Original Research Article

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20172609

A study of clinical and hematological profile of children with sickle cell disease in a tertiary care hospital, Valsad, India

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Received: 03 June 2017 Accepted: 07 June 2017

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ABSTRACT

Background: Sickle cell disease is commonly seen in rural population of south part of Gujarat in India. It is one of the common causes of recurrent hospitalization, morbidity and mortality in pediatric population. This study was therefore undertaken to evaluate the clinical profile of sickle cell disease in a tertiary care hospital.

Methods: This was the prospective observational study done from November 2015 to October 2016. All the hospitalized diagnosed case of sickle cell disease and trait in age group of 6 months to 14 years were taken in this study. Sickle cell disease with some genetic or metabolic disease and sickle-beta-thalassemia patients were not included in this study.

Results: Total 61 patients were admitted over a one year of study period, out of which 47 were sickle cell disease and 14 sickle cell trait patients. Morbidity events were commonly observed in 5-12 years of age groups (68.85%). Seasonal variation also observed, 47.54% of total cases are seen in winter season. Pain (60.65%) was the most common presenting symptom. Severe pallor (39.34%) and splenomegaly (24.59%) was the most common sign in both groups. Vaso-occlusive crisis (59.01%) was the most common morbidity event observed, of which abdominal pain was the most common site of pain involvement. On laboratory analysis, there was statistically significant difference observed in disease and trait. In patients with sickle cell disease acute painful crisis (59.57%) was the common morbidity event observed while in sickle cell trait patient's acute febrile illness (71.42%) observed.

Conclusions: Vaso-occlusive crisis is the commonest manifestation in pediatric age group. Comprehensive medical care and management is required to decrease the morbidity and mortality.

Keywords: Acute painful crisis, Morbidity events, Sickle cell disease, Vaso-occlusive crisis

INTRODUCTION

During its 59th World Health Assembly held in 2006, WHO recognized sickle-cell disease (SCD), an inherited disorder of hemoglobin as a priority of public health.1 A Sickle-cell anemia, one of the most common forms of SCD, is due to a point mutation within the sixth codon of the β -globin chain. The produced abnormal variant-hemoglobin S (HbS) is responsible for chronic hemolytic

anemia and vaso-occlusion which are the underlying causes of the clinical presentation of SCD. Individuals who express the homozygous form (HbSS) manifest the disease, while those with the heterozygous form (HbAS), also known as sickle-cell trait (SCT), are usually asymptomatic carriers. Inheritance of the sickle cell trait follows an autosomal recessive pattern. Sickle cell disease initially limited to the sub-Saharan Africa, the Middle-East and some parts of India, but currently spread

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to all continents with the migration of populations. The β S-globin gene is found on five common haplotypes in Africa (Bantu, Benin, Cameroon and Senegal) and Asia (Saudi Arab-Indian) that can be used as a marker of genetic diversity and population origin. Approximately 300,000 children with severe hemoglobin disorders are born every year worldwide.

In the United States, sickle cell disease is the most common genetic disease identified through the statemandated newborn screening programme, occurring in 1:2647 births.3 In the Unites States; it affects around 72,000 people, most of whose ancestors come from Africa. The disease occurs in about 1 in every 500 African-American births and 1 in every 1000 to 1400 Hispanic-American births. About 2 million Americans or 1 in 12 African Americans carry the sickle cell allele.²

In India, sickle cell disease (SCD) is common in Vidarbha, Chhattisgarh, Madhya Pradesh, Orissa, Gujarat, Tamil Nadu and Andhra Pradesh. The need for hospital care is more frequent in children with Sickle cell disease than adult patients. In addition, SCD children younger than five years of age, especially those between 1-3 years of age are most vulnerable to mortality. There are limited data on the events leading to hospitalizations and death in younger children with SCD from India. Hence, we studied the morbidity pattern in hospitalized patients with sickle cell disease.

METHODS

This study was conducted at a tertiary care hospital GMERS medical college Valsad for the period of one year. This was the prospective observational study. The study period was from November 2015- October 2016.

