Original Research Article

Clinical and hematological profile of sickle cell disease affected children in rural tertiary level hospital

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Abstract

Introduction: Sickle cell disease is commonly seen in rural population of western part of India. It is one of the common causes of recurrent hospitalization, morbidity and mortality in pediatric population. As there are limited studies addressing the pattern of sickle cell disease amongst pediatric population, this study was taken up to evaluate the clinicohematological profile of pediatric population with sickle cell disease in a rural tertiary care hospital in western part of India. **Methods:** This was a retrospective observational study. Data was retrieved from pediatric sickle cell clinic of the department. Data of children diagnosed with sickle cell disease from June 2013 to September 2016 was collected and analyzed to assess the hematological profile at the time of diagnosis and to find if there was any correlation between various hemoglobin variants and the hematological parameters. **Results:** About 173 patients were included in the study. Vasoocclusive crisis was the most common presentation (43.93%) followed by generalized body ache joint pain (36.99%) and acute febrile illness (26.39%), while 45 (26.01%) patients presented with severe anemia. Hematological finding was suggestive of moderate anemia, low Mean corpuscular volume and low Mean hemoglobin concentration. **Conclusion:**At the time of diagnosis vasoocclusive crisis and generalized bodyache are the most common manifestations in pediatric population with sickle cell disease while hematological picture is suggestive of microcytic hypochromic anemia. There is a positive correlation between age at presentation and severity of anemia at the time of diagnosis.

Key words - Sickle cell disease, Pediatric, Morbidity, Anemia

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Introduction

Haemoglobinopathies are the most common single gene disorder in the world. Sickle cell disease (SCD) is the commonest genetic disease worldwide [1]. It is an autosomal recessive genetic condition due to a mutation in the beta-globin gene resulting in replacement of glutamic acid in sixth position of the beta-globin chain by valine resulting in abnormal sickle haemoglobin (HbS) molecule. Homozygous sickle cell disease (HbSS) leads to polymerization of deoxygenated sickle hemoglobin within rigid red blood cells (RBC) which then occlude microvasculature, resulting in acute complications, chronic organ damage, high rate of morbidity and mortality [2]. Sickle cell anemia was first described in south Indian tribal groups [3] and subsequently in central India [4]. The clinical manifestations of sickle cell anemia (SCA) begin early in life and continue with an increased incidence of adverse events coincident with the physiologic decline in fetal hemoglobin (HbF)[5]. Vaso-occlusive pain episodes are one of the predominant clinical features associated with SCA [6]. This study is aimed to identify the pattern of sickness and clinical manifestation of children presenting to a rural tertiary level hospital in western part of India.

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Methodology

This retrospective study was carried out in department of pediatrics S.B.K.S MIRC & Dhiraj Hospital catering to the rural and tribal populations of Gujarat and adjacent states Madhya Pradesh and Rajasthan. Data was retrieved from departmental sickle cell clinic register of the children from June 2013 to May 2016. In the departmental sickle clinic, all the suspected cases are screened by solubility test which has a limitation

that below the level of 20% HbS, it may give false negative results. Hence, it is not suitable for neonatal screening and in post transfusion patients. False negative results are also obtained when Hb is low or the reagents are out dated or contaminated.

False positive results are obtained in severe leukocytosis and hyperproteinemia. So, all patients with positive solubility test and strongly suspected clinically but sickle negative were subjected to high performance liquid chromatography (HPLC) for confirmation and to differentiate sickle cell disease from other variants such as sickle cell trait, Sickle Beta thalassemia etc. All the homozygous confirmed cases are further investigated for complete blood count which is done by using KX 21 Sysmex auto analyzer.

All the tests are carried out in institution's laboratory. Institutional ethics committee permission was taken before conducting study.

