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CORRELATION OF CLINICAL AND HEMATOLOGICAL PROFILE IN HOSPITALISED CASES OF SICKLE CELL DISEASE

General Medicine

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ABSTRACT

Introduction: The Sickle cell diseases (SCD), a group of autosomal recessive disorders characterized by chronic anaemia with a Hb concentration of around 8 g/dl. Almost 5-50% of sickle cells are irreversibly sickled cells (ISC). Pain crisis is a predictor of early mortality6. It is now known to be widespread among people of the Deccan plateau of central India. In Maharashtra sickle cell gene in widely spread in all districts of Vidarbha region, North Maharashtra. This study was under taken to analyse sickle cell disease patients for their clinical presentation, haematological details, need for blood transfusion and correlation of clinical profile with haematological profile. **Material and Methods:** The present observational cross-sectional study was carried out in the hospital settings of Department of General Medicine in Tertiary Care Centre & Government Medical College between Jan 2020 to Oct 2021. 50 hospitalized cases of sickle cell disease (homozygous/heterozygous) of age > 12 years, who admitted in wards and MICU were included. Complete clinical and hematological profile was taken. 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. All the data were tabulated, and then analyzed with appropriate statistical tools SPSS 27th version. **Results:** Most common sickle cell pattern in hospitalized patients was SS pattern (86%) in comparison to AS pattern (14%). Males were (60%). Most common age group was 12-20 years (44%). Mean age for SS pattern was 22.74±07.11 and for AS pattern, 34.71±10.87 years. Most common clinical feature was weakness presented by 100% patients in both groups. Hb concentration, hematocrit, RBCs, and MCV were lower in SCD (SS pattern) patients($p<0.01$). Mean Hb concentration, Hematocrit and platelet count were low in patients presenting with limb pain and weakness ($p<0.01$). One way ANOVA was used as statistical analysis and it was found that correlation for clinical manifestations with hematological profile was statistically significant in all comparisons with p-value <0.05. Mean Hb concentration, RBC, WBC, MCV, and Hematocrit were lower in hospitalized cases of sickle cell disease (SS pattern) ($p<0.01$). Most common duration of hospital stay was 0-3 days, 26 patients (52%) (SS 48.83% and AS 71.42%). Mean Hb, hematocrit, and MCV were lower in patients with prolonged hospital stay(>10days). who needed blood transfusion and who died. Most common presentation was VOC (vaso-occlusive crisis) seen in 30 cases (60%) all were SS pattern patients. **Conclusion:** Most common sickle cell pattern in hospitalized cases was SS pattern. Males were more commonly hospitalized. Most common age group was 12-20 years. Most common presentation was VOC Low levels of Hb concentration, hematocrit and platelets were associated with limb pains and weakness, need of blood transfusion, prolonged hospital stay, and poor outcome. Regular health check-ups and monitoring of hematological profile may help to guide the clinician to prevent vaso-occlusive crisis and further complications.

KEYWORDS

Sickle cell diseases, hematological profile, AS and SS pattern Vaso-occlusive crisis

INTRODUCTION:

The Sickle cell diseases (SCD), a group of autosomal recessive disorders is caused by point mutation at the 6th position in β globulin chain of hemoglobin, substituting valine for glutamic acid resulting in formation of hemoglobin S (HbS). Such haemoglobinopathies, mainly thalassemia and sickle-cell anaemia, are globally widespread[1]. About 5% of the world's population carries genes responsible for haemoglobinopathies. Each year about 300,000 infants are born with major haemoglobin disorders – including more than 200,000 cases of sickle-cell anaemia in Africa[2].

First described in the Nilgiri Hills of northern Tamil Nadu in 1952[3], the sickle cell gene is now known to be widespread among people of the Deccan plateau of central India with a smaller focus in the north of Kerala and Tamil Nadu[4]. In Maharashtra sickle cell gene in widely spread in all districts of Vidarbha region, North Maharashtra (Satpuda ranges) and some part of Marathwada region.

Most affected people of sickle-cell anaemia have chronic anaemia with a Hb concentration of around 8 g/dl. The main problems arise from the tendency of the red blood cells to become sickle-shaped and block capillaries at low oxygen tension, which often become trapped in the spleen, leading to a serious risk of death and a sudden profound anaemia associated with rapid splenic enlargement or because lack of splenic function permits an overwhelming infection. Some patients have such severe problems that they need regular blood transfusion and iron-chelation therapy[5].

