ORIGINAL RESEARCH PAPER

Paediatric Medicine

CLINICOPATHOLOGICAL PROFILE IN A STUDY ON SICKLE CELL DISEASES

KEY WORDS:

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INTRODUCTION

Hemoglobinopathies are the disorders affecting the structure, function, or production of hemoglobin. These conditions are usually inherited and different forms may present as hemolytic anemia, erythrocytosis, cyanosis, or vaso-occlusive stigmata. Sickle cell disorders are structural hemoglobinopathies which occur when mutation alter the amino acid of a globin chain, altering the physiological properties of the variant hemoglobin and producing the characteristic clinical abnormalities. Red blood cell are rendered less deformable, sticky and altered shape like a sickle and abnormally adhere to endothelium of small venule and to each other during to production of sticky ends[1]. These abnormalities provoke unpredictable episodes of microvascular vaso-occlusion and premature RBC destruction (hemolytic anemia), episodes of ischemic pain and ischemic malfunction or frank infarction in the spleen, central nervous system, bones, liver, kidneys and lungs.

MATERIALS AND METHODS:

Study design:

Retrospective observational study.

Inclusion criteria:

Children between the age group from six months to twelve years who were addmitted from june 2018-october 2020, at tertiary care centre of the state and presented with signs and symptoms of chronic hemolysis or acute crisis (vaso-occlusive, hemolytic, aplastic) and further comfirmed by HPLC suggestive of Sickle Cell Disease were included in the study.

RESULTS

Out of total 23257 admissions during the study period, there were 30 cases of Sickle Cell Disease which constituted to 0.13% of all.

The pooled birth prevalence (per 1,00,000 live births) of SCD in the world is reported 112. Sickle cell disease is prevalent in many parts of India, where the prevalence has ranged from 9.4 to 22.2 percent in the endemic areas & tribal belt of certain district[2]. In Gujarat, the prevalence of SCD ranged from 0 % to 30 % depending on the endemic belt[3].

Table 1.Sickle cell disease variants[4]

SICKLE CELL DISEASE	CASES[5] (n=30)	%
Sickle cell homozygous	21	70
Sickle cell trait	5	13.3
Compound heterozygotes	4	16.67

All children showed sickling test positive whereas on HPLC, 21 patients were of Sickle cell homozygous, 5 patients of sickle cell trait & 4 were of compound hetrozygous for HbS & other hemoglobins like HbC or beta thalessemia.

Table 2. Age at first presentation

AGE AT DIAGNOSIS	PRESENT STUDY (n=30)		PATEL KG et al (n=61)[7] (2017)	
	CASES	%	CASES	%
< 1 Year*	1	3.33	0	0
1 – 4 Years	4	13.34	8	13.11
5 - 8 Years	17	56.67	23	37.70
9 - 12 Years	8	26.67	19	31.14
> 12 Years	0	0	11	18.03

* Primary diagnosis of brain abscess and the peripheral smear detected sickled RBCs.

56.67 % of children presented for the first time between the age of 5-8 years followed by 26.67% between 9-12 years of age.

In present study, out of 30, 17 were males and 13 were female child, with male to female ratio being 1.3:1.

Table 3. Immunisation status.

IMMUNIZATION STATUS	CASES (n=30)	%
Unimmunized	6	20
Partially Immunized	14	46.67
Immunized For Age	10	33.33

In the present study, only 10 patients were completely immunised for their age (33.33%) and 6 patients were totally unimmunised (20%).

Table 4a. Nutritional Status(Age<5years)

PEM grading	Cases (n=11)	Percentage
Normal	1	9.09%
Grade I	5	45.45%
Grade II	3	27.27%
Grade III	2	18.18%
Grade IV	0	0

Table 4b. Nutritional status(Age>5 years)

Undernutrition grading(BMI)	**Cases(n=19)**	**%**
Severe (<13)	05	26.31

Moderate(13-15)	13	68.42%
Normal(>15)	01	5.26%

Under the age of 5 years, 2 patients had severe malnutrition (Grade III & Grade IV PEM) (18.18%). Beyond 5 years of age, 13 patients had moderate undernutrition (68.42%) and 5 patients had severe undernutrition (26.31%).

