Clinical and hematological profile of sickle cell disorder patients in a tertiary care hospital of Central India

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Abstract
Sickle cell anemia is the best known hereditary blood disorder; there are serious complications associated with the condition. It is an autosomal recessive genetically transmitted hemo-globinopathy responsible for considerable morbidity and mortality. Vaso-occlusive pain episodes are one of the predominant clinical features associated with sickle cell anemia. The study was conducted to study clinical and hematological profile of sickle cell disorder patients of Lata Mangeshkar hospital. Blood was collected in EDTA test tube and hematological indices were measured by C.B. Counter machine along with blood smear examination and confirmed by sickling method and electrophoresis test. Out of total 110 cases, 13 (11.81%) and 97(88.18%) cases were of sickle cell disease (SS) and sickle cell trait (AS) respectively. Females were more affected. Hematological profile showed decreased values of Hb%, Hematocrit (HCT), Red Blood Cell (RBC) count, Mean Corpuscle Hemoglobin (MCH), Mean Corpuscle Hemoglobin Concentration (MCHC) and raised values of Red blood cell distribution width (RDW).Platelet count, Mean Corpuscle Volume (MCV), Mean Platelet Volume (MPV) was found to be normal. Peripheral smear showed anisopoikilocytosis (60%) and hypochromic cells (74.54%). Approximately half of the patients reported weakness and fatigue.

Keywords: Electrophoresis test, Hematological profile, Sickle cell disease, Sickle cell trait, Sickling test.

Introduction
Sickle cell disorder is a group of diseases caused by a point mutation at sixth position in beta Globin chain, Valine substituting Glutamic acid due to which in deoxygenated state, shape of erythrocytes change to sickle shape and also the fragility of cell membrane increases.[1] It is a hereditary disorder characterized by the production of abnormal sickle-shaped red cells, with variable degree of hemolytic anemia and acute and chronic tissue damage due to vaso-occlusion leading to many serious complications.[2] Taking into our huge population size, more than 50 % of the world's sickle cell anemia cases are in India. It is estimated that most of the cases are in the Central and South India.[3] In individuals with sickle cell anemia (SS),the HbS level is more than 90% while in sickle cell trait, the HbS level is less than 50% and hence the clinical manifestations of disease are usually absent or mild among sickle cell trait patients as compared to with sickle cell disease.[4]

In India, sickle cell disease is more common hemoglobinopathy, next to thalassemia. It is an autosomal recessive genetically transmitted hemo-globinopathy responsible for considerable morbidity and mortality.[5] Although the sickle cell disease is present from birth, symptoms are rare before the age of the three to six months due to persistence of fetal hemoglobin (HbF). Sickle cell anemia was first described in south Indian tribal groups and subsequently in central India.[6] 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).[7] Vaso-occlusive pain episodes are one of the predominant clinical features associated with SCA.[8] The study was conducted to analyze clinical symptoms and hematological profile of sickle cell disorder patients.

Materials and Methods
After taking permission from Institutional Ethical Committee, record based cross sectional study of diagnosed patients of sickle cell disorder was conducted in Department of Pathology of NKPSIMS Nagpur from Consecutive records of 5 months from 01/01/2017 to 31/05/2017. Confidentiality of participants was maintained. Out of 112 patients of sickle cell disorder, 110 patients were included in this study and 2 patients were excluded because of one patient was on hydroxyurea medication and the other had received blood transfusion 7 days earlier. The cases were selected by using Non-Probability (convenient) sampling technique.

Blood sample was collected in EDTA test tube and hematological indices HB%, HCT, PLATELET, MCV, MCH, RDW, MPV were measured by C.B. counter machine (Horiba ABX, MICROS 60) along with blood smear examination and confirmed by sickling method and electrophoresis test. Sickling test was done by slide method test and electrophoresis test done by using cellulose acetate strip at alkaline Ph to differentiate and confirmation of sickle cell disease and sickle cell trait.

Sampling Method:
Inclusion Criteria: All diagnosed patients of sickle cell disorder.
Exclusion Criteria:

1. Patient on hydroxyurea medication.
2. Patient received blood transfusion recently within 3 months.

The data was entered into an MS Excel spreadsheet and imported into Epi-Info software for statistical analysis was done by calculating frequencies and proportions for qualitative variables and mean were calculated for quantitative variables.

