



## A Study on Cardiovascular Manifestations of Leptospirosis

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### Abstract

**Background:** *Leptospirosis is now identified as one of the emerging diseases. It is a very common zoonotic disease across the world, caused by the bacteria of the genus Leptospira, family Leptospiraceae and order Spirochtales<sup>2</sup>. Clinical manifestations vary from mild to serious or even fatal. Cardiac involvement in leptospirosis is often underestimated. The aim of this study was to throw light on this aspect of the disease.*

**Materials and Methods:** *100 patients who satisfied the inclusion according to the modified Faine's Criteria were enrolled in the study. They were subjected to a through history and physical examination. Basic investigations were done in all patients, along with ECG, ECHO and cardiac enzyme CK MB. The clinical profile of the disease was studied and the correlation between the outcomes and complication with the ECG and ECHO findings were done.*

**Observations:** *100 patients were enrolled in the study, during the period of 1 year. Majority of the patients were in the age group of 40- 49 years (34%), followed by 24% in the age group of less than 30 years. Mean age group was 43 years. Among the study population 62 were males and 38 were females, with a male to female ratio of 1.63:1. Among the study population, 70% showed ECG changes. Sinus tachycardia was the commonest ECG change noted(60%). Those with ECG changes had higher incidence of renal and hepatic impairment, but no relation with thrombocytopenia. They also had higher incidence of dialysis and ventilation. Among the ECG changes, it was first degree AV block that was associated with renal impairment, hepatic impairment, dialysis and ventilation. Those with QTc prolongation had higher rates of intervention and poor outcomes like death. Those with ST T changes also had higher degree of renal and hepatic impairment. Among the 100 patients, ECHO was abnormal in 6 patients. In spite of optimal treatment we had a mortality of 4 %. All those who died had significant changes in ECG, ECHO and renal and hepatic impairment.*

### Background

Leptospirosis is now identified as one of the emerging diseases, exemplified by the large outbreaks in India, Brazil, Nicaragua, South East

Asia, and United States. It is presumed to be one of the most widespread zoonosis in the world and its incidence is significantly higher in warmer countries than in temperate regions. This is mainly

due to longer survival of the leptospire in the warm, humid conditions. The disease is also known by several names like mud swamp, fort bragg fever etc<sup>1</sup>.

It is a very common zoonotic disease across the world, caused by the bacteria of the genus *Leptospira*, family *Leptospiraceae* and order *Spirochetales*<sup>2</sup>. They can live in both animals and man freely. Infection is maintained in nature by chronic renal infection of carrier animals. They infect humans by entering through intact mucosal surface like conjunctiva, oronasal cavity, genitourinary tract, disrupted skin or through intact skin upon prolonged immersion in water. Human transmission occurs by indirect contact with contaminated animal urine through surface waters, moist soil or other wet environments or direct contact with urine and other excreta (products of parturition or placenta) of infected animals. Human infection may be acquired through occupational, recreational or avocational exposures. Farmers, veterinarians, rodent control workers, sewer workers, miners, soldiers, fish farmers, canal workers, rice field workers account for most of the cases. Usual portal of entry is through abrasions or cuts in the skin or via the conjunctiva.

Leptospiral entry is followed by extensive proliferation of the organism in many tissues. The resulting leptospiremia causes widespread dissemination in multiple organs. The organism can be isolated in the blood and CSF during the first 4 -10 days of the infection. These then damage the wall of small blood vessels, which leads to vasculitis with leakage and extravasation leading to hemorrhages. The most important property of leptospire is adhesion to cell surface and cellular toxicity. This vasculitis ultimately leads to increased capillary permeability, resulting in fluid leakage and hypovolemia.

After the leptospiremic stage, the organism disappears from blood and is followed by leptospiruric phase. Second stage of acute leptospirosis is also referred to as immune phase, in which the disappearance of the organism from

blood stream coincides with the appearance of antibodies.

Clinical manifestations vary from mild to serious or even fatal. More than 90 % of the cases develop relatively mild and anicteric form of leptospirosis, with or without meningitis. Weils syndrome, the most severe form of leptospirosis is characterized by jaundice, renal dysfunction and hemorrhagic diathesis.

Cardiac involvement in leptospirosis is often underestimated. Many patients develop atrial fibrillation, paroxysmal atrial flutter and ventricular tachycardia. Ventricular dysfunction is uncommon. The postulates range from possible concomitant myocarditis to changes secondary to hypokalemia. Repolarization abnormalities and arrhythmias on electrocardiogram were considered poor prognostic indicators in severe leptospirosis.

In contrast to the ECG abnormalities that are frequently reported, clinical signs of cardiac failure in leptospirosis are rarely seen, although the latter might be responsible for the mortality. Patients can have hypotension, cold clammy extremities, tachycardia and thread pulse. Echocardiography reveals normal systolic function of left ventricle. Hence hypotension is either due to dehydration or peripheral vasodilation.

In autopsy studies, it is noted that the heart and the main vessels are involved during the septicemic phase of the disease, and bacterial migration, toxins, enzymes and/or antigenic products liberated by bacterial lysis might account for the cardiac pathology. Most of the fatal cases demonstrate evidence of interstitial myocarditis.

Mortality ranges from < 5% to 40 %<sup>3</sup> depending upon the stage at which the patient seeks treatment. Serious patients may die within 24 hours of hospitalization due to renal failure, shock, ARDS or myocarditis<sup>2</sup>. Cardiac changes may add to the morbidity or be contributory to the mortality associated with the disease.

Antibiotics and other supportive treatment should be started early in the course of the disease and is found to decrease the morbidity and mortality. It

is therefore necessary to suspect a diagnosis of leptospirosis as early as possible and sometimes even under unusual circumstances in order to be able to provide a treatment which would definitely be more efficient when started earlier.

### Materials and Methods

It was a descriptive study conducted in a tertiary care centre over a period of 1 year.

### Inclusion Criteria

All individuals above 13 years of age, who satisfied the Modified Faine`s Criteria.

### Modified Faine`s Criteria

PARTICULARS	SCORE
(A) CLINICAL FEATURES	
Fever	2
Head ache	2
Temperature >39 degree celcius	2
Myalgia	4
Conjunctival suffusion	4
Meningism	4
Jaundice	1
Albuminuria/ elevated BUN	2
(B) EPIDEMIOLOGICAL FACTORS	
Rainfall	5
Contaminated environment	4
Animal Contact	1
(C) LABORATORY CRITERIA	
Culture	Diagnosis certain
ELISA IgM	15
MSAT	15
MAT- Single positive high titre	15
MAT- rising titre (paired sera)	25

- Each feature is given an appropriate scoring.
- Presumptive diagnosis of Leptospirosis is made if, Part A or Part A + Part B of > or equal to 26. Part A+Part B+ Part C = 25 or more, among serological tests only one should be used.

### Exclusion Criteria

Known case of cardiovascular disease, which includes, ischemic heart disease, valvular heart disease, pre existing arrhythmias.

Diabetes mellitus

Hypertension

Other infections: Malaria, Viral hepatitis, UTI, Enteric fever.

