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A study of Electrocardigraphic and Echocardiographic changes in sickle cell anemia patients – Observational Study

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ABSTRACT

Background: 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. Cardiovascular manifestations of SCD have been attributed to chronic hemolytic anemia, which is typically found in this disorder. **Aim & Objective:** 1. To evaluate ECG and 2D Echo abnormalities in patients with sickle cell Disease.2. To study of Clinical profile of sickle cell disease. **Method: Study design:** Observational study. **Study setting:** Department of General Medicine, Shri Vasantrao Naik Govt. Medical College, Yavatmal. **Study duration:** 2 years from December 2020 to December 2022. **Study population:** The study population included all the cases with sickle cell disease patients visiting OPD and admitted at a tertiary care center such cases included in the study. **Sample size:** 100. **Results:** majority of cases were found in 12-30 years age group e.g. 42 cases (42%) followed by 24 cases in 31-45 years age group,19 cases in 46-60 years age group and 15 cases in >60 years age group. Most of cases were males e.g. 64 cases (64%) and 36 cases were females (36%). majority of cases presented with T-inversion 34 cases followed by sinus tachycardia 24 cases, Left axis deviation 22 cases, right axis deviation 14 cases,12 right ventricular hypertrophy,10 cases with left ventricular hypertrophy, 9 cases with arrhythmia,5 sinus bradycardia,5 cases with P-pulmonale, low voltage complex 3 cases,Poor progression of R-wave 2 cases and P-mitrale 1 case. majority of cases presented with pulmonary hypertension 34 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. majority of cases complained joint pain 60 cases followed by chest pain 42 cases, palpitation 38 cases, breathlessness 38 cases and fever 22 cases **Conclusions:** Majority of cases were found in 12-30 years age group**.** Most of cases were males. Majority of cases presented with T-inversion. Most common Cardiographic changes were pulmonary hypertension

Keywords: Electrocardigraphic changes, Echocardiographic changes, sickle cell anemia.

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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 cell even when the oxygen pressure is increased.

This causes reduced red cell life span as a result of 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 vasoocclusion 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 [3]. Chronic anaemia causes increased cardiac output with minimal increase in heart rate [3].

Left ventricular stroke volume increases with significant dilatation of the left ventricle [4]. The dilated left ventricle adapts to the increased wall stress by developing eccentric hypertrophy in which wall thickening increased and myofibrils are elongated [5].There is therefore increased left ventricular mass with age and left ventricular filling impairment [5–7].

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 [8]. 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 [9].

These are secondary to an increase in cardiac output in an effort to compensate for chronic anaemia that is seen in sickle cell anaemia [9]. There is a high output state and the resulting cardiomegaly increases the preload [10]. The increased preload and decreased after load compensate for the left ventricular dysfunction and maintain normal ejection fraction and high cardiac output [11].

Other reported electrocardiographic abnormalities amongst the adult Nigerians are increased p-wave, QTc depression, and ST segment elevation [12, 13]. These show evidence of myocardial stress. Skin fat and thin chest wall in addition to normal racial variation in black population may contribute to high voltages recorded in black sickle cell population [12, 13].Hence caution should be taken in interpreting electrocardiogram in sickle cell patients.

AIM AND OBJECTIVES:

1. To evaluate ECG and 2D Echo abnormalities in patients with sickle cell Disease.
2. To study of Clinical profile of sickle cell disease

MATERIAL AND METHODS

Study design: Observational study.

Study setting: Department of General Medicine, Shri Vasantrao Naik Govt. Medical College, Yavatmal.

Study duration: 2 years from December 2020 to December 2022.

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Study population: The study population included all the cases with sickle cell disease patients visiting OPD and admitted at a tertiary care center such cases included in the study.

Sample size: 100

INCLUSION CRITERIA:

1. Sickle cell disease patients with "SS" pattern and "AS" pattern.
2. Patients age more than 12 years.
3. Patients who are willing to give consent for studies

EXCLUSION CRITERIA:

1. Patients with acute pulmonary embolism, circulatory shock, and respiratory failure requiring endotracheal intubation and mechanical ventilation.
2. Pregnant females
3. Not willing to participate in the study
4. Loss to follow up
5. Patients below the age of 12 years

Approval for the study:

Written approval from Institutional Ethics committee was obtained beforehand. Written approval of Medicine and Related department was obtained. After obtaining informed verbal consent from all patients with the definitive diagnosis of Sickle cell disease admitted to Medicine ward of tertiary care centre such cases were included in the study.

