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"Study Of Nt-Pro Bnp Levels In The Severity Of Heart Failure In Tertiaryhealth Care Hospital"

Author

Abstract
Background: Chronic heart failure (CHF) is a prevalent clinical syndrome that primarily affects the elderly, characterized by high mortality and morbidity rates. Many patients with CHF remain asymptomatic or present with atypical symptoms, leading to late-stage diagnosis and poor prognosis. Clinical trials have shown that early use of ACE inhibitors, beta-blockers, and spironolactone significantly reduces mortality and morbidity. However, conventional diagnostic tools like echocardiography are expensive and often unavailable, prompting the need for cost-effective alternatives such as neurohormonal markers, including NT-pro-BNP. This study aims to estimate NT-pro-BNP levels and correlate them with the severity of heart failure, providing a cost-effective and early diagnostic tool for heart failure management.
Material and Method: This hospital-based observational study was conducted at Adichunchanagiri Hospital and Research Center over 18 months, involving 100 patients aged over 18 years diagnosed with heart failure according to Framingham criteria. Data collection included detailed patient history, physical examination, and various diagnostic tests, including ECG, 2D ECHO, and NT-pro-BNP levels. Statistical analysis was performed using SPSS v23.0, with significance set at $p < 0.05$.
Results: The study population had a mean age of 54.88 years, with 70% male and 30% female. Hypertension was present in 59% of patients, and 49% had type 2 diabetes mellitus. Symptoms included chest pain (40%), palpitations (41%), and various grades of breathlessness. NT-pro-BNP levels were significantly correlated with declining ejection fractions and were higher in patients with dilated cardiomyopathy, chronic right heart failure, old ischemic heart disease, and LV dysfunction. Non-survivors had significantly higher NT-pro-BNP levels compared to those who improved or were discharged against medical advice.
Conclusion: This study underscores the significant role of NT-pro-BNP as a biomarker for assessing the severity and prognosis of heart failure. Elevated NT-pro-BNP levels were associated with worse outcomes, particularly in non-survivors, highlighting its potential utility in clinical practice for identifying high-risk patients and guiding treatment strategies.
Keywords: *Chronic Heart Failure, NT-pro-BNP, Heart Failure Diagnosis, Cardiomyopathy, Ejection Fraction, Prognostic Biomarker*

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I. Introduction

Chronic heart failure is a clinical syndrome that primarily affects elderly people. The syndrome is associated with high mortality and morbidity.[1] As most of the patients remains asymptomatic or may present with atypical symptoms and may be misdiagnosed. And prognosis also will be poor as they are diagnosed in later stages. Clinical trials shown that ACE inhibitors and beta blockers and spironolactone reduce mortality and morbidity significantly if used early in heart failure.[2,3]

As costs for various diagnostic investigations like Echo and radio nucleotide ventriculogrqphy are all costly as well as mostly not available in many centres newer diagnostic tools like neurohormonal markers could be effective in the diagnosis of heart failure.[4,5]

Natriuretic peptides are produced primarily within the heart and released into circulation in response to increased wall tension. Nt-pro-BNP are raised in both symptomatic and asymptomatic patients with heart failure. Recently a reliable Elisa method for analysis of NT pro BNP has been developed therefore suitable for the diagnosis of heart failure.[6,7]

Its already proven that NT-pro-BNP is diagnostic indicator for heart failure. But in this study focus about the levels of NT-pro-BNP values in various grades of heart failure and thus grading heart failure by knowing the values of NT pro-BNP values.[8,9]

This study is aimed to estimate the values of NT pro BNP in diagnosis of severity of Heart failure.

II. Review Of Literature

Heart failure is defined as abnormality of cardiac structure and or function resulting in clinical symptoms such as dyspnea, fatigue and signs such as edema, rales, hospitalisation, poor quality of life and shortened survival. It is very important to identify the underlying cause of the cardiac disease and factors that precipitate acute chronic heart failure (CHF).[10]

Despite repeated attempts to develop a mechanistic definition that encompasses the heterogeneity and complexity of heart failure (HF), no single conceptual paradigm has withstood the test of time. The current American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) guidelines define HF as a complex clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood, which in turn leads to the cardinal clinical symptoms of dyspnea and fatigue and signs of HF, namely edema and rales. symptoms of volume overload, the term "heart failure" is preferred over the older term "congestive heart failure".

Epidemiology

HF is a growing global disease, affecting over 20 million individuals. In affluent nations, the total prevalence of HF in adults is 2%. HF prevalence rises exponentially with age and affects 6-10% of adults over the age of 65. Although women have a lower proportional prevalence of HF than males, women account for at least half of all HF patients due to their greater life expectancy. For a 40-year-old in North America and Europe, the lifetime chance of having HF is about one in five. The overall prevalence of HF is expected to be rising, in part because modern treatments for cardiac illnesses such as myocardial infarction (MI), valvular heart disease, and arrhythmias allow patients to live longer. [10]

In India, Huffmann et al., estimate that the prevalence of heart failure in India due to coronary heart disease, hypertension, obesity, diabetes, and rheumatic heart disease to range from 1.3 to 4.6 million, with an annual incidence of 491 600-1.8 million, based on disease-specific estimates of prevalence and incidence rates of heart failure.[11]

Because of the scarcity of population-based research in these countries, little is known regarding the prevalence or risk of developing HF.

HF was long assumed to be caused largely by a low left ventricular (LV) ejection fraction (EF); however, epidemiologic studies have revealed that nearly half of individuals who develop HF have a normal or maintained EF (EF ≥50%). As a result, the previous designations "systolic" and "diastolic" heart failure have been abandoned, and HF patients are now generically classified as having HF with a decreased EF (HFrEF; formerly systolic failure) or HF with a preserved EF (HRpEF; formerly diastolic failure). [10]

Etiology

Any disorder that causes a change in the structure or function of the LV might predispose a patient to developing HF. Although the aetiology of HF in individuals with maintained EF differs from that of patients with lowered EF, there is significant overlap in their aetiologies. In developed nations, coronary artery disease (CAD) has become the leading cause of heart failure (HF) in both men and women, accounting for 60-75% of cases. In 75% of patients, including the majority of CAD patients, hypertension leads to the development of HF. Diabetes mellitus, CAD, and hypertension all combine to increase the risk of HF. [10]

The actual etiologic foundation of HF with a low EF is unknown in 20-30% of instances. If the reason is unknown, these individuals are diagnosed with nonischemic, dilated, or idiopathic cardiomyopathy. Prior viral infection or toxin exposure (for example, alcoholic or chemotherapeutic) can also cause dilated cardiomyopathy.[12,13]

Furthermore, it is becoming obvious that a considerable proportion of instances of dilated cardiomyopathy are caused by particular genetic abnormalities, most notably those affecting the cytoskeleton. The majority of familial dilated cardiomyopathies are inherited in an autosomal dominant manner. So far, mutations in genes encoding cytoskeletal proteins (desmin, cardiac myosin, and vinculin) and nuclear membrane proteins (laminin) have been found. Dilated cardiomyopathy has also been linked to Duchenne, Becker, and limb-girdle muscular dystrophies.[12,13]

High cardiac output situations (e.g., arteriovenous fistula, anaemia) are seldom responsible for the development of HF in a healthy heart; nevertheless, in the context of underlying structural heart disease, these diseases can lead to overt HF.

Table 1: Etiologies of heart failure[10]

Depressed ejection fraction (less than 40%)	
Coronary artery disease • Myocardial infarction • Myocardial ischemia	Chronic pressure overload • Hypertension • Obstructive valvular disease
Chronic volume overload	Toxic / drug induced

• Regurgitant valvular disease • Extracardiac shunting • Intracardiac shunting Chagas' disease Disorder of rate and rhythm • Chronic bradyarrhythmias • Chronic tachyarrhythmias	• Metabolic disorders • Viral Chronic lung disease • Cor-pulmonale • Pulmonary vascular disorders
Preserved ejection fraction (>40 – 50%)	
Restrictive cardiomyopathy • Infiltrative disorders (sarcoidosis, amyloidosis) • Storage diseases (hemochromatosis) Endomyocardial disorders	Pathologic hypertrophy • Primary (hypertrophic cardiomyopathies) • Secondary (hypertension) Ageing Fibrosis
High output state	
Metabolic disorders • Thyrotoxicosis Nutritional disorders (beriberi)	Excessive blood flow requirements • Systemic arteriovenous shunting • Chronic anemia

Table 2: New York Heart Association classification[10]

Functional capacity	Limitation	Objective assessment
Class I	None	Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitations, dyspnea, or anginal pain.
Class II	Slight	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
Class III	Marked	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.
Class IV	Severe	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Rheumatic heart disease continues to be a prominent cause of HF throughout Africa and Asia, particularly among the young. In the African and African-American communities, hypertension is a major cause of heart failure. Chagas disease is still a leading cause of heart failure in South America. Not surprisingly, anaemia is a common co-morbidity in many underdeveloped countries. As developing countries progress socioeconomically, the epidemiology of heart failure (HF) is becoming more comparable to that of Western Europe and North America, with CAD emerging as the single most prevalent cause of HF. Although the role of diabetes in heart disease is unknown, diabetes hastens atherosclerosis and is frequently related with hypertension.

In primary care, the overall 5-year survival rate after an HF diagnosis is 50%. The 1-year death rate for people with severe HF may be as high as 40%. In the United States, one in every eight fatalities has HF listed on the death certificate. The vast majority of these individuals die from cardiovascular causes, most typically from gradual heart failure or abrupt cardiac death. Several clinical and laboratory indicators have been shown to be independent predictors of death. Hospitalisations were prevalent after an HF diagnosis in population-based research, with 83% hospitalised at least once and 67%, 54%, and 43% hospitalised at least twice, three times, and four times, respectively. Mortality rates after an HF hospitalisation range from 8-14% at 30 days to 26-37% at 1 year and up to 75% at 5 years. Heart failure readmission is very prevalent, ranging from 20-25% at 60 days to over 50% at 6 months. The chance of mortality increases with each consecutive hospitalisation.

Phenotype and causes

HF with reduced versus preserved Ejection fraction

According to epidemiologic research, around one-half of individuals who develop HF have a lower left ventricular ejection fraction (EF; 40%), whereas the other half have a near-normal or intact EF (50%). Because the majority of HF patients (regardless of EF) have problems in both systolic and diastolic function, the traditional concepts of systolic and diastolic heart failure have gone out of favour. Because of disparities in demographics, comorbidities, and responsiveness to medications, classifying patients based on their EF (HF with decreased EF [HFrEF] versus HF with preserved EF [HFpEF]) is crucial.

HF with Recovered EF:

A subset of individuals identified with HFrEF and treated with guideline-directed treatment experience a quick or gradual return to normal EF and are referred to as having HF with recovered EF (HFrecEF). Younger age, shorter duration of HF, nonischemic aetiology, smaller ventricular sizes, and lack of myocardial fibrosis are

all predictors of HFrecEF. Fulminant myocarditis, stress cardiomyopathy, peripartum cardiomyopathy, and tachycardia-induced cardiomyopathy are specific clinical instances, as are reversible toxin exposures such as chemotherapy, immunotherapy, or alcohol. Despite regaining EF, individuals may remain symptomatic due to chronic diastolic function deficits or exercise-induced pulmonary hypertension. Withdrawal of medication may result in resumption of HF symptoms and a decline in EF in individuals who have been asymptomatic. In general, patients with HFrecEF have a better prognosis than those with HFrEF or HFpEF.

Heart Failure with Mildly Reduced EF (HFmrEF):

Patients with HF and an EF between 40 and 50% are treated similarly to patients with HFrEF for risk factors and comorbidities, as well as with guideline-directed medication treatment. They are thought to have modest systolic dysfunction with diastolic dysfunction traits. They may also include people with impaired EF who improve their EF or those with originally maintained EF who have a minor reduction in systolic performance. Unlike the ACCF/AHA and HFSA guidelines, the ESC guideline has designated HFmrEF as a distinct entity in order to spur research into the underlying features, pathogenesis, and therapy.

Acquired versus familial, congenital and other disorders:

In affluent nations, coronary artery disease accounts for almost two-thirds of all instances of heart failure, with hypertension accounting for up to 75% and diabetes mellitus accounting for 10-40%. While most cardiovascular illness that causes HF develops in middle and later life, a variety of congenital and hereditary conditions that cause HF can be detected in children and young people. It is now estimated that more than 1.4 million people in the United States have congenital heart disease (CHD), which outnumbers the number of infants with CHD.[14–16] Adults with CHD who develop HF can be classified into three pathophysiologic groups: uncorrected defects with late presentation due to missed diagnosis, non-intervention, or lack of access to care; repaired or palliated defects with late valvular and/or ventricular failure; and failing single-ventricle physiology. Furthermore, each adult with CHD frequently has distinct anatomic and physiologic problems that impact HF and its management.

Inherited cardiomyopathies are also becoming more common in individuals with HF. These include more frequent illnesses including hypertrophic and arrhythmogenic cardiomyopathies, as well as less common heart muscle disease caused by pathogenic variations in lamin and titin genes, muscular dystrophies, and mitochondrial disease. The majority of familial cardiomyopathies are inherited in an autosomal dominant manner. The need of taking a full family history, as well as the criteria for (and limitations of) clinical genetic testing, has been documented in society recommendations.

