

Original Research Article

Clinical and haematological profile of children with sickle cell anaemia admitted to a rural medical college of Chhattisgarh, India

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ABSTRACT

Background: Sickle cell disease (SCD) is the most common single gene disorder resulting in hemolytic anemia. Aim of the study was to describe the clinico-haematological profile of children with sickle cell anaemia admitted to Paediatric ward/PICU with any acute clinical event and to find out the association between high HbF level, frequency of crises episodes and requirement of blood transfusion in sickle cell anemia.

Methods: Hospital based descriptive study. Retrospective data analysis was done from medical records of patients between 0-15 years age group admitted to hospital from March 2014 to August 2017.

Results: Total 68 clinical events were recorded in 60 patients during the study period. More than half of the children were in 0-5 years age group. Mean age of diagnosis was 2.79 years. Severe anemia requiring blood transfusion was the most common cause of hospitalization followed by painful crises. Mean Hb level in the children was 6.65(±2.38). More than one third of children had associated nutritional anemia. Children with high HbF level were found to have less number of painful crises episodes.

Conclusions: Severe anemia followed by painful crises were the commonest presentations requiring admission in our hospital. Chronic anemia with microcytosis and high HbF level is the hematological profile of the present study group. Children with high HbF level suffered from less number of painful crises episodes when compared to children with low HbF. But the requirement of blood transfusion was similar in both groups.

Keywords: HbF, Painful crises, Severe anaemia, Sickle cell anaemia

INTRODUCTION

Sickle cell disease (SCD) is the most common single gene disorder resulting in haemolytic anaemia. Global burden of sickle cell anemia is very high. In 2010 number of new-borns with SCA was 305800 globally and population estimates proposed by Piel et al in their geostatistical model estimated that it will be around 40 lakhs by mid half of 21st century.¹ It is highly prevalent in Africa, Saudi-Arabia and parts of central India. This disease is most commonly seen in tribal population of central India. Sickle cell gene frequency in India varies from 2 to 35%. Prevalence of sickle cell anemia in

Chhattisgarh is around 11 percent.² It presents as a chronic haemolytic anaemia with intermittent episodes of crises. Vaso-occlusive crises are most common presentation. Other acute presentations are, sequestration crises, haemolytic crises, aplastic crises etc. Due to progressive developments in health care facilities, routine monitoring and availability of adequate and appropriate health care services quality of life of sickle cell patients are improving and patients are also presenting with chronic complications in adolescence and adulthood. The subtype of SCD in central India is more similar to Arab-Indian haplotype with high level of HbF and less severe clinical manifestations. There are many researches done

in central India describing prevalence and spectrum of clinical manifestations. As per them, though Indian variety is less severe, complications of the disease can be life threatening and risk of associated sepsis and related morbidity is also high in underprivileged tribal communities where access to health care services is poor and level of awareness about the disease is also less in uneducated tribal population.

Our medical college (CCM Medical College) is located in a rural area of Durg district of Chhattisgarh which mainly serves patients from the nearby villages. Both tribal and non-tribal population with sickle cell anaemia are present in this area of Chhattisgarh and children with SCD routinely come to OPD and emergencies. We have done this study to observe various acute clinical presentations of children with SCA and to analyse their haematological profiles.

METHODS

The aim of this study was to describe the clinico-haematological profile of children with sickle cell anaemia admitted to Paediatric ward/PICU with any clinical event and to find out the association between high HbF level, number of painful crises episodes and requirement of blood transfusion in sickle cell anaemia.

This was a hospital based descriptive study. Retrospective data analysis was done from medical records of patients admitted to hospital from March 2014 to August 2017. Complete clinical and haematological profile was collected from the records in a pre-structured proforma of sickle cell clinic. All cases of sickle cell anaemia (diagnosis confirmed by HPLC) in the age group 0-15 years with any severe episode/clinical event as proposed by the SCD co-operative study group requiring hospitalisation, admitted to Paediatric ward/PICU were included.³ Children with SCD admitted to Paediatric ward with incomplete database were excluded.