Sample Size: With reference to study by Naoman SG et al [13] He found that the prevalence of Echocardiographic changes among Sickle cell disease cases was 59% had a TRV ≥2.5 m/s

Formula for sample size = 4* P* Q / L2

Where P = 59%

Q = 100-59 = 41

L = Allowable error = 10% (Absolute error)

Sample size = 4 × 59×41 / 92.16 =104.99

Sample size Rounded to = 100

Sampling technique:

Convenient sampling technique used for data collection. All patients admitted in the Medicine department of tertiary care center from December 2020 to December 2022 with sickle cell disease such cases were included in the study.

Methods of Data Collection and Questionnaire: 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 complain, past history, general examination, systemic examination

After taking written and informed consent about enrolment in the study and maintaining adequate privacy and confidentiality, 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

Procedure:

Age, weight, height, BMI, sex, and medications of all patients were recorded. Ten leads 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

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recorded after the connection of the limb and chest leads. 2D echocardiograms with Doppler flow imaging.

Blood Investigations:

- CBC
- KFT
- LFT
- Blood glucose
- Sr. Electrolyte (Sodium, Potassium)

Blood samples:

Venous blood samples will be collected and centrifuged in cooling centrifuge and serum was separated.

Diagnosed cases of sickle cell disease during the period of 1st January 2021 to December 2022. Patients on treatment were followed up for changes in pre decided parameters and treatment response was decided. All the procedures and investigations conducted under direct guidance and supervision of pg guide. Proforma of HCV notes maintained.

Data entry and analysis:

The data were entered in Microsoft Excel and data analysis was done by using SPSS demo version no 21 for windows. The analysis was performed by using percentages in frequency tables and correlation of sickle cell disease with various risk factors and prevalance of Electrocardigraphic And Echocardiographic Changes In Sickle cell disease. $p<0.05$ was considered as level of significance using the Chi-square test.

RESULTS AND OBSERVATIONS

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

Table No. 1: Distribution of cases according to age (N=100)

Age in years	Frequency	Percentage
12-30	**42**	**42%**
31-45	**24**	**24%**
46- 60	**19**	**19%**
>60	**15**	**15%**
Total	**100**	**100 (100%)**

Above table shows that majority of cases were found in 12-30 years age group e.g. 42 cases (42%) followed by 24 cases in 31-45 years age group,19 cases in 46-60 years age group and 15 cases in >60 years age group