Pathophysiology

HFrEF is a progressive condition with an initial event followed by months or years of structural and functional cardiovascular remodelling. The initial event may be rapid, as in an acute myocardial infarction, or more progressive, as in chronic pressure or volume overload; hereditary, as in genetic cardiomyopathies; or congenital illness. Despite an initial decrease in heart function, individuals may be asymptomatic or minimally symptomatic for extended periods of time due to compensatory processes that eventually lead to disease development. [10]

Different forms of ventricular remodelling occur in response to increased cardiac strain, as evidenced in both animal and human research. Concentric hypertrophy, defined as increased mass that is out of proportion to chamber volume, efficiently decreases wall stress in pressure overload circumstances (e.g., hypertension, aortic stenosis). In volume overload circumstances (e.g., aortic regurgitation, mitral regurgitation), an increase in cavity size or volume (eccentric hypertrophy) develops. An increase in ventricular mass is followed at the cellular level by myocyte hypertrophy and interstitial fibrosis, at the protein level by changes in calcium-handling and cytoskeletal function, and at the molecular level by foetal gene re-expression.[17,18]s

Mechanism of disease progression:

A number of compensatory mechanisms become activated during the development of HF and contribute to disease progression.

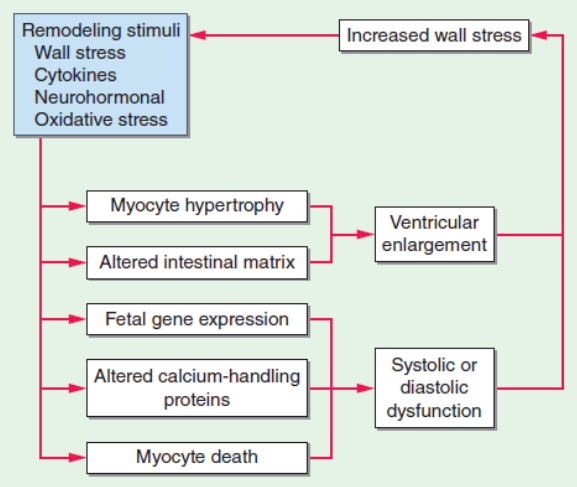

Figure 1: Remodeling stimuli in heart failure[10]

Table 3: Mechanism of ventricular remodeling	
Changes in myocyte biology	Fetal gene expression (e.g., β-myosin heavy chain) Myocyte hypertrophy Abnormal excitation-contraction coupling and crossbridge interaction β-Adrenergic receptor desensitization Impaired cytoskeletal proteins
Changes in myocardial make-up	Matrix degradation Myocyte necrosis, apoptosis, and autophagy Interstitial and perivascular fibrosis
Changes in ventricular geometry	Increased sphericity and displacement of papillary muscles Ventricular dilation and wall thinning Atrioventricular valve regurgitation

Neurohormonal activation:

The sympathetic nervous system (SNS) and the renin-angiotensin-aldosterone system (RAAS) are both activated in the development and progression of HF. Initially, neurohormonal activation raises heart rate, blood pressure, and cardiac contractility, as well as salt and water retention, in order to augment preload and sustain cardiac output at rest and during exercise. Unchecked compensatory reactions result in excessive vasoconstriction and volume retention, electrolyte and renal problems, baroreceptor dysfunction, direct myocardial damage, and cardiac arrhythmias over time.[11,19]

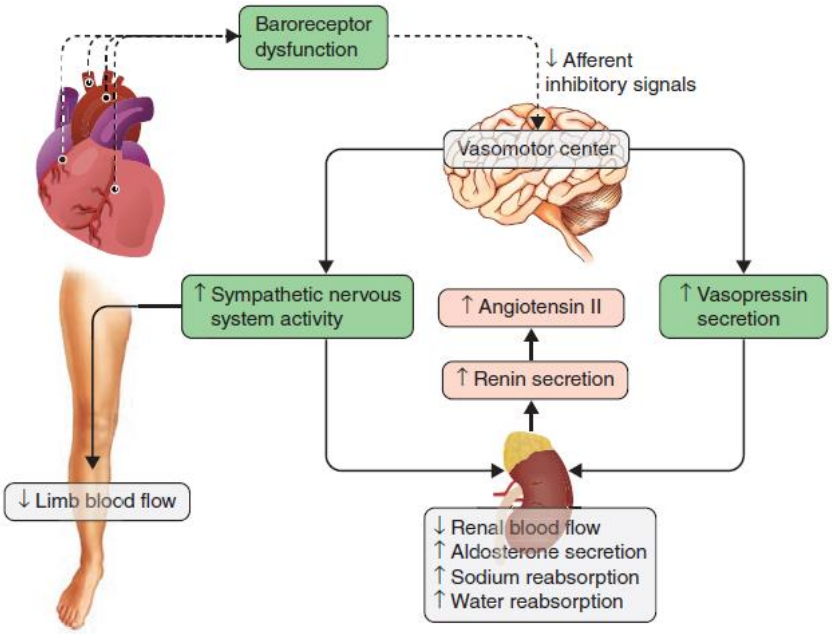

Figure 2: Showing the activation of neurohormonal system in heart failure[10]

Neurohormonal activation leads to tissue remodelling of the heart, blood arteries (atherosclerosis), kidneys, and other organs, as well as the development of symptomatic HF. Antagonism of the RAAS and SNS using renin-angiotensin system inhibitors, mineralocorticoid receptor antagonists, and beta blockers attenuates or reverses ventricular and vascular remodelling and decreases morbidity and death in heart failure.

Vasodilatory hormones:

While RAAS and SNS activation contributes to disease development in heart failure, a variety of counterregulatory hormones are elevated and have positive effects on the heart, kidney, and vasculature. Natriuretic peptides (atrial natriuretic peptide [ANP] and B-type natriuretic peptide [BNP]), prostaglandins (prostaglandin E1 [PGE1] and prostacyclin [PGI2]), bradykinin, adrenomedullin, and nitric oxide are among them. In reaction to increasing stretch or pressure, ANP and BNP are largely stored and released from the atria and ventricles, respectively.[20–22]

Dyssynchrony and electrical instability:

The QRS interval is related with disease progression in up to one-third of HF patients. An aberrant ventricular contraction is caused by electrical dyssynchrony in the form of left bundle branch block (LBBB) or intraventricular conduction delay. Electrical dyssynchrony can be corrected with left or biventricular pacing, which can enhance contractile performance, decrease mitral regurgitation, and reverse ventricular remodelling. Cardiac resynchronization treatment is appropriate in individuals with symptomatic HFrEF and LBBB who are receiving guideline-directed medical therapy to minimise morbidity and mortality. Other types of electrical instability, such as atrial fibrillation with poor rate control and frequent premature ventricular complexes, can also aggravate HF.

Secondary mitral regurgitation:

Mitral regurgitation is seen in a substantial proportion of individuals with HFrEF. This is caused by deformation of the mitral valve apparatus and includes the activity of several pathophysiological processes, including diminished contractile force, which results in decreased attachment of the leaflets to the mitral valve's spheroid. Papillary muscle length and function are influenced by the ventricles. structural, increased mitral annulus size (and annulus inability to contract during systole) with poor leaflet alignment and dilatation of the posterior wall of the left atrium, deforming the leaflets at the valve's rear.

High output states:

Although the majority of patients with HF have low or normal cardiac output (CO) accompanied by raised systemic vascular resistance (SVR), a minority of individuals with HF have a high-output condition with low SVR. High-output states are seldom the cause of HF on their own, but their emergence in the presence of underlying cardiovascular illness can induce HF. Chronic anaemia, for example, is connected with high CO when haemoglobin levels fall dramatically, for example, to ≤8 g/dL. Low SVR is caused by a rise in vasodilatory metabolites and arteriolar vasodilation in response to decreased oxygen-carrying capacity of the blood, as well as a decrease in blood viscosity. In the absence of a particular cardiac anomaly such as ischemia or valvular heart disease, anaemia, even when severe, seldom produces high-output HF.

When chronic anaemia is aggravated by increased flow through an arteriovenous fistula, patients with end-stage renal disease are especially vulnerable to developing high-output HF. Obesity (31%), liver disease (23%), lung disease (16%), arteriovenous shunts (23%), and myeloproliferative diseases (8%), were the most prevalent causes in a recent group of patients with high-output HF.

Symptoms of congestion:

The most common symptoms of HF are related to volume overload with elevation in pulmonary and or due to systemic venous pressure.

Shortness of breath is a cardinal manifestation of left HF, which may arise with increase severity as exertional orthopnea, dyspnea, paroxysmal nocturnal dyspnea and dyspnea at rest.

Symptoms of reduced perfusion:

Related to decreased carbon dioxide, sometime refer to low-output syndrome.

Fatigue and weakness particularly of the lower extremities.

Other symptoms include mood disturbance, poor sleep or both which may be exacerbated by nocturnal dyspnea and obstructive or central sleep apnea.

Diagnosis

When a patient exhibits classic HF signs and symptoms, the diagnosis is very simple; nevertheless, HF signs and symptoms are neither specific nor sensitive. It is also critical for doctors to have a high index of suspicion for HF, especially in patients who are at high risk, such as older patients with underlying cardiovascular disease and those with comorbidities such as hypertension, diabetes, and chronic renal disease.

Standard laboratory testing in patients with HF includes a comprehensive metabolic panel, complete blood count, coagulation studies, and urinalysis. Selected patients should have assessment for diabetes, dyslipidemia, and thyroid function. Blood urea nitrogen and creatinine levels are often elevated in moderate-severe HF due to reduced renal blood flow and/or increased renal venous pressure.

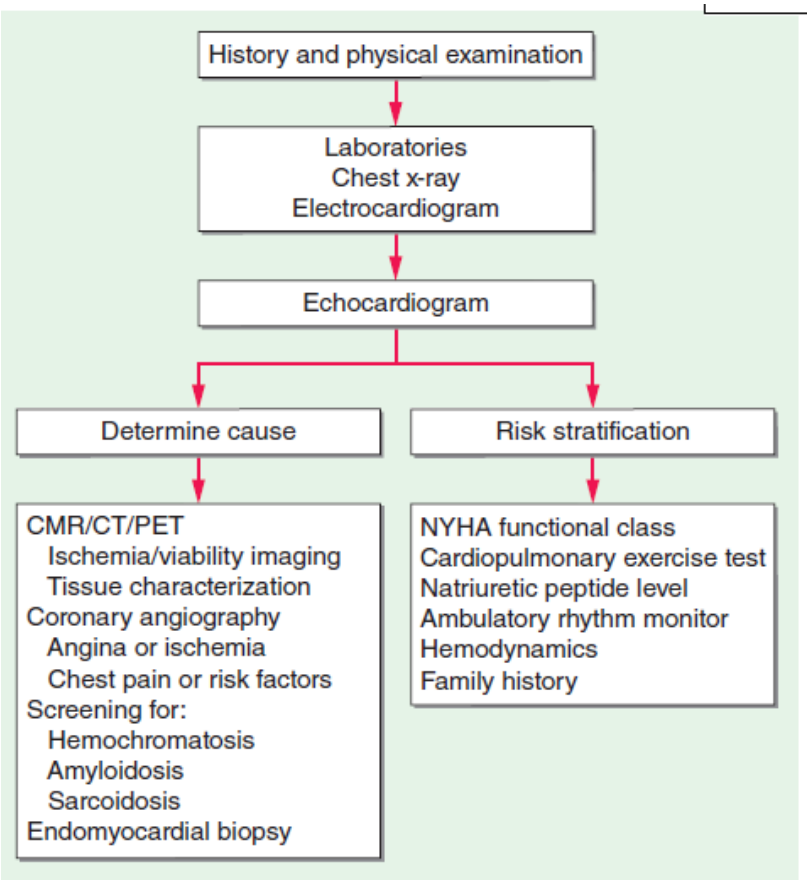

Figure 3: Assessment of patients presenting with heart failure[10]

Chest X-ray:

Chest imaging findings that are related with left HF include an enlarged cardiac silhouette (cardiothoracic ratio >0.5) and pulmonary venous congestion. Upper zone venous redistribution and interlobular septal thickening are early radiologic markers of acute HF. Alveolar edema can manifest as widespread haziness spreading downhill towards the lower lung fields when the pulmonary capillary wedge pressure is moderate to severely raised. The lack of these signs in individuals with chronic HF shows the lymphatics' enhanced ability to clear interstitial and/or pulmonary fluid. In biventricular HF, pleural effusions of varied size and location are prevalent. A chest x-ray can also be performed to rule out noncardiac causes of dyspnea (for example, pneumonia or COPD).

Electrocardiogram:

There is no unique electrocardiographic (ECG) pattern that can be used to diagnose heart failure. Rather, the ECG may reveal vital information about the existence of underlying heart illness. Left ventricular hypertrophy and left atrial enlargement imply hypertension, aortic stenosis, or hypertrophic cardiomyopathy as the cause of HFpEF. The presence of Q waves or infarction indicates ischemic heart disease, although Q waves with decreased QRS voltage (pseudo-infarct pattern) may be found with restrictive or infiltrative cardiomyopathies (e.g., amyloid). In the correct clinical situation, conduction system illness should raise the

possibility of cardiac sarcoid or Chagas cardiomyopathy. Anticoagulation is indicated in up to 40% of patients with chronic HF who had paroxysmal or persistent atrial fibrillation.

Abnormal electrocardiogram findings can increase the likelihood of diagnosing heart failure.[23] Additionally, it can provide information about the potential causes of heart failure, such as a history of myocardial infarction indicating coronary artery disease or arrhythmias suggesting transmedial cardiomyopathy. Certain electrocardiogram patterns, such as tachycardia in the context of heart failure, left ventricular hypertrophy indicating hypertensive cardiomyopathy, a wider QRS complex or left bundle branch block pointing towards idiopathic dilated cardiomyopathy, and heart block observed in patients with cardiac sarcoidosis, can guide treatment decisions. For instance, anticoagulants may be recommended for patients with atrial fibrillation, pacemakers may be considered for certain bradycardias, and cardiac resynchronization therapy (CRT) may be indicated for individuals with an enlarged QRS complex.

