Trends in Clinical and Medical Sciences

PSR Press

Original Research Article

Study of electrocardiographic and echocardiographic changes in sickle cell anaemia patients

Dr. Sandeep P Chaurasia[1,*], Dr. Shekhar Ghodeswar[2] and Dr. Rahul Manvar[3]

[1] Assistant Professor, Department of Cardiology, SVNGMC and SSH Yavatmal, Maharashtra, India.
[2] Associate Professor, Department of Medicine, SVNGMC and SSH Yavatmal, Maharashtra, India.
[3] Resident, Department of Medicine, SVNGMC and SSH Yavatmal, Maharashtra, India.
* Correspondence: schaurisia@rediffmail.com

Received: 12 January 2023; Accepted: 20 May 2023; Published: 24 May 2023.

Abstract: Background: Sickle cell anaemia is a genetic abnormality involving the haemoglobin. Patients present with a wide spectrum of disorders because of a single-point mutation in which thymine substitutes for adenine, thereby encoding valine instead of glutamine in the sixth position of the beta-chain. The repeated sickling and unsickling damage the red cell membrane leading to irreversibly sickled red cell even when the oxygen pressure is increased.
Methodology: Patients admitted in the Medicine department of tertiary care center from December 2020 to December 2022 with sickle cell anaemia were included in the study. Sample size taken for this study was 100 patients. Predesigned and pretested questionnaire was used to record the necessary information.
Result: In this study, association of LVH and severe anemia in sickle cell patients was not statistically significant($P > 0.05$) Association between anaemia and pulmonary artery hypertension in sickle cell patients was found to be statistically significant.
Conclusion: Most common electrocardiographic finding was sinus tachycardia followed by T-inversions. Most common echocardiographic changes were pulmonary hypertension.

Keywords: Electrocardiography; Echocardiography; Sickle cell; Anaemia; Hypertension.

1. Introduction

Sickle cell anaemia is a genetic abnormality involving the haemoglobin. Patients present with a wide spectrum of disorders because of a single-point mutation in which thymine substitutes for adenine, thereby encoding valine instead of glutamine in the sixth position of the beta chain. The repeated sickling and unsickling damage the red cell membrane leading to irreversibly sickled red cells even when the oxygen pressure is increased. This causes a reduced red cell life span due to membrane damage. Haemolysis consequent on the damaged red cell membrane could be intravascular or extravascular, causing chronic anaemia. Chronic anaemia is largely responsible for cardiac manifestations of sickle cell disease. [1] Sickle cell cardiomyopathy may also result from recurrent vaso-occlusion with episodes of ischemia-reperfusion injury to multiple organ systems. [2] Progressive vasculopathic complications due to inflammatory and oxidative stress associated with sickling, intravascular haemolysis, and increased expression of cellular adhesion molecules contribute to progressive cardiac lesions. Chronic anaemia causes increased cardiac output with minimal increase in heart rate. [3] Diastolic dysfunction by Doppler parameters is common in children and adults, and it is an independent risk factor for mortality with a risk ratio of 4.8. [4] The combination of diastolic dysfunction and pulmonary hypertension increased this risk to above 13. [5] Electrocardiographic evidences of cardiomegaly, and biventricular hypertrophy are common findings in sickle cell disease patients. [6]

These are secondary to an increase in cardiac output to compensate for chronic anaemia seen in sickle cell anaemia. [6] There is a high output state, and the resulting cardiomegaly increases the preload. [7] The increased preload, and decreased afterload compensate for the left ventricular dysfunction and maintain normal ejection fraction and high cardiac output. [8] Other reported electrocardiographic abnormalities amongst adult Nigerians are increased p-wave, Q-Tc depression, and ST-segment elevation. These show evidence of myocardial stress. In addition to normal racial variation in the black population, skin fat and thin

chest walls may contribute to high voltages recorded in a black sickle cell population. [9,10] Hence caution should be taken in interpreting electrocardiogram in sickle cell patients. The cardiovascular complications of sickle cell disease (SCD) are being recognized more often and include cardiac enlargement, myocardial ischemia, biventricular dysfunction, and pulmonary hypertension, among others. [11–15] Cardiovascular manifestations of SCD have been attributed to chronic haemolytic anaemia, which is typically found in this disorder. [16,17] Patients with severe SCD frequently have hyper dynamic hearts with high ejection fractions and a cardiac index substantially exceeding normal values. However, it is important to recognize that SCD can affect heart function in multiple ways. The characteristic widespread vascular occlusions in SCD can involve virtually every body organ, including the heart. [18] Likewise, iron overload from long-standing transfusion therapy places these patients at higher risk of developing cardiac hemosiderosis. [19]