Results

In our study, total 110 cases were diagnosed as sickle cell disorder. Among them 97 (88.18%) were heterozygous (Sickle cell trait, AS) and 13 (11.81%) were homozygous (Sickle cell disease, SS). Females (93 cases, 84.54%) were more affected than males (17 cases, 15.45%). Most of the cases were in the age group from 11 to 30 years. Screening of females during antenatal period and screening of girls in school camps, might be the reason for present findings. (Table 1 and 2)

Table 1: Age wise distribution of sickle cell disorder patients

Age in yrs	AS n=97		SS n=13		Total (%) n=110
	Male	Female	Male	Female	
0-10	3	3	0	1	7 (6.36)
11-20	2	34	0	3	39 (35.45)
21-30	5	35	1	3	44 (40)
31-40	2	3	0	3	8 (7.27)
41-50	1	7	1	1	10 (9.09)
51 and above	1	1	0	0	2 (1.8)
Total	14	83	2	11	110 (100)

Table 2: Sex wise distribution of sickle cell disorder patients

Gender	SS type (%) n=13	AS type (%) n=97	Total (%) n=110
Male	2 (15.38)	14(14.43)	16 (14.54).
Female	11 (84.61)	83(85.56)	94 (85.54)
Total	13(100)	97(100)	110(100)

SS-Sickle cell disease (Homozygous), AS-Sickle cell trait (Heterozygous)

Hematological profile showed decreased value of mean Hb%. Mean Hb% value for sickle cell trait was 10.2 gm/dl and for sickle cell disease patient was 7.72 gm/dl. In this study values of HCT, total RBC count, MCH, MCHC were decreased with normal MCV, MPV and platelets count. Value of RDW was high due to variation in red blood cell size. (Table3)

Table 3: Hematological profiles of Sickle cell disorder patients

S. No.	Parameters	Normal Reference Range	Mean value (AS+SS)	Mean value	
				AS	SS
1	Hb (gm/dl)	Male: 13-18 Female: 11.5-16.5	9.87	10.2	7.72
2	HCT (%)	35-47	31.106	32	24.33
3	RBC (millions/cmm)	M : 4.74 -5.49 F: 4.14-4.79	4.105	4.24	3.10
4	PLATELET (lacs/cmm)	1.5-4.0	3.02	3.05	2.82
5	MCV (fL)	75-100	76.90	76.9	76.92
6	MCHC (%)	31-38	24.25	31.48	30.94
7	MCH (pgm)	25-35	24.30	24.2	24.87
8	RDW (%)	11-5-16.5	18.6	18.6	18.85
9	MPV (fL)	6.5-11.0	8.09	8.07	8.28

Among 13 patients of sickle cell disease, peripheral smear showed anisocytosis (90.32%) and poikilocytosis (90.32%), hypochromic cells (90.32 %). Among 97 patients of sickle cell trait, peripheral smear showed anisocytosis (55.67%) and poikilocytosis (55.67 %), hypochromic cells (71.39%). (Table 4)

Table 4: Peripheral smear examination of sickle cell disorder patients

S. No.	Parameters	Sickle cell disorder (AS+SS) n=110		AS (n=97)		SS (n=13)	
		Cases	Percentage	Cases	Percentage	Cases	Percentage
1	Normocytic	36	32.72	35	36.08	1	7.69
2	Normochromic	29	26.36	28	28.86	1	7.69
3	Hypochromic	81	74.54	69	71.13	12	90.32

4	Anisocytosis	66	60	54	55.67	12	90.32
5	Poikilocytosis	66	60	54	55.67	12	90.32

Among 13 patients of sickle cell disease, main complaints were weakness and fatiguability in 11 patients (84.61%), recurrent fever with bone pain in 6 patients (46.15%), recurrent periodic abdominal pain in 4 patients (30.76%). Recurrent jaundice, breathlessness, recurrent fever with cough and pleuritic chest pain were observed in 1 patient each. One patient of one day old newborn baby had difficulty to suck breast milk. One patient was hospitalized 4-5 times in tertiary care hospital during vasooclusive crises. Among 97 patients of sickle cell trait (AS), main complaints were weakness and fatiguability in 44 patients (45.36%), painful and swollen disease in 8 patients (8.24%). Other observed symptoms were recurrent abdominal pain in 6 patients (6.18%), recurrent fever with cough and pleuritic chest pain in 3 patients (3.09%), breathlessness in 3 patients (3.09%), having headache in 2 patients (2.06%). (Table 5)