Almost 5-50% of sickle cells are irreversibly sickled cells (ISC). Its characteristics are a low MCV, high MCHC and low HbF. Pain crisis is a predictor of early mortality[6]. Despite the high prevalence of SCD in the tribal population of Vidarbha region of Maharashtra, very few studies were carried out in adult SCD patients. There is need to find most suitable and practically feasible parameters that could predict clinical disease severity and aid in early therapy. Thus, this study was under taken to analyse sickle cell disease patients for their clinical presentation, haematological details, need for blood transfusion and correlation of clinical profile with haematological profile.

MATERIAL AND METHODS:

The present observational cross sectional study had been carried out in the hospital settings of Department of General Medicine in Tertiary Care Centre & Government Medical College between Jan 2020 to Oct 2021. 50 hospitalized cases of sickle cell disease (homozygous/heterozygous) of age > 12 years, who admitted in wards and MICU were included.

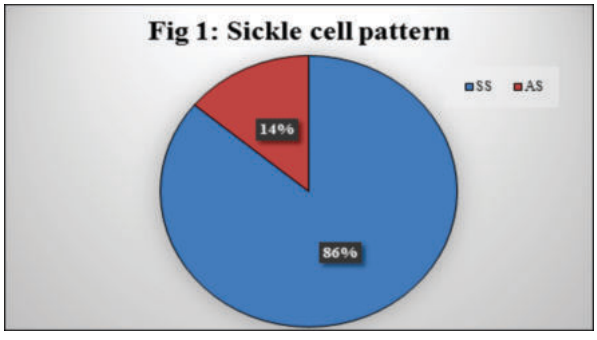
After taking written informed consent, a detailed history and clinical examination of enrolled cases was done as per the pre-structured case proforma. Baseline hematological investigations were done at the time of admission and on discharge. Complete clinical and hematological profile was taken. Hematological indices HB%, HCT, PLATELET, MCV, MCH, MCHC, RBC, WBC were measured by C.B. counter machine (Horiba ABX, MICROS 60) 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. Written informed consent was obtained from patient relatives and/or patient of all study participants.

All the data were tabulated, and then analyzed with appropriate statistical tools SPSS 27th version. Data were presented as mean with standard deviation or proportions as appropriate. Student's T-test was used as the statistical tool to test for significance of observed mean differences. A p-value was considered to be significant if <0.05. Ethical committee approval was obtained from ethics committee. The confidentiality of the participants was ensured.

RESULTS:

Present study revealed that most common sickle cell pattern among hospitalized cases was SS, 43 (86%) and AS 07(14%). (Fig 1) Based on gender distribution, males were 30(60%) [SS-25(58.14%) & AS-05(71.43%)] and females were 20(40%) i.e. [SS-18(41.86%) & AS-02(28.57%)] respectively. Most common age group was 12-20 years, 24(48%) [SS-22(51.16%) & AS-02(28.57%)] followed by 21-30 years, 15(30%) i.e.[SS-15(34.88%) & AS-00(00.00%)] respectively. Results were not significant. For SS, mean age was 22.74±07.11 years, for AS, 34.71±10.87 years. Results were statistically significant (p-value<0.001).



Clinical manifestations:

Most common clinical symptom were weakness presented by 100% patients in both groups, followed by limb pain and cough i.e. 72.09% and 55.81% for SS group. For AS group weakness (100%) followed by cough (57.14%) and fever (42.85%) were most common presentations. (Fig 2)

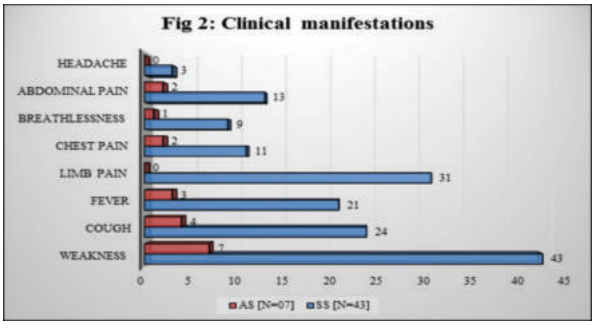


Table 1: Hematological profiles and sickle cell pattern:

Hematological Profile	SS [N=43]	AS [N=07]	t-value	p-value
Hb (gm/dl)	06.68±03.09	07.64±02.31	2.984	0.002S
HCT (%)	21.20±03.75	26.34±06.42	4.109	<0.001HS
RBC*	2.87±01.28	03.24±01.11	3.06	0.042S
TLC	6841.20±2932.30	14158.40±7559.80	3.012	0.045S
Platelets#	02.10±00.35	00.67±00.14	0.510	0.114NS
MCH	26.36±07.15	25.17±05.51	0.593	0.556NS
MCV	80.35±18.56	82.99±21.41	3.734	<0.001HS
MCHC	32.74±05.98	31.88±06.57	0.418	0.678NS

RBCs shows in units millions/cumm and Platelets in lacs/cumm

As per the table 1, mean values of Hb, HCT, RBC and MCV were significantly high in AS group compared to SS group. Difference in mean values of TLC, Platelets, MCH and MCHC were not significant between two groups.

