RESEARCH BRIEF

Sickle Cell Anemia from Central India: *A Retrospective Analysis*

DIPTY JAIN, *KHUSHNOOMA ITALIA, VIJAYA SARATHI, * KANJAKSHA GHOSHAND AND *ROSHAN COLAH

*From the Department of Pediatrics, Government Medical College, Nagpur, India; and *National Institute of Immunohaematology, KEM Hospital Campus, Parel, Mumbai, India.*

Correspondence to:
Dr Dipty Jain, Professor,
Department of Pediatrics,
Government Medical College, Nagpur,
Maharashtra, India.
dipty47@rediffmail.com
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Although sickle cell anemia in India is believed to have a mild clinical presentation, few studies report severe disease in many patients from central India. Hence, we have retrospectively studied 316 children with SCA who were followed up for a period of 5.8±5.7 years. There were 55.4 blood transfusions, 43.3 episodes of vaso-occlusive crises requiring hospitalization, and 108.9 hospitalizations per 100 person years. Ninety six (30%) patients had severe disease whereas 74 patients also fulfilled the criteria for hydroxyurea therapy. Significant proportion of children with sickle cell anemia from central India present with severe clinical presentation and require regular medical attention.

Key words: *Sickle cell anemia, Central India, Children*.

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The prevalence of the sickle gene in India is found to vary from 2-34% [1,2]. It has often been stated that sickle cell anemia (SCA) in Indians being linked to the Arab-Indian haplotype has a mild clinical presentation which goes unnoticed, sometimes throughout life. This has been attributed to the high fetal hemoglobin and associated α–thalassemia commonly seen among these patients [3-6]. However, the phenotype of SCA varies significantly among different population groups of India and there is limited regional data. In this study we report the clinical events in sickle cell anemia patients followed up for several years at a Sickle cell clinic at Nagpur in central Maharashtra where the frequency of the sickle cell gene is very high among some non-tribal populations.

METHODS

This retrospective study included children (<18 years of age) with SCA registered before 2007 at the Sickle Cell Clinic, Department of Pediatrics, Government Medical College, Nagpur. Only those patients who had at least one year of follow-up were included in the study after obtaining a written informed consent from all the patients and/or their parents. At the time of registration, the sickle homozygous status of all patients was confirmed by standard procedures. These patients were followed up regularly the clinic with documentation of all relevant clinical and laboratory data in a detailed proforma. Clinical records of these patients were evaluated for clinical events since the time of registration at the clinic till the last available follow-up or initiation of hydroxyurea therapy. Appropriate treatment was given as and when needed. All children with age less than 5 years were offered penicillin prophylaxis. Patients having any one of the criteria mentioned in ***Table* I** were considered to have severe disease. Children older than five years, having any one of these criteria were offered hydroxyurea therapy.

Results

The study included 316 patients (122 females and 194 males) with SCA who were followed up for a period of 5.8±5.7 years (1832.8 person-years). The median age at presentation was 3.84 years (range: 15 days to 16 years). There were 1725 hospitalizations in 282 patients (***Table* II**). Severe anemia requiring blood transfusion was the most common reason for hospitalizations and 1015 blood transfusions were given to 242 children. Majority (62%) of the blood transfusions were needed when age of the patients was <5 years. The most common (80%) reason for blood transfusions was severe anemia (hemoglobin <5g/dL) while the rest were given for

TABLE I CRITERIA TO DEFINE SEVERE DISEASE

1	Frequent vaso-occlusive crisis (≥3/year) requiring hospitalization
2	Frequent blood transfusion requirement (≥3 per year)
3	At least one cerebro-vascular event
4	At least one episode of acute chest syndrome
5	At least one episode of avascular necrosis of bone

TABLE II CLINICAL EVENTS IN CHILDREN WITH SICKLE CELL ANEMIA (N=316)

	No. of patients affected	*No. of events*	*No. of events per 100 person years*	*Median age (y) at event occurrence*
Hospitalizations	282	1725	94.1	5.7
Blood transfusions	242	1015	55.4	4.3
Painful crises requiring hospitalization	166	793	43.3	7.2
Severe infection requiring hospitalization	107	175	9.5	5.0

stroke, splenic sequestration, hypersplenism or severe vaso-occlusive crisis (VOC).

Moderate episodes of VOC were managed either as outpatient or on home-basis with analgesics and oral hydration. All children had at least one episode of painful crisis by 12 years of age. There were 175 episodes of severe febrile illness requiring hospitalization including 62 episodes of blood culture proven bacterial septicemia in 42 patients.

Other common events were splenic sequestration among 26 patients, cerebrovascular accidents among 17 patients, dactylitis among 14 patients, a vascular necrosis of bone among five patients, non-bacterial infections like malaria among 14 patients, hepatitis B among 12 patients, human immunodeficiency virus among three patients and tuberculosis among three patients. The chronic complications included sickle hepatopathy among 16 patients and sickle nephropathy among four patients. Leg ulcer and priapism were seen in only one patient each. There were 10 deaths which were attributed to severe anemia with hypoxic encephalopathy among three patients, severe bacterial infection among two patients, sequestration crises among two patients, tuberculosis with acquired immunodeficiency syndrome in one patient and unknown reasons in two patients (home deaths). Ninety six (30%) patients had at least one criterion to define severe disease among whom 74 children aged >5 years fulfilled the criteria for hydroxyurea therapy and were treated with hydroxyurea.

DISCUSSION

Our study reports a very high incidence of significant clinical events in SCA children, with 30% patients having severe disease. A previous study from Nagpur, also reported similar findings with 1.25 episodes of sickle cell crises and 1.38 episodes of infections per patient per year in a group of 325 children over a short period of follow-up (146.84 person-years) [7]. The disease is also reported to be severe in patients from Orissa [3,8].

A study on tribal patients with SCA from Gujarat reported lesser number of patients with ≥3 painful crises per year (23.7%) and >3 hospitalizations per year (2.6%) compared to 52% and 16.4% children, respectively in our cohort. The milder disease is partly attributed to high frequency of α-thalassemia in them [4].

Children from central India where the sickle gene is linked to the Arab-Indian haplotype are stated to have a milder disease than those with African haplotypes [9]. The cooperative study including SCA patients with African haplotypes, reported 2.9-49 episodes of painful crises and 0.0-9.9 episodes of bacteremia per 100 person- years as compared to 43.3 episodes of painful crises and 3.38 episodes of bacteremia (despite penicillin prophylaxis) in our study cohort [10]. Thus, our study cohort had SCA as severe as those with African haplotypes.

Since this is a retrospective analysis of a hospital-based cohort with documentation of clinical events from the time of registration at our Sickle cell clinic, we might have missed many events which would have occurred before their registration. On the other hand, many patients may still remain undiagnosed while some others might have died before achieving the diagnosis. The ideal way to understand the natural history of sickle cell anemia is to undertake neonatal screening, identify homozygotes and follow them up from birth [9-11]. With the introduction of newborn screening for sickle cell disease in our hospital since 2010, we have now formed a birth cohort of sickle cell disease children whom we are following at regular intervals.

Ninety eight percent of the younger children received penicillin prophylaxis till they reached five years. Still, we report high rates of bacteremia, 50% of which occurred when children were less than five years of age. Although 74 patients received hydroxyurea, since we have included events till the initiation of hydroxyurea, it has no effect on the number of clinical events considered for the study. Hydroxyurea was found to be beneficial in our patients with severe disease (data not shown). To conclude, a significant proportion of

SCA children from central India present with a severe clinical presentation and require regular medical attention.

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