Non-invasive imaging:

Noninvasive cardiac imaging is critical for the diagnosis, assessment, and treatment of heart failure. Two-dimensional echocardiography determines ventricular size and function, as well as valvular morphology and function, and can identify intracavitary thrombi and pericardial effusions. Systolic function is considered normal when the left ventricular ejection fraction (LVEF) is 50%. Speckle tracking myocardial strain rate imaging can offer added value to LVEF and has prognostic relevance.

In patients with HFpEF, Doppler methods can be utilised to quantify CO, pulmonary artery pressures, and valve areas, as well as detect anomalies in left ventricular diastolic filling. Echocardiography is essential for assessing right ventricular function before and after mechanical circulatory support and heart transplantation in patients with end-stage HF. Transesophageal echocardiograms are used to rule out atrial thrombi prior to cardioversion and to evaluate aortic or mitral valve disease in preparation for transcatheter valvular replacement or repair.

Cardiac magnetic resonance imaging (CMR) is highly accurate and quantitative tool for evaluation of left ventricular mass, volume and function for determining the specific cause for CHF. Other include the cardiac computed tomography which help to rule out pericardial disease or left ventricular apical thrombus. Positron emission tomography, which is limited with availability and cost may play a role in evaluating the extent of ischemia or infarction in patients with coronary artery disease.

Cardiopulmonary exercise testing: While not routinely performed in HF, cardiopulmonary exercise testing using a symptom limited, ramp protocol can provide an objective assessment of peak functional capacity in patients being evaluated for mechanical circulatory support or heart transplant.

Biomarkers: Natriuretic peptide levels in the blood are important adjunctive tools in the diagnosis of heart failure. In response to increasing wall stress, the atria and ventricles produce BNP and N-terminal pro-BNP (NT-proBNP). individuals with HFrEF have larger levels than individuals with HFpEF, although levels in obesity may be erroneously low. BNP or NT-proBNP testing in ambulatory patients with dyspnea is valuable to enhance clinical decision-making about the diagnosis of HF, particularly in the case of clinical ambiguity or concurrent lung illness. Furthermore, in stable outpatients, natriuretic peptide levels can be utilised to determine illness severity and prognosis, as well as to recommend appropriate dose of medicinal therapy. Many noncardiac variables, such as age, female sex, and chronic renal illness, raise natriuretic peptide levels. BNP levels can also be raised by other cardiovascular illnesses such as atrial fibrillation, pulmonary embolism, and pulmonary arterial hypertension. Galectin-3 and soluble ST2 are novel biomarkers that have been authorised for prognostic evaluation in HF but are not frequently used. In HF, biomarkers of renal damage deserve additional investigation.

BNP and N-terminal pro-BNP (NT-proBNP)

Natriuretic peptides (NP) are important proteins that help and regulate circulation. They are important proteins that cause blood arteries to dilate or expand. These peptides are mostly produced by cardiomyocytes with a mixed secretory-contractile character in the atrial and ventricular walls. NPs prevent heart hypertrophy and remodelling in addition to controlling blood pressure.[24,25] A treatment-induced decline in wedge pressure is frequently accompanied by a fast drop in NP levels in patients with decompensated heart failure due to volume overload. Thus, measuring NP levels might help with hemodynamic evaluation and subsequent therapy titration. NPs are also present in the kidneys, where they induce this vital organ to discharge more water and salt.[19,24,26]

B-type natriuretic peptide (BNP) belongs to the NP family, which also includes atrial natriuretic peptide (ANP), C-type natriuretic peptide, D-type natriuretic peptide, and urodilatin. Pro-BNP is a 108-amino acid precursor protein of BNP present in the heart's ventricles and atria. ANP and BNP in humans are encoded by genes on chromosome 1. ProBNP is elevated at the genomic level in circumstances of volume overload and cardiac muscle strain.[27–29]

BNP is present in modest amounts in the cytoplasmic granules of myocytes. ProBNP is cleaved by corin into equimolar levels of the physiologically active BNP hormone and the biologically inactive amino-terminal proBNP (NT-proBNP), which is also released into circulation as the unprocessed precursor protein when stimulated for synthesis and release. When the effects of this peptide on vascular smooth muscle cells, cardiac fibroblasts, and myocytes were examined, it was discovered that it had no biological activity.[28,30]

Pathophysiology

BNP is a peptide hormone that contains 32 amino acids and has a molecular weight of 3472 daltons.[31] The molecule has a 9-amino acid N-terminal tail, a 6-amino acid C-terminal tail, and a 17-member ring connected by a disulfide link between two cysteine residues. Eleven amino acids in the ring are conserved across the natriuretic peptide family. BNP binds to natriuretic peptide receptors A and C, causing water and electrolyte loss, vasodilation, and RAAS suppression. Neutral endopeptidases remove BNP from the blood.[31,32] Dipeptidyl peptidase IV removes the first two amino acids from the N-terminal sequence (serine and proline) shortly after BNP is released into circulation.[29]

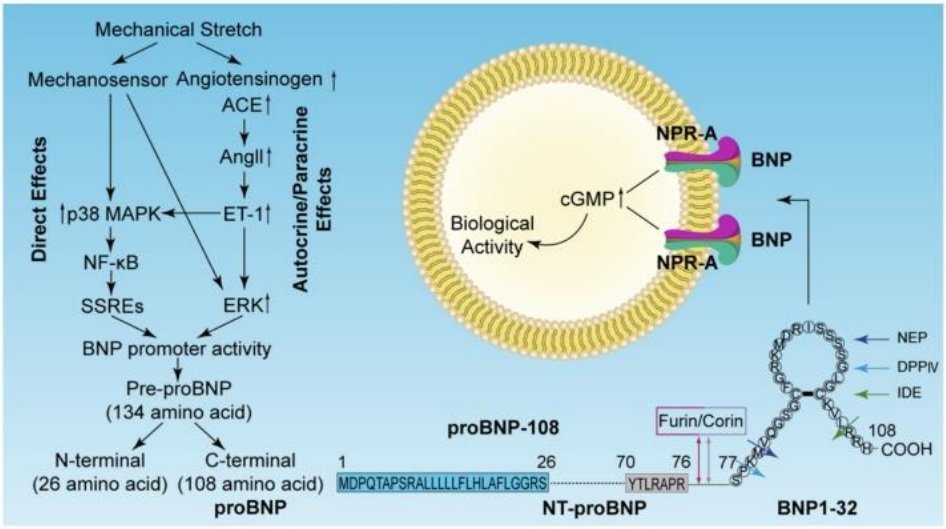

Figure 4: Signal transduction pathway for mechanical stretch inducing brain natriuretic peptide[28]

Following systemic release, natriuretic peptides activate transmembrane guanylate cyclases on surface endothelial cells, raising intracellular levels of cyclic guanosine monophosphate (cGMP) and therefore causing vasodilation. Other systemic effects include diuresis and natriuresis, both of which result in decreased blood pressure. The peptides have also been shown to antagonise unfavourable pathways that are over-activated in heart failure, such as RAAS, which has anti-diuretic effects, and the transforming growth factor-beta pathway, which enhances cardiac remodelling and fibrosis.[33,34]

BNP has an estimated half-life of 20 minutes, but NT-proBNP has a half-life of 120 minutes; this discrepancy explains why NT-proBNP serum levels are about six times greater than BNP levels, despite the fact that both molecules are produced in equimolar amounts. NT-proBNP concentrations, like BNP, change with age; the typical threshold for people under 50 is 450 pg/mL, while it is 900 pg/mL for those over 50.[35,36]

Various studies to assess the NT-pro-BNP for heart failure;

In a study conducted by Bay M et al., (2003) to assess the utility of NT-proBNP to differentiate between patients with normal and reduced left ventricular systolic function. Study shows clear increase in age related increase in NT pro BNP concentration . Concentrations of NT pro BNP increased with increasing age across three different intervals of LVEF. Furthermore, the results suggest that a patient with a measured value of NT pro BNP below that predicted has a 97 percent certainty of more than 40 percent. Study conclude that a single measurement of NT pro BNP at the time of admission to hospital can provide important information about LVEF in unselected patients.[6]

Sakhuja R et al., (2004) Aggregate data now point to the exceptional value of NT pro BNP for the diagnosis, prognosis, and management of patients with acute CHF. While many studies suggest that NT pro BNP is a more discerning marker in many common clinical scenarios, such as diastolic CHF. In addition, the value of NT pro BNP for diagnosis and prognosis extend to other cardiovascular disease states such as, ACS and PE. This versatile marker should help to optimize the care of a wide range of patients with prevalent cardiovascular illness.[37]

Cleland JGF et al., (2007) in their study shows raised plasm concentrations of NT Pro BNP, and probably other peptides of this family, predicts an increase in cardiovascular events and mortality in patients with a clinical diagnosis of heart failure but a preserved LVEF. Echocardiogram, at least using conventional imaging and Doppler, is of limited use in identifying patients whose symptoms and prognosis are driven by cardiac disease. Therefore, an elevated plasma concentration of BNP/ NT pro BNP might be used as a key aspect of the definition of diastolic heart failure in further guidelines.[38]

In a study conducted by Ozturk TC et al., (2011) to assess the NT-proBNP used as criterion for heart failure in emergency room. The study shows that Nt pro BNP has been shown as an easy diagnostic method among routine emergency service tests in the most recent guidelines on CHF. The mean NT-proBNP value of the patients was 9741.9 ± 8973 pg/ml (range: 245-35000) while the mean NT-proBNP value of patients diagnosed with non-decompensated congestive heart failure was 688.9 ± 284.5 pg/ml. However, it is not currently included among the classic criteria for hospitalization. A certain cut off value may be determined in further multicentre controlled trials conducted with larger patient groups. As a result in emergency departments as more benefit in diagnosis and treatment of CHF.[39]

In a prospective study conducted by Sokhanvar S et al., (2011) to assess the relation of serum NT-proBNP levels with prognosis of patients with systolic heart failure. Ten individuals with heart failure who entered in this clinical investigation were lost to follow-up. NT-proBNP mean is substantially linked with ejection fraction ($p=0.003$) and NYHA class ($p<0.001$). The mean NT-proBNP level was substantially greater in patients who died vs patients who survived. In addition, the mean NT-proBNP level was considerably lower in individuals with a favourable prognosis compared to those with a poor prognosis. This study, like others, indicates that NT-proBNP is highly associated to mortality and morbidity. This might be used to predict negative outcomes and stratify people with heart failure. It is suggested that additional study be conducted in Iran. [40]

In a prospective study conducted by Onur S et al., (2015) to assess the association between serum level of ubiquinol and NT-proBNP for chronic heart failure. In healthy aged people, greater blood ubiquinol levels are related with decreased serum NT-proBNP levels. Prospective studies are needed to determine how much ubiquinol in the blood is a protective factor for heart failure. [41]

In a study conducted by Pan et al., (2017) to assess the NT-proBNP test with improved accuracy for diagnosis of chronic heart failure. In their study provides diagnostic model for the diagnosis of NYHA 2 to 3 chronic heart failure. The corrected NT – pro BNP test was established by inclusion of multivariate regression analysis. It was found that compared with uncorrected NT Pro BNP, the diagnostic formulation of corrected NT Pro BNP could improve the diagnostic accuracy of chronic heart failure.[42]

Sahal K, et al., (2019) to assess the prognosis and NT-proBNP in heart failure patients with preserved versus reduced ejection fraction. Study shows that there is no difference between patients with HFpEF and HFrEF in relative risk prediction of 6-month mortality by absolute discharge NT pro BNP levels or by percentage NT pro BNP changes. To explain the similar long term mortality in HFpEF as in HFrEF , despite lower NT pro BNP discharge levels in HFpEF, Study raised possibility that larger burden of prognostic relevant comorbidities in patients with low NT pro BNP levels unfavourably affects their prognosis.[43]

In a study by Shi L et al., (2020) to assess the application of blood pre-albumin and NT-proBNP in evaluating prognosis of elderly chronic heart failure patients. Multivariate regression analysis revealed that serum PA and plasma NT-pro BNP were independent risk variables for the incidence of cardiac events during follow-up. PA decline and NT-pro BNP elevation show a substantial link with poor prognosis in elderly CHF patients, and they can be utilised for clinically assessing disease states, directing therapy, and improving prognosis. [44]

Toppo A et al., (2021) to assess the role of NT-proBNP in diagnosis of diastolic heart failure and its correlation with echocardiography. In their Study they showed serum NT pro BNP levels provide reliable diagnostic accuracy to detect heart failure and its correlates well with increasing severity of diastolic dysfunction as assessed by well-established modality of Echocardiogram.[45]

Athavale B et al., (2022) study shows that the values of NT pro BNP vary with factors like age, BMI, and creatinine, clearance in addition to LVEF. This may lead to falsely positive or falsely negative diagnosis of HF. With the above observations in mind, it may be concluded that NT pro BNP can help diagnosis HF but only in addition to clinical findings.[46]

In a prospective study conducted by Chen S et al., (2022) to assess the value of echocardiography combined with NT-proBNP level in assessment and prognosis of diastolic heart failure. NT-pro BNP was found to be overexpressed in the serum of DHF patients. NT-pro BNP levels were considerably greater in the P-MACE group than in the N-MACE group, and the degree of elevation was associated to NYHA class. The ratio of peak velocity of left atrial early diastolic blood flow to early diastolic peak velocity of mitral annulus (/Ea) and serum NT-pro BNP level were risk variables for NYHA class and prognosis, according to the multivariate logistic regression analysis. However, LVEF, LVEDD, and flow propagation velocity (Vp) might all be

advantageous. Furthermore, the ROC curve demonstrated that echocardiography coupled with NT-pro BNP concentration had superior accuracy in NYHA class and prognostic evaluation of DHF than either alone. The diagnosis of echocardiography combined with NT-pro BNP levels has the potential to distinguish the NYHA class in heart function of patients with DHF and determine the prognosis of patients. [47]

III. Aims & Objectives

Aim:
Present study aimed to estimate the values of NT pro BNP and associate with severity of Heart failure

Objective:
1) Study of Nt pro BNP levels in population aged more than 18 years diagnosed with heart failure and to know Nt pro BNP values in severity of heart failure
2) Find the association between the grading heart failure with NT pro BNP levels
3) Cost effective and early diagnostics in diagnosis of heart failure

IV. Material & Method

Study place: Department of Medicine, Adichunchanagiri Hospital and Research Center, B G Nagara-571448

Study Design: Hospital Based Observational Study

Study Period: 18 months (August 2022 – February2024)

Sample Size: 100 cases of heart failure during study period

Inclusion criteria:
- Patients with Diagnosis of heart failure and fulfil Framingham criteria of heart failure admission aged >18 years
- NT pro BNP levels will be assessed within 24 hours from admission.
- Patients who agree to give informed consent.