This study was undertaken to study the Electrocardigraphic and Echocardiographic Changes in Sickle Cell Anaemia Patients.

2. Materials and Methods

This observational study was conducted at the Medicine department of a tertiary care centre after getting written approval from the Institutional Ethics Committee. The study was conducted for two years (December 2020 to December 2022), and the sample size taken for this study was 100 patients. All the patients admitted to the Medicine department who had Sickle cell anaemia with "SS" pattern and "AS" pattern, aged more than 12 years, and those willing to consent to studies were included in this study.

Patients who were less than 12 years & more than 65 years, having cardiorespiratory diseases either congenital or with acquired causes, haemoglobinopathies other than sickle cell AS and SS pattern, significant renal insufficiency with Stage 3 or more CKD, patients with AKI, pregnant females, patients having Co-morbidity like HTN, DM, Asthma, and Thyroid disorders, haemolytic and sequestration crisis and those who were not willing to give consent were excluded from this study.

Informed written and verbal consent was obtained from the patients. Predesigned and pretested questionnaire was used to record the necessary information. Questionnaires included general information, such as age, sex, religion, occupation, residential address, and marital status, date of admission. Medical history- chief complaint, history, general examination, systemic examination. All patients were subjected to a standardized interview. Detailed medical history was taken, and complete general and systemic examinations were done to establish the diagnosis of sickle cell disease and rule out association of various risk factors and electrographic and Echo graphic changes.

Age, weight, height, BMI, sex, and medications of all patients were recorded. Ten leads were placed at precise anatomical locations to obtain quality data. The four limb lead electrodes were applied to the extremities starting with the right leg and then the left leg, right arm, and left arm. All the chest leads also be applied at the precordial electrode locations (V1-V6). ECG was recorded after the connection of the limb and chest leads. 2D echocardiograms with Doppler flow imaging. Blood investigations like CBC, LFT, KFT, Blood glucose, and Serum electrolyte (sodium, potassium) were done. Venous blood samples will be collected and centrifuged in a cooling centrifuge, and serum will be separated. Patients on treatment were followed up for changes in pre-decided parameters, and treatment response was decided.

The data were entered in Microsoft Excel, and data analysis was done by using SPSS demo version no 21.

3. Results

The present observational study was done among 100 sickle cell anaemia cases admitted to tertiary care center during study period.

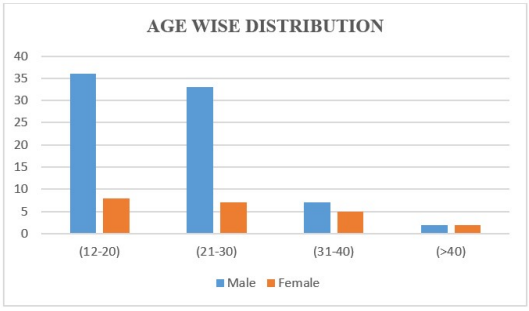

Figure 1. Distribution of cases according to age

Table 1. Severity of Anaemia in study subjects

		FREQUENCY	PERCENTAGE
SEVERITY OF ANEMIA	MILD(11-12.9GM%)	03	4%
	MODERATE (8-11GM%)	44	63.4%
	SEVERE (<8GM%)	20	32.6%
	TOTAL	74	

In this study, majority of patients had moderate anaemia 63% of anaemia patients, and 32.4% of patients had severe anaemia. Figure 1 Table 2