Prior to data collection and analysis permission was obtained from concerned authority through proper channel. Ethical clearance was obtained from ethical committee of the institution.

Definition of various clinical events was taken as per CSSCD group criteria. Painful crisis was defined as pain in extremities, back, abdomen, chest, or head for which no other explanation could be found. Sequestration crisis was defined as decrease in hemoglobin or PCV level at least 20% from baseline with an increase in spleen size of at least 2 cm from baseline. Acute chest syndrome and pneumonia were difficult to differentiate clinically, and they were taken as a single group with fever and/or tachypnoea and/or hypoxemia with observation of new pulmonary infiltrate on X-ray. Stroke was defined as acute neurologic syndrome secondary to occlusion of an artery or to hemorrhage with resultant neurologic symptoms and signs which lasted >24 hour. Severe

anaemia was not defined in CSSCD group, but since it is a common presentation in central India, Hb<5 gm/dl was defined as severe anaemia in the present study group. Children with fever >101°F were diagnosed as acute febrile illness and all children with this presentation were admitted to Pediatric ward for sepsis work up and I.V. antibiotic administration. After hospitalization patients were managed according to standard protocols. Only HPLC test reports (by Bio-rad system) done at the time of diagnosis were included. Complete blood count using HORIBA Micros 60, 3-part Coulter system), reticulocyte count, peripheral smear, liver function test, renal function test done at the time of admission.

Statistical analysis was done using Microsoft excel, SPSS. Chi-square test was used to find out the association between high HbF level and frequency of painful crises and requirement of blood transfusion.

RESULTS

Out of total 67 patients, 7 were excluded as per the exclusion criteria. In the remaining 60 patients, 68 clinical events were documented during the above-mentioned period. Out of all the patients 43 were males. Mean age was 6.34 years (range 6 months to 14 years). More than half (n=36) of the children were in 0-5 years age group. Around one third (n=20) were in 11-15 years range. Mean age at the time of diagnosis was 2.79 years (SD±2.26) with lowest age of diagnosis at 6 months and highest at 12 years. Among all children 95% were from Durg district and rest 5% were from adjacent districts.

Most common clinical event requiring admission was severe anaemia followed by painful crises. Pneumonia/ACS, acute febrile illness, haemolytic crisis were other common causes of hospitalisation. Table 1 describes the diagnoses of children with SCD admitted to our hospital.

Table 1: Clinical profile of sickle cell anaemia patients admitted to Paediatric ward/PICU.

Diagnosis	Number of events (n)
SCD with severe anaemia	24
SCD with painful crises	22
Pneumonia/ACS	9
Acute febrile illness	5
Hemolytic crisis	5
Sequestration crisis	3
Right sided classical hemiplegia (stroke)	1
Aplastic crisis	1
Megaloblastic anaemia	1
Cerebral malaria	1

In the age group 0-5 years severe anaemia was most common presentation followed by painful crisis. Two cases of sequestration crisis and hemolytic crisis each

were recorded in this age group. In 6-10-year age group severe anaemia and acute febrile illness were most common presentations.

Painful crisis was most common clinical event in 11-15-year age group followed by severe anaemia. Table 2 depicts the age wise distribution of clinical events of SCA in our study population.

Table 2: Age wise distribution of clinical events of SCA.

Diagnosis	0-5 years	6-10 years	11-15 years
Painful crisis	11	3	8
Pneumonia	6	2	1
Severe anaemia	14	4	5
Sequestration crisis	2	0	1
Hemolytic crisis	2	0	3
Acute febrile illness	1	4	1

As far as symptoms are concerned fever and pain were the most common complaints (n=29 and 31 respectively) followed by cough and respiratory distress. Generalised weakness and lethargy resulting from gradual pallor was the presenting complaint in 15 patients. One patient had altered sensorium due to cerebral malaria and 1 patient had right sided classical hemiplegia resulting from stroke. Five children had haematuria at the time of admission.

Most patients (90%) had significant pallor at the time of admission. Icterus was clinically detected in 35 (51%) children. Around 80% of cases (n=54) had splenomegaly at the time of admission. But only 3 cases of sequestration crises were admitted. Thirteen patients had features of congestive cardiac failure secondary to severe anaemia at the time of admission.