All patients aged between 6 months to 18 years were eligible for inclusion. All the known cases of sickle cell disease who were diagnosed outside and were already taking hydroxyurea or had received blood transfusion were excluded from the study. The cases of sickle cell trait and sickle cell B thalassemia were not considered for further analysis. Complete demographic, socio-economic, clinical and hematological profile were collected from the sickle clinic register and recorded in a prestructured proforma. Statistical analysis was done using SPSS software version 10.

Results

Total 1360 children with positive solubility test were enrolled in sickle cell clinic during June 2013 and Sept 2016. All these children were subjected to HPLC as per the departmental protocol. Out of these 1160 (85.2%) were heterozygous with sickle cell trait 173 (12.72%) children were diagnosed as homozygous sickle cell disease and 26 (1.95%) were double heterozygous for Hb-S. 1 (0.001%) child was double heterozygous for Hb-S and hemoglobin E (Hb-E). Double heterozygotes for sickle plus beta thalassemia minor were diagnosed solely on basis of elevated hemoglobin A2 (Hb A2) levels on HPLC. We studied the clinical and hematological profile of homozygous sickle cell disease exclusively.

Out of total 173 patients homozygous sickle cell disease 108 (62.4%) were males and 65 (37.6%) were females. Mean age of the children was 10.32 ± 3.79 years with the range of 1.2 and 17 year. As hospital is situated in rural area and caters rural tribal population of Gujarat with adjacent parts of Madhya Pradesh and Rajasthan, majority of the patients were from tribal community. Caste and sub caste wise distribution of sickle cell disease patients was Bhilala 62(35%), Bariya 34 (19%), Rathwa 20 (11.5%), Parmar 12 (6.9%) and Adivasi 3(1.73%). About 42 (24.27%) belonged to other communities.

Table-I Base line distribution of study population on basis of caste and clinical manifestation.

	N (%)
Male	108 (62.4%)
Female	65 (37.6%)
Bhilala tribe	62 (35.83%)
Bariya	34(19.65%)
Rathwa	20 (11.56%),
Parmar	12 (6.93%)
Adiwasi	3(1.73%)
Others	42 (24.27%)
Vasoocclusive crisis	76 (43.93%)
Febrile illness	41 (23.69%)
Bodyache and Joint Pain	64 (36.99%)
Severe anemia	45 (26.01%)
Hepatomegaly	14 (8.09%)
Splenomegaly	26 (15.02%)
Hepato-splenomegaly	12 (6.93%)
Jaundice	36 (20.80%)

Clinical profile-Common clinical features with which the SCD patients presented to hospital were - 76 (23.6%) with Vasoocclusive Crisis (VOC) (i.e. abdominal pain, acute chest syndrome etc.), 64 (36.99%) with generalized bodyache and joint pain, 41 (23.69%) with febrile illness and 36 (20.80%) with clinically detectable jaundice. Isolated splenomegaly and hepatomegaly were noticed in 26 (15.02%) & 14 (8.09%) cases respectively, while hepatosplenomegaly was seen in 12 (6.93%). Severe anemia was seen in (30%). Stroke and avascular necrosis of femur was noted in one patient each. Huge splenomegaly was noted in four patients. None of the patients had morbid and events like priapism, leg ulcers or Hand-Foot syndrome (Table I).

Hematological profile- Complete blood count was done in all the homozygous cases. Most notable finding were microcytic anemia with low Hemoglobin (Hb), Mean Corpuscular Volume (MCV), Hematocrit (HCT) and Mean Cell Hemoglobin (MCH) values. Mean Hb concentration was 8.21 ±2.07 gm%, MCV-71.22 ±11.96 fl, MCH -22.48 ±3.70pg. Mean Corpuscular Hemoglobin Concentration (MCHC) was 32.97 ± 2.63gm/dl and Mean HbF was 16.78 ±8.60 gm%. (Table -II).

Table-II Hematological data of sickle cell disease patients.