Table 2: Correlation of clinical manifestation with hematological profile:

Clinical Manifestation	Hb	HCT	RBC	TLC	PC	MCH	MCV	MCHC	p-value
Weakness	9.86±1.21	31.24±2.22	2.95±1.12	7125.30±1589.20	3.25±1.10	24.32±4.32	76.98±7.80	31.47±4.68	0.001S
Cough	8.62±2.10	30.41±4.65	2.66±1.24	7265.41±1642.61	2.10±0.78	23.12±24.65	72.32±8.50	30.21±5.61	0.001S
Fever	8.21±2.41	30.25±6.55	2.59±1.34	6534.90±1647.30	2.54±0.87	21.39±5.21	77.65±6.58	29.65±6.40	0.031S
Limb pain	7.25±2.71	29.40±6.80	2.11±1.56	6564.10±1457.10	1.90±0.61	20.14±4.38	74.30±6.34	29.87±5.70	0.014S
Chest pain	7.65±1.24	29.65±5.10	2.47±1.45	6934.97±1587.62	2.98±0.91	23.41±3.54	75.65±6.54	32.35±5.40	0.0041S
Breathlessness	6.21±2.31	29.41±3.21	2.44±1.65	7435.68±1478.90	3.24±1.07	25.32±4.65	72.35±6.40	33.56±6.23	0.001S
Abdominal pain	7.45±3.44	31.24±3.21	2.57±1.88	7126.30±1258.10	1.45±0.56	21.34±4.30	70.35±6.52	35.14±5.41	0.001S
Headache	6.24±2.11	33.54±6.41	2.77±1.89	8734.69±1348.70	1.98±0.87	20.35±3.59	76.35±6.24	34.11±3.24	0.001S

Correlation of clinical manifestation with mean values of hematological profile with standard deviation is shown in table 2. One way ANOVA was used as statistical analysis and it was found that correlation for clinical manifestations with hematological profile was statistically significant in all comparisons, with p-value <0.05.

Hospital stays of studied cases: Based on hospital stay most common was 0-3 days 26(52%) i.e. SS (21, 48.83%) & AS(05, 71.42%) followed by 3-10 days 18(36%) i.e. SS(16, 37.20%) & AS(02, 28.58%) respectively.

Table 3. Correlation of Mean Hematological profile with hospital stay of studied cases

Hematological Profile	0-3 days	3-10 days	>10 days	p-value
Hb (gm/dl)	10.32±03.41	09.62±03.91	08.11±02.41	0.009S
HCT (%)	31.78±03.90	30.18±03.30	22.10±05.40	<0.001HS
RBC*	4.41±01.22	4.31±01.02	03.21±01.24	0.042S
TLC	11158.30±5559.10	10158.30±5059.10	5841.20±1032.30	0.023S
Platelets#	01.55±00.59	01.05±00.39	02.42±00.36	<0.001HS
MCH	20.74±03.65	19.41±03.32	24.30±03.61	<0.001HS
MCV	78.87±05.62	74.36±04.62	73.30±02.61	<0.001HS
MCHC	23.58±02.38	24.65±03.65	25.11±02.57	<0.001HS

RBCs shows in units millions/cumm and Platelets in lacs/cumm

As per table 3, mean Hb, mean HCT, mean RBC, mean TLC and mean MCV were decreased over period of hospital stay and one way ANOVA shows that the correlation was statistically significant. Mean Platelets, mean MCH and mean MCHC improved over duration of hospital stay and one way ANOVA shows that the correlation was statistically significant.

Blood transfusion given to studied cases:

Most cases were not given blood transfusion i.e. 39(78%) and only 22% cases received blood transfusion i.e. SS- 11(25.58%) & AS-00(00%) respectively.

As per table 4, mean Hb, mean HCT, mean RBC, mean TLC and mean MCV were significantly high in patient who didn't require blood transfusion and the difference was statistically significant. Mean Platelets, mean MCH and mean MCHC were low high in patient who

required blood transfusion but lacks statistical significance.