Table 2. Distribution of laboratory parameters of study subjects

Investigations	Mean ± S.D.
Hemoglobin (gm/dl)	7.88± 3.92
Total leucocyte count (cells/mm3)	8613.8 ± 3349.1
Platelet (lacs/mm3)	2.26 ± 0.59
Hematocrit (%)	23.6 ± 3.43
Total bilirubin (mg/dl)	2.34 ± 2.11
Direct bilirubin (mg/dl)	0.84 ± 0.34
Indirect bilirubin (mg/dl)	1.42 ± 1.89
Serum creatinine (mg/dl)	0.78 ± 0.17
Blood urea level (mg/dl)	14.54 ± 3.11
Serum glutamic oxaloacetic transaminase (SGOT)/ Aspartate transaminase (AST) (IU/L)	24± 3.22
Serum glutamic pyruvic transaminase (SGPT) /Alanin transaminase (ALT) (IU/L)	21± 4.21
Serum sodium (meq/L)	141.1±2.23
Serum potassium±(meq/L)	4.2±1.83

Table **??** Mean value of hemoglobin, TLC, platelet, and hematocrit are 7.88 ± 3.92 gm/dl, 8613.8 ± 3749.1 cells/mm3, 2.26 ± 0.59 lacs/mm3 and 23.6 ± 3.43% respectively. Mean levels of total bilirubin, direct bilirubin, indirect bilirubin, serum creatinine and blood urea level of study subjects were 2.34 ± 2.11 mg/dl, 0.84 ± 0.34 mg/dl, 1.42 ± 1.89 mg/dl, 0.78 ± 0.17 mg/dl and 14.54 ± 3.11 mg/dl respectively. The mean values of SGOT, SGPT, Sr. Sodium and Sr. Potassium were found to be 24± 3.22 IU/L, 21± 4.21 IU/L, 142.1±2.23meq/L and 4.2±1.83 respectively.

Table 3. Electrocardiographic Findings in study subjects.

Parameter	Gender		Total	Percentage
	Male	Female		
Abnormal ECG	31	10	41	41%
Normal ECG	47	12	59	59%
Total	78	22	100	

Table 3 In this study, 41% of the cases enrolled were having abnormal ECG changes out of which 31 subjects were male and 10 subjects were females, while 59% were having normal ECG.

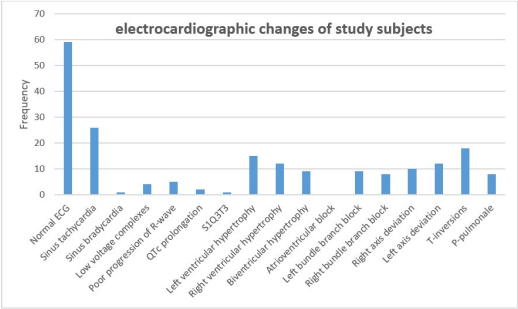

Figure 2. Distribution of electrocardiographic changes of study subjects.

The above Figure 2 shows majority of cases presented with sinus tachycardia 26 cases followed by T-inversions in 18 cases, left axis deviation 12 cases, right axis deviation 10 cases,12 right ventricular hypertrophy,15 cases with left ventricular hypertrophy, 01 case of sinus bradycardia, 8 cases with P-pulmonale, low voltage complex in 4 cases and Poor progression of R-wave in 5 cases.

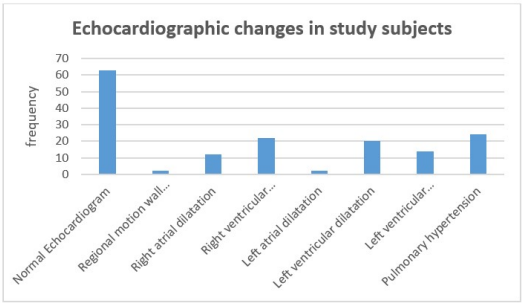

Figure 3. Distribution of cases according to echocardiographic changes in study subjects

The above Figure 3, shows majority of cases presented with pulmonary hypertension 24 cases followed by 22 cases presented with right ventricular dilatation,20 cases with left ventricular dilatation, left atrial dilatation 2 cases, left ventricular hypertrophy 14 cases, global hypokinesia was found in 2 cases.

Table 4. Association between Severe Anaemia and Left ventricular hypertrophy in Sickle Cell patient.

