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Comparison of adverse prognostic haematological parameters in sickle cell anaemia patients with splenomegaly and without splenomegaly

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Abstract:
Aim: *To compare the adverse prognostic haematological parameters in patients of sickle cell anaemia with and without splenomegaly.*
Material and methods: *This prospective, cross sectional study was conducted in Jawaharlal Nehru Medical College, AcharyaVinobha Bhave Rural Hospital (A.V.B.R.H), a 1200 bedded tertiary teaching hospital of Datta Meghe Institute of Medical Sciences University. Fifty cases of diagnosed SCA patients were included in the study. After Physical examination and ultrasound examination the cases were divided as SCA patients with splenomegaly and without splenomegaly. Adverse haematological parameters like haemoglobin (Hb%), platelet counts, serum lactate dehydrogenase (LDH), neutrophil counts were estimated and compared between the groups.*
Results: *Fifty cases of sickle cell anemia were studied. Out of the cases 20 (40%) had splenomegaly and 30 (60%) did not have splenomegaly. All the adverse hematologic parameters existed in significant percentage in both the groups. These parameters did not have any statistical significance when compared in both the groups separately.*
Conclusion: *This study concluded that SCD with splenomegaly posses complications related to the spleen proper. As per the natural history is concerned autosplenectomy is usually the rule. But as far as the adverse hematologic parameters are concerned , presence or absence of splenomegaly doesn't dictate their occurrence.*
Key words: *Sickle cell disease, splenomegaly, autosplenectomy, LDH*

I. Introduction:

Herrick (1861–1954) in 1904 first described sickle red blood cells. [1] The term sickle cell anemia was coined by Mason in 1922. [2] Later it was demonstrated by Pauling and his that sickle-cell anemia (SCA) occurs as a result of an abnormality in the hemoglobin molecule. [3] In SCA , in the beta 6th position of globin chain aminoacid glutamic acid is replaced by valine. results from a single change of one amino acid, valine leading to polymerization of the hemoglobin when the oxygen saturation is lowered, resulting in deformity of the red blood cells and microvascular occlusion. [4,5] This as well as its subsequent effects including cellular dehydration, inflammatory response, and reperfusion injury which are important pathophysiological mechanisms leads to the different manifestations of SCA.

The main cause of sickle cell-associated morbidity and mortality is microvascular occlusion. Direct adherence of sickle red blood cells (RBC) to the endothelial cell surface is the main pathology which in turn results in delayed passage with concomitant enhancement of RBC sickling, ultimately leading to tissue hypoxia and infarction. Clinically this process manifests as painful vasoocclusive episodes, and damage to multiple organ systems causing morbidity and mortality.

During infancy and early childhood, the spleen commonly enlarges in patients with sickle cell anaemia (SCA), and it thereafter undergoes progressive atrophy due to repeated episodes of vaso-occlusion and infarction, leading to autosplenectomy in adult life. Splenic complications amongst others are common as a consequence of progressive injury resulting from repeated sickling of red blood cells. In early life, splenomegaly has been known to be common. In later years, however, "autosplenectomy" commonly occurs, because of recurrent infarctions. The spleen becomes firm, smaller and nodular with depressed scars and finally reduced into a small wrinkled remnant often buried in adhesions. However, is not the case always and sometimes splenomegaly persists into an older age group or even into adulthood necessitating splenectomy for a variety of reasons including acute splenic sequestration crisis, hypersplenism, massive splenic infarction and splenic abscess. [6–10] Splenic complications of SCA are associated with an increased morbidity and in some it may lead to mortality.

Another school of thought suggests that the presence of a palpable spleen in a patient with sickle cell disease after age five suggests a coexisting hemoglobinopathy, e.g., thalassemia, hemoglobin C or sickle-HbE . Patients with sickle thalassemia and sickle-HbE tend to have similar, slightly milder, symptoms, perhaps because of the ameliorating effects of production of other hemoglobins within the RBC .

Hematologic adverse parameters that determine poor prognosis in SCD are increased platelet counts. Platelet activation is another known component of hemostatic activation in patients with SCD. Increased percentages of platelets are activated during steady state in patients with SCD, and this accelerates during vaso-occlusive crisis (VOC)

Increased platelet activation is another known component of hemostatic activation in patients with SCD. Increased percentages of platelets are activated during steady state in patients with SCD, and this accelerates during vaso-occlusive crisis (VOC). [11-14]

Other factors associated with increased morbidity are, decrease haemoglobin levels, chronic neutrophilia, increased LDH levels. It will be interesting to study the adverse hematologic parameters in SCD patients with and without splenomegaly.[15-17]

So this study was done to compare the adverse hematologic parameters in cases of sickle cell anaemia with and without splenomegaly.