All the patients satisfying the inclusion criteria were subjected to a detailed history, with special emphasis to occupation or activities likely to increase the exposure to leptospirosis. A detailed physical examination was done with special emphasis on signs of cardiac failure, hepatic or renal impairment and evidence of bleeding manifestations.

Base line investigations were sent, which included, a complete hemogram, RFT, LFT and electrolytes were done in all patients. Serological investigations were done by detecting Ig M Antibody to Leptospira ( ELISA)

An ECG was done at the time of admission and, day 3, day5 and on the day of discharge in patients with ST-T changes.

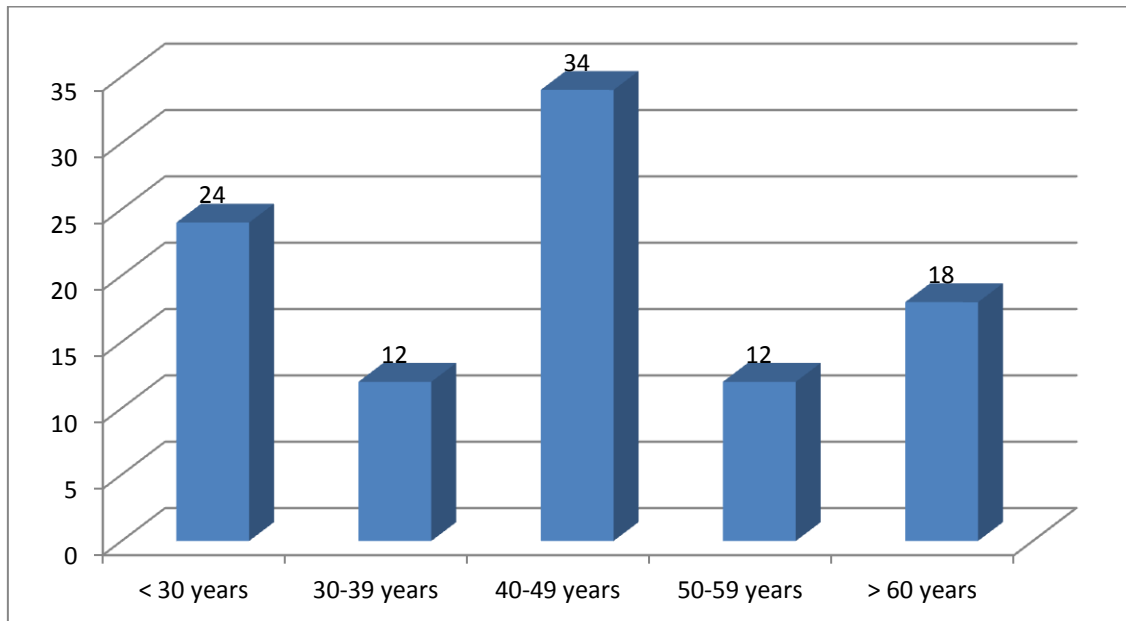
Repeat serum potassium was done in patients with ECG changes. Creatinine Phosphokinase MB sub fraction was measured at admission and at 24 hours in patients who had ST-T changes or in whom the initial value was raised.

Echocardiogram was done in patients with ST-T changes/raised CK MB or with a likelihood of having myocarditis, ie, presence of undue tachycardia, elevated JVP, hypotension, muffled heart sounds, new onset murmurs, basal creps etc. changes in ECHO included, global LV hypokinesia, chamber dialation, Mitral or tricuspid Regurgitation, decreased ejection fraction, pericardial effusion etc were checked.

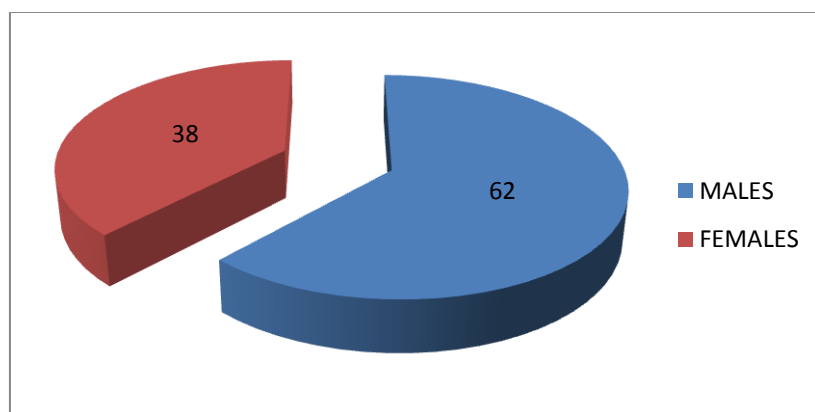
Data were analyzed using SPSS version 15. To elucidate the associations, Chi square tests, students t test and Mc Nemar Test were used. For all statistical evaluations, a two-tailed probability value of < 0.05 was considered significant.

**Observations**

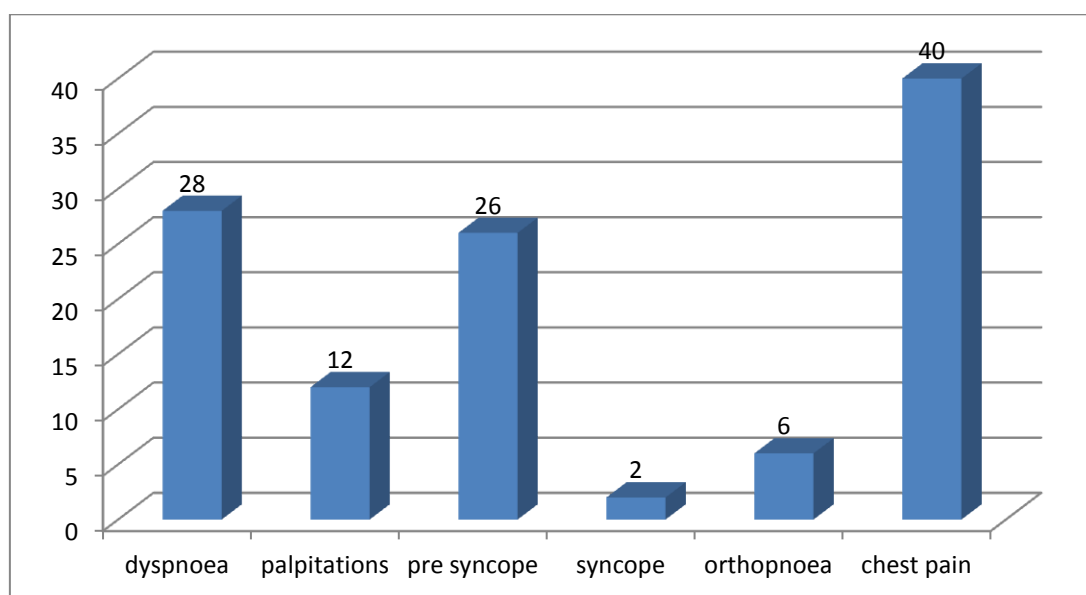
Total of 100 patients who satisfied the inclusion criteria were taken into the study.



