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Overview of the Distribution and Presentation of Patients with Sickle Cell Disorders: A Report from a Tertiary Care Centre in Eastern Part of India

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Authors' contributions

This work was carried out in collaboration among all authors. Author AS collected the data, analyzed the data and wrote the manuscript. Authors TKD and AC analyzed and reviewed the study. All authors read and approved the final manuscript.

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ABSTRACT

Aims: With globalisation, patients with Sickle cell disorders can be found all over the world. Depending on the original genotype, the disease manifestations vary.
This study aimed to assess the distribution and clinical presentation of patients with Sickle homozygous/ heterozygous diseases in the eastern part of India.
Study Design: Retrospective analysis.
Place and duration of study: Department of Hematology at NRS Medical College, Kolkata, between 1st January 2018 to 31st May 2020 (2 years and 4 months).
Methodology: Patients having hemoglobinopathies with any type of Sickle haemoglobin (HbS), such as, Sickle cell anemia/homozygous Sickle cell disorders(SCA); compound heterozygous diseases, like Sickle cell/β thalassemia(HbS/β), Sickle cell/Delta thalassemia (HbS/D), Sickle cell Haemoglobin/E thalassemia(HbS/E); or Sickle cell trait(HbS trait), have been included.
Thorough history was elicited and every patient was clinically examined. Published literature was analysed to assess the differences in disease presentation.
Results: Total 95 patients with a component of HbS were assessed and HbS/β (53.7%) patients comprised the majority, followed by SCA (30.5%). Median age of presentation to our clinic was 17years (range 2-50years). HbS/β and SCA patients had a median age of presentation of 17.5years

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and 12years, respectively.
Commonest clinical presentation was pain crisis (32,33.7%) - abdominal (11,11.6%) or bone pain (13,13.7%). Other presentations were pallor (26,27.4%), jaundice (12,12.6%) and fever (4,4.2%). Most patients had more than one complaint. Occasional patients required hospital admission for pain, fever or convulsions. HbS trait (5,5.3%) was diagnosed incidentally.
Most patients who attended our center hailed from the nearby district of North 24 Parganas (26,27.4%), and fewer patients came from distant districts and neighbouring states.
Patients were treated with Hydroxyurea, with/without blood transfusions or chelation.
Conclusion: Most studies conducted in India have highlighted the prevalence of Sickle cell disorders among specific endemic populations, unlike in our analysis.
HbS/β was more common than SCA, and, median age of disease presentation was later than that in published literature. There is a variation in the severity of disease manifestation in our cohort. Commonest painful crisis was bone pain, followed by abdominal pain. Stroke, a common manifestation of SCA in other countries, was rare in our cohort.

Keywords: Sickle cell disorders; distribution; clinical presentation.

1. INTRODUCTION

Sickle cell disorders were originally found in the African regions, Arabian Peninsula and parts of India [1]. However, in today's age of globalisation patients with homozygous or compound heterozygous Sickle cell disorders can be found all over the world. The clinical presentation of patients with Sickle cell anemia/homozygous Sickle cell disorders (SCA) varies depending on the original genotype- African or Arab-Indian and other associated factors [2].

The primary aim of our study was to assess the distribution and clinical presentation of patients with Sickle homozygous or heterozygous diseases in the eastern part of India.

2. MATERIALS AND METHODS

Patients who attended the Thalassemia Clinic in our tertiary care center, between 1st January 2018 to 31st May 2020 (2 years and 4 months) were retrospectively analysed and the ones who had any type of Sickle haemoglobin (HbS), either in the form of SCA or compound heterozygous diseases, like Sickle cell/β thalassemia (HbS/β), Sickle cell/Delta thalassemia (HbS/D), Sickle cell Haemoglobin/E thalassemia (HbS/E), were included in this descriptive study. Patients having Sickle cell trait (HbS trait), have also been included for the analysis. At our tertiary care hospital, patients are usually referred from other hospitals or departments, either for or after diagnosis. Once the patient is diagnosed with a hemoglobinopathy, they are followed up regularly and treated accordingly.

The demographic details of the patients, including the age, sex and address of the patients were collected.

Thorough history of pain crises, family history, blood transfusions, treatment history was enquired, and every patient was clinically examined. The patients were diagnosed by High Pressure Liquid Chromatography (HPLC) or Thalassemia Mutation analysis by Polymerase Chain reaction (PCR).