Exclusion criteria:
- Pregnant women.
- Patients with known case of Pulmonary diseases like COPD, ILD , lung carcinoma
- Patient less than 18-year-old
- Patients with CVA, CKD, on chemotherapy,
- Patients with sepsis

Method of collection of data

Present study was planned as a single center, prospective, and controlled trial. Data were collected from total of 100 patients with pre diagnosis of heart failure either by 2D ECHO OR according to the Framingham criteria, aged above 18 years and volunteered to participate in the study admitted to Adichunchanagiri medical college

In all the selected patients detailed history and physical examination was noted. Every patient were subjected to ECG, Trop I, 2D ECHO and NT pro BNP and relevant investigations. NT pro BNP was done on the day the subject with diagnosis of Congestive heart failure admitted to the hospital. Subjects were followed up till the mortality or discharge/ improvement.

Does the study require any investigations or interventions to be conducted on patients or other humans or animals? If so describe briefly?

YES
1. Complete Hemogram
2. Urine Routine and Microscopy
3. Renal Function Test and Serum Electrolytes
4. Liver Function Test
5. ECG
6. Chest X Ray
7. 2D Echo
8. NT pro BNP levels
9. Trop I

Statistical Analysis

Data were entered with MS Excel and analysed using SPSS v23.0 software operating on windows 10. Descriptive statistics were expressed using mean, standard deviation, frequency and percentages. The mean difference between the continuous data were analysed using unpaired t-test and the categorical data were analysed using Chi-square test. For statistical purpose, a p value < 0.05 was considered statistically significant.

V. Results

Present study total of 100 patients fulfilling inclusion criteria are included with mean age of 54.88yrs.

Table 4: Showing the mean age of the patients

	Minimum	Maximum	Mean	SD
AGE	30.0	74.0	54.88	11.52

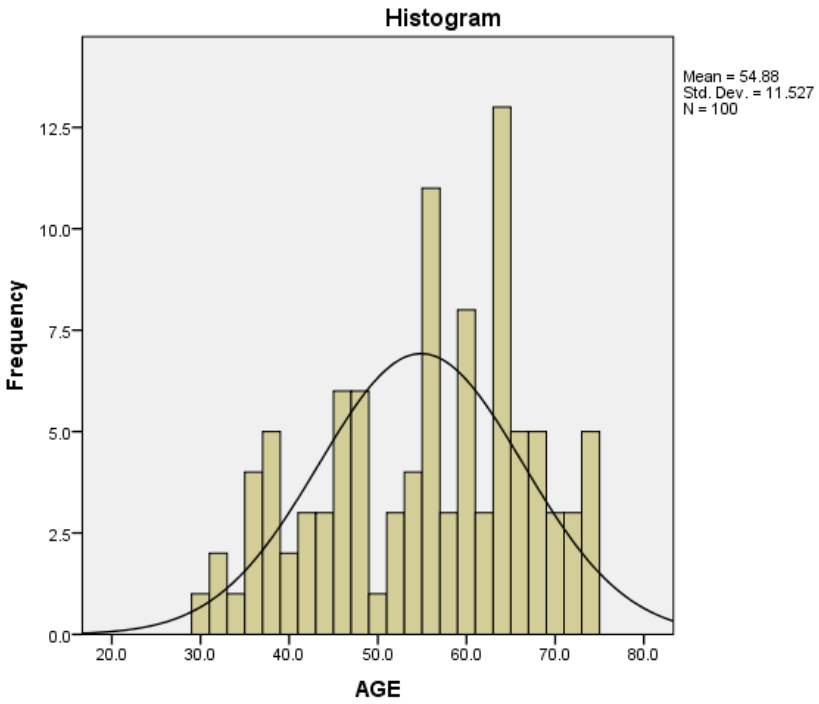

Figure 5: Showing the mean age of the patients

Table 5: Gender distribution of patients

		Frequency	Percent
GENDER	Female	30	30.0
	Male	70	70.0
	Total	100	100.0

Among the included patients, 70% were male and 30% were female with male preponderance in the study.

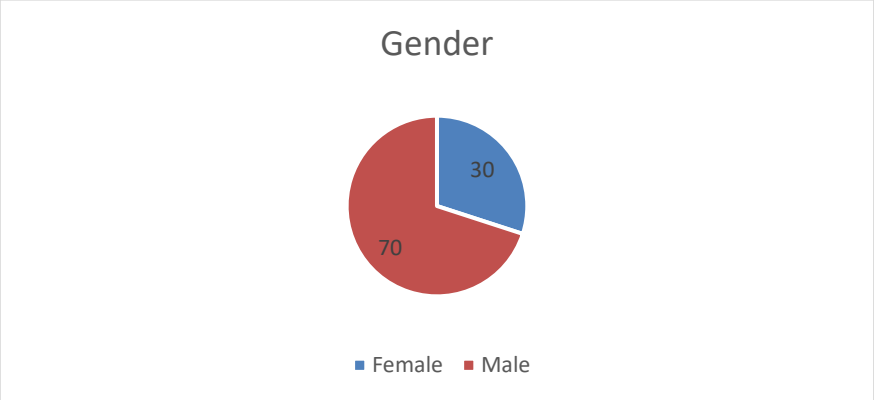

Figure 6: Gender distribution of patients

Table 6: Presence of hypertension

		Frequency	Percent
HTN	No	41	41.0
	Yes	59	59.0
	Total	100	100.0

Hypertension was present in 59% of the patients.

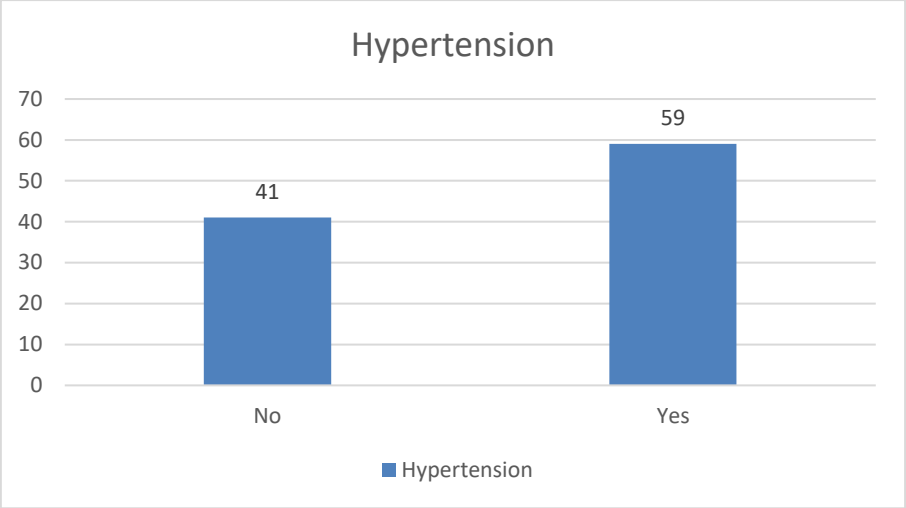

Figure 7: Presence of hypertension

Table 7: Presence of diabetes mellitus

		Frequency	Percent
T2DM	No	51	51.0
	Yes	49	49.0
	Total	100	100.0

Type 2 diabetes mellitus was present in 49% of the patients.

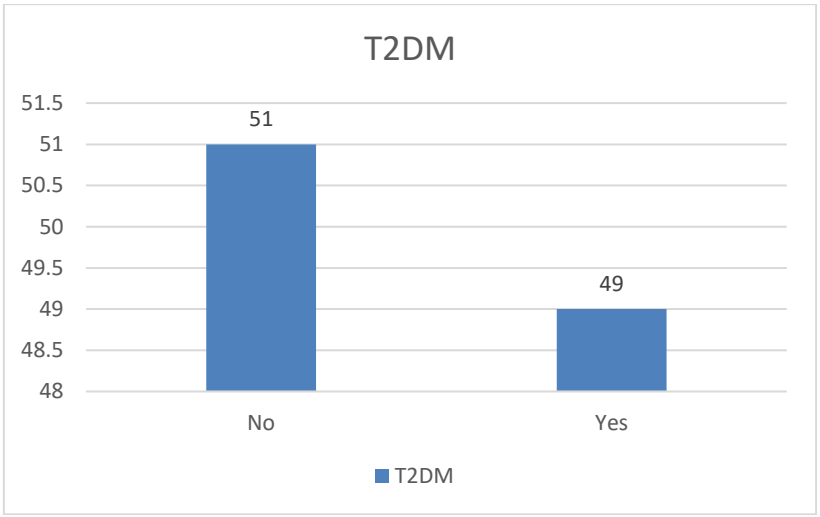

Figure 8: Presence of diabetes mellitus

Table 8: Presence of history of ischemic heart disease

		Frequency	Percent
IHD	No	72	72.0
	Yes	28	28.0
	Total	100	100.0

Previous history of ischemic heart disease was present in 28% of the patients.

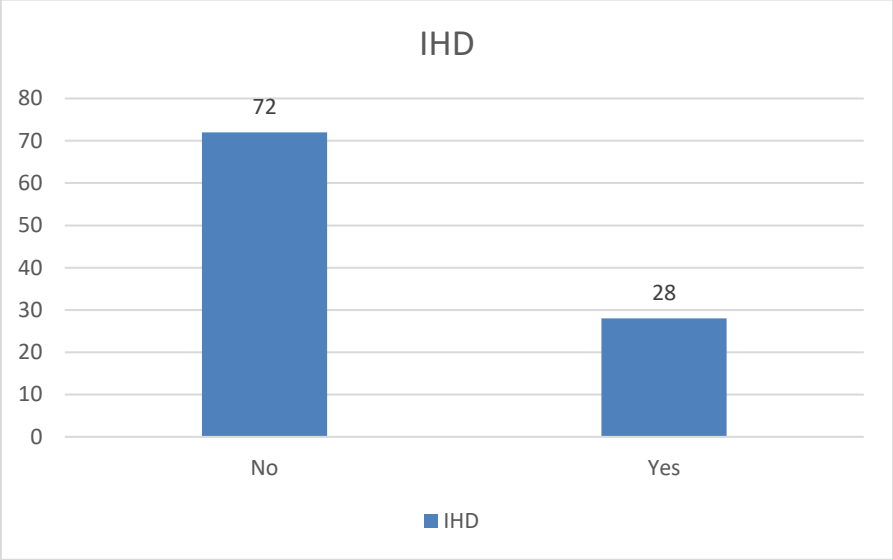

Figure 9: Presence of history of ischemic heart disease

Table 9: Showing other habits among patients

		Frequency	Percent
Others	Alcoholic	20	20.0
	Arthritis	15	15.0
	No	60	60.0
	Smoker	5	5.0
	Total	100	100.0

Habits were with alcoholism in 20%, smoking history in 5% of the patients.

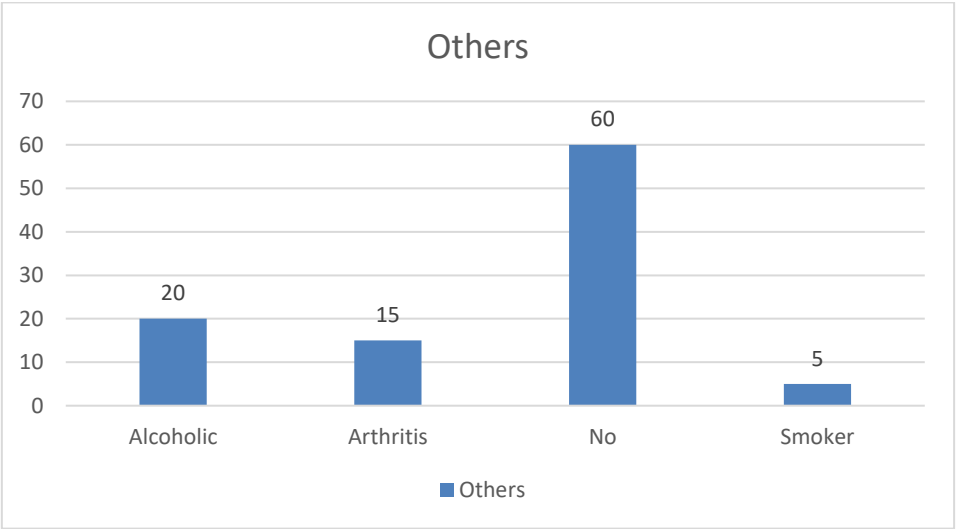

Figure 10: Showing other habits among patients

Table 10: Showing presence of chest pain

		Frequency	Percent
Chest pain	No	60	60.0
	Yes	40	40.0
	Total	100	100.0

Chest pain was recorded in 40% of patients.