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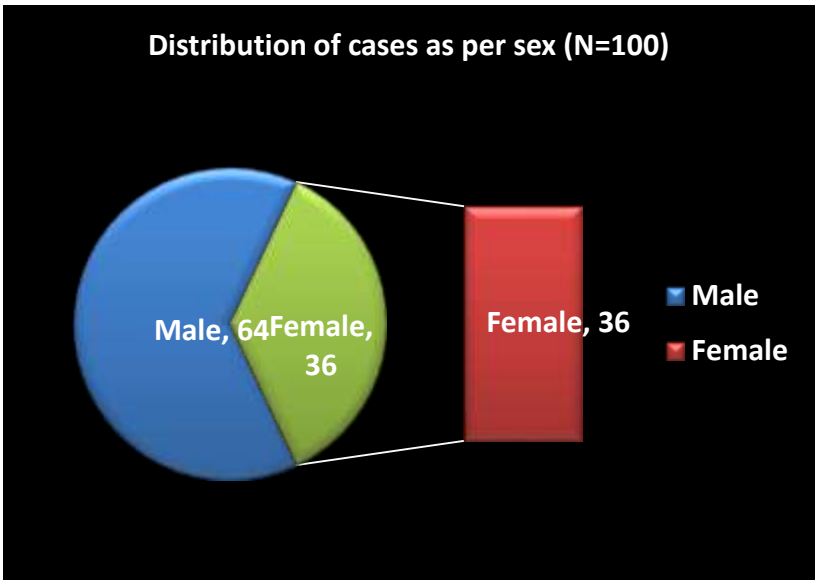
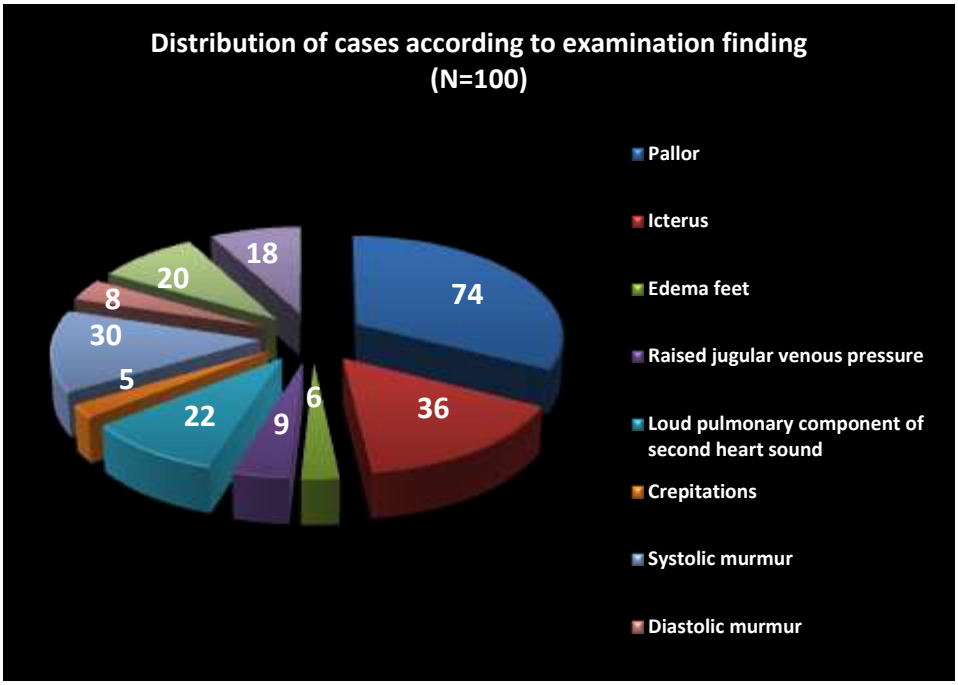


The above figure shows majority of cases were males e.g. 64 cases (64%) and 36 cases were females (36%).

Table No.2: Distribution of cases according to Hb electrophoresis (N=100)

Hb electrophoresis	Frequency	Percentage
AS	48	48%
SS	52	52%
Total	100	100 (100%)

The above table shows majority of cases 52 with homozygous sickle cell haemoglobinopathy (HbSS variant) and 48 with heterozygous sickle cell haemoglobinopathy (HbAS variant).



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The above figure shows majority of cases presented with pallor 74 cases followed by icterus 36 cases, systolic murmur 30 cases, Loud pulmonary component of second heart sound 22 cases, Splenomegaly 20, Displaced apex beat 18 cases, Raised jugular venous pressure 9, Diastolic murmur 8 cases, Edema feet 6 cases, Crepitations 5 cases.

Table no 3: Distribution of cases according to ECG changes (N=100)

ECG changes	Frequency	Percentage
T-inversion	34	34%
Left axis deviation	22	22%
Right axis deviation	14	14%
Right ventricular hypertrophy	12	12%
Left ventricular hypertrophy	10	10%
P-pulmonale	05	05%
P-mitrale	01	01%
Low voltage complexes	03	03%
Poor progression of R-wave	02	02%
Sinus bradycardia	05	05%
Sinus tachycardia	24	24%
Arrhythmia	09	09%

The above table shows majority of cases presented with T-inversion 34 cases followed by sinus tachycardia 24 cases, Left axis deviation 22 cases, right axis deviation 14 cases,12 right ventricular hypertrophy,10 cases with left ventricular hypertrophy, 9 cases with arrhythmia,5 sinus bradycardia,5 cases with P-pulmonale, low voltage complex 3 cases,Poor progression of R-wave 2 cases and P-mitrale 1 case.

Table no 4: Distribution of cases according to Cardiographic changes (N=100)

2D Echo changes	Frequency	Percentage
Regional motion wall abnormality	02	2%
Right atrial dilatation	12	12%
Right ventricular dilatation	22	22%
Left atrial dilatation	16	16%
Left ventricular dilatation	20	20%
Left ventricular hypertrophy	14	14%
Pulmonary hypertension	34	34%
Ejection fraction Median(IQR)	60(58 - 62)	

The above table shows majority of cases presented with pulmonary hypertension 34 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.

