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VARIABILITY IN CLINICAL MANIFESTATIONS OF SICKLE CELL DISEASE

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ABSTRACT

Sickle cell disease is one of the most commonly encountered hemoglobinopathies, widely distributed in tribal populations of Central & Eastern part of India. The prevalence in India ranges between 9 to 22 percent in endemic areas.[1] This disease load calls for the need of identifying the affected children at the earliest possible. Varied clinical presentations of sickle cell disease poses problems in diagnosing during the first encounter. Thus the aim of our study was to identify and observe the different clinical presentations of sickle cell disease in the tribal dominated region of jharkhand. **Material and Methods:** This study was conducted in pediatric ward of tertiary care unit of Jharkhand state. Subjects included were the cases of sickle cell disease admitted between the months of January to March 2018 **Results:** Anemia and Vaso-occlusive crisis were the commonest presenting complaint, followed by sequestration crisis. A handful of cases also presented with respiratory tract infections. Rare complications such as hematuria, low back pain and headache were also noted. **Conclusion:** The study showed that sickle cell disease can present as a manifestation of any systemic involvement and can mimic a large number of other conditions. Thus, it is necessary to have a high index of suspicion & knowledge of multiple clinical presentations, while working in endemic regions to promote early diagnosis of sickle cell disease.

KEYWORDS: Sickle cell disease, Tribal population, Anaemia.

INTRODUCTION

Sickle cell disease was the first disease for which clear molecular basis was identified. HbS is the result of single base-pair change, thymine for adenine at the sixth codon of β-globin chain. This change encodes valine instead of glutamine. Sickle cell anemia (HbSS), a homozygous condition occurs when both β-globin alleles have the sickle cell mutation. Sickle cell disease refers to compound heterozygotes where one β -globin allele includes the sickle cell mutation and the secondβ -globin allele includes a gene mutation other than the sickle mutation such as HbC, Hb β thalassemia, HbD, HbO. Sickle hemoglobin (HbS) polymerizes on deoxygenation, reducing the deformability of red cells. Patients have intensely painful vaso-occlusive crises, leading to irreversible organ damage, poor quality of life, and reduced life expectancy.[2]

Epidemiology

The prevalence in United States is approximately 1 in 5000, mostly affecting Afro-Americans. Sickle cell disease is noted primarily in African descent, Hispanics, middle eastern, Indian, Latin American, Native American and Mediterranean region. Studies indicate that besides the heterozygote advantage against malaria, the uneven regional distribution of HbS trait is because of restricted movement of two different populations due to meagre communication channel in olden days. That's why Dravidian from the south and Tibeto-Burman from the east, failed to meet into the Indian mainland, (due to severe climatic conditions (deserts and heat) prevailing through parts of central India).[3] Jharkhand was a part of older Indian mainland endemic region, spreading from Orissa to Chhattisgarh including Madhya Pradesh.[6]

Manifestations

For the first 6 months of life, infants are protected largely by elevated levels of Hb F; soon thereafter, the condition becomes evident. One of the common presenting clinical manifestations of Sickle Cell Disease is vaso-occlusive crisis, as patients do not report during early asymptomatic state. It is the leading cause of emergency

department visits and hospitalizations for affected patients.

Anemia is universally present. It is chronic and hemolytic in nature and usually very well tolerated. Their tolerance for exercise and exertion tends to be very limited. Anemia may be complicated with megaloblastic changes secondary to folate deficiency.

Splenic sequestration occurs with highest frequency during the first 5 years of life in children with sickle cell anemia. This complication is characterized by the onset of life-threatening anemia with rapid enlargement of the spleen and high reticulocyte count.[7]

Functional asplenia results in extreme susceptibility to infection.

Organisms that pose the greatest danger include encapsulated respiratory bacteria, particularly Streptococcus pneumoniae.

During childhood and adolescence, SCD is associated with growth retardation, delayed sexual maturation, and being underweight.

Infants with SCD may develop hand-foot syndrome, known as dactylitis, presenting as exquisite pain and soft tissue swelling of the dorsum of the hands and feet. Hand-foot syndrome occurs between age 6 months and 3 years; it is not seen after age of 5 years because hematopoiesis in the small bones of the hands and feet ceases at this age.[1]

The acute chest syndrome consists of chest pain, fever, cough, tachypnea, leukocytosis, and radiological appearance of new pulmonary infiltrates.