Hematological Parameter	Mean (SD)	Range
Hb (gm %)	8.21 (2.07)	2 - 12.7
HCT (%)	25.87 (8.67)	4.31 - 96.4
Platelet count (10^3/µl)	285.48 (193.20)	37 -330
WBC (10^3/µl)	12.32 (6.00)	2.4 - 33.50
RBC (10^6/ µl)	3.82 (3.42)	0.72 - 41.6
MCV (fl)	71.22 (11.96)	7.02 - 112
MCH (pg)	22.48 (3.40)	18.2- 38.8
MCHC (gm/dl)	32.97 (2.63)	15.4 - 39.5
HbF (%)	16.78 (8.60)	0.2 - 34.7

Hb-Hemoglobin, HCT hematocrit, WBC white blood cells, RBC red blood cells, MCV mean cell volume, MCH mean cell hemoglobin, MCHC mean cell hemoglobin concentration, HbF fetal hemoglobin,

On correlation analysis we did not find any significant correlation of percentage of variant hemoglobin with age, Hemoglobin level or any other hematological parameter.

Discussion

In this retrospective study 173 (12.72%) cases diagnosed as homozygous sickle cell disease were included. 26 (1.95%) were double heterozygous for Hb-S. There were more males as compared to females which may be due to the fact that male child gets more attention as compared to female child and thus present to hospital in higher numbers. In this study, the age of cases showed a wide range age which were similar to other studies [7,8].

In present study, the most common presentation in homozygous cases was vasoocclusive crisis - musculoskeletal pain, abdominal pain and chest pain which was similar to previous studies [8, 9, 10]. Another hospital based study also found that the common presentations in homozygous cases were musculoskeletal pain in 64%, abdominal pain in 35% and chest pain in 7% which was similar to our outcome [9]. Similarly in our study isolated splenomegaly was more common than hepatomegaly as reported in other studies [8]. Huge splenomegaly was noted in few patients similar to previous studies carried out in India [11,12].

An Indian study reported pain abdomen in 4.7% cases, musculoskeletal pain in 0.6% and splenomegaly in 30% [12]. The lower incidence in their study may be attributed to the fact that it was a community based study. In our study there were no cases of leg ulcer or priapism similar to the previous studies [8]. Though we

found low mean Hb levels in case of HbSS having VOC, but overall there seemed to be no correlation between hemoglobin level and VOC. This is in conformity to observations by earlier workers [13,14]. According to National Family Health survey (NFHS-3), anemia is common in India among the schedule caste and tribes and among the children with low socio-economic status [15].

Hb, MCH and MCHC were low in our study which is comparable to other studies [16,17,18]. It is said that MCV is high in SCD patients because of the increasing need of erythropoiesis due to chronic hemolysis leading to macrocytosis, It is also suggested to be related to a folic acid deficiency. However, MCV was low in our study similar to some other studies from different parts of our country [18,19, 20]. Low MCV in these studies may be due to co-existing iron deficiency anemia.

Conclusion

We conclude that in rural area any child presenting for detecting sickle cell anemia, the signs and symptoms like pallor, icterus, musculoskeletal pain, abdominal pain, splenomegaly and hepatomegaly should lead to high suspicion of sickle cell anemia where its prevalence is more. We also observed that vasoocclusive crisis is the commonest manifestation in pediatric age group and that despite being hemolytic in nature, hematological parameters were suggestive of hypochromic microcytic anemia which may be due to associated iron deficiency in these patients.

Abbreviations

SCD- Sickle cell disease

HbS- Sickle Hemoglobin

HbSS – Homozyzous Sickle cell disease

RBC- Red blood cell

SCA- Sickle cell anemia

HbF- Fetal hemoglobin

HPLC- high performance liquid chromatography

HbE – Hemoglobin E

HbA2 – Hemoglobin A2

MCV –Mean corpuscular volume

Hct- Hematocrit

MCH – Mean corpuscular hemoglobin

SD – Standard Deviation

MCHC – Mean corpuscular hemoglobin concentration

VOC –Vaso- occlusive crisis

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