Comparison of the sickle cell disorders prevalent in our area of investigation (eastern part of India), with different parts of the world, were primarily undertaken based on a thorough literature search using Pubmed. The comparison between countries was based on established literature, without considering the time period or age and sex matched populations. The presentation and management of sickle cell disorders in countries such as, USA, UK, UAE were considered.

3. RESULTS

A total of 95 patients with a component of HbS were detected among our patient cohort. Depending on the age of presentation to our Clinic, patients ranged between 2-50 years age. Most patients in our cohort had HbS/β (53.7%). They presented at a median age of 17.5 years. This was followed by SCA (30.5%) and the median age of patients was 12 years. Their demographic distribution is depicted in Table 1.

The most common clinical presentation was pain crisis (32,33.7%), be it abdominal pain (11,11.6%) or bone pain (13,13.7%). Other

presenting complaints were pallor (26,27.4%), jaundice (12,12.6%) and fever (4,4.2%). Some rarer presenting manifestations were fatigue (4,4.2%), splenic infarction (1,1%), convulsions (1,1%), Raynaud`s phenomenon (1,1%), headache (1,1%) or itchy skin lesions (1,1%). Few patients (4,4.2%) had recurrent pregnancy loss, while one patient was diagnosed incidentally when she came for antenatal check-up. Most patients had more than one complaint. Very occasionally patients required admission and the reasons were varied: chest pain, fever, convulsions, or abdominal pain.

The HbS trait patients were diagnosed incidentally on evaluation during an antenatal check-up (2,40%) or during evaluation of pallor (3,60%): one patient was later diagnosed with iron deficiency anemia. Most patients were from the nearby district of North 24 Parganas (26,27.4%), followed by South 24 Parganas (16,16.8%). Other places from where patients attended our Clinic were: West Midnapore (8,8.4%), East Midnapore (7,7.4%), Kolkata (7,7.4%), Nadia (6,6.3%), Birbhum (5,5.3%), Hooghly (5,5.3%), Bankura (3,3.2%), Howrah (3,3.2%) or Purulia (2,2.1%). Least number of patients came from faraway districts, such as Burdwan (1,1%), Jalpaiguri (1,1%), Malda (1,1%), Uttar Dinajpur (1,1%); or neighbouring states, such as, Jharkhand (2,2.1%) and Bihar (1,1%). (Fig.1).