**Figure 1:** Age distribution of cases.



**Figure 2:** Showing Gender distribution



**Figure 3:** Showing symptoms at presentation

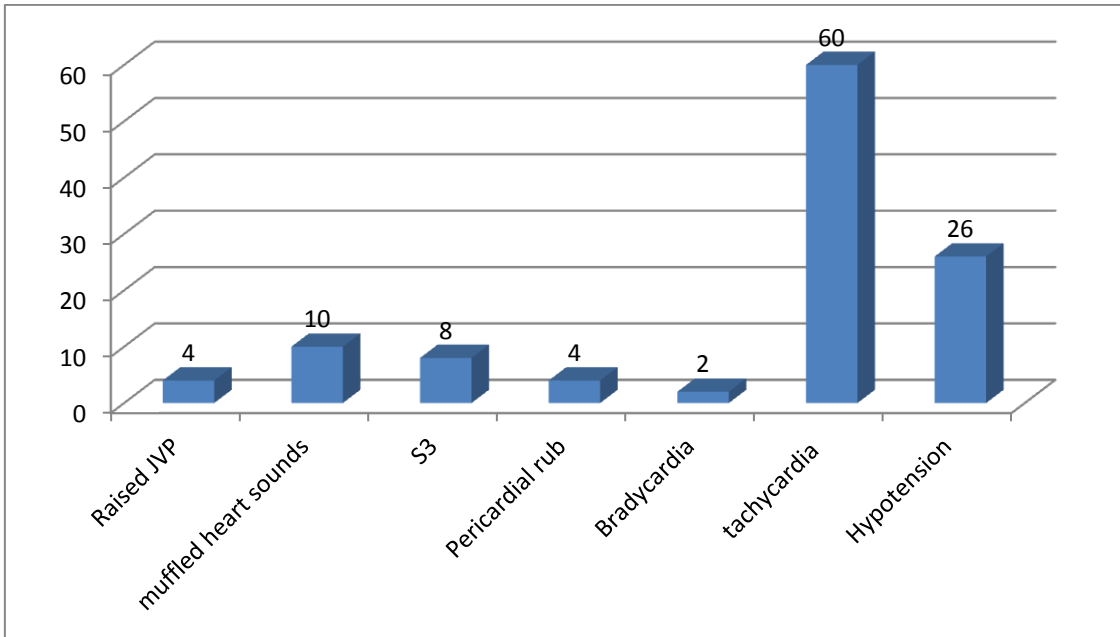


Figure 4: Showing physical signs

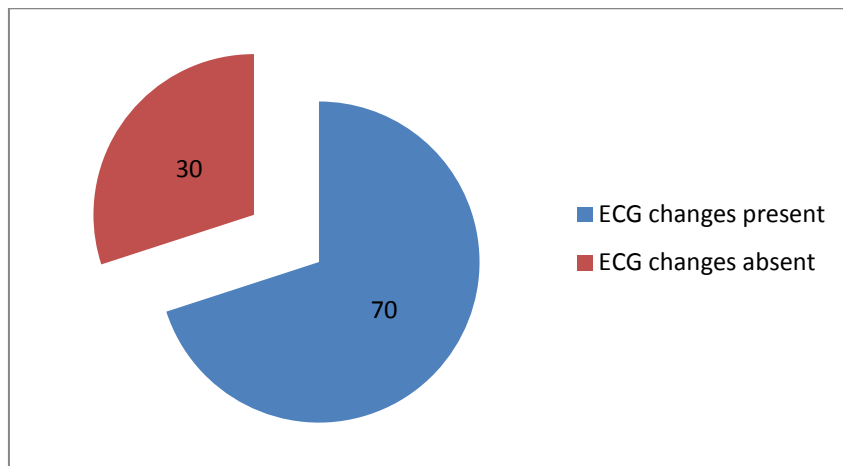


Figure 5: Showing frequency of ECG changes

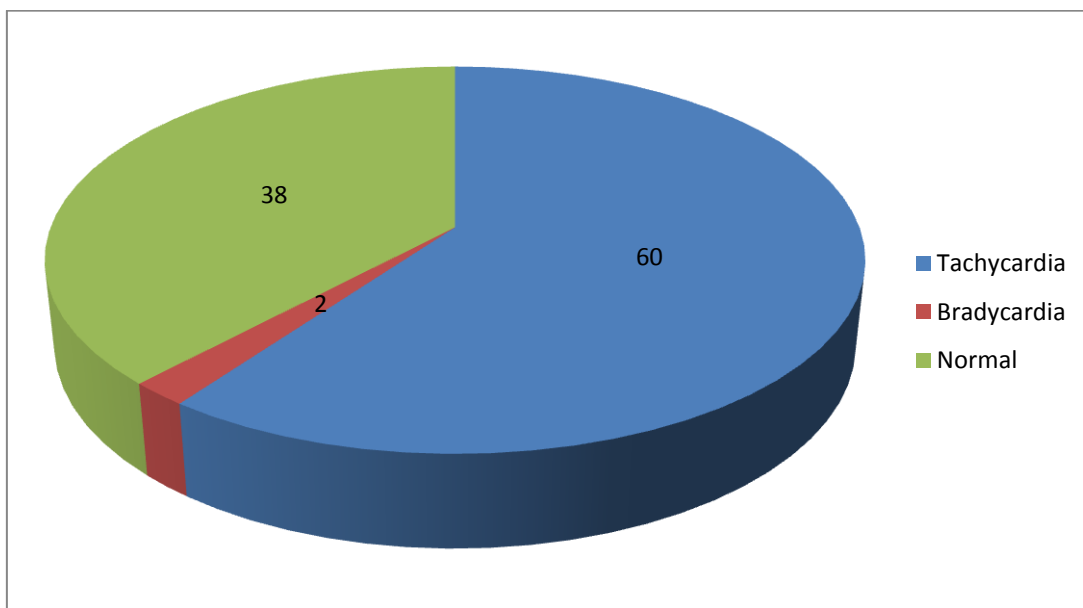


