of sickle cell disease or recently diagnosed cases of sickle cell disease in children and adolescents of age group 5-18 years of either sex attending OPD, IPD and PICU.
2. Children whose parents gave informed consent to participate by

signing in consent form.

Exclusion Criteria:

1. Cases of other causes of anaemia like nutritional deficiency anaemia, thalassemia and other haemoglobin abnormalities.
2. Patients with chronic diseases like chronic kidney disease, chronic liver disease.
3. Patients with history of co-morbidities like congenital heart disease or rheumatic heart disease and chromosomal abnormalities.

A self-structured questionnaire was used to obtain the socio-demographic characteristics, academic performance and economic burden on the families of the patients.

Health-Related Quality of Life (HRQOL) assessment: The paediatric population was evaluated for Generic questionnaire Medical Outcome Study-36- items-Short Form health survey SF-36 (RAND) to assess the health-related quality of life (9). The answers were linearly transformed into a score.

Statistical Analysis

Mean and standard deviation or percentage values of the numerical variables were estimated. The two-sample t-test was used to calculate two tailed p-value. The data was entered into an Excel spreadsheet and the statistical analyses were performed using the Statistical Package SPSS-20. Ethical approval was obtained from the Institutional Ethics Committee, before commencement of the study. An informed written consent in a consent form (ICF) was obtained from the parents/ guardian of patients attending OPD, IPD and PICU by free will through explaining to them before proceedings.

RESULTS

Mean age of population with SCD was 10.60(3.62) years and with other anemias was 09.76(3.48) years. About 62% males and 38% females from rural area (81%) and urban area (19%) participated in the study. The haemoglobin was 6.55(2.45) gm/dl & 7.79(0.75) gm/dl in SCD and control. 72% population were classified as HbSS; 28% as HbAS and HbS beta-thalassemia genotype. (Table 1)

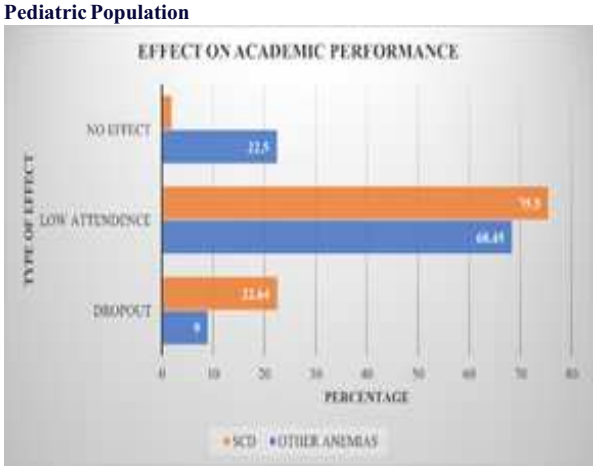
Academic performance of SCD group showed high percentage of dropouts than controls. (Table 1, Graph 1) 62.26% families of SCD group had to compromise on the number of working days which was higher than controls. (Table 1, Graph 2)

The SCD patients scored minimum in Role Physical 47.41(14.58); maximum score in Social Functioning 62.02(18.15). While, control scored minimum in Bodily Pain 54.25(10.59); maximum in Social Functioning 73.43(12.6). Thus, patients with SCD had significantly lower HRQOL as compared with control in both physical and mental health components of SF-36(p-value<0.001).(Table 2, Graph 3)

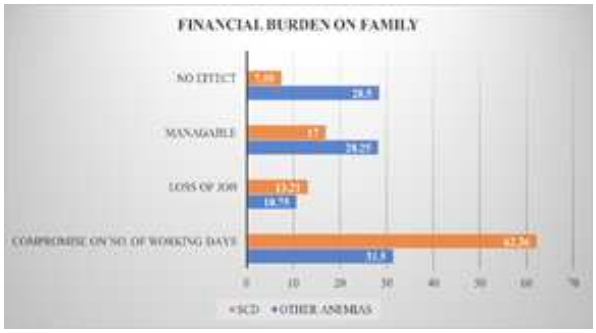
Table 1. Socio-demographic Characteristics Of The Study Pediatric Population

