Clinical Profile of Patients of Sickle Cell Crisis in a Rural Tertiary Care Hospital

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ABSTRACT

BACKGROUND

Sickle cell disease (SCD) is a part of the spectrum of sickle cell syndromes which occurs due to a genetic mutation causing substitution of glutamic acid to valine at the 6th position of the β- globin chain. This can cause patients to present with a wide spectrum of crises including acute bone pain, pulmonary crises, vaso-occlusive crises, aplastic crises, and splenic crises. Central and western part of India harbours the majority of the sickle cell disease burden. Thus, this study was conducted to assess the clinical profile of patients with SCD who were admitted at a tertiary care hospital with sickle cell crisis.

METHODS

This was a cross-sectional study conducted in the Dept. of Medicine, and Central Clinical Laboratory, Acharya Vinoba Bhave Rural Hospital (AVBRH), Sawangi (Meghe), Wardha, for a period of 10 months from 1st January 2018 to 31st October 2018. Fifty sickle cell patients were selected as study population, the sample size was taken based on the convenience of the study, and a proforma detailing relevant clinical history was filled first, followed by collection of blood sample for assessment of laboratory parameters including haemoglobin levels, platelet counts, and S. LDH levels. Data was compared and contrasted between the Recovery group and the Mortality group.

RESULTS

Most common crises amongst patients encountered was vaso-occlusive crisis 23 out of 50 (60.5%) in recovery group versus 9 out of 50 (75%) in mortality group, and the most common trigger for it was dehydration. While no statistically significant differences were found between the Recovery group and Mortality group on comparison of age groups, gender, or caste of patients, serum haemoglobin levels were statistically lower ($p < 0.001$), and platelet and S. LDH (4302.41 ± 2560.34 U/L) versus (504.98 ± 223.82 U/L), were statistically higher ($p<0.001$) in the Mortality group compared to the Recovery group. Duration of stay in the hospital was also significantly higher ($p<0.001$) in the Mortality group compared to the Recovery group.

CONCLUSIONS

Thus, haemoglobin levels, platelet counts, and S. LDH appear to act as good prognostic markers to assess and follow-up in cases of sickle cell crises. Early detection and correction of these variables can ensure better patient outcomes in sickle cell disease.

KEY WORDS

Sickle Cell, Sickle Crises, Haemoglobin, Serum LDH

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BACKGROUND

Sickle cell disease is a part of the spectrum of sickle cell syndromes which occurs due to a genetic mutation causing substitution of glutamic acid to valine at the 6th position of the β- globin chain.[1] This mutation leads to the sickling of the biconcave RBCs. The sickle haemoglobin (HbS) polymerizes reversibly under deoxygenated conditions increasing stiffness and viscosity, decreases pliability to traverse small vessels, forms abnormal sticky membranes adherent to endothelium of small venules, a culmination of all these processes results in microvascular mainly venocclusion (VOC) and haemolytic anaemia leading to crisis and the varied clinical features of SCD.[2] With the current knowledge of the clinical heterogeneity of sickle cell haemoglobinopathies, the quintessential representation of any patient with SCD in crisis both clinically and in the form of laboratory investigation can be summarized as the following characteristic crises. Painful crises exhibit ischemia, pain, tenderness, fever, hand and foot syndrome, priapism, and chronic leg ulcers due to added superinfection. Acute Chest syndrome tends to present as chest pain, tachypnoea, fever, cough, decreased oxygen saturation. Widespread renal papillary necrosis presents as renal failure a late common cause of death, bone and joint ischaemia presenting as avascular necrosis of femur etc.[3,4] Recent studies have shown that patients with the lowest RBC deformability have enhanced haemolysis and would be more prone to develop several complications such as priapism, leg ulcers and glomerulopathy. In contrast, patients with the highest deformability, and not under hydroxyurea therapy, seem to develop more frequently vaso-occlusive like events.[5] Although less studied, RBC aggregation properties are very different between SCA and healthy individuals and it was demonstrated that increased RBC aggregates strength could be involved in some complications. Finally, several studies have established that the vascular system of SCA patients could not fully compensate any increase in blood viscosity because of the loss of vascular reactivity, which may result in vaso-occlusive crises.[6] Laboratory findings in sickle cell disease commonly involves haemoglobin values from 2 to 10 gm/dl depending on the severity of crisis, reticulocytosis, raised LDH, MCV being 80 to 100, and leucocyte count is highly variable but is commonly raised.[7] The provocative factors include dehydration, infection, fever, excessive exercise, anxiety, temperature changes, hypoxia, and hypertonic dyes.[8] Central and western part of India harbours the majority of the sickle cell disease burden. Thus, thus study was conducted to obtain a clinical profile of patients with SCD who are admitted at a tertiary care hospital with sickle cell crisis, audit the diverse presentations, review the past history and ongoing treatment and interpret as to how all these factors exert an impact on the prognosis and final outcome of the patient.