Figure 6: Showing rate abnormalities in ECG

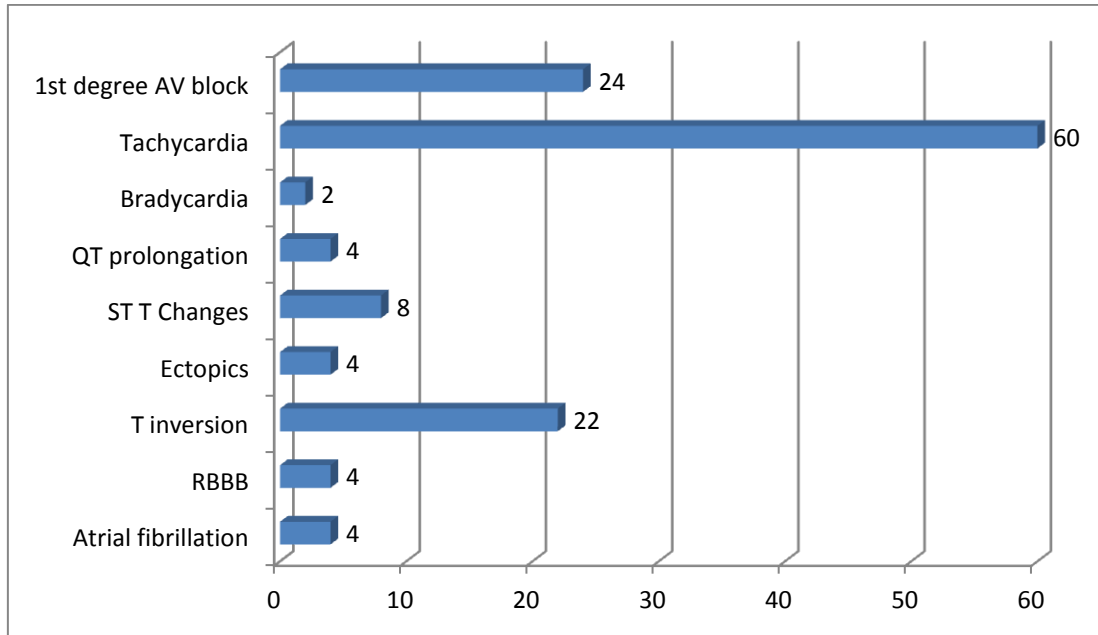


Figure 7: Showing rhythm abnormalities in ECG

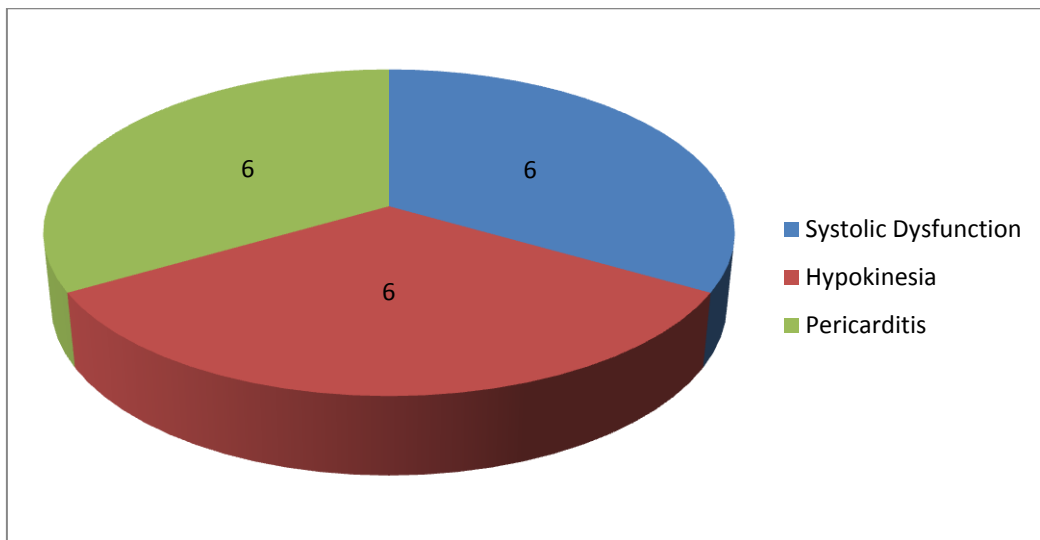


Figure 8: Showing ECHO changes

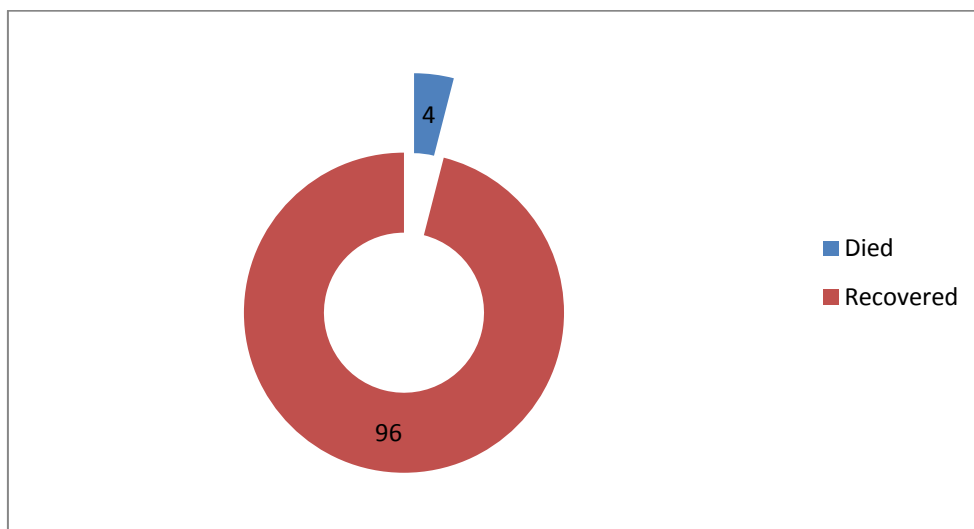
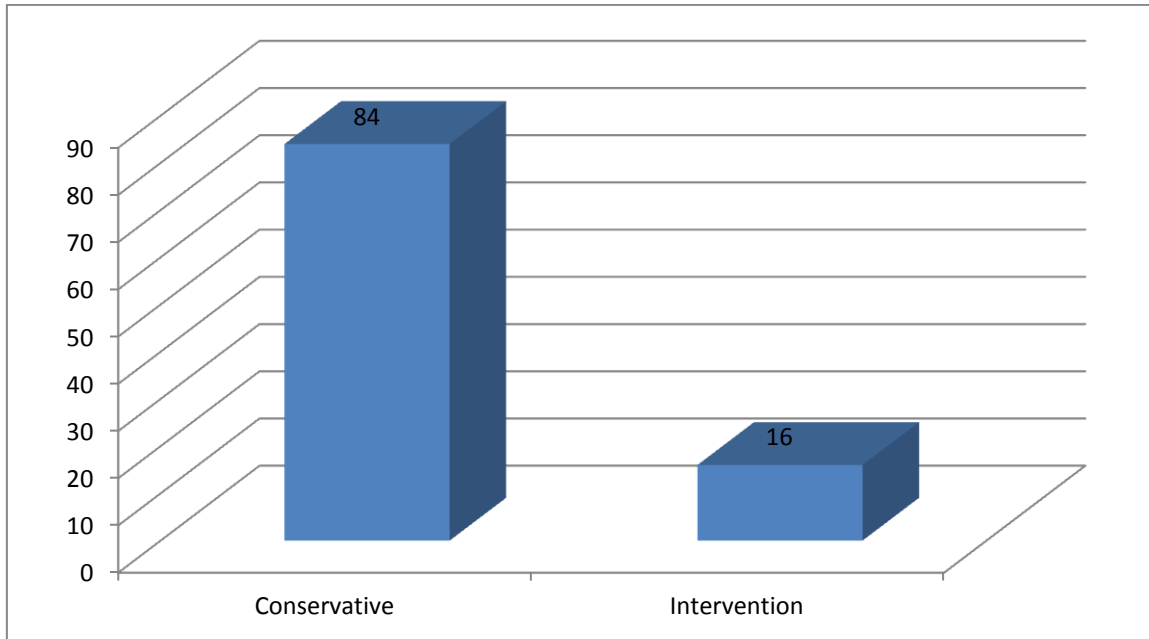
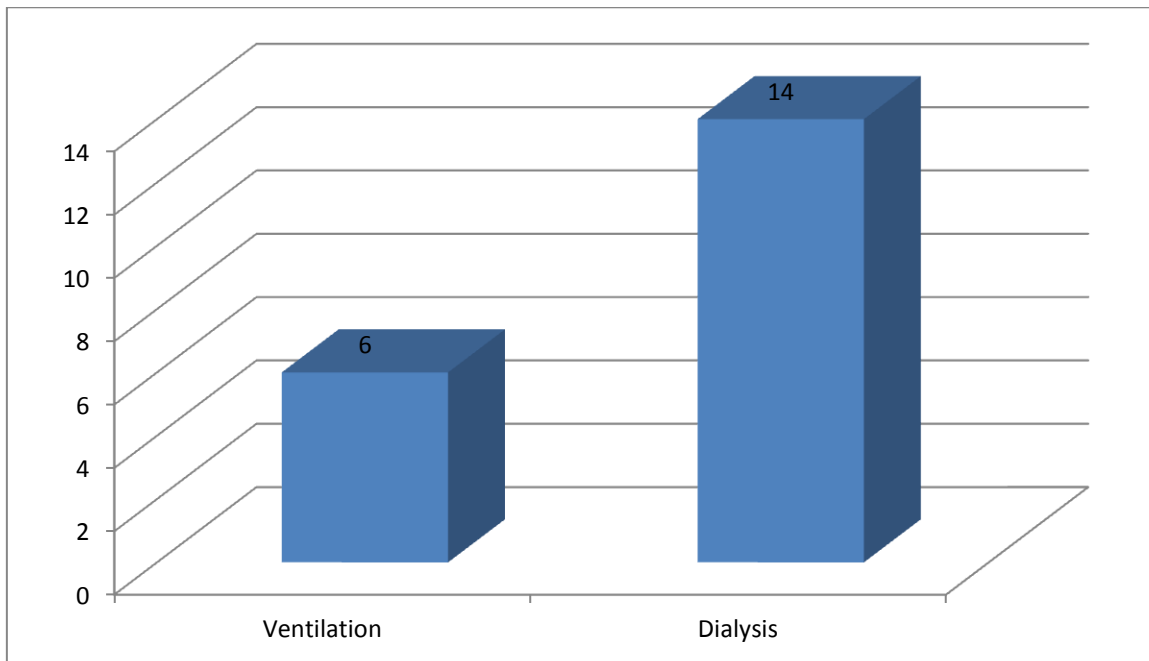