Parameters	Patients with SCD (n-68)	Other anemias(n-51)
Age (mean (SD) years)	10.60(03.62)	09.76(03.48)
Gender		
• Male (%)	62.26%	62.00%
• Female (%)	37.73%	38.00%
Socioeconomic status	-	-
• High (%)	7.55%	12.00%
• Middle (%)	92.45%	88.00%
• Low (%)		
Caste		
• Scheduled Tribe (%)	58.49%	20.00%
• Scheduled Caste (%)	15.09%	10.00%
• Other Backward Castes (%)	20.75%	36.00%
• Other (%)	5.66%	34.00%
Place of residence		
• Urban (%)	18.17%	32.00%
• Rural (%)	81.13%	68.00%
Economic burden on family		
• Compromise on working days	62.26%	31.50%
• Loss of job (%)	13.21%	10.75%
• Manageable (%)	17.00%	28.25%
• No effect (%)	7.55%	28.50%
Academic performance		
No effect (%)	1.90%	22.50%
Low attendance (%)	75.50%	68.45%
Drop out (%)	22.64%	9.00%
Haemoglobin (Mean (SD))	06.55 (2.45)	07.79(0.75)
9. Diagnosis*		
• Pre diagnosed (%)	25.26%	-
• Diagnosed first time (%)	74.72%	-
10. SCD in the family*		
• Yes (%)	17.00%	-
• No (%)	83.00%	-

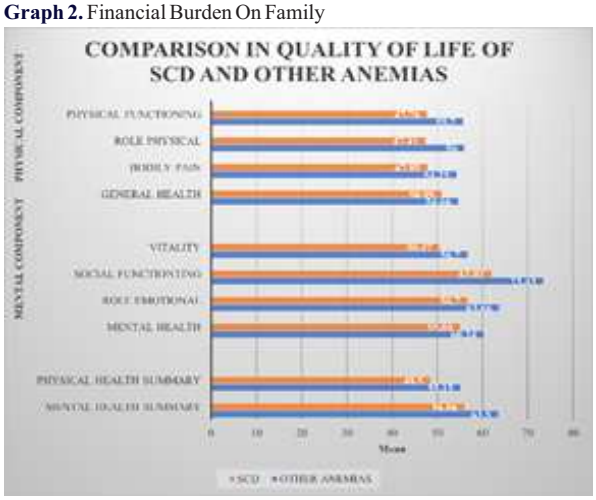
***Only SCD patients**



Graph 1. Effect On Academic Performance



Graph 2. Financial Burden On Family



Graph 3. Comparison In Quality Of Life Of SCD And Other Anemias

Table 2. Health Related Quality Of Life Scores Of Pediatric Populations Suffering From Sickle Cell Disease Compared To Other Anemias Using sf-36 (RAND)

Domain	SF	Items	SCD (N-68)	Other anemias (N-51)	p-value
Physical Functioning	PF	10	47.76 (07.20)	55.70 (08.57)	<0.001
Role Physical	RP	4	47.41 (14.58)	56.00 (16.41)	0.005
Bodily Pain	BP	2	47.85 (13.88)	54.25 (10.59)	0.008
General Health	GH	5	50.99 (11.82)	54.66 (06.24)	0.042
Vitality	VT	4	50.47 (12.84)	56.70 (08.12)	0.003
Social Functioning	SF	2	62.02 (18.15)	73.43 (12.60)	<0.001

Role Emotional	RE	3	56.70 (08.12)	63.66 (11.19)	<0.001
Mental Health	MH	5	55.04 (08.97)	60.24 (07.25)	<0.001
PHYSICAL HEALTH	PHCS		48.50 (01.45)	55.15 (0.72)	<0.001
COMPONENT SUMMARY					
MENTAL HEALTH	MHCS		56.06 (04.13)	63.50 (6.23)	<0.001

Acknowledgement:
The 36-items Health survey was developed at RAND as part of the Medical Outcomes Study (MOS).