Table 4: Correlation of hematological profile with need for blood transfusion:

Hematological Profiles	Blood transfusion	No Blood transfusion	t-value	p-value
Hb (gm/dl)	06.27±01.98	11.32±03.61	3.003	0.007S
HCT (%)	22.04±05.78	32.78±03.60	6.609	<0.001HS
RBC*	03.60±01.71	4.30±01.02	2.68	0.018S
TLC	4841.20±1932.30	10148.30±4569.10	2.748	0.025S
Platelets#	02.36±00.76	01.15±00.49	0.987	0.550NS
MCH	23.27±03.59	21.44±03.05	0.473	0.667NS
MCV	74.09±02.01	78.87±05.62	4.054	<0.001HS
MCHC	25.18±02.17	23.08±02.18	0.689	0.547NS

RBCs shows in units millions/cumm and Platelets in lacs/cumm

Diagnosis of SCD cases:
Most common diagnosis was VOC (vaso-occlusive crisis) 30 (60%) i.e. SS 30 (60%) followed by anemia 28 (56%) i.e. [SS- 25 (50%) & AS- 03 (06%)] respectively.

Outcome:
Based on outcome only two cases died i.e. 4%, rest were survived.

Table 5 shows that mean values of Hb, HCT, RBC, TLC and MCV were significantly high in patient who survived and the difference was also statistically significant. Mean MCH was also high in patient who survived but lacks statistical significance. Mean Platelets, and mean MCHC were low high in patient who survived but difference was not significant.

Table 5: Correlation of hematological profile with outcome

Hematological Profiles	Survived	Death	t-value	p-value
Hb(gm/dl)	10.45±03.67	06.08±01.41	2.014	0.004S
HCT(%)	31.08±04.02	22.47±05.28	4.870	<0.001HS
RBC*	4.12±01.23	03.27±01.61	2.987	0.012S
TLC	11108.30±3569.29	4041.20±1232.28	2.562	0.004S
Platelets#	01.35±00.29	02.06±00.47	0.789	0.589NS
MCH	22.40±03.25	21.27±03.08	0.771	0.889NS
MCV	76.17±05.08	74.47±02.17	5.147	<0.001HS
MCHC	24.18±02.09	25.89±02.69	0.358	0.578NS

RBCs shows in units millions/cumm and Platelets in lacs/cumm

DISCUSSION:
A correlational study of clinical and hematological profile of hospitalized cases of SCD carried out from Jan 2020 to Oct 2021 on 50 hospitalized cases at Department of General Medicine of Tertiary Care Centre & government medical college.

Sickle cell pattern:
In present study, most common sickle cell pattern was SS i.e. 43 (86%) in comparison to AS i.e. 07 (14%). Similar to present study, in Brahme K et al[7] study, out of total 41 patients 34 had Sickle cell anemia, 4 had Sickle β – Thalassemia and 4 were Sickle cell trait. In contrast to present study, Gaikwad V et al[8] study most common sickle cell pattern was AS i.e. 97 (88.18%) in comparison to SS i.e. 13 (11.82%) and Jadhav A et al[9] study, total of 122 subjects in the age group 18-40 participated in the study, which included 36 diagnosed sickle cell disease patients (SS), and 43 were sickle cell carriers (AS).

Age and Gender distribution:
In present study, males were 30 (60%). Male to female ratio was 1.5:1. Patel KG et al[10] study reported out of which 47 were homozygous sickle cell disease and 14 heterozygous sickle cell trait patients. Total male patients were 39(63.93%) and female 22(36.06%). Male to female ratio was 1.7:1. Based on age distribution with respect to sickle cell pattern, most common age group was 12-20 years 24 (48%) i.e. [SS- 22 (51.16%) & AS- 02 (28.57%)]. 12-20 years was the most common age group in our study. This could be due to repeated infections in this age, nutritional deficiencies and increased nutritional requirement in the growing age in addition to chronic hemolytic process and frequent crisis in this period. Gaikwad V et al[8] study found that 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. Patel KG et al[10] found, morbidity events were commonly observed in 21-40 years of age groups (68.85%). Seasonal variation also observed. Rao SS et al[11] and Shah V et al[12] revealed similar findings to our study with mean age 29.6±3.2 and 30.32 ± 3.79 years respectively.