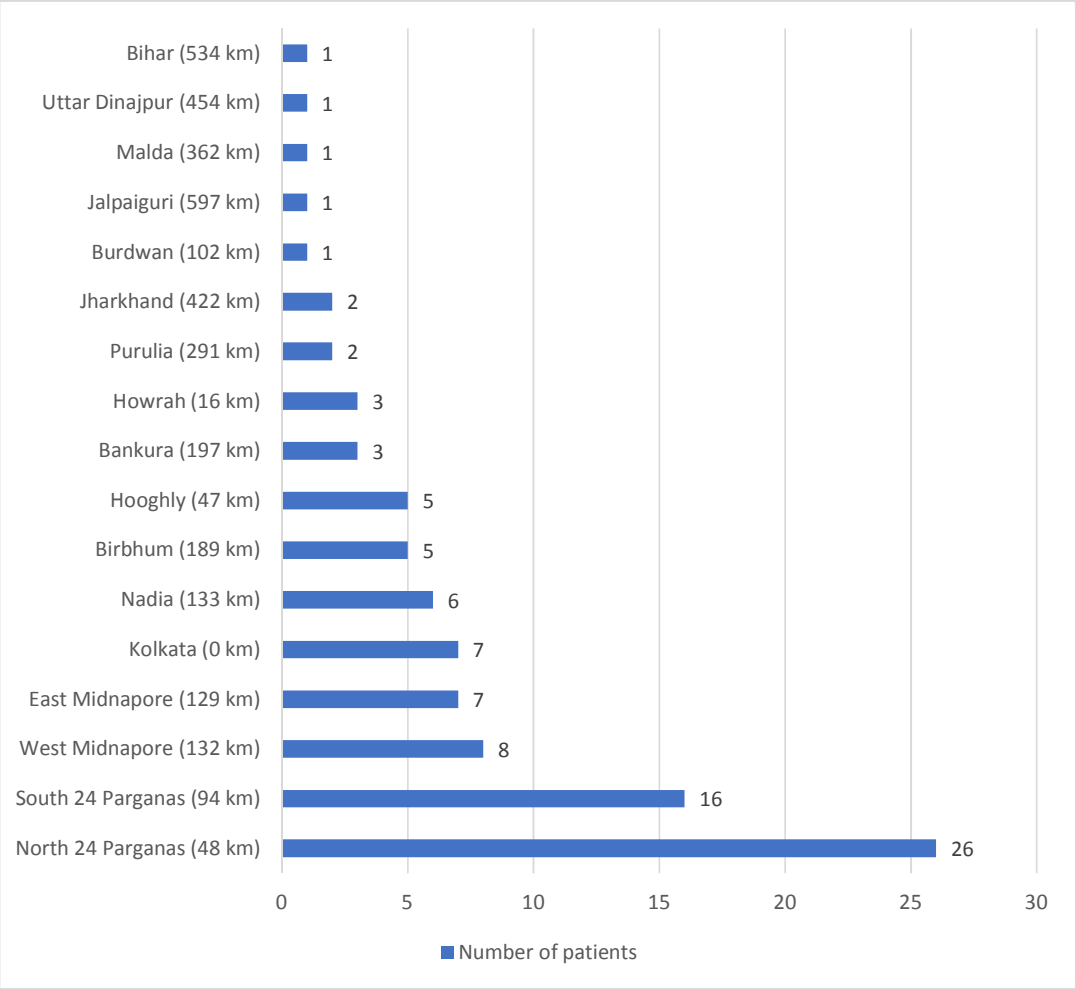

Fig. 1. Demographic distribution of patients attending our hospital according to address

Legends: Demographic distribution of patients attending our hospital, from different districts and neighbouring states of West Bengal, n=95. The numbers within brackets indicate the average distance of the districts or states from Kolkata, which is taken as the starting point (0 km). Abbrev: km=kilometres.

Table 1. Demographic distribution of patients with Sickle cell disorders

Parameters evaluated	Total Cohort	HbS/β	SCA	HbS/D	HbS/E	HbS trait
Number of patients (%)	95(100%)	51(53.7%)	29(30.5%)	6(6.3%)	4(4.2%)	5(5.3%)
Median age in years (Range in years)	17(2-50)	20(2-50)	13(2.5-50)	15.3(4-20)	14(9-30)	14(2-24)
Median age of disease presentation (years)	13	17.5	12	10.3	12.5	7.5
Mean age of disease presentation (years)	17.5	20.4	14.4	12.4	16.5	13.4
Male: Female (ratio)	59:36(1.6:1)	34:17(2:1)	16:13(1.2:1)	5:1(5:1)	2:2(1:1)	2:3(1:1.5)
Most common clinical presentation (%)	Pain crises (33.7%), pallor (27.4%)	Pallor (35.3%), crises (29.4%)	Pallor (34.5%), Crises (20.7%)	Pallor (50%)	Pain (75%)	Incidental (40%), pallor (60%)
Treatment	FA ± HU ± BT ± Dsx	HU, BT, Dsx, FA	HU, FA ± BT	HU, FA ± BT	HU, FA ± BT	FA

Footnote: Demographic distribution of patients with Sickle cell homozygous or heterozygous diseases, n=95. Abbrev: HbS/β= Sickle cell β thalassemia, SCA= Sickle cell anemia/ Homozygous Sickle cell disease, HbS/D= Sickle cell Delta thalassemia, HbS/E= Sickle cell Hemoglobin E thalassemia, HbS trait= Sickle cell trait, FA= Folic acid, HU= Hydroxyurea, BT= blood transfusion, Dsx= Deferasirox.

The HbS/β thalassemia patients were treated with Hydroxyurea, blood transfusions, chelation therapy with Deferasirox as required and Folic acid supplementation. The SCA patients received Hydroxyurea, Folic acid supplementation and blood transfusions during crises. The HbS/D and HbS/E thalassemia patients were treated with Hydroxyurea, Folic acid supplementation and blood transfusions as required. Patients with HbS Trait continued to receive Folate supplementation. (Table 1).

