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Research Article

Study of clinical profile of painful crisis in hospitalized children of sickle cell anemia

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ABSTRACT

Background: To study the clinical profile of painful crisis in hospitalized children with Sickle cell anemia.
Methods: A prospective cross sectional study; details of onset, perceived precipitating factors, associated symptoms, and pain distribution in the painful crisis have been studied in 195 painful crises in 130 patients of Sickle cell anemia.
Results: The average age was 7.4±3.2 years with male preponderance predominantly from Mahar community (68.46%). Seasonal incidence was more during rainy season (99 patients). Of the perceived precipitating factors decreased oral intake (42.56%) and fever (54.36%) were common. Commonly involved joints were knee (39.18%), elbow (28.62%) and ankle joint (27.18%) while non-articular limb pain was experienced by 78.35% children. Bilateral limb and joint paint was seen in 82.64% and multiple site involvement (≥4 sites) was seen in 40%. Recurrence occurred in 28 patients but showed no significant evidence of involving same sites on successive occasions.
Conclusions: Painful crisis were seen in 7-10 year old children with male preponderance, mainly from Mahar community, more during rainy season. Common precipitating factors were decreased oral intake and fever. Bilateral involvement was common. Duration of hospitalization was significantly longer in males than in females (3.47±1.7 Vs 3.86±2.51days) ($p<0.01$). Mean age (±) SD with spleen size (≥5 cm) was 8.48±1.92 years; indicating late persistence of splenomegaly.

Keywords: Pain, Sickle cell crisis, Sickle cell anemia, Precipitating factors, Children

INTRODUCTION

Sickle cell disease (SCD) is an autosomal recessive genetically transmitted hemoglobinopathy responsible for considerable morbidity and mortality. The prevalence in Central India is high, ranging from 9.4-22.2%.[1,2] The painful crisis is a common and dramatic manifestation of Sickle cell disease. It is defined as pain in any part of the body which may be generalized body ache or joint pain, tenderness, with or without swelling of hand and or foot, warmth, fever, acute abdominal pain and acute chest pain.[3] The Asian/Indian haplotype is associated with higher levels of HbF and milder course than in three African haplotypes.[4] Within the same region also different patient characteristics may influence the clinical course of the illness.5We conducted the study to determine the precipitants and clinical presentation of painful crisis in patients of sickle cell anemia.

METHODS

This was a prospective cross sectional study from December 2007 to November 2009 conducted in the Indira Gandhi Government Medical College, Nagpur a tertiary level hospital.The study was approved by the Institutional Ethics Committee and a written informed consent was obtained from parents of all study participants. Children 9 months to 12 years of age were enrolled who had HbSS pattern on cellulose acetate electrophoresis and high performance liquid chromatography.

Patients having S beta thalassemia, SD disease and any other co-morbidity like pre-existing illness, major congenital anomaly were not included.

We defined painful crisis as defined as pain in any part of the body with smiley pain scale score ≥3, having ruled out acute chest syndrome, osteomyelitis, pyogenic arthritis, fracture of bones, gall stones, hepatitis, urinary calculi, surgical abdomen, intracranial infection, other Sickle cell crisis clinically and by appropriate investigations. Children with pain in small joints were included if there was associated pain in other parts of the body. These patients were not on hydroxyurea treatment. If hydroxyurea treatment was started later child was excluded from the study.

Following data was recorded on structured Case report form: age, gender, caste, anthropometry and immunization status. Patients whose weight for age and height for age Z score was less than 2 were characterized as underweight and stunted respectively.

Information was extracted about precipitating factors like exposure to cold (like getting wet in rain, sleeping under fan or cooler, swimming, traveling during cold hours without adequate protection), exposure to heat (like exposed to sun, playing in sun or traveling during summer where temperature in Central India goes high up to 48 degree Celsius), history of vomiting, history of loose motions, physical exertion (excessive exercise or activity more than normal daily activity), emotional stress (academic evaluation, family problem, peer problem), fever, history of decreased oral intake of fluids (less than normal daily intake), paleness as perceived my mother seeing palm of child; in the 24-48 hours preceding the onset of pain.

The distribution of pain was recorded. All patients were subjected to routine clinical examination. For recording of pain smiley pain scale was used.

Figure 1: Wong-Baker Faces pain rating scale.

Child was explained that face 0 is very happy because he doesn't feel pain at all. Face 1 hurts just a little bit. Face 2 hurts a little more. Face 3 hurts even more. Face 4 hurts a whole lot. Face 5 hurts is maximum score.[6] Rating scale was recommended for children age 3 years and older. The child was asked to choose face that best describes pain and appropriate number was recorded. In subjects <3 years smiley pain scale score was calculated considering discomfort due to pain to child, effect on daily activities, oral intake and sleep pattern of child, by clinician.

Statistical analysis was done using STATA 10/IC software. For continuous data, mean and standard deviation of the characteristics were calculated and for categorical data, frequency distribution of the characteristics was calculated. Chi-square test and ANOVA test were used.

RESULTS

There were 195 episodes of painful crisis in 130 patients.