Parameter		Anemia			Total	Chi square	P value
		mild anaemia	moderate anemia	Severe anemia			
Left Ventricular Hypertrophy	Absent	03	38	16	57	3.08	.0792
	Present	00	08	9	17		
Total		03	46	25	74		

Table 4 Association of LVH and severe anaemia in sickle cell patients was not statistically significant(P>0.05) in the study. 36.6% of patients with severe anaemia had LVH. There was higher percentage of LVH in males as compared to females.

Table 5. Association between anaemia and pulmonary artery hypertension in sickle cell patients

Parameter		Anemia				Total	Chi -square	P -value
		mild	moderate	Severe	Absent			
Pulmonary artery hypertension	Present	0	13	11	0	24	15	0.0017
	Absent	3	33	14	26	76		
Total		03	46	25	26	100		

The above Table 5 showed relationship of anaemia and pulmonary artery hypertension in study subjects, it is found that pulmonary artery hypertension is seen in 24 subjects, and out of which maximum had severe anaemia. This association is found to be statistically significant.

4. Discussion

The present observational study was done among 100 sickle cell anaemia cases admitted to tertiary care center during study period.

In present study Figure 1 shows distribution of cases according to age majority of cases were found in 12-20 year's age group, the youngest patient was of 13 years of age however the oldest patient was found 56 years old. e.g., 44 cases (44%) followed by 40 cases in 21-30 year's age group,12 cases in 31-40 year's age group and 4 cases in >40 year's age group.

Another study Oguanobi NI et al [20] he reported that the mean ages for patients and controls were 28.27 ± 5.58 (range 18 - 44) and 28.37 ± 5.91 (range 18 - 45) years respectively. Pathak et al [21] he reported that the age of patients ranged from 14 to 50 years. Majority of patients were in the age group of 14-20 years (46%).

In Table no.1majority of patients had moderate anaemia 63% of anaemia patients, and 32.4% of patients had severe anaemia. In Table no. 2, Mean value of hemoglobin, TLC, platelet, and hematocrit are 7.88 ± 3.92 gm/dl, 8613.8 ± 3749.1 cells/mm3, 2.26 ± 0.59 lacs/mm3 and 23.6 ± 3.43% respectively. Mean levels of total bilirubin, direct bilirubin, indirect bilirubin, serum creatinine and blood urea level of study subjects were 2.34 ± 2.11 mg/dl, 0.84 ± 0.34 mg/dl, 1.42 ± 1.89 mg/dl, 0.78 ± 0.17 mg/dl and 14.54 ± 3.11 mg/dl respectively. The mean values of SGOT, SGPT, Sr. Sodium and Sr. Potassium were found to be 24± 3.22 IU/L, 21± 4.21 IU/L, 142.1±2.23meq/L and 4.2±1.83 respectively. Table no 3. shows 41% of the cases enrolled were having abnormal ECG changes out of which 31 subjects were male and 10 subjects were females, while 59% were having normal ECG. In current study Graph no. 2 shows distribution of cases according to ECG changes. majority of cases presented with sinus tachycardia, 26 cases followed by T-inversions 18 cases, left axis deviation 12 cases, right axis deviation 10 cases,12 right ventricular hypertrophy,15 cases with left ventricular hypertrophy, 01 case of sinus bradycardia, 8 cases with P-pulmonale, low voltage comples in 4 cases, Poor progression of R-wave in 5 cases.