4. DISCUSSION

This study highlights the distribution of the HbS gene among the population attending a tertiary care center, irrespective of specific area-based population. We have tried to highlight the varied distribution of patients who attend a tertiary care center for therapy. Till date most studies conducted in India have highlighted the prevalence of Sickle cell disorders among specific endemic populations [1,3,4]. In one study conducted in eastern part of India, there were 7 SCA and 14 HbS/β thalassemia patients, and 87 had HbS trait [5]. This is similar to the finding in our study, where HbS/β thalassemia patients were more than SCA patients.

Though, less in number, co-inheritance of HbS with β thalassaemia, HbC, HBE or HbD have been reported [3]. Among our patient cohort, HbS/β thalassemia patients comprised the majority. HbS/β thalassemia patients were reported to be asymptomatic with occasional vaso-occlusive crises or required frequent transfusions with vaso-occlusive crises [6]. Most patients in our study required frequent transfusions, and occasional patients had vaso-occlusive crises.

A study by Serjeant et al, highlights how the severity of disease manifestation varies among different populations in India [1]. This variation in disease manifestation is evident in our cohort. In our study, few SCA patients presented at a later age, partly due to fewer or milder symptoms. Anemia, and vaso-occlusive crises in the form of bone pain, musculoskeletal pains were common in our patients, like the reported literature [7].

The assessment of the distribution of patients attending our tertiary care hospital has highlighted that majority of patients belonged to the North and South 24 Parganas, districts of West Bengal. No specific endemicity of patients with Sickle cell disorders was noted. This is similar to the worldwide observation, that with the advent of globalisation, the disorder is not restricted to a particular region. Knowing the exact distribution of patients will help in better management facilities for these patients.

The clinical manifestations of SCA among our study cohort were compared to the clinical features of patients in different parts of the world. SCA patients with the African variants of HbS (Bantu, Senegal, Benin), usually present with stroke, in addition to vaso-occlusive crisis in the form of bone pain or recurrent infections [8]. SCA and HbS/C disease are the most common Sickle cell disorders in Africa [8]. Anemia with cholelithiasis, aplastic anemia are common manifestations, unlike in our cohort. Vaso-occlusive crises are also common and include, pain (most common), priapism, stroke, avascular necrosis of femoral head [8]. Bacterial infections were commonly seen in children aged <5years. Except pain, the other manifestations are quite rare in patients in India with the Arab-Indian variant, and only seen in occasional patients.

The African variants are also more common in the USA. In USA, the different types of Sickle cell disorders were as follows: SCA 60%, HbS/C thalassemia 30%, HbS/β thalassemia 10% [9-10]. The HbS/C thalassemia patients had a near normal life expectancy compared to general population and patients with SCA had a higher mortality rate than the other types of Sickle disorders [9]. The rates of mortality have reduced in children <4years age [11]. Among patients in Britain, painful vaso-occlusive crises were the commonest causes of hospital admission. The incidence of HbS trait and HbC trait were 3.2% and 0.8%, respectively [12].

In Saudi Arabia, the prevalence of HbS trait ranged from 2-27% and SCA 1.4% [13]. Patients with SCA manifested with anemia or vaso-occlusive crises depending on the Arab-Indian or Benin haplotypes. The vaso-occlusive crisis manifests as pain, acute chest syndrome, splenic infarction, stroke or avascular necrosis [13]. In another study, there were 91 SCA patients, with a mean age of 18.81±11 years and male: female ratio of approximately 1:1. [14].

Africa is the country with highest prevalence and highest mortality of SCA [15]. Hydroxyurea used in Indian patients, was effective in reducing clinical severity among patients with SCA or HbS/β thalassemia [16]. Blood transfusions are indicated in conditions with vaso-occlusive crises

[17]. It has been seen that with early diagnosis and management, the mortality can be drastically reduced. There are reports of improved survival rates in USA or UK, in comparison to Africa, due to early and comprehensive management of the disease [8].

5. CONCLUSION

Thus, in our study, HbS/β thalassemia patients were more prevalent than SCA patients. Variable phenotype of SCA patients were seen among our cohort, and painful vaso-occlusive crises and/or pallor were the most common manifestations. Stroke or ulcerations were uncommon manifestations. People with HbS trait were mostly diagnosed incidentally. Knowing the distribution of patients with Sickle disorders will aid in better diagnostic and management facilities for them.

There is a significant difference of patient presentation, when compared with the western literature. However, there is a similarity with the disease presentation in other parts of India, even though, most of the other studies conducted in India concentrate on specific endemic populations.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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