Haematological profile

The hematological profile of children with SCD admitted to Paediatric ward/PICU presented in the Table 3.

Table 3: Hematologic profile of children with Sickle cell anaemia.

Hematologic indices	0-5 years	6-10 years	11-15 years	P values
Hb	6.60±2.08	5.91±2.17	7.18±2.95	0.347
MCV	87.14±8.54	87.75±11.14	85.25±12.63	0.749
MCH	26.49±2.89	25.84±3.96	24.61±3.10	0.114
MCHC	31.60±1.89	30.67±2.37	31.09±3.03	0.454
RDW	17.81±2.80	18.00±2.22	17.015±2.03	0.440
HbF	19.66±16.12	26.25±9.45	11.44±10.72	0.013
TLC	11725±5232.	13950±7404	12824±5936	0.496

The mean Hb at the time of admission was 6.65(±2.38). Hb level in all age groups were below normal range. There was no statistically significant difference in hematological profile of all three age groups. Leucopenia was detected in 7 (10%) children. Leucocytosis was documented in 24 children with SCD. Nine patients had thrombocytopenia. Two patients had pancytopenia, one of them diagnosed as aplastic crisis and the other one had features of hypersplenism. Peripheral smear of most of the children showed anisopoikilocytosis. Twenty-six (38%) children had microcytic hypochromic anaemia detected from peripheral smear.

The initial diagnostic HPLC reports were reviewed in all patients. From the initial HPLC report children were categorised into 4 groups. Eighteen children were diagnosed as sickle β thalassemia, 32 children were homozygous SCD with high HbF level, 8 were homozygous SS and 2 patients were sickle cell traits.

Association between presence of high baseline HbF (HbF level >10) and number of painful crises was calculated

using χ^2 test. There was statistically significant association between number of hospitalizations for painful crises episodes and presence of high HbF (p value 0.035). There was less number of painful crises in children with high baseline HbF level as compared to children with low HbF level. However, frequency of blood transfusion was similar in both groups. There was no statistically significant association between presence of high HbF and number of blood transfusion in children with SCD (p value 0.285).

DISCUSSION

WHO collaborative study Ichhpujani RL et al has similar SCD is commonly seen in Africa, middle East and parts of central India. The African haplotypes were clinically more severe and associated with more complications. The Arab-Indian haplotype, prevalent in Saudi-Arabia and India is said to have less severe clinical manifestations with lower frequency of complications. However, studies from Maharashtra have also shown that the clinical presentation of Indian children with SCD is highly variable and does not depend only on level of HbF. Till

date newborn screening practice is not followed in all parts of central India, particularly the tribal population of Chhattisgarh and lack of infrastructure also makes this difficult in other parts of the state. Government funded screening programmes done at community level have detected many cases of SCD in the state. Most of the cases come for medical attention during an acute clinical event only. There are only few new-born cohorts in India describing natural history of the disease in our population. Till then we have to rely on hospital based studies to find out the common presentations, clinical profile and disease course in Indian population. Hence, we have tried to describe the common presentations of sickle cell anaemia in our hospital. Out of the 60 patients, 48 (63%) were males. Majority of cases had been diagnosed before 3 years of age with mean age of diagnosis being 2.7 years.

This is similar to the findings reported by Al Saqladi AW et al in Yemeni children and other parts of Saudi Arabia.^{4,5} Retrospective data analysis with prospective cohort study done by Jain D et al in Maharashtra also reported the mean age of presentation at 3.85 years.⁶ However in American and Jamaican cohorts the age of diagnosis is earlier and almost all children were diagnosed during infancy.⁷ In the present study 10% of children were symptomatic before 1 year of age and almost 95% were diagnosed before 6 years age.