Table 5: Clinical manifestations of sickle cell disorder patients

Symptoms	**AS (%) n=97**	**SS (%) n=13**	**Total (%) n=110**
Weakness and fatigue	44 (45.36)	11 (84.61)	54 (49.09)
Recurrent fever with cough, plueritic chest pain	3 (3.09)	1 (7.69)	4 (3.63)
Recurrent fever with bone pain	1 (1.03)	6 (46.15)	7 (6.36)
Breathlessness	3 (3.09)	1 (7.69)	4 (3.63)
Painful, swollen digits of hands and feet	8 (8.24)	1 (7.69)	9 (8.18)
Recurrent jaundice	0	1 (7.69)	1 (0.9)
Recurrent, periodic abdominal pain	6 (6.18)	4 (30.76)	10 (9.09)
Headache	2 (2.06)	0	2 (1.8)
Feeding problem (inability to suck)	0	1 (7.69)	1 (0.9)
Recurrent hospitalization	0	1(7.69)	1 (0.9)

Discussion

In our study 97 cases (88.18%) were diagnosed as sickle cell trait (AS) and 13 cases (11.81%) were diagnosed as sickle cell anemia (SS) by electrophoresis test. Cases of sickle cell trait (AS pattern) were more than trait (SS pattern). Deshmukh PR at al. (2006),[9] found more cases of sickle cell trait (AS pattern) than sickle cell disease (SS pattern).In their study out of total samples found positive on solubility test, 94.4% were having HbAS pattern while 5.6% had HbSS pattern. Deore at al. (2014),[10] found more cases of sickle cell trait than sickle cell disease. In their study 46 cases (82.60%) were diagnosed as sickle cell trait and 37 cases (21.51%) were diagnosed as sickle cell disease.[10] These findings are nearly similar to present study.

Chavda J.at. (2015),[11] found 30 cases (66.66%) of sickle cell disease (SS pattern) and 15 cases (33.33%) were sickle cell trait (AS pattern) by electrophoresis. Cases of sickle cell disease were found more than sickle cell trait. Study conducted by Kamble M et al. (2000),[12] reported 61.6% cases of Hb SS and 38.4% cases of Hb AS.[12] These studies are contradictory to present study. In present study proportion of females was more than males due to screening of females during antenatal period. Screening of females in girls school might be the another reason. In most of the studies proportion of males was more as compared to females. Deore at al. (2014),[10] reported out of 46 cases of sickle cell disorder, males were 27 and females were 19. In study conducted by Chavda J.at al. (2015),[11] total 45 cases were diagnosed as sickle cell disorder, males were more commonly affected than female with male: female ratio 2:1. In studies conducted by Shrikhande et al. (2007),[6] Mandot et al. (2016)[4] found proportions of males more than females.

Mean Hb% value was 9.87 gm/dl that was nearby to other study which was 8.6gm/dl.[11, 6] Values of HCT, total RBC count, MCH, MCHC were found to be low in present study which are comparable to other studies.[11,13,14] Mean RDW value was found to be high i.e.18.85 %. Study conducted by Roberts GT et al. (1985)[15] found elevated mean RDW values in anemic patients, with the highest value seen in sickle cell anemia, sickle cell thalassemia, sickle cell trait, thalassemia trait, and iron deficiency anemia in decreasing order of magnitude. It was found that the RDW was proportional to the reticulocyte count, with the highest values in the patients with the highest reticulocyte count (sickle cell anemia). One clinical value of the RDW therefore may lie in its capacity for reflecting active erythropoiesis. This is similar to present study.

On Peripheral smear anisocytosis, poikilocytosis, hypochromic cells were commonly seen in both sickle cell trait and sickle cell disease. Study conducted by Silvestroni E et al.(1952)[16] found anisocytosis, poikilocytosis, hypochromic, normocytic, target cells on peripheral smear in sickle cell disorder patients. This finding is nearly similar to present study. In present study weakness, fatigability, pain, fever were more common in both sickle cell disease and sickle cell trait patients. The majority of cases had mild to moderate anemia. Study conducted by Mandot at al. (2016)[4] reported pain, fatigability, fever and anemia. This findings nearly similar to present study.

Conclusion

This study showed that hematological profile of sickle cell disorder patients has low value of Hb%, HCT, total RBC count, MCH, MCHC with normal MCV, MPV and platelets count and high RDW. Peripheral smear showed predominantly hypochromic and anisopoikilocytosis cells. Symptoms like weakness and fatigability were mostly seen in sickle cell disease patients, same symptoms were also commonly seen in sickle cell trait patients. Some patients of sickle cell trait had also same clinical features of sickle cell disease along with anemia. So patients having weakness and fatigability, recurrent fever with cough, breathlessness, bone pain, painful, swollen digits of hands and feet, periodic abdominal pain, jaundice along with low values of Hb%, HCT, total RBC count, MCH, MCHC and high value of RDW in presence of anisopoikilocytosis, hypochromic cells on peripheral smear strongly suspect sickle cell disorder.

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