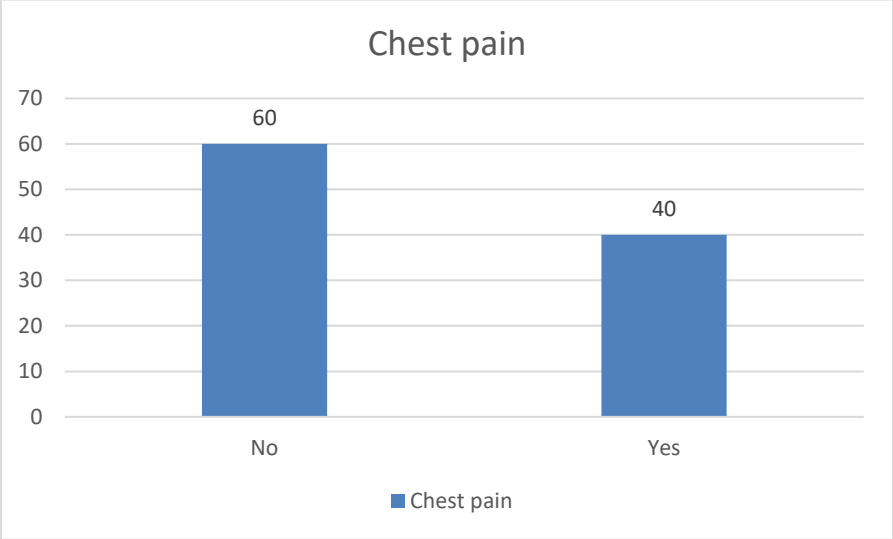

Figure 11: Showing presence of chest pain

Table 11: Showing presence of palpitation

		Frequency	Percent
Palpitation	No	59	59.0
	Yes	41	41.0
	Total	100	100.0

Palpitation was present in 41% of the patients.

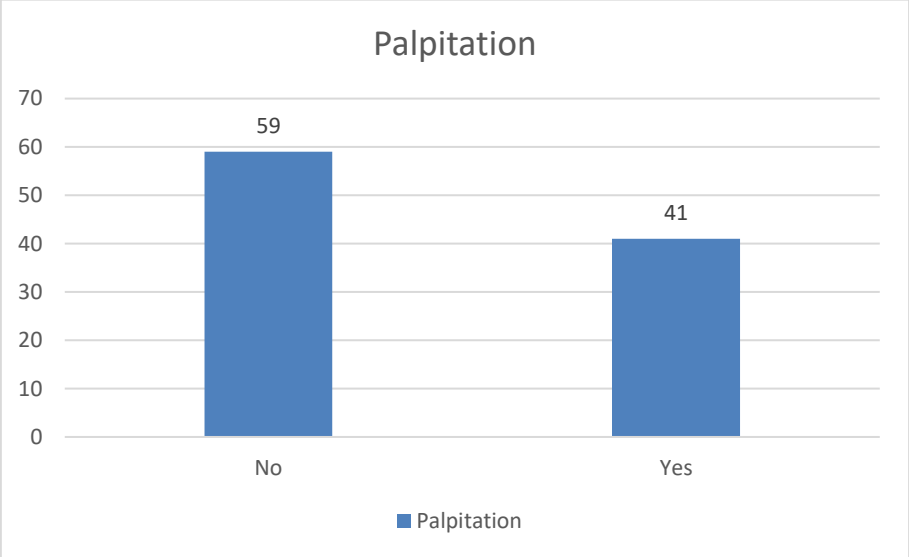

Figure 12: Showing presence of palpitation

Table 12: Showing presence of breathlessness among patients

		Frequency	Percent
Breathlessness NYHA Class	2.0	45	45.0
	3.0	16	16.0
	4.0	39	39.0
	Total	100	100.0

Breathlessness was present in with grade of 4 in 39%, grade 3 in 16% and grade 2 in 45% of the patients.

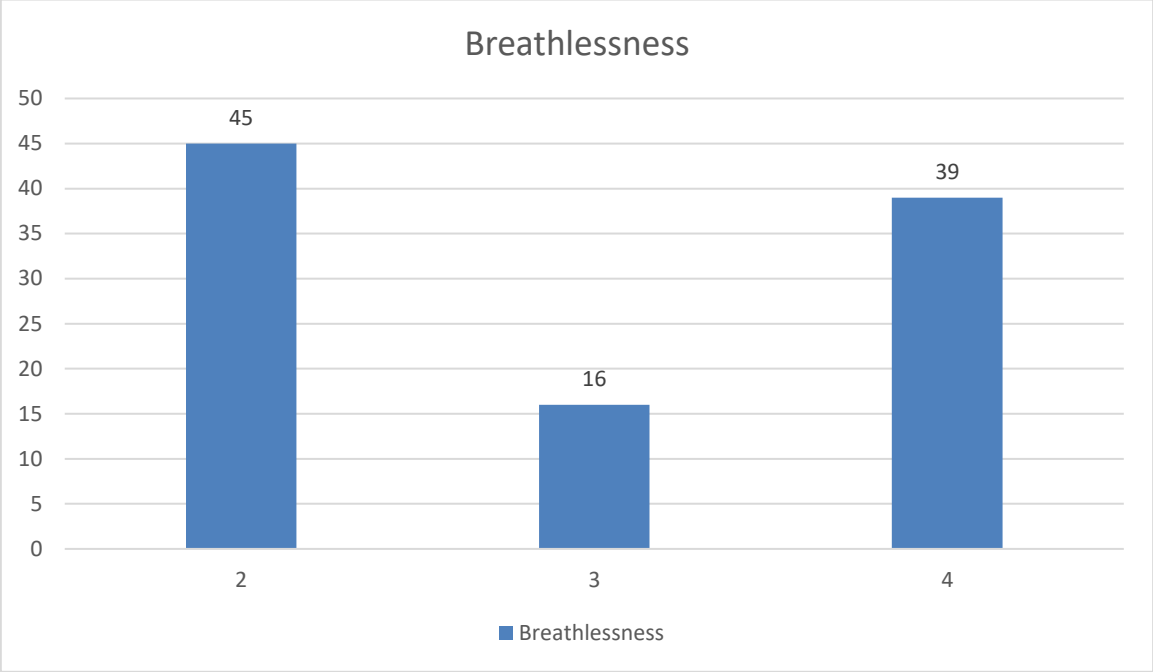

Figure 13: Showing presence of breathlessness among patients

Table 13: Showing presence of PND among patients

		Frequency	Percent
PND	No	64	64.0
	Yes	36	36.0
	Total	100	100.0

PND was present in 36% of the patients.

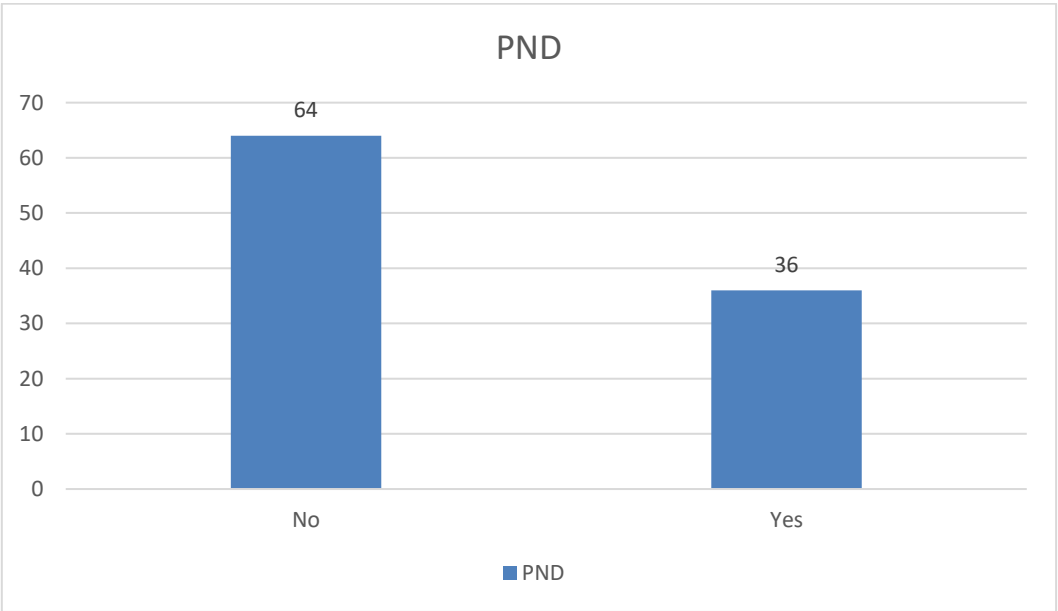

Figure 14: Showing presence of PND among patients

Table 14: Showing presence of orthopnea

		Frequency	Percent
Orthopnea	No	64	64.0
	Yes	36	36.0
	Total	100	100.0

Orthopnea was present in 36% of the patients.

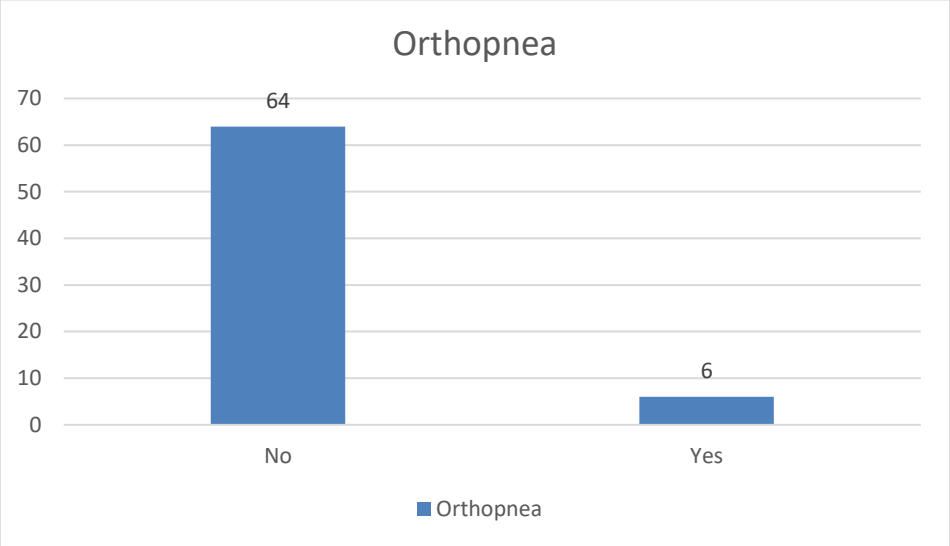

Figure 15: Showing presence of orthopnea

Table 15: Showing presence of lower limb swelling

		Frequency	Percent
Lower Limb swelling	No	55	55.0
	Yes	45	45.0
	Total	100	100.0

Lower limb swelling was present in 45% of the patients

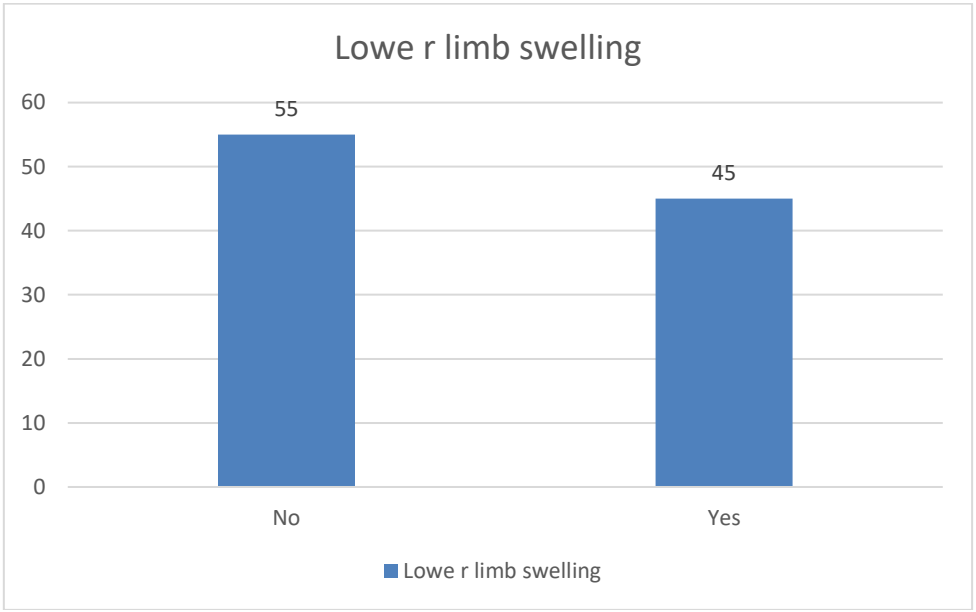

Figure 16: Showing presence of lower limb swelling

Table 16: Showing the presence of syncope among patients

		Frequency	Percent
syncope	No	78	78.0
	Yes	22	22.0
	Total	100	100.0

History of syncope was present in 22% of the patients.