Severe anaemia requiring blood transfusion was the most common cause of hospitalisation in overall all age groups (48%). This is similar to the observation reported by Jain D et al.⁶ But other studies done in Chhattisgarh and Odisha have reported painful episodes as the most common cause of seeking medical attention in SCD, former being a community based study and the later one was a hospital based data analysis. Next to severe anaemia, painful crisis was common requiring hospitalisation.^{3,8}

Severe anaemia was the most common presentation in 0-5 years age group (n=14) and 6-10 years age group. This could be due to associated nutritional anaemia, worm infestations, recurrent minor infections resulting in haemolysis in this age group. Painful crises were most common in 11-15-year age group. Five cases of haemolytic crises and 3 cases of sequestration crises were documented. Although the incidence of splenomegaly was high in the present study group (around 80%), sequestration crises were less commonly seen. A study done in Saudi-Arabia, found higher rates of splenomegaly in SCD cases as compared to African children.⁹ High incidence of splenomegaly in the present study group can be explained by coexistence of thalassemia with sickle cell anaemia and high endemicity of malaria in this area. Another study done by Yadav et al, found higher incidence of splenomegaly in patients with Sickle cell anaemia and sickle β thalassemia.¹⁰ In their study 68.8% children with homozygous SCA and 82.6% children with Sickle β thalassemia had splenomegaly. However,

occurrence of recurrent bacteremia in spite of penicillin prophylaxis does indicate the non-functioning nature of spleen in central India population. Mean duration of hospital stay in the present study group was 6 ± 3.5 days.

Haematological profile of children at the time of admission was studied. Mean Hb level of all the patients was $6.65(\pm 2.38)$. Mean Hb level was lowest in 6-10-year age group. This value is significantly lower than baseline Hb level in steady state of the disease. It may be due to the reason that we have included the patients admitted to hospital with a clinical event and severe anaemia requiring blood transfusion was our most common indication of hospitalisation. Mean HbF level in the present study population was high (18.4 ± 14.4) similar to other studies done in central India. Mean HbF level of SCD cohort at GMC Nagpur diagnosed by neonatal screening and followed up for 3-4 years was $21.4\pm 5.4\%$.¹¹ Study done by Rao et al in children between 5-15 years at south Gujarat have found mean HbF level 12.2 ± 7 .¹² In the present study population children with high HbF level also suffered from painful crises episodes and they had also severe anaemia requiring blood transfusion. High level of HbF may not always protect from crises in SCD. There are also other factors that influence sickling in these children. Moreover, distribution of HbF in F cells also affects the functioning of HbF. Patients with high HbF can have severe presentation of the disease. This occurs due to uneven distribution of fetal hemoglobin in F-cells with mean HbF remaining constant. Even if with high HbF, the F-cells might be insufficient to inhibit HbS polymerization. Theoretically SCD cases should have normocytic normochromic anaemia with anisopoikilocytosis due to frequent hemolysis. In the present study group children had anisopoikilocytosis with predominant microcytosis. MCH and MCHC were also in lower range. This could be due to associated nutritional deficiency. This was similar to the findings obtained by Rao et al in children with SCD in steady state from south Gujarat.

In the present study population, children with high HbF had less number of painful crises episodes as compared to those with low HbF. There was statistically significant association between high HbF level and less number of painful crises requiring hospitalizations. This was similar to the findings by Upadhye et al.¹¹ They have found high level of HbF was inversely associated with vaso-occlusive crises and episodes of severe anaemia. But in the present study, there was no significant difference in the requirement of blood transfusion between these two groups.

This could be due to the reason that we have included hospitalised children with acute clinical event and severe anaemia was the most common cause of hospitalisation. In some children with high HbF level presenting with crisis episode there were other indications of blood transfusion apart from severe anaemia and this could have biased the above finding.

CONCLUSION

Sickle cell anaemia is highly prevalent in both tribal and non-tribal communities of Chhattisgarh. Level of awareness, counselling and monitoring of patients is still inadequate and needs further upgradation so that frequency of crises episodes and hospitalisation with severe life-threatening emergencies decreases. Co-existence of nutritional deficiencies, recurrent infections make the condition worse. Even if level of HbF is high in our population, rates of complications are not lower. Hence, SCD cases should be followed up regularly, immunised and caregivers/parents should be counselled properly for better outcome and a good quality of life.

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