Inclusion criteria

All the diagnosed cases of sickle cell disease and trait admitted in pediatric word with any morbidity events in the age of 6 month to 14 years in both gender.

Exclusion criteria

All the outdoor patient of sickle cell disease and trait. Sickle cell disease with some genetic or metabolic disease and sickle-beta-thalassemia patients were not included in this study.

Patients with Sickle cell disease or trait patients (confirmed to have either homozygous SS pattern or sickle heterozygous pattern on hemoglobin analysis by high performance liquid chromatography) who were hospitalized for any morbidity in pediatrics ward were enrolled for the study. The study was approved by the Institutional Ethics Committee and a written informed consent was obtained from parents of all study participants. A detailed history and clinical examination of enrolled children was done as per the pre-structured

proforma. Baseline hematological investigations were done at the time of admission. Complete demographic, socioeconomic, clinical and hematological profile was taken. The degree of malnutrition was assessed by BMI (body mass index). Statistical analysis was done.

RESULTS

Total 61 sickle cell disease patients were admitted over a period of 1 year. Out of which 47 were homozygous sickle cell disease and 14 heterozygous sickle cell trait patients. Total male patients were 39(63.93%) and female 22(36.06%). Male to female ratio was 1.7:1.

Figure 1 showing that more male patients are affected in 9-12 years, while more female patients in 5-8 years of age group. But there was no significant difference in gender in patients with sickle cell disease. [Chi-square value (at d.f=3)=6.01, p value>0.05]. Most patients belonged to the age group of 5-12 years comprising 68.08% of total sickle cell disease patients.

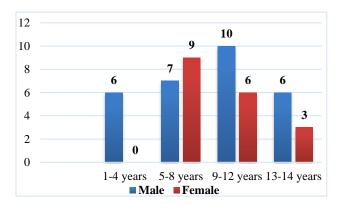


Figure 1: Age and gender wise distribution of patients with sickle cell disease.

Figure 2 showing most patients in both gender belonged to the age group of 5-8 years comprising 50.0% of total sickle cell trait patients. But there was no significant difference in gender in sickle cell trait patients. [Chi-square value (at d.f=3)=2.1, p-value>0.05].

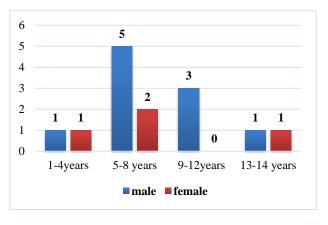


Figure 2: Age and gender wise distribution of sickle cell trait patients.

Table 1 shows that, total 29 (47.54%) patient was admitted in winter season (November-February), while similar number of cases observed in summer and monsoon season.

Table 1: Month wise distribution of sickle cell disease and trait patients.

Month	Sickle cell disease (N=47)	Sickle cell trait (N=14)	Total (N=61)
Nov-Feb	23 (48.93%)	6 (42.85%)	29 (47.54%)
Mar-Jun	12 (25.53%)	5 (35.71%)	17 (27.86%)
Jul-Oct	12 (25.53%)	3 (21.42%)	15 (24.59%)

Nutritional status of these patients was studied. In sickle cell disease patients 63.82% had under nutrition while in sickle cell trait patients only 35.71%.had undernutrition.

Table 2 showing that in both the groups pain (60.65%) was the commonest symptom, seen in more than half of the patients. In sickle cell disease patient pain (65.95%) was the most common symptom followed by fever (36.17%) and cough (17.02%). Pallor (46.80%) and splenomegaly (27.65%) was the common sign observed. Four sickle cell disease patients had massive splenomegaly. In sickle cell trait patients pain was presenting symptom in 42.85% of cases, fever in 28.57% and cough in 28.57% of cases. Severe anemia was seen in 14.28% and splenomegaly in 14.28% of cases.

Table 2: Clinical profile of patients with sickle cell disease and trait.