The monthly distribution of 195 painful crises over the study period (December 2007 to November 2009) showed maximum no. of crisis in July and January (Figure 1).

Table 1: Baseline data of study subjects.

	Character	Total patients n (%) (N=130 no. of patients)
Age group	9 months <2 years	4(3.08)
	2-5 years	32(24.62)
	>5-12 years	94(72.31)
Sex	Male	68(52.31)
	Female	62(47.61)
Nutrition	Underweight	49(37.95)
	Stunted	39(29.74)
Caste	Mahar	89(68.46)
	Kalhar	6(4.62)
	Gond	5(3.85)
	Adiwasi	3(2.31)
	Kunabi	3(2.31)
	Sahu	3(2.31)
	Teli	2(1.54)
Crises frequency	Single episode	102 (78.46)
	Two episodes	16 (12.31)
	Three episodes	7 (5.39)
	≥4 episodes	5 (3.84)

Of the perceived precipitating factors 42.56% had decreased oral intake, 19.49% had vomiting, 17.44% were exposed to cold, 9.23% had loose motions, 6.67% had emotional stress, and 6.15% had physical exertion whereas 2.05% were exposed to heat. Fever was common, seen in 54.36% patients.

As per smiley pain scale, score was 3 in 4.62%, 4 in 34.87% and 5 in 60.15% patients.

Distribution of joint pain is given in Table 2. Non-articular limb pain was present in 78.35%, backache in 22.56% and abdominal pain in 33.88%. Bilateral limb and joint paint was seen in 82.64% and multiple site involvement (≥4 sites) was seen in 40%. Recurrent painful crises occurred in 28 patients but showed no

significant evidence of involving similar sites on successive occasions by analysing first two crises in patients with multiple crises. Clinical features of joint involvement are described in Table 3.

Table 2: Distribution of joint involvement.

No.	Joint involved	No. of patients n (%)
1	Small joints of hand and foot	36(18.46)
2	Shoulder	25(12.08)
3	Elbow	58(28.62)
4	Wrist	37(18.97)
5	Hip	21(10.77)
6	Knee	76(39.18)
7	Ankle	53(27.18)
8	Axial	27(13.85)
Sites involved	1	55(28.21)
	2	42(21.54)
	3	20(10.26)
	≥4	78(40)

N=195; where N is total no. of episodes

Spleen was not palpable in 62.56% patients, between 1-4 cm in 25.13% and >5 cm in 12.30%. Mean age (±) SD with spleen size (≥5 cm) was 8.48±1.92 years shows late persistence of splenomegaly.

Table 3: Characteristics of the involved joints.

No.	Clinical feature	No. of joints n (%)
1	Pain	543(100)
2	Swelling	9(2)
3	Redness	0(0)
4	Raised temperature	1(1)
5	Loss of function	400(73.66)
6	Unilateral involvement of joint	21(17.36)
7	Bilateral involvement of joint	100(82.64)

Total no. of joints involved (N) = 543

Frequency of painful crisis episodes showed that 102 patients had only 1 episode whereas 16 patients had 2 episodes, 7 patients had 3 episodes, whereas 5 patients had ≥4 episodes. In a study done by Ware et al in Jamaica, single crises occurred in 119 (55·1%) patients, two crises in 42 (19·4%) patients, three in 21 (9·7%), four in 16 (7·4%), and five or more in 18 (8%) patients over a study period of around 6 years.[8]

Table 4: Association of pain scale and sex wise distribution with age, anthropometric factors and other factors.

	Pain scale score ≤4 (n=77)	Pain scale score (n=118)	p value	Female (n=68)	Male (n=62)	p value
Age (yrs) mean(±)sd	7.35±2.93	7.47±3.31	0.78	7.18±3.35	7.68 ±22.94	0.205
Underweight n (%)	33(42.86)	41(34.75)	0.25	39(39)	35(36.84)	0.756
Stunted n (%)	23(29.87)	35(29.66)	0.97	31(31)	27(28.42)	0.694
Duration of hospitalization in days mean(±)sd	2.87 ± 1.19	4.17 ± 2.44	<0.01	3.47 ±1.70	3.86±2.51	<0.01
Spleen size(cm) mean(±)sd	1.77 ± 2.91	1.44 ± 2.35	0.37			
No. of painful crisis mean (±) sd				4.7 ±4.22	3.89 ±3.38	0.032

Duration of hospitalization was more in males than in females and this difference was found to be statistically significant (p<0.01) (Table 4).

DISCUSSION

The present study done shows that incidence of painful crisis in 9months to <2 years is less and as age increases the incidence increases till age of 12 years. This differs from early and more severe presentation in African patients who have lower levels of fetal hemoglobin as compared to Asian haplotype.[6,7]

Male preponderance was seen, which was similar to other studies from central India.[9,10] This may be due to a cultural bias or males are more exposed to known precipitating factors as compared to females. [11]A study in Nigeria has reported less severe disease in adult females compared to adult males.[12] This could be due to higher levels fetal hemoglobin levels in females caused by X-linked dominant inheritance of the gene coding for Hb F.[13,14]

Nutritional status of these patients was studied, 37.95% patients were underweight and 29.74% were stunted.