DISCUSSION

In the present study, the mean age of the pediatric population with confirmed diagnosis of SCD was 10.60 ± 3.62 years and with other anemia was 09.76 ± 3.48 years. Overall, 62% males and 38% females about 81% from rural area and 19% from urban area were participated in this comparative study. The mean (SD) haemoglobin of SCD population was 6.55 (2.45) gm/dl and other anemia was 7.79 (0.75) gm/dl. About 72% children and adolescents with SCD were classified as HbSS and the rest 28% as HbAS and sickle–beta-thalassemia genotype. About 75% population was diagnosed with SCD first time after hospitalization and only 17% patients had family history of SCD. About 58.45% Pediatric population suffering from SCD were from Scheduled tribe. Other 15.09% and 20.75% belonged to Scheduled castes and other backward castes respectively. (Table 1).

Academic Performance:

As far as, the academic performance of the SCD children and adolescents was concerned, most of the patients about 75.50% had low attendance in the school, about 22.64 % patients had left the school due to severity of the disease; whereas in case of children and adolescents with other anemia only 9.00 % patients left the school, otherwise 68.45 % patients had low attendance (Table-1; Graph-1).

One of the most commonly cited consequences of SCD was impaired academic functioning; as reflected in evaluations, low attendance, poor performance and school absenteeism. Concerning school achievements of pediatric population with SCD, the result of this study found that more than two third of the study population (75%) was hardly paying attention in classroom because of low attendance. Most of the population often missed school to go to the doctor or hospitals. School absence presented as one of the major stresses to the children and their families. Approximately one quarter population (22.64%) with SCD had trouble keeping up with their school. School problems such as teasing regarding their jaundice, failure to participate in school activities, and embarrassment due to their enuresis were reported in the study of Salih (10). There were significant differences in all school subscales from the other anemia group. These findings were supported by Sadarangani *et al* (11) in Killifish, Kenya; who stated that excessive absence of children with SCD is owing to the complications of the disease and sometimes affect a child's ability to meet up with class work regarding all social well-being scales. Similar studies done by other researchers also (1,12**,**13,14**)** showed lower scores in school functioning.

Economic Burden On Families:

Economic burden on the families of SCD patients was miserable, about 62.26% families had to compromise on the number of working days and 13.21% families had to face the loss of job to manage the pediatric patient. On the other hand in case of patients with other anemia the economic burden was not so high. Only 10.75% families had to face loss of job (Table-1; Graph-2).

Because of poor socioeconomic status and remote habitation of the tribal population, health care-seeking is poor. Management of SCD can be very expensive given its chronicity, recurrent hospitals admissions for acute VOCs, treatment of complications, repeated blood transfusions, use of intensive care facilities, and multi disciplinary approach to management. As a result the families with children affected by SCD often face financial challenges, loss of job and compromise on the number of working days as shown in our study. In our study, about 62.26% of the parents did compromise on the number of working days to look after their child and 13.21% parents had to face the loss of jobs. On the other hand, parents of children with other anemia 31.5% compromised on the number of working days and only 10.75% lost their job to manage the disease of their child. In developing countries like India, national health insurance or social welfare programs are lacking, thus placing the financial burden for care of children with chronic disease on the individual family according to Pandarakutty *et al* (15**).** About 92.45% families of SCD patients belonged to low socio-economic status.

Health-related Quality Of Life:

The SF-36 scores applied to pediatric population were significantly lower than those obtained in the group with other anemia in all studied aspects (physical, emotional, social and psychological). Pediatric population with SCD had significantly lower health related quality of life scores as compared with patients of other anemias in all 8 SF-36 subscales. They scored minimum scores in domain of Physical Functioning 47.76 (7.20) and Role Physical 47.41 (14.58); whereas maximum score were noticed in Role Emotional 56.70 (08.12) and social functioning domain 62.02 (18.15). On the other hand, patients of other anemia scored minimum in bodily pain 54.25 (10.59) and general health 54. 66 (6.24). Maximum score obtained by them was in social functioning 73.43 (12.60) and Role Emotional 63.66 (11.19) (Table-2; Graph-3).

Physical health component summary (PHCS) of SCD patients contained 48.50 (01.45) scores, while patients with other anemia obtained 55.15(0.72) scores; Mental health component summary (MHCS) of SCD patients scored 56.06(04.13) and patients with other anemia contained 63.50(06.23) scores. The two-tailed p-value was calculated and found < 0.001 in between PHCS and MHCS. It means this difference was considered to be statistically significant. (Table-2; Graph-3).