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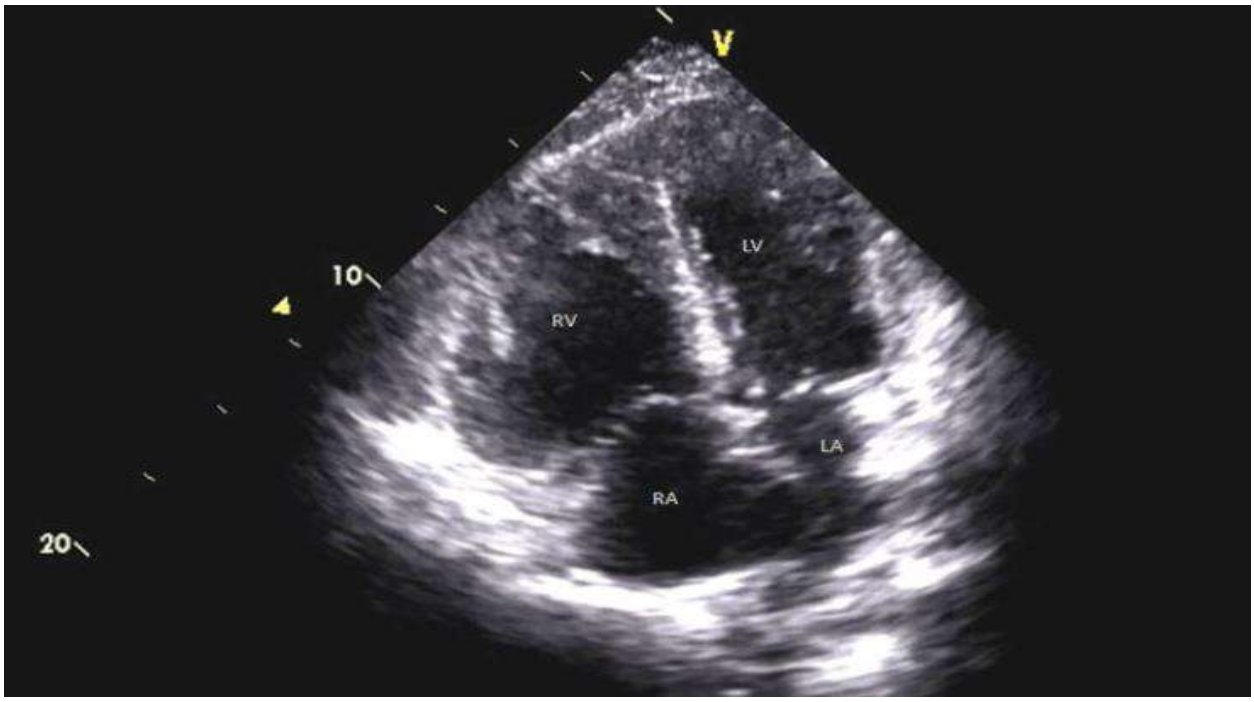

Figure no: 1 Echocardiographic image (apical 4-chamber view) from a SCD patient showing dilated, dysfunctional right ventricle.