We wanted to assess the pattern, most commonly implicated aetiologies in causation, prognosis and outcome of sickle cell crises.

METHODS

After obtaining due approval from the Institutional Ethics Committee, a cross-sectional study was conducted in the Dept. of Medicine, and Central Clinical Laboratory, Acharya Vinoba Bhave Rural Hospital (AVBRH), Sawangi (Meghe), Wardha, for a period of 10 months from 1st January 2018 to 31st October 2018. Study participants were 50 Sickle cell patients aged 18 to 60 years, attending the Medicine OPD and Sickle Cell clinic, and/or admitted to the Medicine Ward/ICU with a current, ongoing Sickle Cell crisis, confirmed by Qualitative and/or Quantitative Hb electrophoresis. Participants were selected on the basis of simple random sampling in order to eliminate any bias.

Patients having sickle cell trait, sickle cell- β thalassemia, or Sickle cell Hb C disease, patients on treatment including glucocorticoids, anti-coagulants, or anti-platelet drugs, or those presenting with febrile illness were excluded from the study.

Written consent of the participant was obtained first, having explained in detail about the purpose, methodology, and implications of the study. Next, a proforma detailing relevant clinical history was obtained, with emphasis on number, frequency, duration, and severity of Emergency Department admissions brought on by vaso-occlusive crisis. This was then followed by a meticulous clinical examination to assess the presence of any infection, pallor, jaundice, or related signs of sickle cell anaemia.

Skin over the median cubital vein was first disinfected by applying surgical spirit over the cubital fossa, along with application of a tourniquet proximal to the fossa. Then, using a sterile standard venipuncture needle, blood was collected in a potassium ethylene diamine tetra acetate (EDTA) bulb for sampling and CBC, and analyzed within 15 minutes of collection.

The blood collected was placed in a siliconed, graduated centrifuge tube containing 0.3 ml of 45 % disodium ethylene diamine tetraacetic acid (EDTA), and mixed. Then, the sample was spun at 900 r.p.m. for 15 minutes, and supernatant plasma separated. 20 mm^3 of platelet-rich plasma obtained was then diluted in 100 ml of 0.85 % saline giving a dilution ratio of 1/5,000.

Statistical Analysis

Following collection of data, statistical analysis was done by using descriptive and inferential statistics using chi square test and Multivariate regression analysis. Software used in the analysis were SPSS 22.0 version and GraphPad Prism 7.0 version and $p<0.05$ is considered as level of significance.

RESULTS

The study involved 50 Sickle cell patients aged 18 to 60 years, attending the Medicine OPD and Sickle Cell clinic, and/or

admitted to the Medicine Ward/ICU with a current, ongoing Sickle Cell crisis, confirmed by Qualitative and/or Quantitative Hb electrophoresis. 38 patients were found to recover from sickle cell crises, termed as the Recovery group, while 12 patients suffered mortality, included in the Mortality group.

On comparison of age groups of patients, mean age of Recovery group was found to be 30.84±10.68 years, while mean age of Mortality group was found to be 29.66±7.53 years. p-value was found to be 0.66, hence considered to be statistically non-significant. On comparison of gender percentages in both groups, p-value was found to be 0.25, hence considered to be statistically non-significant as well. Comparison of tribes of patients was carried out next, namely Gond, Kalhar, Kunbi, Mahar, and Teji. p-Value was found to be 0.52, hence considered to be statistically non-significant as well. The data is represented in Table 1: Comparison of patient demographics.