Aims: To compare the adverse prognostic haematological parameters in patients of sickle cell anaemia with and without splenomegaly.

Objectives:
1) To study the adverse haematological parameters among the patients with sickle cell disease patients who have undergone autosplenectomy.
2) To study the adverse haematological parameters among the patients with sickle cell disease patients who have palpable spleen or have ultrasound evidence of enlarged spleen.
3) To compare these adverse hematologic parameters between these two groups.

II. Materials and Methods:

Study setting: This prospective, cross sectional study was conducted in Jawaharlal Nehru Medical College, AcharyaVinobha Bhave Rural Hospital (A.V.B.R.H), a 1200 bedded tertiary teaching hospital of Datta Meghe Institute of Medical Sciences University. This hospital runs a sickle cell OPD every week. All diagnosed cases of Sickle cell anemia (Hb electrophoresis SS pattern) attend the OPD for periodic evaluation and getting free drugs (Folic acid, Hydroxyurea, hematinics).

Study duration: Study was conducted over a period of 2 months, January 2014 to March 2014, with due clearance of institutional ethical committee.
A total of 50 SCA patients were studied over this duration.

Inclusion Criteria:
All the patients diagnosed with sickle cell disease attending sickle cell OPD.

Exclusion Criteria:
Patients with infections
Patients on other drugs that can affect hematologic profile
Patients not willing to sign consent

Study Design:

Patients willing to participate and sign the inform consent were enrolled in the study. The demographics as well as other data like patient's medical history, surgical and other significant history were taken on case record form. The details of the painful crises were recorded in the form of onset, duration, type, frequency, severity and the episodes of painful crises. History of previous hospitalisations was recorded. Detailed clinical examination was done and positive findings were noted. Abdominal examination was done with special reference to palpation and percussion of spleen. Palpation will be done by classical method and percussion was done by Castle's method.

Ultrasonography of the abdomen was done to detect splenomegaly. This technique is the current procedure of choice for routine assessment of spleen size (normal = a maximum cephalocaudal diameter of 13 cm) because it has high sensitivity and specificity and is safe, noninvasive, quick, mobile, and less costly. Patients with cephalocaudal splenic diameter of more than 13 cm were taken as splenomegaly. [18]

All the patients with clinically detected enlarged spleen and USG detected splenomegaly formed one group. Patients without splenomegaly by both the methods formed the other group.

Haemoglobin estimation, peripheral smear particularly the RBC morphology, red cell indices consisting of MCV, MCH, and MCHC, total leucocyte count, differential leucocyte count absolute neutrophil count, Absolute platelet count and LDH will be done and these parameters will be compared in the two groups and analysed.

Statistical Analysis:
The data was analyzed by using descriptive and inferential statistics using Z-test and chi square test. The software used in the analysis were SPSS 20.0 and Graph Pad Prim 5.0 and $p<0.05$ is considered as level of significance.

Observations and results:

Table 1: Age wise distribution of patients

Age(yrs)	Splenomegaly		ℵ2-value	p-value
	Present	Absent		
1-5 yrs	9(45%)	0(0%)	24.19	0.000 S,p<0.05
6-14 yrs	9(45%)	9(30%)		
14-30 yrs	2(10%)	11(36.67%)		
>30 yrs	0(0%)	10(33.33%)		
Total	20(100%)	30(100%)		

Table 2: Gender wise distribution of patients

Gender	Splenomegaly		ℵ2-value	p-value
	Present	Absent		
Male	18(90%)	19(63.33%)	4.43	0.035 S,p<0.05
Female	2(10%)	11(36.67%)		
Total	20(100%)	30(100%)		

Table 3: Distribution of patients according to their symptoms

Presenting Symptoms	Splenomegaly		ℵ2-value	p-value
	Present	Absent		
Abdominal Pain	0(0%)	2(6.67%)	16.98	0.002 S,p<0.05
Fatigue	4(20%)	0(0.00%)		
Headache	0(0%)	2(6.67%)		
Joint pain/ chest pain/ weakness	2(10%)	15(50%)		
No	14(70%)	11(36.67%)		
Total	20(100%)	30(100%)		

Table 4: Correlation of haematological parameters in the patients with and without splenomegaly.