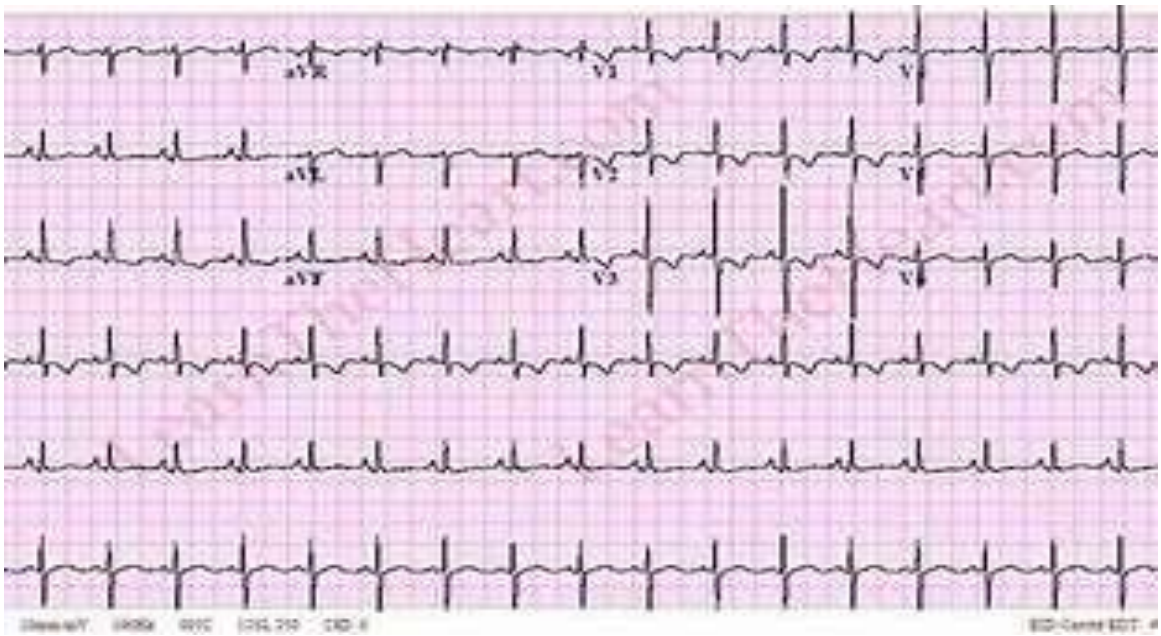

Figure no: 2 ECG changes in Right ventricular hypertrophy in SCD

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DISCUSSION

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

In present study Table No. 1: Distribution of cases according to age. majority of cases were found in 12-30 years age group e.g. 42 cases (42%) followed by 24 cases in 31-45 years age group,19 cases in 46-60 years age group and 15 cases in >60 years age group. Similar result found in the study conducted by **Holloman et al** [14] he reported that the age range was 18 to 55 years with mean age of 27 years. 72% (63 of 87) were ≥30 years of age, while 44 (51%) were 44 ≤25 years, and 43 (49%) were above 25 years of age.

In present study figure No.1: Distribution of cases as per sex. majority of cases were males e.g. 64 cases (64%) and 36 cases were females (36%).Similar result found in the study by **Pathak et al** [15] he reported that the 34 were males (68%) and 16 were females (32%). Contrast result observed in the study by **Holloman et al** [14] he reported that the 38 were men and 49 were women.

In present study Table No.2: Distribution of cases according to Hb electrophoresis. majority of cases 52 with homozygous sickle cell haemoglobinopathy (HbSS variant) and 48 with heterozygous sickle cell haemoglobinopathy (HbAS variant). **Ondze-Kafata LI et al** [16] He reported that the 39 patients with hemoglobin SS (49.4%) and 40 with AS hemoglobin (50.6%).

In present study figure no 2: Distribution of cases according to examination finding. majority of cases presented with pallor 74 cases followed by icterus 36 cases, systolic murmur 30 cases, Loud pulmonary component of second heart sound 22 cases, Splenomegaly 20, Displaced apex beat 18 cases, Raised jugular venous pressure 9, Diastolic murmur 8 cases, Edema feet 6 cases, Crepitations 5 cases. **Adedoyin Dosunmu et al** [17] he reported that the majority of cases presented with pallor 56% cases followed by icterus 32% systolic murmur 28% cases, Splenomegaly 18 %, Diastolic murmur 6%.

In current study Table no 3: Distribution of cases according to ECG changes. majority of cases presented with T-inversion 34 cases followed by sinus tachycardia 24 cases, Left axis deviation 22 cases, right axis deviation 14 cases,12 right ventricular hypertrophy,10 cases with left ventricular hypertrophy, 9 cases with arrhythmia,5 sinus bradycardia,5 cases with P-pulmonale, low voltage complex 3 cases,Poor progression of R-wave 2 cases and P-mitrale 1 case.

Holloman et al [14] he reported that the electrocardiograms (ECGs) of 87 adult patients72% 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 Table no 4: Distribution of cases according to Cardiographic changes. majority of cases presented with pulmonary hypertension 34 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.

Ahmed et al [18] 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 hyperdynamic left ventricle (ejection fraction >70%). Left heart abnormalities included dilated atrium in 14 (37%),

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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.

Conclusions:

Majority of cases were found in 12-30 years age group**.** Most of cases were males. Majority of cases presented with T-inversion. Most common Cardiographic changes were pulmonary hypertension

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