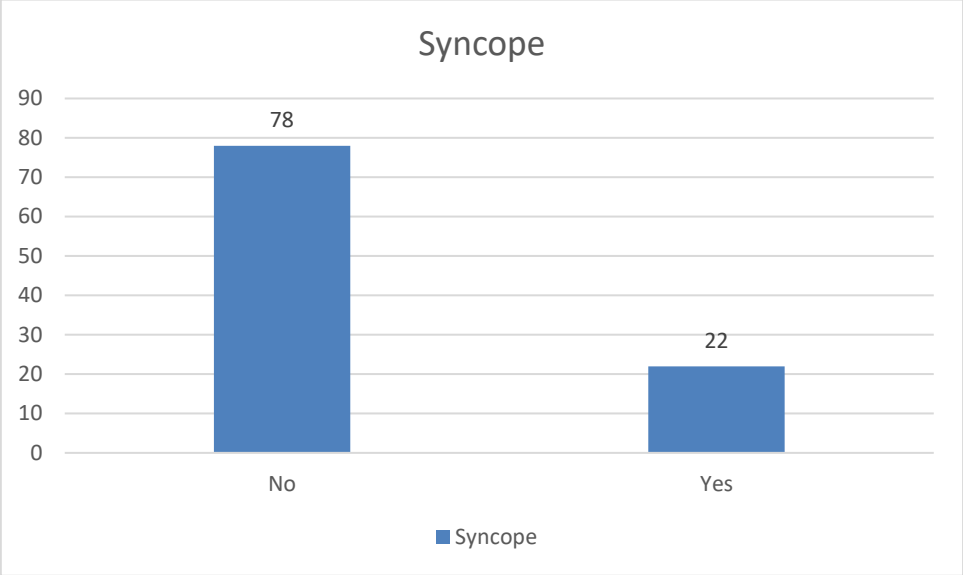

Figure 17: Showing the presence of syncope among patients

Table 17: Showing presence of nocturnal cough

		Frequency	Percent
Nocturnal cough	No	56	56.0
	Yes	44	44.0
	Total	100	100.0

History of nocturnal cough was present in 44% of the patients.

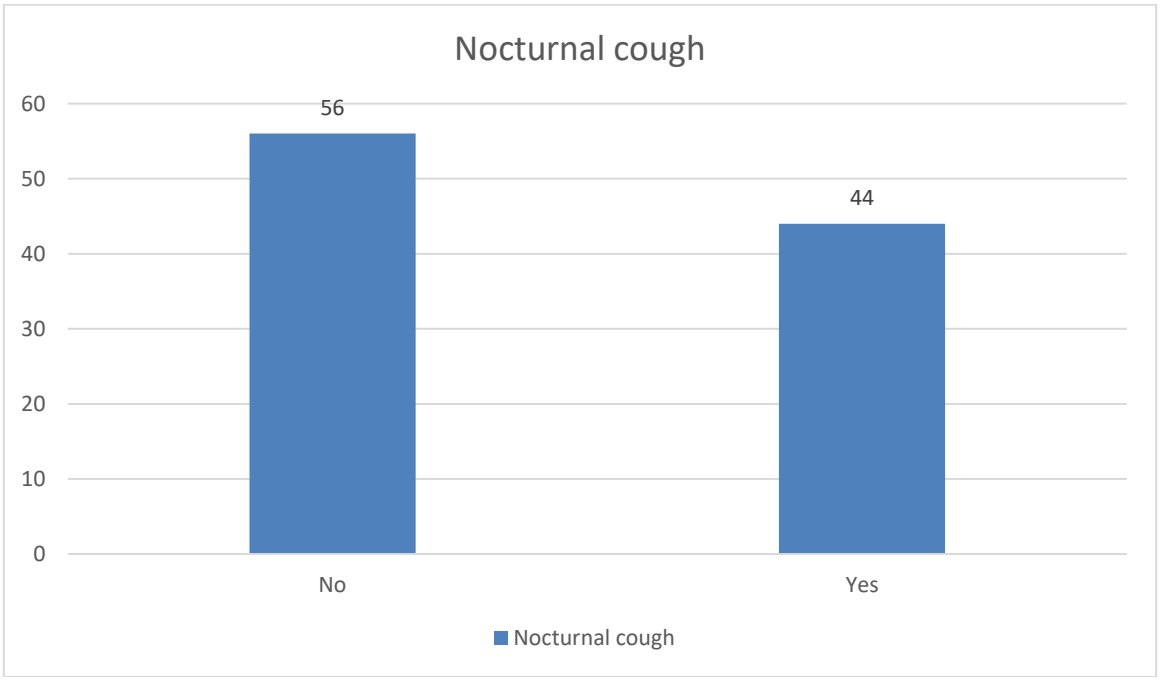

Figure 18: Showing presence of nocturnal cough

Table 18: Showing the presence of JNV

		Frequency	Percent
JNV	No	22	22.0
	Yes	78	78.0
	Total	100	100.0

The JNV elevation was present in 78% of the patients.

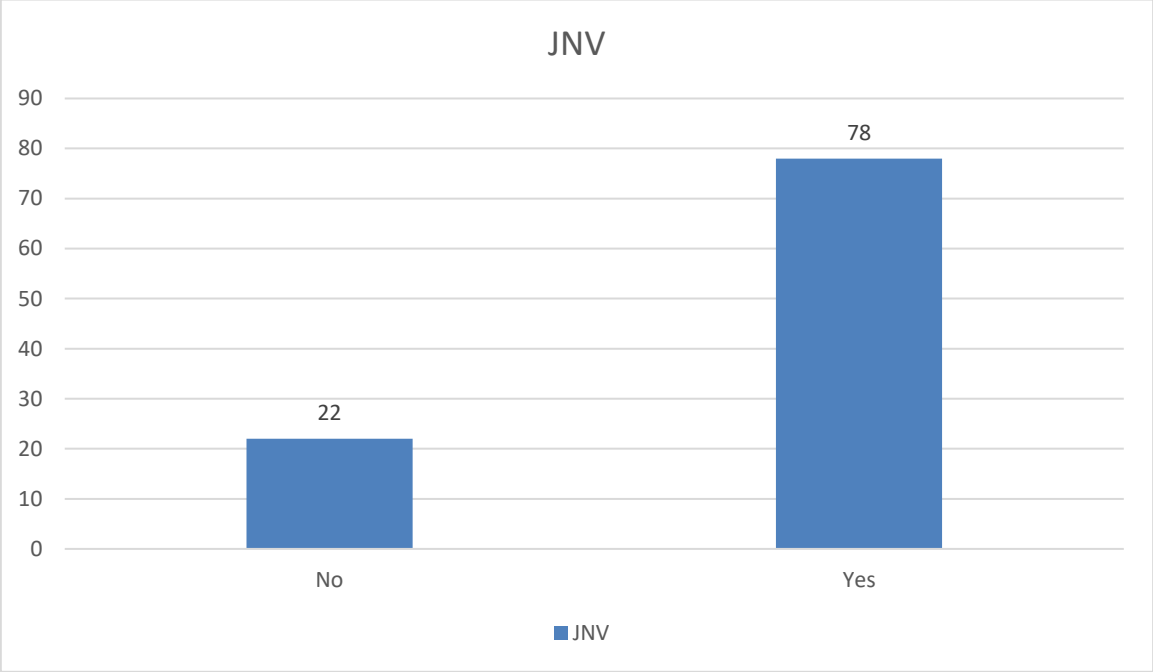

Figure 19: Showing the presence of JNV

Table 19: Showing presence of weight loss or gain among patients

		Frequency	Percent
Weight loss or gain	Gain	56	56.0
	Loss	44	44.0
	Total	100	100.0

History of weight loss was present in 44% of the patients.

Figure 20: Showing presence of weight loss or gain among patients

Table 20: Showing the mean vital parameter among patients

	Minimum	Maximum	Mean	Std. Deviation
SBP	86.0	200.0	122.120	29.7285
DBP	.0	120.0	74.500	17.6415
PR	60.0	130.0	91.440	22.6993
RR	16.0	28.0	23.460	3.9808
TEMP	96.8	104.0	98.979	1.6887

Table showing the mean blood level of the vital parameters

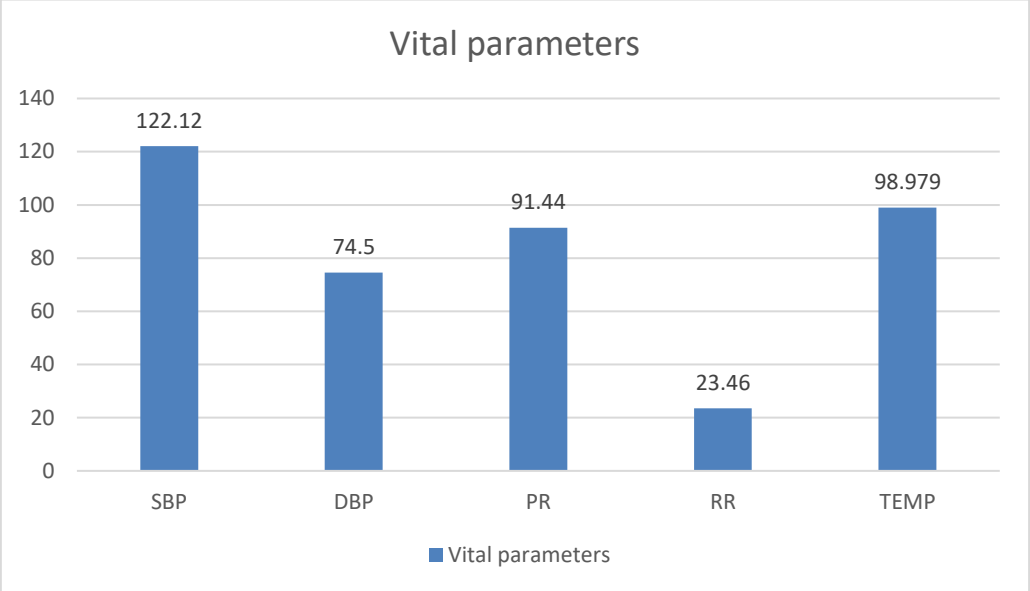

Figure 21: Showing the mean vital parameter among patients

Table 21: Showing various ECG findings among patients

		Frequency	Percent
ECG	LAD	27	27.0
	LBBB	14	14.0
	Mobitz II block	7	7.0
	Q waves in lead II and III	6	6.0
	Q waves in lead V1-V6	1	1.0
	RBBB	18	18.0
	Sinus tachycardia	13	13.0
	ST elevations in V1-V4	14	14.0
	Total	100	100.0

ECG pattern showing majority with LAD in 27%, 18% with RBBB, 14% with LBBB, 13% with sinus tachycardia and ST elevation at v1-v4 in 14% of the patients.

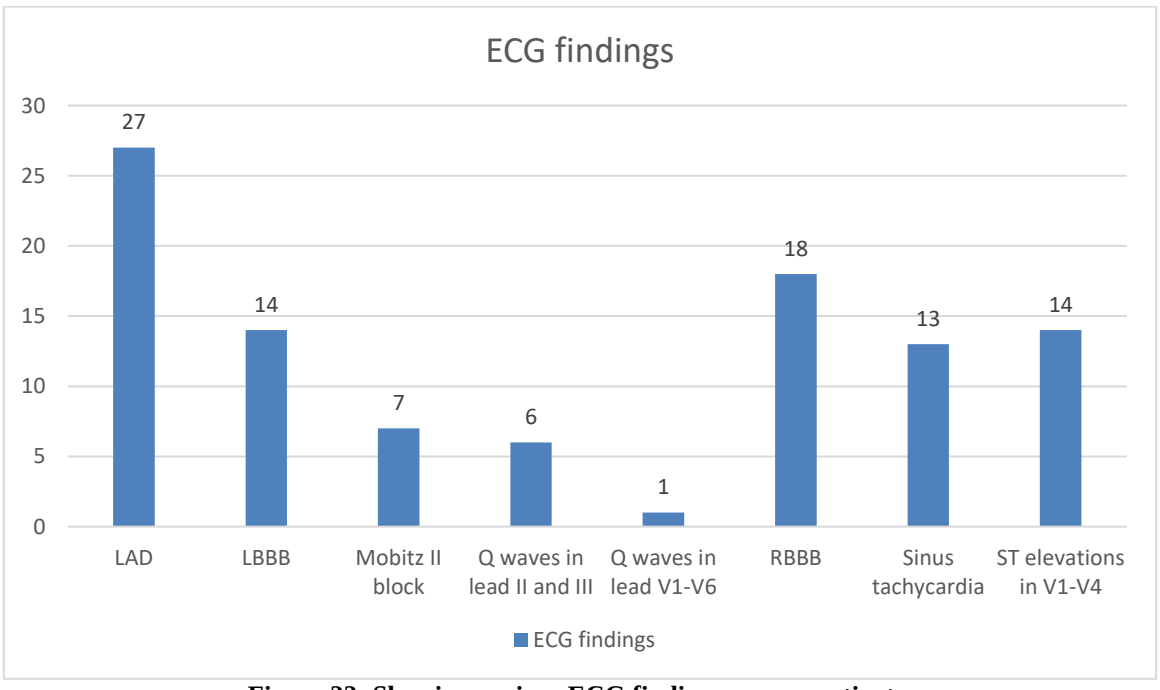

Figure 22: Showing various ECG findings among patients.

Table 22: Showing the presence of 2D Echo findings among patients

		Frequency	Percent
2D ECHO	DCM	20	20.0
	IHD and LV dysfunction	14	14.0
	Ischaemic cardiomyopathy	7	7.0
	LV dysfunction	16	16.0
	Mild lv dysfunction	12	12.0
	Old IHD	15	15.0
	Old IHD and Cardiomyopathy	10	10.0
	RHD and LV dysfunction	6	6.0
	Total	100	100.0

On 2D CHO, majority of the patients presented with dilated cardiomyopathy in 20%, followed with LV dysfunction, Old IHD and mild LV dysfunction.