Table 5. Family Screening

HPLC	MOTHER (17out of 30)	FATHER (19 out of 30)	SIBLING (n=15)
Sickle Cell Heterozygous	10 (58.82%)	13 (68.42%)	5 (33.3%)
Sickle Cell Homozygous	3 (17.64%)	0	3 (20%)
Compound Heterozygous	0	HbD-2(10.52%) HbE - 1(5.26%) Beta-Thal minor -1(5.26%)	0
Normal	4	2	7

HPLC of all the relatives could not be done due to their non availibilty during the hospital stay of the patients.

Hetrozygous abnormality was present in 58.82% of mother & 68.42% of father. 4 fathers were also compound hetrozygous.

Out of 15 siblings that were screened, 5 were sickle cell trait & 3 were sickle cell disease.

Table 6. Presenting complaints

PRESENTING COMPLAINTS	PRESENT STUDY (n=30)		PATEL KG et al [7] (n=61)	
	CASES	%	CASES	%
Pallor	23	76.67%	24	39.34
Fever	13	43.33%	21	34.42
Generalised weakness	12	40%	7	11.48
Abdominal pain	8	26.67%	14	22.95
Musculoskeletal pain	5	16.67%	15	24.6
Chest pain	4	13.3%	1	1.64
Convulsions	2	6.65%	-	-
Shortness of breath	2	6.65%	-	-
Focal deficits	1	3.33%	-	-
Swelling of joints	1	3.33%	-	-

The most common presenting symptom was pallor (76.67%) followed by fever (43.33%) and generalised weakness (40%). The abdominal pain in 8 (26.67%), musculoskeletal pain in 5 (16.67%) and chest pain in 4 (13.3%) were the common acute presenting complaints.

Table 7. Clinical Signs

SIGNS	PRESENT STUDY (n=30)		PATEL KG et al (n=61)[7]	
	CASES	%	CASES	%
Pallor	23	76.67%	24	34.34
Jaundice	9	30%	6	9.83
Clubbing	2	6.67%	-	-
Oedema	1	3.33%	-	-
Abdominal tenderness	8	26.67%	-	-
Splenomegaly	4	13.33%	15	24.59
Hepatomegaly	7	23.33%	4	6.55
Splenohepatomegaly	11	36.67%	-	-
Hand Foot Syndrome (Dactylitis)	1	3.33%	0	0
Hemiparesis	1	3.33%	0	0

Pallor (76.67%) & jaundice (30%) were the most common generalized signs. Organomegaly was present in 73.34% of children (22 out of 30)

Table 8. Comparative analysis of Morbidity events

MORBIDITY EVENTS		PRESENT STUDY (n=30)		PATEL KG et al[7](n=61)	
		CASES	%	CASES	%
SEVERE ANEMIA	Aplastic crisis	1	3.33%	4	6.56
	Sequestration crisis	-	-	-	-
	Hemolytic anemia (Hb<7gm/dl)	8	26.67%	24	39.34
ACUTE VASO-OCCLUSIVE CRISIS	Musculoskeletal pain	11	36.67%	32	54.5
	Splenic infarction	2	6.67%	-	-
	Acute chest syndrome	2	6.67%	1	1.63
	Neurological deficit (acute stroke)	1	3.33%	-	-
ACUTE FEBRILE ILLNESS	Respiratory infections	3	10%	9	14.75
	Viral fever	4	13.34%	9	14.75
	Malaria (P vivax)	1	3.33%	1	1.63
	Urinary tract infection	2	6.67%	0	0
	Gastroenteritis	1	3.33%	3	4.92

Vaso-occlusive crisis was the most common crisis (53.33%). Severe anemia was present in 26.67%. Acute febrile illness was present in 36.67% cases.