Figure 9: Showing outcome of patients



**Figure 10:** Treatment given to patients



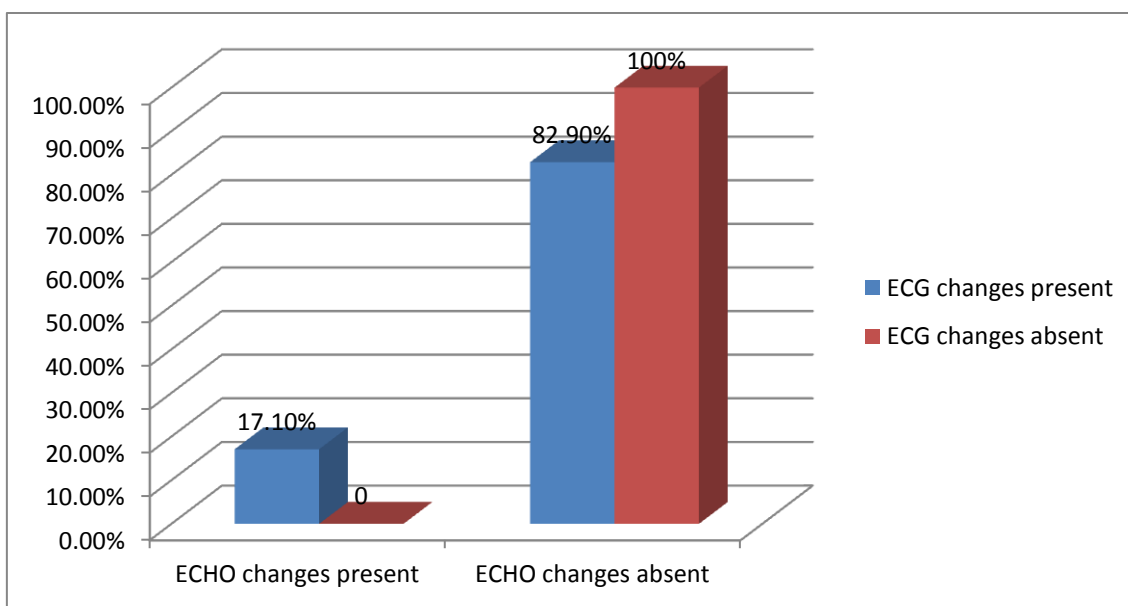
**Figure 11:** Type of intervention

**Table 1:** Showing association of variables in relation to tachycardia

PARAMETERS	TACHYCARDIA		TOTAL	CHI SQUARE	P value
	No	Yes			
ECG Changes	25%	100%	70%	64.286	<0.001
ECHO changes		20%	12%	9.0911	<0.01
Intervention		26.7%	16%	12.698	<0.001
Ventilation		10%	6%	4.255	<0.05
Dialysis		23.3%	14%	10.853	<0.01
Renal Failure		40%	30%	3.573	<0.05
Liver failure		40%	24%	10.526	<0.01
Thrombocytopenia		56.7%	54%	0.215	>0.05
Dyselectrolytemia		36.7%	28%	2.798	>0.05
Death		6.7%	4%	2.778	>0.05