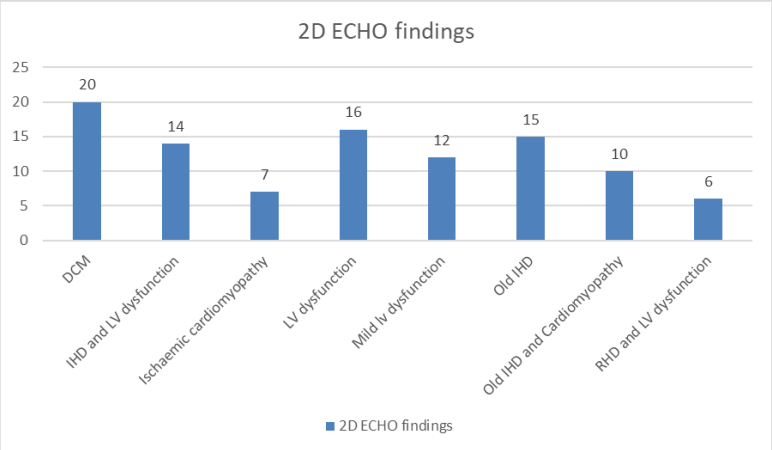

Figure 23: Showing the presence of 2D Echo findings among patients

Table 23: Showing the X-ray findings of chest in patients

		Frequency	Percent
CHEST X-RAY	Aortic knuckle,	10	10.0
	B/L lower lobe consolidation	7	7.0
	B/L non homogeneous opacites	6	6.0
	Cardiomegaly	25	25.0
	Cardiomegaly, interstitial opacity	13	13.0
	COPD changes	11	11.0
	Emphysematous lung,	14	14.0
	Right sided effusion	14	14.0
	Total	100	100.0

Chest X-ray showing majority with cardiomegaly in 25% followed with 14% emphysematous lung and right sided effusion.

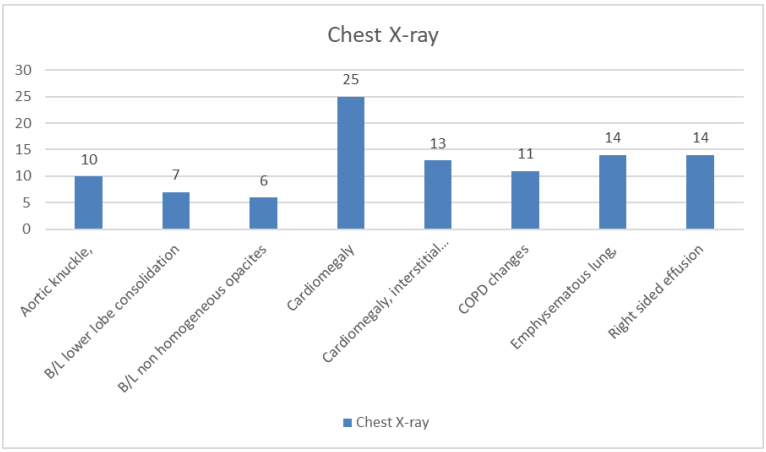

Figure 24: Showing the X-ray findings of chest in patients

Table 24: Showing the diagnosis of the patients

		Frequency	Percent
DIAGNOSIS	Acute LV failure	35	35.0
	Congestive heart failure	18	18.0
	Chronic right heart failure	4	4.0
	COPD with COR pulmonary	8	8.0
	Dilated cardiomyopathy	14	14.0
	Ischemic cardiomyopathy with lv failure	21	21.0
	Total	100	100.0

Among the various diagnosis, 35% presented with acute LV failure, 21% with ischemic cardiomyopathy with LV failure, 18% with congestive heart failure, and 14% with dilated cardiomyopathy.

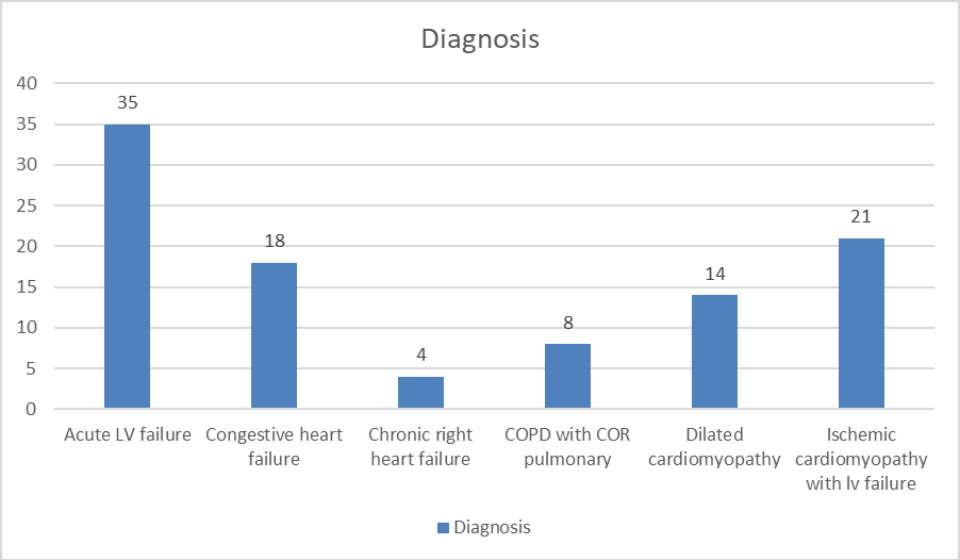

Figure 25: Showing the diagnosis of the patients

Table 25: Showing the outcome among the included patients

		Frequency	Percent
OUTCOME	DAMA	13	13.0
	Died	27	27.0
	Improved	60	60.0
	Total	100	100.0

In present study, 60% patients improved at discharge, 27% died and 13% discharge against medical advice.

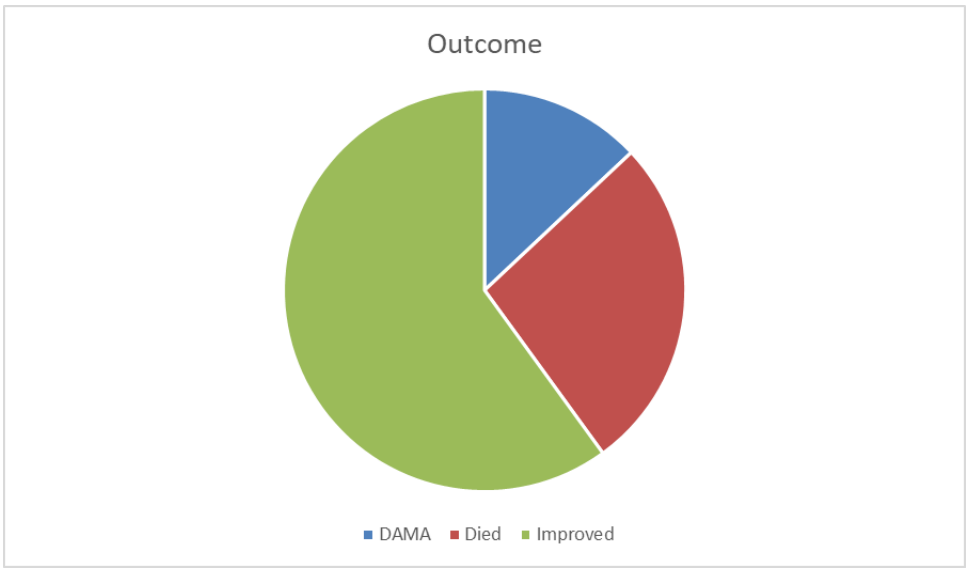

Figure 26: Showing the outcome among the included patients

Table 26: Showing mean level of ejection fraction and blood markers

	Minimum	Maximum	Mean	Std. Deviation
EJECTION FRACTION	16.00	58.00	40.69	11.82
TROP I ng/ml	.10	12.00	2.88	4.15
CKMB U/L	12.0	56.0	31.63	10.39
NTPROBNP Pg-ml	3460.0	12000.0	7210.76	2889.05

Table showing the mean level of ejection fraction, Troponin I level, CKMB and NT-pro-BNP levels among patients.

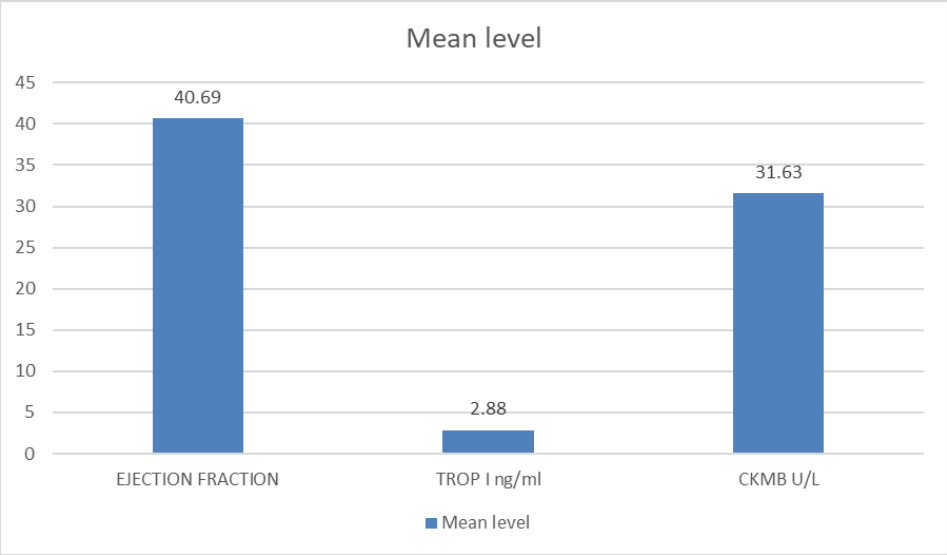

Figure 27: Showing mean level of ejection fraction and blood markers

Table 27: Correlation of blood markers with ejection fraction among patients

Correlations		Ejection fraction
TROP I ng/ml	Pearson Correlation	-.437
	Sig. (2-tailed)	.001*
CKMB U/L	Pearson Correlation	-.210
	Sig. (2-tailed)	.036*
NT-proBNP Pg/ml	Pearson Correlation	-.356
	Sig. (2-tailed)	.05*

On pearson's correlation, there is significant correlation of the NT-pro-BNP with decline in ejection fraction. Similarly the other markers such as Trop I and CKMB also showed negative relation with ejection fraction among patients.

Table 28: Comparison of NT-proBNP with diagnosis of patients

		NT-PROBNP Pg/ml	
		Mean	SD
Diagnosis	Acute LV failure	9230.9	2746.5
	Congestive heart failure	6156.3	2070.9
	Chronic right heart failure	11280.0	46.9
	Copd with cor pulmonary	6368.7	444.7
	Dilated cardiomyopathy	10347.6	648.4
	Ischemic cardiomyopathy with lv failure	4363.3	499.9

The mean level of NT-pro-BNP was found to be higher mean in cases of dilated cardiomyopathy and chronic right heart failure among the patients.

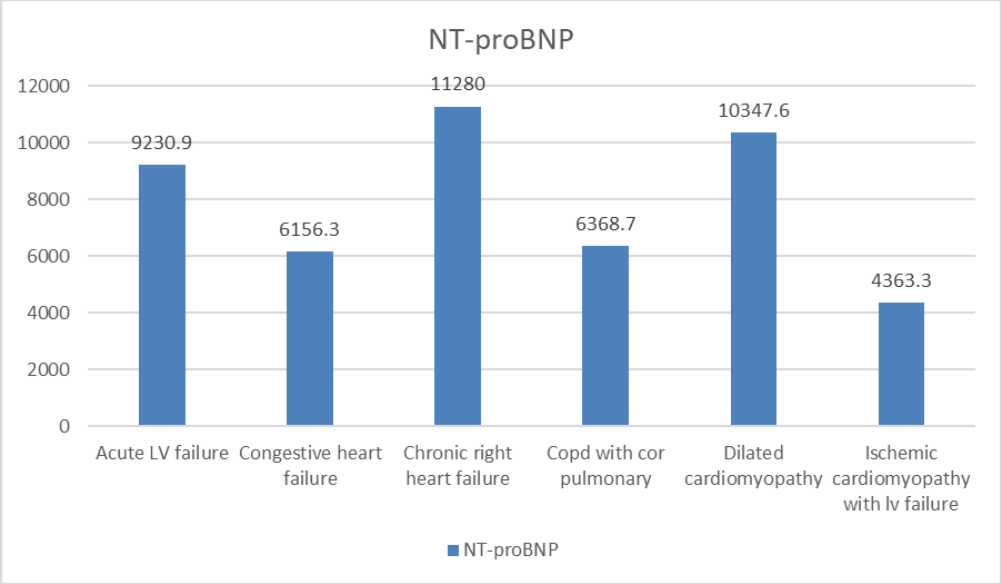

Figure 28: Comparison of NT-proBNP with diagnosis of patients

Table 29: Comparison of the NT-proBNP levels with 2D ECHO findings among patients

		NT-pro-BNP Pg/ml	
		Mean	SD
2D ECHO	DCM	6907.9	3182.8
	IHD and LV dysfunction	6430.7	2501.2
	Ischaemic cardiomyopathy	7300.7	2711.4
	LV dysfunction	7036.1	2654.9
	Mild lv dysfunction	7175.8	3268.0
	Old IHD	8393.3	2969.6
	Old IHD and Cardiomyopathy	8442.0	2801.9
	RHD and LV dysfunction	5462.5	2266.9

The mean level of NT-pro-BNP was higher among the cases with old IHD, cardiomyopathy, and LV dysfunction.