Central nervous system involvement is one of the most devastating aspects of SCD. It is most prevalent in childhood and adolescence. The most severe manifestation is stroke, resulting in varying degrees of neurological deficit.

A serious complication is the aplastic crisis. This is caused by infection with Parvovirus B-19 (B19V). This virus causes fifth disease, a normally benign childhood disorder associated with fever, malaise, and a mild rash. A very rapid drop in Hb occurs. The condition is self-limited, with bone marrow recovery occurring in 7-10 days, followed by brisk reticulocytosis.

The other uncommon complications include leg ulcers, priapism, cholelithiasis, proliferative retinitis, avascular necrosis, pulmonary hypertension, and cardiac involvement.[1]

MATERIAL AND METHODS

This is a retrospective audit study carried out in pediatric ward of tertiary care unit of Jharkhand (Rajendra Institute of medical sciences, Ranchi) over a period of 3 months. Total number of subjects included were 50 cases of sickle cell homozygous and heterozygous variants. Patients were admitted from emergency room and pediatric out patient department and were attended and managed by pediatric residents and pediatricians.

The details of each case were taken from patients case records available in Paediaric units & Medical Records section of RIMS, Ranchi.

The laboratory test that were used for confirming the diagnosis of sickle cell disease was High Performance Liquid Chromatography(HPLC) of blood samples collected in EDTA vial.

RESULTS

Table 1.1: Age wise and sex wise distribution of sickle cell disease.

Age Group (In Years)	Males (%)	Females (%)	Total
1-5	4	6	10(20%)
6-10	22	8	30 **(60%)**
>10	6	4	10(20%)
Total	32(64%)	18(36%)	50

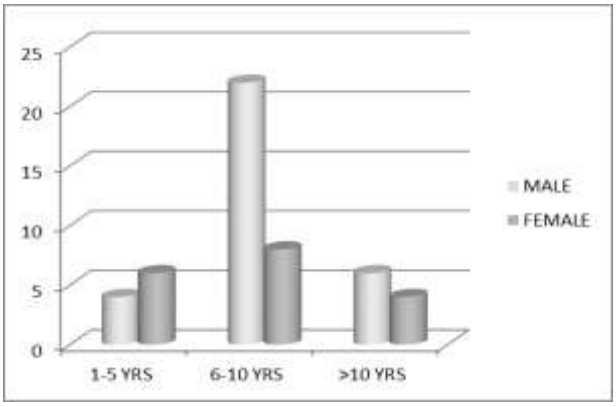

Fig. 1.1: Showing the graphic representation of age and gender wise distribution of the cases.

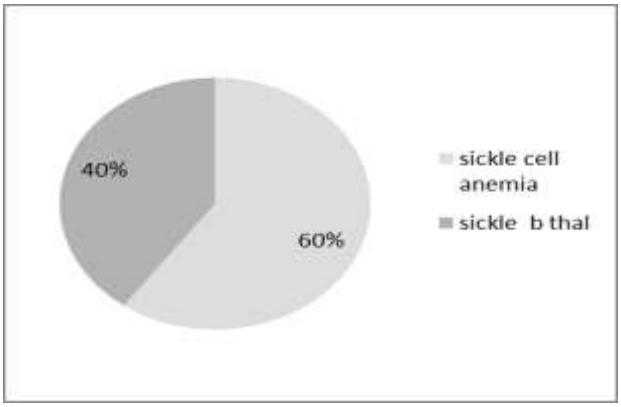

Fig. 1.2: Incidence according to variants of sickle cell disease.

Table 1.2: Showing the relative frequency of manifestations of sickle cell patients.

Manifestations	Number of cases	% of Cases	Complaints
Commonest	35	70%	Anemia
Common	20	40%	Fever, Vaso occlusive crisis
	15	30%	generalized myalgia
Uncommon	10	20%	Sequestration crisis
	1	2%	Hematuria
	4	8%	LRTI
Rare	5	10%	Back pain
	2	4%	Headache