Table 9. Laboratory profile

LABORATORY PROFILE	CASES (n=30)	%
Haemogram		
Hb < 7g/dl	8	26.67%
Hb 7-9 g/dl	10	33.3%
Hb > 9 g/dl	12	40%
Leucocytosis (>30,000/mm3)	3	10%
Leukopenia (<5000/mm3)	3	10%
Thrombocytosis	4	13.33%
Pancytopenia	1	3.33%

cRetic count	Cases	%
< 5 %	4	13.33%
5-10 %	11	36.67%
> 10 %	15	50%
Peripheral smear	Cases	%
Sickled cells	30	100%
Target cells	10	33.33%
Sickling test	30	100%

Laboratory profile showed Hb of < 7gm% in 26.67% & corrected reticulocyte count > 5% in 86.67% of cases.

In peripheral smear examination, sickle shaped RBCs were present in all (100%) while target cells detected in 33.3%. One child had pancytopenia as well. All cases on screening

found to be positive for sickling test.

Table 9.Treatment modalities

TREATMENT	CASES (n=30)	%
Iv fluids	22	73.33%
Analgesics	16	53.33%
Antibiotics	10	33.33%
Anticonvulsant	2	6.67%
Blood Transfusions	25	83.33%
B12, Folic acid supplements	30	100%
Hydroxyurea	19	63.33%
Special vaccines	12	40%
Bone Marrow Transplantation planned	2	6.67%

In the present study, 22 patients received hydration therapy and 25 patients received packed cell volume (73.3 % and 83.3 % respectively). Analgesics were given in 16 cases (53.33%). Hydroxyurea was given in 19 cases (63%).

Bone marrow transplant was planned by haematologists in 2 newly diagnosed cases younger than 5 years of age. The donor for these patients were their normal siblings

DISCUSSION

1. Sickle cell anaemia constituted 0.13 % of the total paediatric admissions in the Civil hospital during the study period.

The proportion is lower in the present study, possibly due to the fact that being in urban location, the hospital caters relatively less tribal population as compared to peripheral rural centres.

2. Out of total 30 patients of Sickle Cell Disease, 70% were homozygous, 16.67% were heterozygous & 13.3% were coumpound heterozygous (sickle cell syndromes).

3. The most common age of first presentation was 5-8 years (56.67%).

In young children, the normaly functioning spleen removes the sickled RBCs from the circulation that prevents intrvascular hemolysis & acute veno-occlusion. After the age of 5 years, abnormal RBCs continue to remained in the circulation leading to continued hemolysis & frequent vaso-occlusion due to functional aspleenia.

4. The male to female ratio in the present study was 1.3:1. No significant gender predilection was noted.

5. Severe malnutrition was present in 18.18% of children < 5 years of age in contrast to children > 5 years of age in whom moderate to sever undernutrition was present in 94.73%. Relatively less proportion of severe malnutrition in children less than 5 years of age may be related to lesser haemolysis & lesser infectious illness due to near to normal splenic function in this age[6].

Associated factors with increasing age that affect the growth are increased resting energy expenditure, low mineral bone density, decreased plasma concentration of micronutrients, low concentration of haemoglobin, recuurent infections and vessel occlusion crisis leading to impaired bone growth..

6. The most common presenting symptom was pallor (76.67%), fever (43.33%), and generalised weakness (40%). Abdominal pain (26.67%), musculoskeletal pain (16.67%) and chest pain (13.3%) were also acute presenting symptoms.

7. Pallor (76.6%) and jaundice (30%) were the most evident general signs observed. Spleno-hepatomegaly (36.67%) was the most common systemic examination finding. Isolated hepatomegaly & spleenomegaly was observed in 23.33% & 13.33% respectively.

8. Acute vaso-occlusive crisis was present in 53.3% off which musculoskeletal pain was the most frequent (36.6%). Aplastic crisis was also present in one patient. Acute febrile illness (36.6%) & severe anemia (26.6%) were common complication amongst all.

9. Laboratory profile showed Hb of < 7gm% in 26.67% & corrected reticulocyte count > 5% in 86.67% of cases.In peripheral smear examination, sickle shaped RBCs were present in all (100%) while target cells detected in 33.3%. One child also had pancytopenia.

10. Packed cell volume required in 83.33% of children. For acute vaso occlussive crisis hydration therapy & analgesics were used in 73.3% & 53.3% respectively.Hydroxyurea was given to 63.3% patients for long-term therapy. Bone marrow transplant was planned in two children as well.

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