	Splenomegaly		t-value	p-value
	Present	Absent		
Hb%				
Mean	8.90	9.27	1.05	0.29 NS,p>0.05
SD	0.71	1.46		
TLC				
Normal	20(100%)	26(86.67%)	2.89	0.089 NS,p>0.05
High	0(0%)	4(13.33%)		
Low	0(0%)	0(0%)		
MCV				
Normal	20(100%)	25(83.33%)	3.70	0.05 NS,p>0.05
High	0(0%)	5(16.67%)		
Low	0(0%)	0(0%)		
MCH				
Normal	20(100%)	30(100%)	3.70	0.05 NS,p>0.05
High	0(0%)	0(0%)		
Low	0(0%)	0(0%)		
ANC				
Normal	4(20%)	3(10%)	0.99	0.31 NS,p>0.05
High	16(80%)	27(90%)		
Low	0(0%)	0(0%)		
PLT				
Normal	5(25%)	5(16.67%)	0.52	0.47

High	15(75%)	25(83.33%)		NS,p>0.05
Low	0(0%)	0(0%)		
LDH				
Normal	4(20%)	2(6.67%)	2.02	0.15 NS,p>0.05
High	16(80%)	28(93.33%)		
Low	0(0%)	0(0%)		

III. Discussion:

This study titled “Comparison of adverse prognostic haematological parameters in sickle cell anaemia patients with splenomegaly and without splenomegaly.” was carried out in ABVR hospital DMIMS University. Fifty cases of sickle cell anemia were studied. Out of the cases 20 (40%) had splenomegaly and 30 (60%) did not have splenomegaly. Ninty percent cases who had splenomegaly were below 15 years of age and as the age increased splenomegaly decreased. Seventy percent of cases above age 15 did not have splenomegaly. None of the patients above 30 years of age had splenomegaly.

Rajan Chopra et al; found that in the eastern Saudi Arabia, out of 44 patients, the reported splenomegaly occurrence in sickle cell disease patients ranges from 68.8% to 82.1%, with an autosplenectomy incidence of 6.6–15.5% ; and the frequency of HbSS (sickle cell

hemoglobin, homozygous) is 3.8% in this region. [19-20] Splenomegaly was more prevalent in male patients in our study (Table 2). In our study fatigue was the predominant complaint in patients with splenomegaly and fatigue, chest pain and joint pains were the predominant complaints in patients without splenomegaly.

As far as adverse hematologic parameters were concerned mean haemoglobin levels in both the groups were not statistically significant. In one study patients of SCD with splenomegaly had increased amount of haemoglobin and Hb F levels were more in these patients. [21]

Comparing the adverse haematological parameters, 43(86%) patients had neutrophlia while 7(14%) patients had normal absolute neutrophil count. Forty (80%) patients had elevated platelet count whereas 10(20%) patients had normal platelet count. Fortyfour (88%) patients had elevated lactate dehydrogenase whereas 6(12%) patients had normal LDH level, irrespective of splenomegaly absent or present. None of the adverse hematologic parameters had any statistically significant variation in the two groups in our study. But each individual parameters were higher in sickle cell anemia patients irrespective of the status of spleen, suggesting that adverse parameters exist as the natural pathophysiologic consequence of the disease and that is not related to persistence of spleen or autosplenectomy. Similar to our study one study in SCD patients in Nigeria also did not find any significant difference in SCD patients with or without splenomegaly. [22]

Freedman et al study [23] , eight adult patients with sickle cell anemia were followed over a 6-mo period. During this time all patients had elevated platelet counts, 1.7-fold (mean, 438,398 +/- 86,223), and megathrombocyte numbers, 2.3-fold (mean, 79,535 +/- 38,907), during asymptomatic periods. Akinbami et al [24]**,** study platelet counts were elevated in half of the SCD cases. In our study also the mean platelet counts were elevated in SCD though the elevation was same in both the groups.

Studies had also depicted the role of LDH in SCD. [25-26] Lactate dehydrogenase usually increases in SCD in vasoocclusive and due to bone marrow infarctions. Another study found out strong correlation of hemolysis, splenomegaly and LDH levels. Though the study emphasized that this occurred in a specific genetic deletion in SCD. In our study LDH was also elevated in SCD patients with and without splenomegaly without any significant difference.

IV. Conclusion:

We concluded that SCD with splenomegaly posses complications related to the spleen proper. As per the natural history is concerned autosplenectomy is usually the rule. But as far as the adverse hematologic parameters are concerned , presence or absence of splenomegaly doesn’t dictate their occurrence.

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