In this study we found that SCD is associated with limitations in different dimensions of HRQOL in SCD pediatric population as compared to the other anemia pediatric population. First, our results showed that the scores of physical and mental health component summary of children with SCD was poor 48.50(01.45) and average 56.06(04.13) respectively. However, their physical HRQOL was worse than their mental domain. In our study, the population with SCD showed statistically significant decrease in the mean scores of all the eight domains of HRQOL than the patients with other anemia as reported with SCD and different chronic non-communicable diseases by Bhagat *et al* (16). Thus, the SF-36 scores of SCD children and adolescents were significantly (< 0.001) lower than that of children and adolescents with other anemia in both physical and mental health component summary. It was not a surprising result as we can find the same result in earlier studies also (12,16,17).

McClish *et al* (18) reported that patients with SCD scored significantly worse than US national norms on all subscales of HRQOL except mental health. HRQOL was equal to or lower than patients with other significant chronic diseases such as cystic fibrosis, asthma and hemodialysis in many domains in their study. Anie *et al* (19) also reported that about SCD patients in UK that they had much lower HRQOL scores than general UK population norms.

On analysis of QOL, for physical health subcategories for children with SCD, it was found that most of the children always felt fatigue, frequent vaso-ocular crisis and repeated hospitalization which interfered with regular routine work, absenteeism from school and hard to do sports. Similar findings were observed in a study carried out by Asnani *et al* (20) and Alharbi *et al* (13). Physical functioning was observed significantly poor in children with SCD, this is why more medical consultations for SCD cases when compared with patients of other chronic diseases according to Bhagat *et al* (16). This negative impact is associated with pain due to SCD and the overload of work due to the care and attention directed to the child or adolescent with the disease.

In addition, studies done by Hooker *et al* (21) and Dampier *et al (1*2) in America had showed lower scores in physical domain. Various studies have reported poor cognitive and psychosocial performance of children and adolescents with SCD. In a study conducted in India, Patel and Pathan (22) reported that children with SCD demonstrated low HRQOL scores in physical, psychosocial and cognitive areas.

Regarding the negative repercussion in the mental health domain of children and adolescents with SCD, it was found that due to a chronic disease in childhood, a risk of psychological and psychosocial

problems was involved in parents as well as children. According to the study of Bhagat *et al* (16), role limitation owing to emotional problems and fatigability were significantly higher in SCD children. Again, these findings were very well supported by others such as Alharbi *et al* (13) and Kumar *et al* (23).

A study conducted in Saudi Arabia examined the QOL of adolescents with SCD and highlighted a number of important factors such as age, gender, education, socio-demographics that are associated with change in QOL in adolescents (24). A study developed in USA by Dampier *et al* (12), showed that the number of complications increased substantially with the age of patients but only a few significantly influenced the reduction in HRQOL in adults with SCD.

CONCLUSION

In central India, particularly in Madhya Pradesh, no diagnostic facilities or dedicated sickle cell disease clinics exist in public health establishment. Most of the tribal population with SCD rely on the primary health care facilities in rural and often remote areas. There is insufficient knowledge about the disease, its severity and its impacts on quality of life in general. Therefore, measuring the quality of life in children with sickle cell disease might provide the degree of severity and significant attention to the health outcome so that the burden of SCD patients and their families to achieve as normal life as possible, can be minimize.

SCD is a chronic disease with financial, emotional and social burden on family, thus affecting growth and QOL of children and adolescents with a genetic disadvantage, so it is important as a pediatrician

- The proper social and genetic counselling.
- Promote follow up.
- Screening – newborn and pre marriage screening.
- Vaccination to improve QOL and reducing morbidity and complications.
- Enhancing availability of medicines and health facilities of patients at low cost.

The advent of newborn screening, newer oral medication and better general medical care in regards of safer blood transfusion and antibiotics will add in decreasing the rate of recurrence and severity of the SCD related complications and hence decrease the cost for health care.

IMPLICATIONS

Special SCD clinics should be opened in the areas with high prevalence of the SCD which can provide- proper information to the local population about the disease, proper screening facilities, required medicines for registered patients, specific vaccinations for SCD patients and prepare a unique database to alert people with disease or trait from marrying similar individuals to prevent further propagation of the SCD.

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