Parameters	Recovery Group (n=38)	Mortality Group (n=12)	χ^2 Value	p Value
Age Group				
20-30	22(57.89%)	9(75%)	1.59	0.66 NS
31-40	11(28.95%)	2(16.67%)		
41-50	3(7.89%)	1(8.33%)		
>50	2(5.26%)	0(0%)		
Total	38(100%)	12(100%)		
Mean ± SD	30.84±10.68	29.66±7.53		
Gender				
Male	23(60.53%)	5(41.67%)	1.31	0.25 NS
Female	15(39.47%)	7(58.33%)		
Caste				
Gond	5(13.16%)	1(8.33%)	2.39	0.52 NS
Kalhar	5(13.16%)	1(8.33%)		
Kunbi	10(26.32%)	6(50%)		
Mahar	10(26.32%)	2(16.67%)		
Teli	8(21.05%)	2(16.67%)		

Table 1. Comparison of Demographic Profiles in Mortality Group and Recovery Group

Parameters	Recovery Group (n=38)	Mortality Group (n=12)	χ^2 Value	p Value
Crisis				
Vaso-occlusive	23(60.5%)	5(41.6%)	1.59	0.18 NS
Acute chest syndrome	7(18.42%)	2(16.6%)		
Splenic Crisis	2(5.6%)	2(16.6%)		
Aplastic crises	6(15.7%)	1(8.3%)		
Bone pain	0(0%)	2(16.6%)		
Treatment with Hydroxyurea				
Yes	28(73.6)	11(91.6)	1.59	0.62 NS
No	10(26.3)	1(8.3)		
Haemoglobin in gm/dl				
<5 gm/dl	0(0%)	8(66.67%)	42.69	0.0001 S
5 to 7 gm/dl	2(5.26%)	4(33.33%)		
7.1 to 10 gm/dl	32(84.21%)	0(0%)		
>10 gm/dl	4(10.53%)	0(0%)		
Mean ± SD	8.73±1.23	4.29±1.08		
Platelet count (lakhs/ mm^3)	10.56±3.00	36.16±5.27	21.17	0.0001 S
Sr. LDH level (U/L)	504.98±223.82	4302.41±2560.34	9.23	0.0001 S
Stay in the Hospital				
1 to 5	23(60.53%)	1(8.33%)	35.07	0.0001 S
6 to 10	15(39.47%)	2(16.67%)		
>10	0(0%)	9(75%)		
Mean ± SD	4.89±2.03	14.08±6.09		

Table 2. Comparison of Clinical Parameters in Recovery Group and Mortality Group

On comparison of clinical parameters amongst both groups, patients most commonly presented with vaso-occlusive crises. Other crises included acute chest syndrome, splenic crisis, aplastic crises, and bone pain. p-value obtained on comparison was found to be 0.18, and hence deemed statistically non-significant. Comparison of history of having received previous treatment with urea also proved to be statistically non-significant, having a p value of 0.62. Comparison of haemoglobin amongst both groups was statistically significant, having p value 0.001. Comparison of platelet counts and serum LDH amongst both groups also proved to yield statistically significant differences, having p values of 0.0001 in each case. Lastly, parameter compared was duration of hospital say amongst both cases. Recover group had a mean duration of 4.89±2.03, while Mortality group had a mean stay of 14.08±6.09 days. p-value obtained was 0.0001, hence deemed clinically significant as well. This data is represented in Table 02: Comparison of clinical parameters.