Sign and symptoms	Sickle cell disease (N=47)	Sickle cell trait (N=14)	Total (N=61)
Pain	31 (65.95%)	6 (42.85%)	37 (60.65%)
Fever	17 (36.17%)	4 (28.57%)	21 (34.42%)
Cough	8 (17.02%)	4 (28.57%)	12 (19.67%)
Vomiting, Diarrhea	2 (4.25%)	3 (21.42%)	5 (8.19%)
Pallor	22 (46.80%)	2 (14.28%)	24 (39.34%)
Icterus	5 (10.63%)	1 (7.14%)	6 (9.83%)
Hepatomegaly	3 (6.38%)	1 (7.14%)	4 (6.55%)
Splenomegaly	13 (27.65%)	2 (14.28%)	15 (24.59%)

The current study shows, musculoskeletal pain in 15 (40.54%), abdominal pain in 14 (37.83%), generalized body ache in 7 (18.91%) and chest pain in 1 (2.7%) of total patients with acute painful crisis. On laboratory analysis, it is observed that hemoglobin level with indices MCV, MCH and hematocrit were low in patients with sickle cell disease as compared to sickle cell trait and statistically significant.

It was found to be high leucocyte count in sickle cell disease that is statistically significant. Platelet count was low in sickle cell disease as compare to sickle cell trait but statistically not significant (Table 3).

Table 4 shows that, acute painful crisis (59.01%) and severe anemia (39.34%) were the common morbidity events in both groups.

Vaso-occlusive crisis was seen in 55.31% of sickle cell disease patient and 42.85% of sickle cell trait patients. Aplastic crisis was seen in 14.28% of sickle cell trait patient.

Respiratory infections were seen in 28.57% and malaria in 7.14% of patients with sickle cell trait. Acute chest syndrome was seen in 2.12% of patient with sickle cell disease. Severe anemia was seen in 46.80% of sickle cell

disease and 14.28% of sickle trait patients. Splenic sequestration crisis, stroke and dactylitis were not seen.

Table 3: Hematological profile of sickle cell disease and trait patients on admission.

Investigation	Disease (N=47)	Trait (N=14)	P value
Hemoglobin (gm/dl)	8.08±2.40	10.07±2.47	< 0.001
Hematocrit (%)	23.34±6.40	31.2±2.75	< 0.05
MCV (micro liters)	75.99±2.12	82.6±3.01	< 0.001
MCH (picograms)	25.02±1.11	25.8±1.19	< 0.05
MCHC (gram/dl)	26.03±1.86	25.57±1.28	0.109
Total leucocyte count (cumm)	14158±7859	6841±2923	< 0.001
Platelet (lac/cumm)	2.75±1.30	3.07±0.86	0.154

DISCUSSION

In this study 47 diagnosed cases of homozygous sickle cell disease and 14 heterozygous cases were enrolled. In the present study male preponderance was seen, which

was similar to other studies from central India.5,6 This could be due the gender-selective use of medical facilities and management of patients. Male to female ratio was 1.7:1. Most patients belonged to the age group of 5-12 years comprising 68.08% of total sickle cell disease

patients. (34.04% in 5-8 years and 34.04% in 9-12 years of age group) In sickle cell trait 50% of patients in both gender belonged to the age group of 5-8 years. There was no statistically significant difference in gender in both groups. Study by Swarnkar K7 shows similar results.

Morbidity events		Sickle cell disease (N=47)	Sickle cell trait (N=14)	Total (N=61)
Ata Dain-falliaia	Vaso-occlusive crisis	26 (55.31%)	6 (42.85%)	36 (59.01%)
Acute Painful crisis	Aplastic crisis	2 (4.25%)	2 (14.28%)	
	Respiratory infection	5 (10.63%)	4 (28.57%)	22 (36.06%)
A	Viral fever	6 (12.76%)	3 (21.42%)	
Acute febrile illness	Malaria	0	1 (7.14%)	
	Acute gastroenteritis	1 (2.12%)	2 (14.28%)	
Acute chest syndrome		1 (2.12%)	0	1 (1.63%)
Severe anemia (Hb<7 gm/dl)		22 (46.80%)	2 (14.28%)	24 (39.34%)

Table 4: Morbidity events in patients with sickle cell disease and trait.