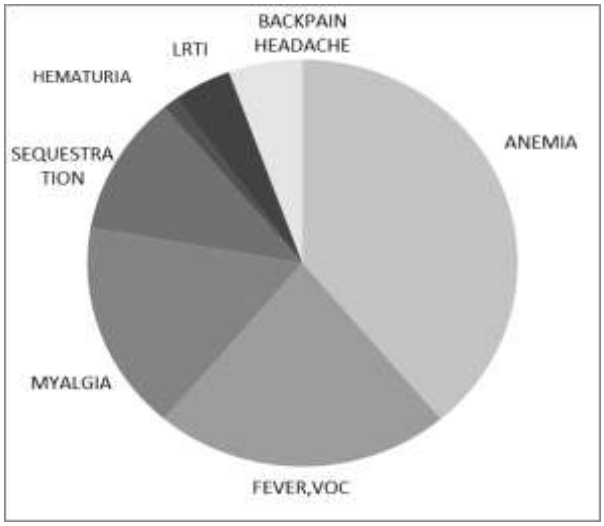

Fig 1.3: Showing incidence of manifestations of sickle cell disease.

Table 1.1. showing that out of the 50 cases included in current study, 32 were males (64%) and 18 were females (36%).

It also shows that maximum cases reported belonged to the age group between 6 to 10 yrs (60%)., followed by equal number of cases, reporting in the age group 1-5 yrs and more than 10 yrs.

Fig 1.2 shows that 60% were diagnosed to be sickle cell homozygous (HbSS) and rest 40% were found to be sickle heterozygous (Hb – b thal).

Fig 1.3 shows that the commonest cause of admission was Anemia **(70%)**. The other common causes include fever with or without vaso occlusive crisis (40%) and generalized myalgia (30%), indicative of chronic pain.

The uncommon complications noted were pain abdomen indicative of sequestration crisis and lower respiratory tract complications (8%), hematuria (2%).

Rare complications such as low back pain (10%) and headache (4%), suspected to be due to sluggish cerebral blood flow and occasional case of paraplegia, were also seen.

DISCUSSION

The study was undertaken with the aim of identifying the common, uncommon and rare manifestations of sickle cell disease presenting in the region of Jharkhand.

The study shows that anemia is the commonest cause of admission, which is in sync with other studies which suggest chronic anemia as one of commonest causes of admission in central India (Patel et al,2015).[4] Vaso-occlusive crisis is the next common presenting complaint, accounting to 40% of the admissions. Vaso occlusive phenomenon occurred most commonly after an episode of acute illness, accompanied by fever as also reported by other authors.[5]

Sequestration crisis, presenting as acute abdominal pain is relatively an uncommon manifestation in our study. Sequestration crises had been found to be more common and severe in Afro-American populations by other authors (John et al, 2012).

Hematuria (2%), has also been documented in current study. Sickle cell nephropathy is also known complication, occurring in a comparatively lesser frequency. Hematuria was corrected by conservative management of sickle cell crisis.[4]

One of the rarest manifestation noted was recurrent headache not amenable to routine treatment and management was noted in our series. CNS manifestations, due to sluggish cerebral blood flow has been described as an uncommon but serious complication .Thus, headache as the initial presenting complaint, while being diagnosed for the first time as a case of sickle cell disease has been observed in the study. This may be an early red flag sign of impending vaso occlusive crisis.

Low back pain is common in older children when the hematopoietic activity is gradually increased in the long bones and vertebra. Due to increased marrow activity and repeated episodes of marrow infarction, vertebral collapse, manifesting as low back pain was also noted during the course of study.

Some studies conducted in Jharkhand and other parts of central India, suggested that anemia and hematological crisis were the main causes of repeated episodes of

hospitalizations accounting to more than 50 % of total admissions (Roshan et al).[6] In endemic regions of African subcontinent, intercurrent infections particularly of the respiratory tract, fever, abdominal/skeletal pain, haematologic and bone pain crises were the main causes of morbidity.[5]

CONCLUSION

Manifestations of sickle cell disease are multi-systemic involving respiratory, neurological, renal, musculo skeletal system etc in the region of Jharkhand .Any systemic involvement can also present with a variety of symptoms.

Thus, due to varied clinical presentations of sickle cell disease, a high rate of suspicion is necessary to diagnose sickle cell disease in endemic regions. Any patient, belonging to tribal population in these endemic regions, reporting for any complaint may fall in the spectrum of sickle cell disease. This should always raise the question of possibility of sickle cell disease, in addition to the other conditions in differential diagnoses. A variety of screening programs can be undertaken in these endemic areas to identify the burden of sickle cell disease in these populations. Creating awareness regarding sickle cell disease in the general tribal population can also prompt the early reporting of patient to the health care facility and thus facilitate the early diagnosis of the patient.

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