Holloman et al [22] he reported that the electrocardiograms (ECGs) of 87 adult patients, 72% of all patients had abnormal ECGs. Non-specific ST-T (NS ST-T) wave abnormalities (53%) and QT interval prolongation (12%) were frequent. 11% had sinus tachycardia and 80% of those were women (P <0.05). Fifteen of 21 (71%) patients with arrhythmias had NS ST-T abnormalities. Systemic hypertension and ECG evidence for right-sided heart disease were rare, as was the incidence of LVH by ECG. In present study Graph no.3 shows distribution of cases according to echo cardio graphic changes. majority of cases presented with pulmonary hypertension 24 cases followed by 22 cases presented with right ventricular dilatation,20 cases with left ventricular dilatation, left atrial dilatation 16 cases, left ventricular hypertrophy 14 cases, regional motion wall abnormality 2 cases. Similar results were found in study of Ahmed et al. [23] He found that the estimated mean left ventricle ejection fraction was 61.29 ± 11.29% (range 20-76%). Eight (21%) patients had evidence of a hyper dynamic left ventricle (ejection fraction >70%). Left heart abnormalities included dilated atrium in 14 (37%), dilated ventricle in 5 (13%), ventricle hypertrophy in 5 (13%), and ventricle dysfunction in 3 (9%) patients. Right heart abnormalities included dilated atrium in 9 (24%), dilated ventricle in 6 (16%), and ventricle dysfunction in 3 (9%) patients. One of these 3 patients had evidence of biventricular failure, and all 3 patients with right ventricular dysfunction had moderate to severe pulmonary hypertension.

Pulmonary hypertension was the most common abnormality identified in 22 (58%) patients. Another study Ondze- Kafata LI et al. [24] He reported that the Left ventricular dilatation was observed in 26 patients (31.7%), right ventricle in 14 patients (17.1%), left atrial dilatation in 36 patients (43.9%), right atrial in 11 patients (13.4%). Left ventricular hypertrophy was observed in 13 patients (15.9%). The Pulmonary arterial hypertension was found in 43 patients (52.4%).

In the present study, Table 4 shows association of LVH and severe anaemia in sickle cell patients was not statistically significant(P>0.05) in the study, 36.6% of patients with severe anaemia had LVH similar results were found in study conducted by Adedoyin Dosunmu et al. [25] 2016 reported a total of 43% SCA patients had left ventricular hypertrophy (LVH) and this was found to be more frequent in males than females. This is much lower than 75% of participants reported by Oguanobi et al. though they reported a higher percentage (96.7%)

of ECG abnormalities amongst SCA patients. The higher mean age of participants reported by Oguanobi et al. compared with the present study could account for a higher prevalence of LVH in their study. Increasing age was reported to be directly proportional to increasing LV filling. [10]

In present study Table no. 5 showed relationship of anaemia and pulmonary artery hypertension in study subjects, it is found that pulmonary artery hypertension is seen in 24 subjects, and out of which maximum had severe anaemia.

5. Conclusion

Majority of cases were found in 12-20 year's age group. Most common electrocardiographic finding was sinus tachycardia followed by T-inversions. Most common echocardiographic changes were pulmonary hypertension. In this study, association of LVH and severe anemia in sickle cell patients was not statistically significant(P>0.05) Association between anaemia and pulmonary artery hypertension in sickle cell patients was found to be statistically significant.

Author Contributions: All authors contributed equally to the writing of this paper. All authors read and approved the final manuscript.

Conflicts of Interest: "The authors declare that they do not have any competing interests."

References

[1] R.H. Falk and W. B. Hood Jr., "The heart in sickle cell anemia," Archives of Internal Medicine, vol. 142, no.9, pp. 1680-1684, 1982.

[2] R. B. Francis Jr. and C. S. Johnson, "Vascular occlusion in sickle cell disease: current concepts and unanswered questions," Blood, vol. 77, no. 7, pp. 1405-1414, 1991.

[3] M. T. Gladwinand, V. Sachdev, "Cardiovascular abnormalities in sickle cell disease," Journal of the American College of Cardiology, vol. 59, no. 13, pp. 1123-1133, 2012.

[4] V. Sachdev, R. F. Machado, Y. Shizukuda et al., "Diastolic dysfunction is an independent risk factor for death in patients with sickle cell disease," Journal of the American College of Cardiology, vol. 49, no. 4, pp. 472-479, 2007.

[5] L. A. Lester, P.C. Sodt, N. Hutcheon, and R. A. Arcilla, "Cardiac abnormalities in children with sickle cell anemia," Chest, vol. 98, no. 5, pp. 1169-1174, 1990.

[6] I. C. Balfour, W. Covitz, H. Davis, P. S. Rao, W. B. Strong, and B. S. Alpert, "Cardiac size and function in children with sickle cell anemia," American Heart Journal, vol. 108, no. 2, pp. 345-350,1984.