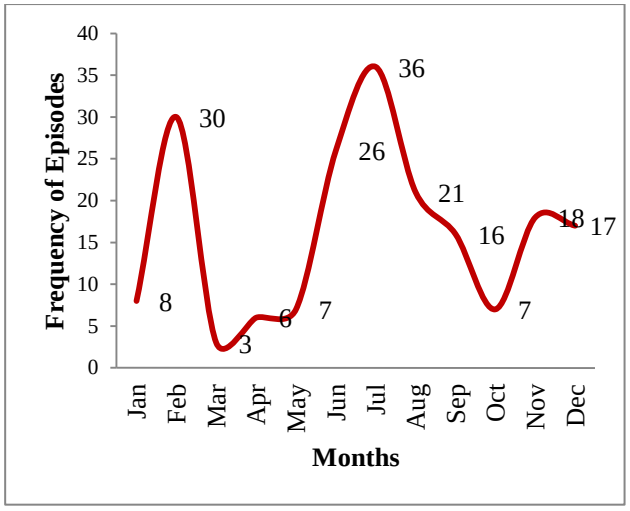

Figure 1: Monthly distribution of patients with painful crisis (Dec. 2007 - Nov. 2009).

Nutritional intake is compromised in any chronic illness; however recent studies have also reported that basal metabolic rate is higher in children with Sickle cell disease as compared to healthy children.[15,16]

The children were predominantly from the Mahar community (68.46%). Similar finding was found in the study done in central India.[9,10]

Seasonal incidence of painful crisis shows more cases are during rainy season (June to August), and winter season (January, February) due to cold and humid climate.

In other study done in central India the maximum hospitalizations were seen during the late monsoon and early post monsoon season (August-October).[9] This finding was similar to previous reports from India.[17,18]

However, the studies from other countries have shown rainy season, low temperature or high wind speed and low humidity as precipitating factors for vasoocclusive crisis in SCD subjects.[19-22]

The mechanism of cold-induced painful crises is postulated to result from cold-induced diuresis, cold agglutinins, cryoglobulins or cutaneous vasoconstriction with shunting of blood to deeper vascular bed as per a study done in Jamaica.[3]

The structure of the study did not allow independent confirmation of the perceived precipitating factors for pain, because no control observations were available. The observations were therefore confined to precipitants as perceived by the patient and direct questions were asked about precipitants for which there is some support from the literature.[3]

In our study fever was common finding (54.36%). According to study done in Jamaica mostly fever gets resolved without antibiotics and also the greater prevalence of fever with multiple site involvement raises the possibility that fever is characteristic of the inflammatory response involved in the removal of uninfected avascular marrow and does not necessarily imply infection as is frequently assumed. [3]

In this study most painful crises affected bones and abdomen. The origin of bone pain appears to be avascular necrosis of bone marrow on the basis of aspiration of necrotic marrow from painful sites, loss of marrow function on scintigraphy and the limitation of pain to sites occupied by active bone marrow.[23,24]

The tendency to simultaneous, bilateral involvement is more consistent with a hypothesis that marrow necrosis results from a centrally mediated reflex shunting of blood away from the bone marrow. [25]

Difference in the duration of hospitalization in pain scale score ≤4 and with pain scale 5 was found to be statistically significant. Longer duration of hospitalization in children with pain scale score 5 was due to severity of symptoms.

Duration of hospitalization was more in males than in females and this difference was found to be statistically significant. Also similar finding was found in study done in Saudi Arabia.[26] This aspect needs to be studied more as it may be due to more severe nature of painful crisis in males than in females and also higher HbF in females leading to milder course in females.[27]

In patients with ≥5 cm spleen size mean age (8.48±1.92 years) was more, this may be due to persistence of splenomegaly due to more frequent α+ thalassemia in Asian patients and higher HbF values.[28,29]

There was no mortality of Sickle cell patients admitted with painful crisis in our study however sickle cell patients with crisis had mortality d/t splenic sequestration, severe sepsis.[10]

CONCLUSION

Comparing various studies in other parts of World and India we found that in our study painful crisis in HbSS pattern was more common in males than in females and common in rainy season.

Bone and abdominal involvement was common and mostly associated with fever, with simultaneous bilateral multiple joint involvement along with persistence of splenomegaly. Duration of hospitalization was longer in males than in females.

Limitation of our study is that we did not compare HbF levels in each patient with severity of painful crisis. Etiology of fever was not identified in all cases in our

study. Also many patients were not started on hydroxyurea therapy due to financial constraints.

Considering the high prevalence of Sickle cell disease in Central India and high burden of morbidity and mortality due to Sickle cell disease it is recommended to study in detail the clinical profile of Sickle cell disease and vasoocclusive crisis in order to identify the precipitating factors, common infections, clinical presentation, complications and preventive measures required to be taken to avoid the morbidity and mortality due to the disease.

Informed consent was obtained from all individual participants included in the study.

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