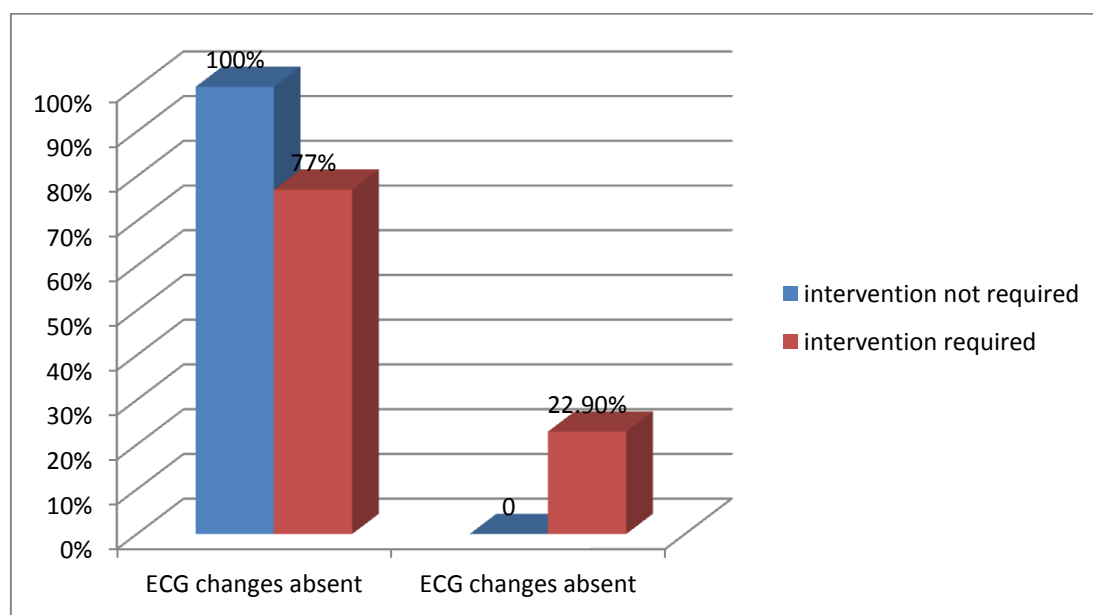
**Table 2:** Showing association of variables with hypotension.

PARAMETERS	HYPOTENSION		TOTAL	CHI SQUARE	P Value
	NO	YES			
ECG changes	59.5%	100%	70%	15.058	<0.001
ECHO changes	8.10%	23.1%	12%	4.082	<0.05
Intervention	5.4%	46.2%	16%	23.771	<0.001
Ventilation		23.1%	6%	18.167	<0.001
Dialysis	5.4%	38.5%	14%	17.462	<0.001
Renal failure	21.6%	53.8%	30%	4.757	<0.05
Liver failure	13.5%	53.8%	24%	8.581	<0.01
Thrombocytopenia	43.2%	84.6%	54%	6.629	<0.01
Dyselectrolytemia	21.6%	46.2%	28%	2.872	<0.05
Death		15.4%	4%	11.859	<0.01
Tachycardia	45.9%	100%	60%	23.423	<0.001



**Figure 12:** Association between ECG and ECHO changes

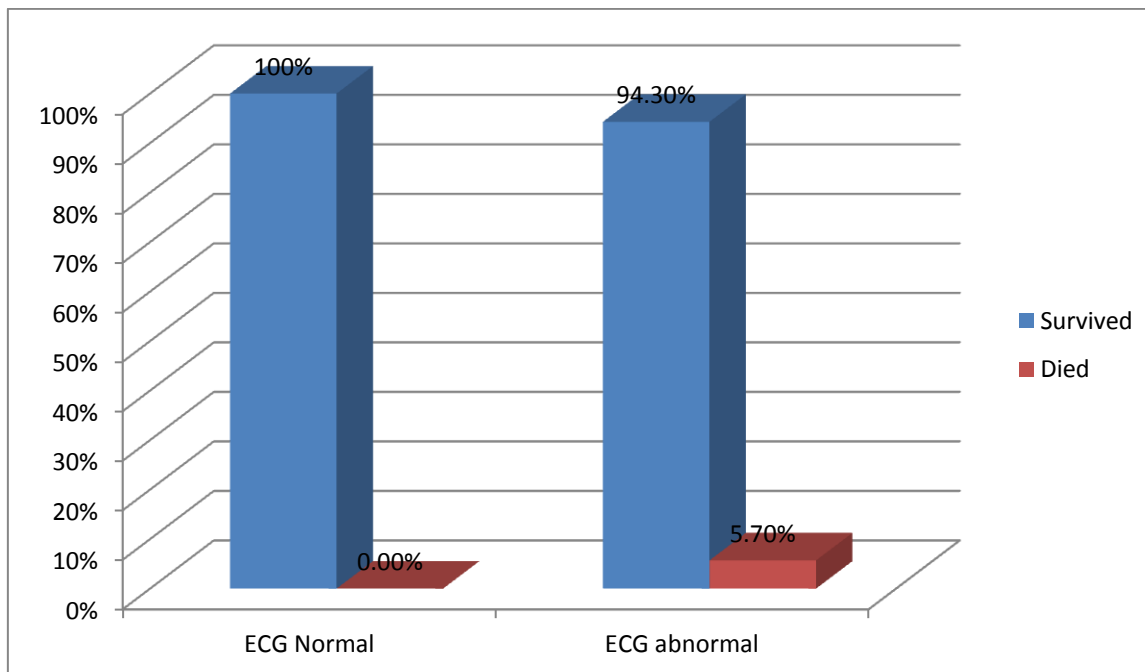
Chi square is 5.884 and p value is <0.05



**Figure 13:** Association between ECG changes and requirement of intervention.

Chi square 8.163, p value <0.01.