Clinical manifestations:
Most common clinical features in present study were weakness presented by 100% patients in both groups, followed by limb pain and cough i.e. 72.09% and 55.81% for SS group. For AS group weakness (100%) followed by cough (57.14%) and fever (42.85%) were most common presentations. Very close to present study, Shah V et al[12] study found that common clinical features with which the SCD patients presented to hospital were - 76(23.6%) with Vasoocclusive Crisis (VOC) 64(36.99%) with generalized bodyache and joint pain, 41(23.69%) with febrile illness and 36(20.80%) with clinically detectable jaundice. In a study by Chandra et al[13], 55 patients of sickle cell disease were prospectively studied and in their cohort of patients, symptoms at presentation included pain (80%), jaundice (85%) and anemia (60%). In another study from south India (Karnataka), Meera et al[14] studied 60 patients of sickle cell disease, anemia was most common symptom (83.3%) followed by bone pains (60%).

Hematological profiles:
We found lower levels of Hb concentration, RBC, WBC, MCV, and hematocrit in patients with SS group. Increased rate of hemolysis during oxygenation and deoxygenation process associated with recurrent infections in sickle cell anemic patients could account for these decreased values. Nutritional deficiencies because of low socio-economic status, increased nutritional demands in adolescents can also contribute to this. Sickle cell patterns shows significant correlation with most hematological parameters i.e. Hb, RBC, WBC, MCV, and hematocrit. Similarly, Jadhav A et al[9] study reported Hb concentration, RBC count and PCV was significantly low (P<0.05) while the MCV was significantly high (P<0.05) and MCHC was significantly low (P<0.05) in SCD patients. Shah V et al[12] study reported 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%. Kaur M. et al[15] study & Rao SS et al[11] study also show comparable results with present study.

Correlation of clinical manifestation and hematological profile:
All clinical features in correlation with hematological profile show significant results. Increased rate of hemolysis during oxygenation and deoxygenation process associated with recurrent infections which may account for these decreased values. There could also a blunted response to erythropoietin secretion in sickle cell anemia. Jadhav A et al[9] study explains results on the hematological profile most probably appears due to lack of balanced nutritional dietary intake or due to poverty and/or blood loss in females during menstruation or repeated abortions could be other possible reasons responsible for low haemoglobin concentration, RBC count and PCV in sickle cell carrier females. Patel KG et al[10] found Hemoglobin, MCH and MCHC were low in their study and also comparable to other studies. Normally sickle cell disease patients are at a critically balanced state of Vit B-12 and folic acid so slight increase in demand due to increase need for erythropoiesis because of chronic hemolysis or haematuria can precipitate deficiency state. However, MCV was low in our study similar to some other studies from different parts of our country. Low MCV in these studies may be due to co-existing iron deficiency anemia. Behera SK et al[16] study also explains average Hb was low in both cases and it was significantly much lower in homozygous cases than heterozygous cases. This may be explained by hemolysis, blood loss, hematuria, repeated infections and nutritional deficiency, which are more in homozygous cases. Female were more anemic (low Hb value) than male in both cases. However, the findings were not significant.

Hematological profile and need for blood transfusion:
Hematological parameters (Hb, RBC, WBC, MCV, and hematocrit) correlated with need for blood transfusion. In present study, most cases were not given blood transfusion (78%) and only 22% cases received blood transfusion i.e. SS (25.58%) and none from AS. In a study from Tamil Nadu, Roshan R et al[17], 167 patients (72.6%) had past history of

blood transfusion at the time of diagnosis. This is higher as compared to study by Chandra et al[13] (52% versus 72%), while in a study of pediatric patients with SCD by Jain et al[18], 85% of patients received blood transfusion. The difference of blood transfusion practices is variable in our country and there are no specific guidelines for blood transfusion in sickle cell disease, which can account for the difference in frequency of blood transfusion in different studies.

Hospital stays of studied cases:

Based on hospital stay in present study, most common was 0-3 days (52%) i.e. SS (48.83%) & AS (71.42%). Belala A et al[19] study found that homozygous cases consumed 49% of these hospital days, heterozygous 18%.

CONCLUSION:

Present study revealed that most common sickle cell pattern in hospitalized cases was SS pattern. Males were more commonly hospitalized. Most common age group was 12-20 years. Predominant symptom was weakness in all patients in both groups, followed by limb pain and cough. Most common presentation was VOC followed by anemia. Low levels of Hb concentration, hematocrit and platelets were associated with limb pains and weakness. Most cases were not given blood transfusion. Low levels of Hb, RBC, WBC, MCV and hematocrit were associated with need of blood transfusion. Low levels of Hb concentration and MCV on admission were associated with prolonged hospital stay. Low levels of Hb concentration, MCV and hematocrit on admission were associated with poor outcome.

Thus, regular health check-ups and monitoring of hematological profile may help to guide the clinician to prevent vaso-occlusive crisis and further complications. The data so obtained would help in the management, prevention and control programme for SCD patients at the primary health centers in India.

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