Original Article:

Clinical profile of sickle cell syndromes: experience at a tertiary care centre in South India

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ABSTRACT

Background: Sickle cell syndromes are commonly encountered inherited haematological disorders regarding which sparse published data are available from Telangana State.

Methods: Prospective study of 55 patients diagnosed to have sickle cell syndromes at our tertiary care teaching hospital in Hyderbad, Telangana State, South India.

Results: Their mean age was 19.9 (range 3-48) years; there were 35 males. Consanguinity was noted in 31%. History of cholecystectomy was evident in 5 cases. Blood transfusions were received in the past in 52% of cases. Symptoms at presentation were jaundice (85%), pain (80%), fatiguability (60%), pallor (30%), dyspnoea (29%), lump abdomen (7%) and leg ulcer (3%). Acute chest syndrome was seen in 10.9% cases. Physical examination revealed pallor (90%), icterus (80%) hepatomegaly (49%) and splenomegaly (41%). Mean haemoglobin at presentation was 8.3 g/dL. Sickle cells were seen in peripheral smear in 51%. Sickling test was positive in all after induction. Characterization of haemoglobin by high performance liquid chromatography revealed homozygous sicke cell anaemia was evident in 22/43 (51.2%), sickle thalassemia in 16/43 (37.2 %) and sickle cell trait in 5/43 (11.6 %).

Conclusions: Sickle cell disease should be considered in the differential diagnosis while evaluating patients presenting with anaemia and skeletal pains. Prompt recognition and management improves survival and eventual prognosis in these patients.

Key words: *Sickle cell disease, Diagnoses, India*

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INTRODUCTION

Sickle cell syndromes are one of the most common inherited haematological disorders. In patients with sickle cell disease, morbidity, frequency of crisis, degree of anaemia and organ systems involved at the time of presentation varies considerably from person to person.[1] Sickle cell disease is caused by a mutation in beta-globin gene that changes the sixth amino acid to valine resulting in haemoglobin S (HbS). Inheritance of HbS from one parent and another haemoglobinopathy, (for e.g., beta-thalassemia) from another parent results various sickle cell syndromes. Prevalence of sickle syndromes is highest in tropical Africa, but occurs with significant frequency in India.[1,2] There are some studies on the epidemiological patterns in various endemic belts and among specific communities in India.[2] Since little recent published data are available on this topic from Hyderabad, Telangana State, we under took the present study.

MATERIAL AND METHODS

We prospectively studied patients presenting with one or more of the following, (i) presence of sickle cells on peripheral smear, (ii) positive silckling positivity after induction with sodium

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metabisulphate (either immediately or after incubation), (iii) evidence of haemoglobin S (HbS) on laboratory testing to Nizam's Institute of Medical Sciences (NIMS), Hyderabad, Telangana, a tertiary care centre in South India, during the period February 2003 to May 2005. The study was carried out after getting clearance from Institute Ethics Committee. After obtaining a detailed history, thorough clinical examination was done and relevant laboratory evaluation were carried out.

High performance liquid chromatography (HPLC) (Bio-rad D-10 Dual Program machine) was used to measure haemoglobin A (HbA), haemoglobin A_2 (HbA_2), haemoglobin S (HbS), foetal haemoglobin (HbF), haemoglobin C (HbC) and haemoglobin D (HbD).

Patients were treated symptomatically. Wherever necessary, packed red cell transfusions were given. Other complications were managed accordingly.

Penicillin prophylaxis was advised to patients who were asplenic. All were advised pneumococcal, meningococcal and *Haemiophilus influenza* vaccination; precautions to prevent vaso-occlusive phenomenon. Hydroxyurea therapy was given wherever indicated in a dose of 500 mg/day.

RESULTS

Of the 680 patients with anaemia screened during the study period, sickle cell syndromes were noted in 55 (8.1 %). Their mean age was 19.9 (range 3-48) years; there were 35 males.

Community distribution (available in 43 patients) included *Mala* (n=21; 48.8%); *Lambadi* (n=8, 18.6%); *Kapu* (n=5, 11.6%); *Madiga, Padmasali* (n=3 each); *Perika, Pelli* and *Telaga* (n=1 each).

Consanguinity was noted in 17 of the 54 patients (31.4%) for whom such data could be recorded. Past history of cholecystectomy was noted in 5 cases. History of blood transfusions was present in the past in 29 (52%) of cases. Non-steroidal anti inflammatory drugs (NSAID) use was observed in 34/54 (61.8%) patients.

Symptoms at presentation included jaundice in 47 patients (85%), pain in 44 (80%), fatiguability in 33 (60%), pallor in 17 (30%), dyspnoea in 16 (29%), lump abdomen in 4 (7.9%) and leg ulcers in 2 (3.6%). Mean duration of painful episodes 4.9 days. Acute chest syndrome was seen in 6 patients (10.9%). Young patients frequently presented with acute complications while middle-aged patients usually presented with evidence of organ dysfunction.