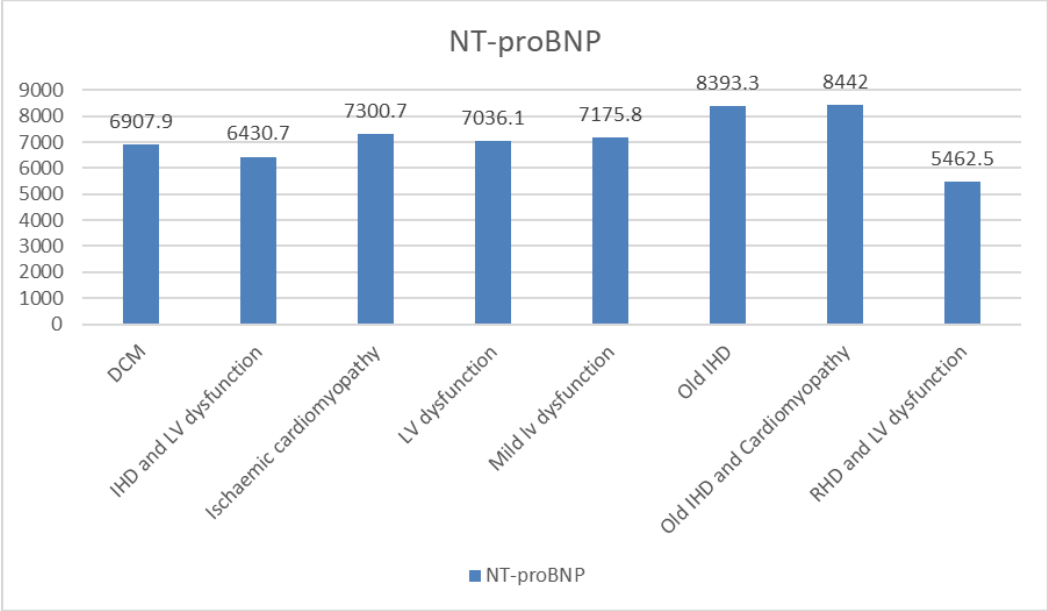

Figure 29: Comparison of the NT-proBNP levels with 2D ECHO findings among patients

Table 30: Comparison of the NT-proBNP level with outcome of the patients.

		NT-proBNP Pg/ml	
		Mean	SD
Outcome	DAMA	6363.7	3420.8
	Died	9138.7	2817.7
	Improved	6526.7	2406.6

Among the outcome, the patients with non-survivor had the significant higher mean level of NT-pro-BNP levels compared to the patients improved or discharged from hospital against medical advice. The NT-pro-BNP was significantly higher among the cases with mortality compared to discharged.

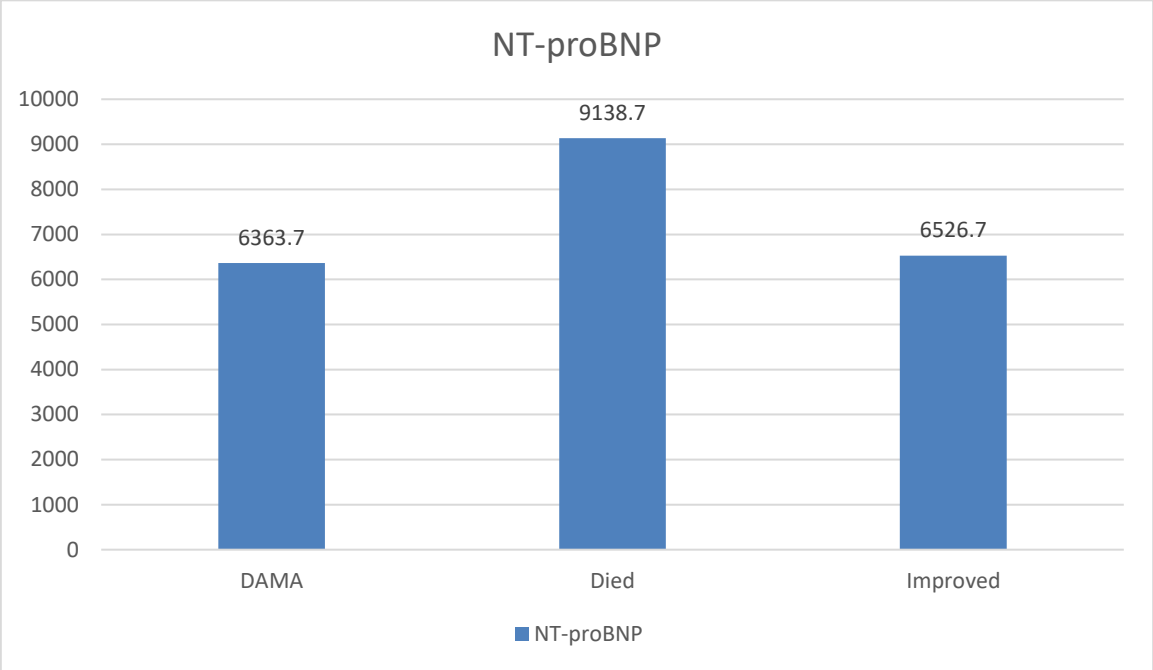

Figure 30: Comparison of the NT-proBNP level with outcome of the patients

VI. Discussion

Heart failure (HF) is a prevalent and debilitating condition that significantly impacts patient morbidity and mortality. In tertiary healthcare settings, accurate assessment of HF severity is crucial for effective management and treatment. NT-proBNP (N-terminal pro b-type natriuretic peptide) has emerged as a pivotal biomarker in this regard. Elevated NT-proBNP levels are strongly associated with the severity of heart failure, providing valuable diagnostic and prognostic information. This discussion aims to explore the role of NT-proBNP in assessing heart failure severity within a tertiary healthcare hospital, examining its clinical utility, diagnostic accuracy, and implications for patient care and outcomes. By understanding the nuances of NT-proBNP levels, healthcare providers can enhance their strategies for managing heart failure, ultimately improving patient prognosis and quality of life.

Present study total of 100 patients fulfilling inclusion criteria are included with mean age of 54.88yrs. Among the included patients, 70% were male and 30% were female with male preponderance in the study. among them 59% were hypertensive, 49% with diabetes mellitus, 28% with previous history of IHD.

In concordance study by Sokhanwar S et al., documented with mean age of 58.7yrs, among them 60% were male patients and 40% were female patients, with male preponderance in the study. [40] In study by Toppo A et al., documented mean age of 54.5yrs with female preponderance in their study. among them 29.2% were diabetic and 70.8% were non-diabetic patients. Majority presented with dyspnea, pedal edema, orthopnea and chest pain. [45]

ECG pattern showing majority with LAD in 27%, 18% with RBBB, 14% with LBBB, 13% with sinus tachycardia and ST elevation at v1-v4 in 14% of the patients. On 2D ECHO, majority of the patients presented with dilated cardiomyopathy in 20%, followed with LV dysfunction, Old IHD and mild LV dysfunction. On pearson's correlation, there is significant correlation of the NT-pro-BNP with decline in ejection fraction. Similarly the other markers such as Trop I and CKMB also showed negative relation with ejection fraction among patients. The mean level of NT-pro-BNP was found to be higher mean in cases of dilated

cardiomyopathy and chronic right heart failure among the patients. The mean level of NT-pro-BNP was higher among the cases with old IHD, cardiomyopathy, and LV dysfunction.

In line study by Chen S et al., ROC curve demonstrated that echocardiography coupled with NT-pro BNP concentration had superior accuracy in NYHA class and prognostic evaluation of DHF than either alone. The diagnosis of echocardiography combined with NT-pro BNP levels has the potential to distinguish the NYHA class in heart function of patients with DHF and determine the prognosis of patients. [47] In conclusion of study by Athavale B et al., that NT pro BNP can help diagnosis HF but only in addition to clinical findings.[46]

Also in study by Toppo A et al., NT pro BNP levels provide reliable diagnostic accuracy to detect heart failure and its correlates well with increasing severity of diastolic dysfunction as assessed by well-established modality of Echocardiogram.[45] Multivariate regression analysis revealed that serum Pre-albumin (PA) and plasma NT-pro BNP were independent risk variables for the incidence of cardiac events during follow-up. PA decline and NT-pro BNP elevation show a substantial link with poor prognosis in elderly CHF patients, and they can be utilised for clinically assessing disease states, directing therapy, and improving prognosis in study by Shi L et al. [44]

The patients in study by Ozturk TC et al., documented mean NT-proBNP value was 9741.9 ± 8973 pg/ml (range: 245-35000) while the mean NT-proBNP value of patients diagnosed with non-decompensated congestive heart failure was 688.9 ± 284.5 pg/ml. They stated, NT-proBNP result in emergency departments as more benefit in diagnosis and treatment of CHF.[39] elevated plasma concentration of BNP/ NT pro BNP might be used as a key aspect of the definition of diastolic heart failure in further guidelines as concluded by Cleland JG et al.[38]

In present study, 60% patients improved at discharge, 27% died and 13% discharge against medical advice. Among the outcome, the patients with non-survivor had the significant higher mean level of NT-pro-BNP levels compared to the patients improved or discharged from hospital against medical advice. The NT-pro-BNP was significantly higher among the cases with mortality compared to discharged.

In concordance to present study Sokhanvar S et al., documented the mean NT-proBNP level was substantially greater in patients who died vs patients who survived. In addition, the mean NT-proBNP level was considerably lower in individuals with a favourable prognosis compared to those with a poor prognosis. NT-proBNP is highly associated to mortality and morbidity. This might be used to predict negative outcomes and stratify people with heart failure.[40]

The study's laboratory findings included mean levels of vital blood parameters. Pearson's correlation analysis showed a significant correlation between NT-pro-BNP levels and a decline in ejection fraction, with other markers like Troponin I (Trop I) and CKMB also negatively correlating with ejection fraction. NT-pro-BNP levels were found to be higher in patients with dilated cardiomyopathy and chronic right heart failure. Similarly, higher NT-pro-BNP levels were observed in cases with old IHD, cardiomyopathy, and LV dysfunction. Importantly, non-survivors had significantly higher mean levels of NT-pro-BNP compared to patients who improved or were discharged against medical advice, indicating that NT-pro-BNP levels were significantly higher among those who succumbed to their conditions. The data indicated that patients with old ischemic heart disease (IHD), cardiomyopathy, and left ventricular (LV) dysfunction had significantly elevated NT-pro-BNP levels compared to those without these conditions. This elevation suggests a direct correlation between higher NT-pro-BNP levels and the presence of chronic cardiac issues. Specifically, old IHD patients exhibited elevated NT-pro-BNP due to the long-term impact of ischemic events on heart tissue, leading to sustained stress and damage. Similarly, individuals with cardiomyopathy showed higher levels, reflecting the progressive weakening of the heart muscle, which exacerbates cardiac stress and elevates NT-pro-BNP.

Moreover, the study found that LV dysfunction, which impairs the heart's ability to pump blood effectively, also significantly raised NT-pro-BNP levels. This finding underscores the role of NT-pro-BNP as a marker of cardiac strain and heart failure severity. The increased levels in these conditions emphasize the importance of NT-pro-BNP in diagnosing and monitoring heart disease progression and tailoring appropriate treatment strategies.

VII. Summary

- Present study total of 100 patients fulfilling inclusion criteria are included with mean age of 54.88yrs.
- Among the included patients, 70% were male and 30% were female with male preponderance in the study.
- Hypertension was present in 59% of the patients.
- Type 2 diabetes mellitus was present in 49% of the patients.
- Previous history of ischemic heart disease was present in 28% of the patients.
- Habits were with alcoholism in 20%, smoking history in 5% of the patients.
- Chest pain was recorded in 40% of patients.
- Palpitation was present in 41% of the patients.
- Breathlessness was present in with grade of 4 in 39%, grade 3 in 16% and grade 2 in 45% of the patients.

- PND was present in 36% of the patients.
- Orthopnea was present in 36% of the patients.
- Lower limb swelling was present in 45% of the patients
- History of syncope was present in 22% of the patients.
- History of nocturnal cough was present in 44% of the patients.
- The JNV elevation was present in 78% of the patients.
- History of weight loss was present in 44% of the patients.
- Table showing the mean blood level of the vital parameters
- ECG pattern showing majority with LAD in 27%, 18% with RBBB, 14% with LBBB, 13% with sinus tachycardia and ST elevation at v1-v4 in 14% of the patients.
- On 2D CHO, majority of the patients presented with dilated cardiomyopathy in 20%, followed with LV dysfunction, Old IHD and mild LV dysfunction.
- Chest X-ray showing majority with cardiomegaly in 25% followed with 14% emphysematous lung and right sided effusion.
- Among the various diagnosis, 35% presented with acute LV failure, 21% with ischemic cardiomyopathy with LV failure, 18% with congestive heart failure, and 14% with dilated cardiomyopathy.
- In present study, 60% patients improved at discharge, 27% died and 13% discharge against medical advice.
- Table showing the mean level of ejection fraction, Troponin I level, CKMB and NT-pro-BNP levels among patients.
- On pearson's correlation, there is significant correlation of the NT-pro-BNP with decline in ejection fraction. Similarly the other markers such as Trop I and CKMB also showed negative relation with ejection fraction among patients.
- The mean level of NT-pro-BNP was found to be higher mean in cases of dilated cardiomyopathy and chronic right heart failure among the patients.
- The mean level of NT-pro-BNP was higher among the cases with old IHD, cardiomyopathy, and LV dysfunction.
- Among the outcome, the patients with non-survivor had the significant higher mean level of NT-pro-BNP levels compared to the patients improved or discharged from hospital against medical advice. The NT-pro-BNP was significantly higher among the cases with mortality compared to discharged.

VIII. Conclusion

In conclusion, this study highlights the demographic, clinical, and diagnostic profiles of patients with various cardiac conditions, emphasizing the significant role of NT-pro-BNP as a biomarker for assessing heart disease severity and prognosis. Elevated NT-pro-BNP levels were notably associated with worse outcomes, particularly among non-survivors, underscoring its potential utility in clinical practice for identifying high-risk patients and guiding treatment strategies