DISCUSSION

The present study outlines the clinical course of sickle cell disease among 50 patients from the rural population visiting AVBRH, Wardha located in central India. The mean age of patients at enrolment was 30 years, with all patients with positive Hb SS pattern confirmed by Hb electrophoresis. It was found that the maximum number of crisis episodes occurred in the age group 20 to 30 years similar to the findings when considering from first year of life, the highest mortality is seen in the first 5 years of life.[7] Male preponderance with regards to number of crisis episodes was observed in this study which is a finding common to other studies in central India[4] whereas equal male to female ratio was noted in a recent study conducted in western India.[7] The death rate upon admission due to sickle cell crisis was higher in females than males. Vasocclusive crisis outnumbered all other described crisis in this patient population, while going back to a study published in 1982 the most common cause of death was attributed to acute chest syndrome in a study conducted at Jamaica as well as by authors J. Brambilla et al in their study published in the new England journal.[6] Vaso-occlusive crisis is also the most common cause leading to mortality in this study group claiming 41% as cause of death which can also be seen in a study conducted in basra by authors Zeina et al.[9] Authors such as Acharya et al have also noted correlation of sickle cell nephropathy to ophthalmic manifestations in patients, and other unusual presentations such as renal tubular acidosis with hyperkalemia.[10,11] Specific lab parameters such as Mean Platelet Volume and other platelet indices have been found useful to estimate frequency of crises in such patients as well.[12,13] An important factor that has thus been noted is to improve awareness regarding such complications amongst patients in sickle-endemic areas, that can greatly improve clinical outcomes.[14]

Pain is the principle clinical feature that leads to morbidity[15] and mortality, it is also observed in most patients and most common presentation after the age of 2 years,[16] pain in the limbs and anaemia are the most commonly observed presentation characteristic in this study population which coincides with the findings obtained from a study in Maharashtra[7] in 2002. Joint pain was a very common finding in most of the patients with 30 % experiencing pain in the hip

joint, 18 % complaining of non-articular pain, and 16 % suffering from pain in the knee joint. Awasthy N, Aggarwal K C in their study at a tertiary center reported high incidence of joint pain in patients with HbSS phenotype.[3] Seasonal variation is seen in 38 percent of the patients which is a feature described earlier by S. L. Kate and D. P. Lingojwar[7] and also in a recent study conducted in 2016 by Anjali Parekh, Leena Dhande[5] which also brings to light an apparent increase in the incidence of crises during monsoon amongst the paediatric patient population. In our study, dehydration was the most common precipitant of a crisis episode, it is well known that dehydrated erythrocytes have an increased tendency to polymerize and sickle[17] Dehydration was followed by fever precipitating crisis in 30 percent of the patients which is a common citing in many studies in almost all regions. Though dehydration was the commonest cause grouping fever and infection together contributes as a major precipitant as seen in previous studies.[10] Comparison of history of blood transfusion history and past hospitalisation of the patients between those who recovered after crisis and those who died subsequent to crisis was found to be statistically significant ($p<0.05$).

Another observation noted is how duration of hospital stay and outcome after treatment when analysed, signified that with the increase in the number of days of hospitalisation chances of a negative outcome is most likely. Hydroxyurea, a myelosuppressive agent, is the only effective drug proven to reduce the frequency of painful episodes and decreases the rate of painful episodes by 50 %.[14] In our study hydroxyurea didn't show any statistically significant effect on patient outcome, but those on hydroxyurea mostly had a positive outcome. Narrowing down to the laboratory evaluation, three important parameters total leukocyte count, platelet count and serum LDH compared between those who recovered and those who died wherein statistically significant figures were obtained with $p<0.05$. Emergence of this significance is due to raised TLC apparent in both Asian and African populations as noted by Emmanuel Chide, Charle, Uchenna and also found in this study.[17] Serum LDH as marker for disease severity was considered and as expected it was raised in most patients during crisis, a finding reported by Ballas S in his study as well. It is also seen that serum LDH was markedly elevated in those who died due to crisis than those who recovered from it.

Haemoglobin percentage was mostly <5 gm% and in between 5 to 7 gm% for those who succumbed to death whereas those who recovered had Haemoglobin >7%. On assessment of caste, the prevalence in this study group was found to be highest in the Kunbi caste (32%), followed by Mahar and Teli (20%) castes. Another study conducted in Wardha shows highest prevalence in the tribals namely among Pardhan, Gowari and Gond communities whereas Teli ranked first with 25% followed by Kunbi which are scheduled castes.[18]

CONCLUSIONS

While age, gender, and caste, appeared to have no significant correlation to patient outcome in our study, haemoglobin levels, platelet counts, and S. LDH were found to be statistically significant. Thus, these parameters appear to act as good prognostic markers to assess and follow-up in cases of sickle cell crises. Early detection and correction of these variables can ensure better in-patient management of sickle cell crises, and thus, better patient outcomes in sickle cell disease.

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