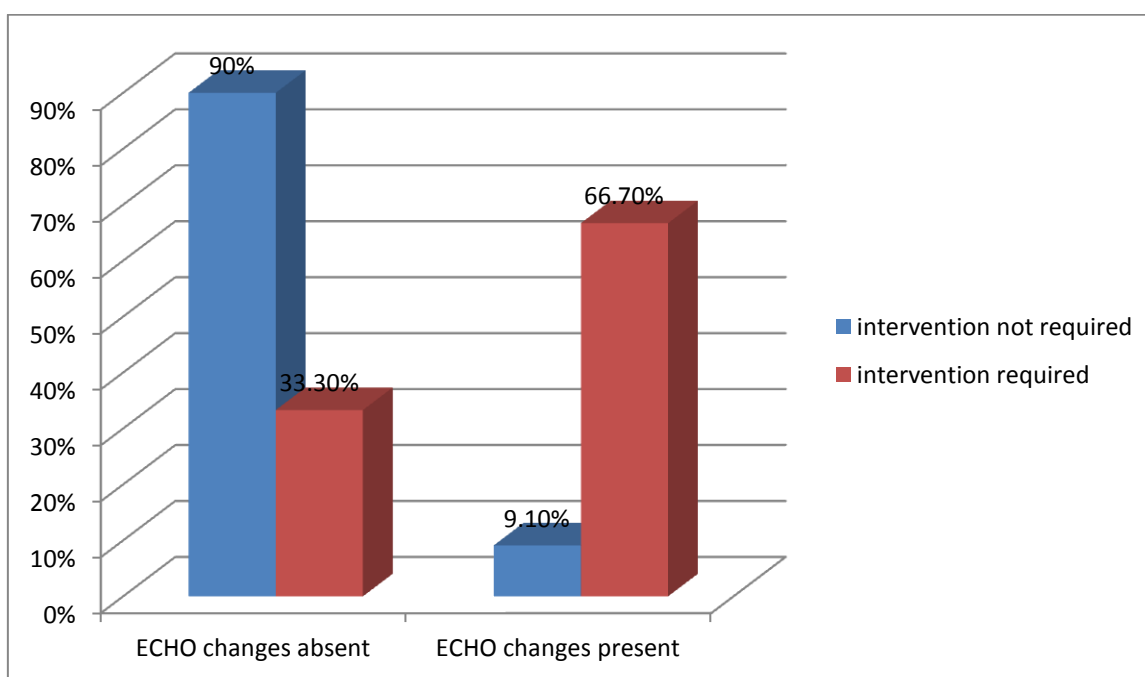


**Figure 14:** Association between ECG changes and survival

Chi square 1.789, P value >0.05

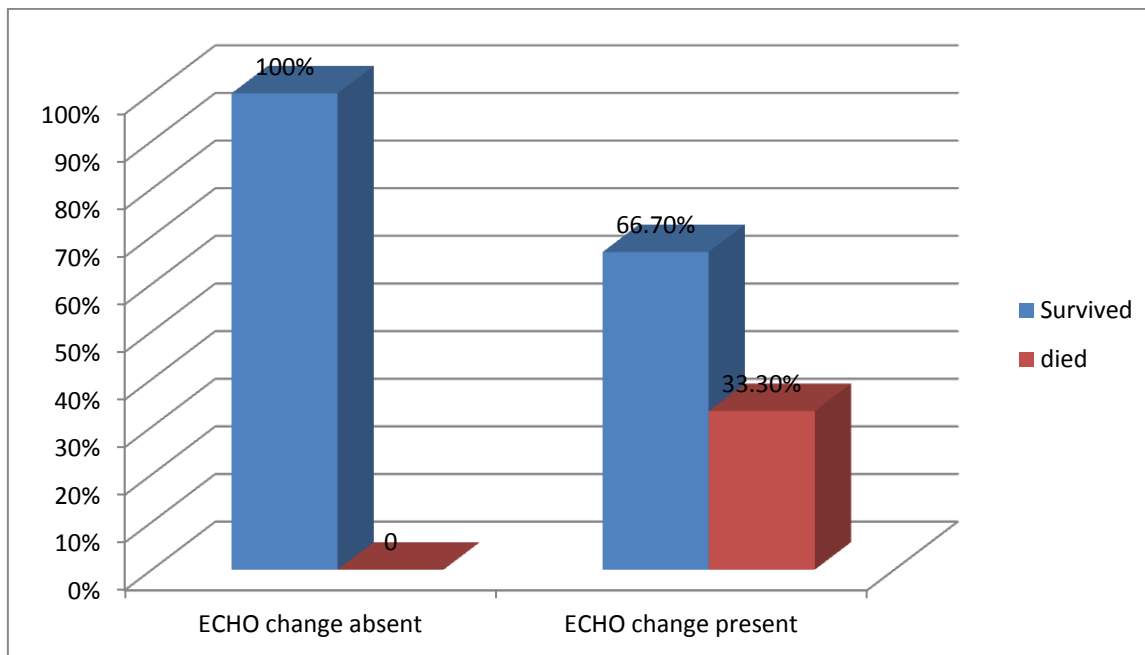
**Table 3:** Association of variables with ECG changes

PARAMETERS	ECG CHANGES		TOTAL	CHI SQUARE	P VALUE
	No	Yes			
Renal failure	6.7%	40%	30%	5.556	<0.05
Liver failure		34.3%	24%	6.767	<0.01
Thrombocytopenia	46.7%	57.1%	54%	0.464	>0.05
Dyselectrolytemia	6.7%	37.1%	28%	4.837	<0.05
Ventilation		8.6%	6%	2.736	>0.05
Intervention		22.9%	16%	8.163	<0.01



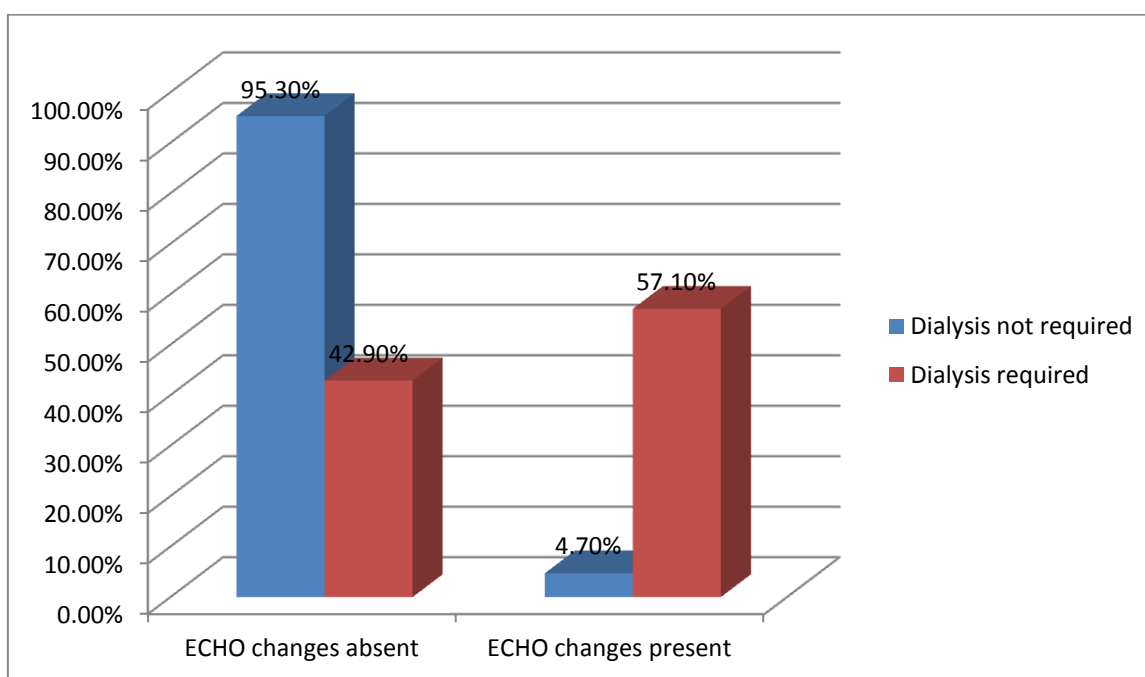
**Figure 15:** Association between ECHO changes and requirement of intervention

Chi square 26.001, p value <0.001



**Figure 16:** Association between ECHO findings and survival

Chi square 30.556, p value <0.001



**Figure 17:** Association between ECHO findings and requirement of dialysis.

Chi square 31.415 and p value <0.001

**Table 4:** Association of variables with ECHO changes

PARAMETERS	ECHO CHANGES		TOTAL	CHI SQUARE	P VALUE
	NO	YES			
Renal failure	25%	66.7%	30%	4.365	<0.05
Liver failure	18.2%	66.7%	24%	4.805	<0.01
Thrombocytopenia	52.3%	66.7%	54%	0.441	>0.05
Dyselectrolytemia	27.3%	33.3%	28%	0.096	>0.05
Ventilation	2.3%	33.3%	6%	8.064	<0.001
Intervention	9.1%	66.7%	16%	26.046	<0.001
Death	0	33.3%	4%	30.556	<0.001