In the present study, maximum hospitalizations were seen during the winter season (November to February). The mechanism of cold-induced painful crises is postulated to result from cold-induced diuresis, cold agglutinins or cutaneous vasoconstriction with shunting of blood to deeper vascular bed as per a study done in Jamaica.⁸

However, the studies from other countries have shown rainy season, low temperature or high wind speed and low humidity as precipitating factors for vaso-occlusive crisis in sickle cell anemia patients. 9,10

Pain was the most common presenting complains seen in 65.95% of sickle cell disease and 42.85% of sickle trait patients. Splenomegaly was seen in 27.65% of sickle disease and 14.28% of sickle trait. In present study, isolated splenomegaly was more common than hepatomegaly as reported in other studies. Huge splenomegaly was noted in four patients, similar to previous studies carried out in India. He present study shows, musculoskeletal pain in 40.54%, abdominal pain in 37.83%, generalized body ache in 18.91% and chest pain in 2.7% of cases. Study by Subhramanyam shows musculoskeletal pain in 64%, abdominal pain in 35% and chest pain in 7% of cases.

Hemoglobin, MCH and MCH were low in our study which is comparable to other studies. 14,15 It is said that MCV is high in sickle cell disease patients because of the increasing need of erythropoiesis due to chronic hemolysis leading to macrocytosis. It is also related to a folic acid deficiency. However, MCV was low in our study similar to some other studies from different parts of our country14,15. Low MCV in these studies may be due to co-existing iron deficiency anemia. According to National Family Health survey (NFHS-3), anemia is

common in India among the schedule caste and tribes and among the children with low socioeconomic status. 16

Current study shows that, acute painful crisis (59.01%) was the most common cause for hospitalization, followed by severe anemia (39.34%) and infections (36.06%). In a study by Akar NA.¹⁷ Vaso-occlusive crisis was the most common cause of hospitalization in SCD children. Another study from central India has reported severe anemia requiring blood transfusion as the most common cause of hospitalization in SCD childrens. 18 Study by Sinde S showing respiratory infections in 37%, gastrointestinal infection in 9%, urinary tract infection in 2% and malaria in 9% cases. 19 The present study shows similar results. In this study malaria was seen in 7.14% of cases. Previous studies have shown that SCT protects against severe forms and mild malaria infections, although the precise mechanism remains poorly understood.²⁰

There was no mortality of Sickle cell patients admitted with painful crisis in our study however sickle cell patients with crisis had mortality due to splenic sequestration or severe sepsis. This study was a hospital based study and hence, does not represent the true rate of events for SCD children in the general population. The ideal study should be a community-based cohort study or a birth cohort study. A second limitation of this study is the absence of long-term follow-up to estimate the outcomes of children and the proportion and causes of death mainly among those living with SCD.

CONCLUSION

Comparing various studies in other parts of India, It was found that in our study morbidity events were common in males patients in 5-12 years of age groups. In hospitalized

children with sickle cell anemia, acute painful crisis was the most the common morbidity events followed by severe anemia and acute febrile events. Morbid events most commonly occurred during the winter season. It was also observed that vaso-occlusive crisis is the commonest manifestation in pediatric age group and that despite being hemolytic in nature; hematological parameters were suggestive of hypochromic microcytic anemia which may be due to associated iron deficiency in these patients.

Sickle cell disorders in children are indistinguishable both clinically and hematologically. Parental counseling and preventive measures like regular folic acid supplementation, early treatment of infection with antibiotics and management of pain with simple analgesics will be helpful in decreasing morbidity and mortality in patients with sickle cell anemia. With comprehensive medical care health status and life expectancy of these patients can be improved considerably.

ACKNOWLEDGEMENTS

Authors would like to thank to the G.M.E.R.S Medical College and Government of India for the infrastructural support.

Funding: No funding sources Conflict of interest: None declared

Ethical approval: The study was approved by the

Institutional Ethics Committee

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Cite this article as: Patel KG, Chaudhari C, Sharma D. A study of clinical and hematological profile of children with sickle cell disease in a tertiary care hospital, Valsad, India. Int J Contemp Pediatr 2017;4:1317-21.