[7] L. Leight, T. H. Snider, G. O. Clifford, and H. K. Hellems, "Hemodynamic studies in sickle cell anemia," Circulation, vol. 10, no. 5, pp. 653-662, 1954.

[8] B. S. Denenberg, G. Criner, R. Jones, and J. F. Spann, "Cardiac function in sickle cell anemia," American Journal of Cardiology, vol. 51, no. 10, pp. 1674-1678, 1983.

[9] R. Macruz, J. K. Perloff, and J. K. Case, "A method for the electrocardiographic recognition of atrial enlargement," Circulation, vol. 17, no. 5, pp. 882-885, 1958.

[10] N. I. Oguanobi, B. J. C. Onwubere, S. O. Ike, B. C. Anisiuba, E. C. Ejim, and O. G. Ibegbulam, "Electocardiographic findings in adult Nigerians with sickle cell anaemia," African Health Sciences, vol. 10, no. 3, pp. 235-241, 2010.

[11] Falk R, Hood W. The heart in sickle cell anemia. Arch Intern Med 1982; 142:1680-1684.

[12] Simmons BE, Santhanam V, Castaner A, et al. Sickle cell heart disease. Two-dimensional echo and Doppler ultrasonographic findings in the hearts of adult patients with sickle cell anemia. Arch Intern Med 1988;148: 1526-1528.

[13] Sutton LL, Castro O, Cross DJ, Spencer JE, Lewis JF. Pulmonary hypertension in sickle cell disease. Am J Cardiol 1994; 74:626-628.

[14] San M, Demirtascedil M, Burgut R, et al. Left ventricular systolic and diastolic function in patients with sickle cell anemia. Int J Angiol 1998;7: 185-187.

[15] Norris S, Johnson C, Hayward J. Sickle cell anemia: does myocardial ischemia occur during crisis? J Natl Med Assoc 1991; 83:209-213.

[16] Stone RM, Bridges KR, Libby P. Hematological-oncological disorders and cardiovascular disease. In: Braunwald E, Zipes DP, Libby P, editors. Heart disease: a textbook of cardiovascular medicine. 6th edition. Philadelphia: W.B. Saunders; 2001. p 2223-2241.

[17] Mardelle T, Ekra A, Bertand E. LV function in sickle cell anemia. Am Heart J 1986; 112:1356-1357.

[18] Bunn HF. Pathogenesis and treatment of sickle cell disease. N Engl J Med 1997; 337:762.

[19] Ballas SK. Iron overload is a determinant of morbidity and mortality in adult patients with sickle cell disease. Semin Hematol 2001; 98:30-36.
[20] NI O. Cardiovascular System Abnormalities in Sickle Cell Anaemia: Clinical Findings in Steady State Adult Nigerian Patients. J Clin Exp Cardiolog 2016;07(03):6-11.
[21] Pathak J, VadiVelan M, Mathew C. Evaluation of Cardiac Status of Patients with Sickle Cell Disease by 2D Echocardiography with Specific Reference to Pulmonary Hypertension. Indian J Clin Pract 2013;23(11):694-7.
[22] Holloman KL, Johnson CS, Haywood LJ. Electrocardiogram analysis in adult patients with sickle cell disease. J Natl Med Assoc 1987;79(8):809-14.
[23] Ahmed S, Siddiqui AK, Sadiq A, Shahid RK, Patel D V., Russo LA. Echocardiographic abnormalities in sickle cell disease. Am J Hematol 2004;76(3):195-8.
[24] Ondze-Kafata LI, Sanouiller A, Hedreville M, Hedreville S, Larifla L. Echo-cardiographic aspects in sickle cell disease Guadeloupe. Pan Afr Med J 2014; 18:1-7
[25] Adedoyin Dosunmu, Akinsegun Akinbami, Ebele Uche, Adewumi Adediran, Sarah John-Olabode, "Electrocardiographic Study in Adult Homozygous Sickle Cell Disease Patients in Lagos, Nigeria", Journal of Tropical Medicine, vol. 2016, Article ID 4214387, 5 pages, 2016.