**Table 5:** Association of variables with systolic dysfunction

PARAMETERS	SYSTOLIC DYSFUNCTION		TOTAL	CHI SQUARE	P VALUE
	NO	YES			
Renal failure	25%	66.7%	30%	4.365	<0.05
Liver failure	18.2%	66.7%	24%	6.805	<0.01
Thrombocytopenia	52.3%	66.7%	54%	0.441	>0.05
Dyselectrolytemia	27.3%	33.3%	28%	0.096	>0.05
Ventilation	2.3%	33.3%	6%	18.064	<0.001
Intervention	9.1%	66.7%	16%	26.046	<0.001
Death	0	33.3%	4%	30.556	<0.001
Dialysis	6.8%	66.7%	14%	31.415	<0.001

**Table 6:** Association between variables and first degree heart block

PARAMETERS	FIRST DEGREE BLOCK		TOTAL	CHI SQUARE	P VALUE
	NO	YES			
Renal failure	23.7%	50%	30%	3.125	<0.05
Hepatic failure	18.4%	41.7%	24%	2.702	>0.05
Thrombocytopenia	47.4%	75%	54%	.803	>0.05
Dyselectrolytemia	21.1%	50%	28%	3.791	<0.05
Ventilation	2.6%	16.7%	6%	6.371	<0.05
Intervention	10.5%	33.3%	16%	7.059	<0.01
Death	2.6%	8.3%	4%	1.544	>0.05
Dialysis	10.5%	25%	14%	3.174	<0.05

**Table 7:** Association between variables and QTc prolongation

PARAMETERS	QTc PROLONGATION		TOTAL	CHI SQUARE	P VALUE
	NO	YES			
Renal failure	29.2%	50%	30%	0.398	>0.05
Hepatic failure	22.9%	50%	24%	0.772	>0.05
Thrombocytopenia	54.2%	50%	54%	0.013	>0.05
Dyselectrolytemia	29.2%	0	28%	0.812	>0.05
Ventilation	4.2%	50%	6%	14.303	<0.001
Intervention	14.6%	50%	16%	3.584	<0.05
Death	2.1%	50%	4%	22.961	<0.001
Dialysis	12.5%	50%	14%	4.485	<0.05

**Table 8:** Association between variables and ST segment changes

PARAMETERS	ST SEGMENT CHANGES		TOTAL	CHI SQUARE	P VALUE
	NO	YES			
Renal failure	26.1%	75%	30%	4.193	<0.05
Hepatic failure	19.6%	75%	24%	6.201	<0.05
Thrombocytopenia	52.2%	75%	54%	0.772	>0.05
Dyselectrolytemia	26.1%	50%	28%	1.044	>0.05
Ventilation	2.2%	50%	6%	29.849	<0.001
Intervention	10.9%	75%	16%	22.522	<0.001
Death	0	50%	4%	47.917	<0.001
Dialysis	8.7%	75%	14%	26.847	<0.001

**Table 9:** Association between variables and T inversions:

PARAMETERS	T INVERSION		TOTAL	CHI SQUARE	P VALUE
	NO	YES			
Renal failure	25.6%	45.5%	30%	1.604	>0.05
Hepatic failure	20.5%	36.4%	24%	1.182	>0.05
Thrombocytopenia	48.7%	72.7%	54%	1.991	>0.05
Dyselectrolytemia	12.8%	81.8%	28%	20.261	<0.001
Ventilation	5.1%	9.1%	6%	0.478	>0.05
Intervention	12.8%	27.3%	16%	2.667	>0.05
Death	5.1%	0	4%	1.178	>0.05
Dialysis	12.8%	18.2%	14%	0.412	>0.05

## Discussion

100 patients were enrolled in the study, during the period of 1 year. Majority of the patients were in the age group of 40- 49 years (34%), followed by 24% in the age group of less than 30 years. Mean age group was 43 years. Existing studies also show similar findings<sup>4,5</sup>.

Among the study population 62 were males and 38 were females, with a male to female ratio of 1.63:1. This was in concordance with previous studies<sup>7</sup>.

Tachycardia was found to be significantly associated with ECG changes, ECHO changes, interventions like dialysis and ventilation and morbidities like hepatic and renal impairment. It was also associated with poor outcomes as death. There was no relation between parameters like thrombocytopenia.

Similarly, hypotension was associated significantly associated with ECG changes and ECHO changes and more of poor outcomes like hepatic and renal impairment. Again they had increased incidence of interventions like dialysis and ventilation. Those with hypotension had significant tachycardia.

Among the study population, 70% showed ECG changes. According to the previous studies, the incidence of ECG changes fell between 50-80%<sup>2,4,5,6</sup>. Sinus tachycardia was the commonest ECG change noted(60%). Other changes noted were, first degree AV block, RBBB, Atrial fibrillation, non specific T inversions, ectopics, ST-T changes, QT prolongation, bradycardia and normal ECG. Among the tachycardia patients, 56 had sinus tachycardia and 4 had AF. Those with ECG changes had higher incidence of renal and hepatic impairment, but no relation with thrombocytopenia. They also had higher incidence of dialysis and ventilation. Among the ECG changes, it was first degree AV block that was associated with renal impairment, hepatic impairment, dialysis and ventilation.

Those with QTc prolongation had higher rates of intervention and poor outcomes like death.

Those with ST T changes also had higher degree of renal and hepatic impairment. Also higher chances of interventions and death. There was no significant relation with thrombocytopenia.

In this study in variance with previous studies, it was found that first degree heart block, ST T changes and QT prolongation were associated with morbidity and mortality, where as in previous studies only QT prolongation had a significant association<sup>5</sup>.

Among the 100 patients, ECHO was abnormal in 6 patients. Abnormalities found were systolic dysfunction (6), hypokinesia (6), pericarditis (6). Among the 96 recovered, 6 had abnormal ECHO and 90 had normal ECHO and the difference between 2 groups were statistically significant in terms of recovery( p value <0.001). ECHO changes were significantly associated with poor outcomes like requirement of intervention and death.

The previous studies did not have any significant ECHO findings<sup>4,5</sup>.

Among the cardiac markers, Troponin was not done because of financial constrains. CK MB was done instead. But it could not be considered significant.

Regarding the treatment, most recovered with conservative management, while 16% required interventions. Of them 14% underwent dialysis and 6% were ventilated and 4% required both. In spite of optimal treatment we had a mortality of 4 %. All those who died had significant changes in ECG, ECHO and renal and hepatic impairment.

## Conclusions and Limitations

- Atypical chest pain and dyspnoea were the most common symptoms.
- Tachycardia and hypotension were the most common signs.
- Non specific ECG changes were seen in 70% but were asymptomatic.
- First degree AV block was the most common cardiac arrhythmia.

- ECHO findings seen were, systolic dysfunction, global hypokinesia, RWMA and pericarditis.
- Tachycardia was significantly associated with organ impairment, but not with death.
- Hypotension was associated with significant morbidity and mortality.
- ECG changes like AV block, ST T changes and prolonged QT interval had significant association with morbidity.
- ECG changes as a whole was not significantly associated with mortality, where as ECHO changes were significantly associated with mortality.
- We had a very small sample size.
- Cardiac troponins were not done.

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