Physical examination revealed pallor in 50 (90.9%), icterus in 44 (80%), hepatomegaly in 27 (49%), splenomegaly in 23 (41%) and ejection systolic murmur in 43 (78.1%). Acute arthropathy was noted in 3 cases. Splenomegaly was mild in 15 patients, moderate in 7 and large in 1 patient.

Mean haemoglobin at presentation was 8.3 g/dL (range 5.2-10.1 g/dL) and mean reticulocyte count was 4.3% (range 1%-6.9%). Peripheral smear revealed sickle cells in 28 (51%), target cells in 35 (63.6%) and anisopoikilocytosis in 35 (63.6%). Features suggestive of hyposplenism in peripheral smear were noted in 8 patients. Total leukocyte count was elevated (>10,000/mm^3) in 23. The platelet count was elevated (>400,000/mm^3) in 13.

Serum lactate dehydrogenase levels (>400 IU/L) were elevated in 14 of the 20 patients in whom it was tested. Unconjugated hyperbilirubinemia was seen in 35 (94.8%). Sickling test was positive in all 55 after treatment with sodium metabisulphate.

Albuminuria was noted in 5 of 23 patients (21.7%) and serum creatinine was elevated (>1.5 mg/dL) in 2/22 patients tested. HPLC profile of sickle cell syndromes (n=43; 78.2%) is shown in Table 1.

Table 1: Profile of sickle haemoglobinopathies

Diagnosis	Number of patients	Percentage
Homozygous sickle cell anaemia	22	51.2
Sickle β^{O} thalassemia	8	18.6
Sickle β+ thalassemia	8	18.6
Sickle cell trait	5	11.6

Ultrasonography of abdomen showed shrunken/absent spleen suggestive of outo-splenectomy in 8, splenomegaly in 7, gall stones in 4 and renal papillary necrosis in 1.

Pain arising from bones or joints was noted in 44 (80%) patients. Of the 44 patients for whom such data were available, there were 1628.4 painful episodes per 480 patient years yielding a pain rate of 3.4 per person per year. Bone pains were reported in 36 of the 44 (81.8%) patients. Joint pains were reported in 31 of the 44 (70.5%) patients; spine involvement was seen in 7 (15.9%) patients. Other complications encountered included acute chest syndrome in 6 (10.9%), recurrent haemolytic episodes requiring multiple transfusions in 5 (9%), megaloblastic crisis in 2 (3.6%), cholelithiasis requiring surgery in 5 (9%), splenic infarcts in 2 (3.6%), avascular necrosis of femur in 3 (5.4%), renal failure in 2 (3.6%) and pneumonia in 2 (3.6%).

DISCUSSION

The patients in our study were mostly young males in their second and third decades of life. In comparison with other studies,[2,3] our patients were older. This could possibly be due to referral bias, as the present study was based in a tertiary care teaching hospital.

A substantial number of patients came from Khammam district indicating clustering of cases. Other studies[4,5] also describe clustering of sickle cell anaemia in certain areas in Andhra Pradesh and adjoining districts of Orissa. The community distribution observed in the present study as do the observations from earlier studies[2,6] suggest need for further research in this area.

The prevalence of pains at presentation (80%) in our study was similar to the observations (86.5%) reported in one study[5] but were more than the figure reported in two other studies.[2,3]

Pain rate seen in the present study (3.4 episodes / person / year) was higher in comparison to the figure of 0.8 reported in another study.[7-2.3] The average duration of each pain episode in our study was 4.9 days and this was similar to the observations from another study. Leg ulcers were noted in 5.4% of our population. In contrast to an incidence figure of 2.5% reported in another study.[8] In a study from Orissa[5] chronic leg ulceration was though to be rare. Occurrence of leg ulcers in a higher proportion of patients in the present study could be due to late presentation in the course of the disease.

We observed homozygous sickle cell disease in 51.1% patients. This figure is lower than the figure of 61% reported in one study,[2] but higher than the 21.6% reported in another study.[9] Whether these epidemiological pattern are true variations or due to selection bias requires further research.

Acute chest syndrome noted in 10.9% patients in our study is comparable to the figure documented in another study.[3] Recurrent haemolytic crises noted in 9% patients in our study is less than that (16%) noted in another study.[2] We observed avascular necrosis of femur in 5.4% and renal failure in 3.6% patients. The observations are similar to the figures reported in other studies.[5,10]

History of blood transfusions observed in almost half the patient in the present study was similar to the figure (62%) reported in another study.[11] We found consanguinity in a high

proportion of patients (31.4%) compared to the observations from another study (7%) from India.[2] While 61.8% patients in the present study gave history of NSAID use compared to 88% reported in another study.[12]

Our observations suggest that sickle cell syndromes are an important cause of morbidity and mortality.

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