“STUDY OF IRON DEFICIENCY IN CHRONIC HEART FAILURE SUBJECTS.”

By

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Dr. DHEERAJ KUMAR REDDY A

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LIST OF ABBREVIATIONS

GLOSSARY	ABBREVIATIONS
2SD	Two standard deviations
AHA	American Hospital Association
AHF	Acute heart failure
AOCD	Anemia of chronic disease
BNP	B-type natriuretic peptide
BP	Blood pressure
CHF	Chronic heart failure
CI	Confidence interval
CN-HF	China national heart failure registration study
CO	Cardiac output
COPD	Chronic obstructive pulmonary disease
CRF	Chronic renal failure
CRP	C-reactive protein
DM	Diabetes mellitus
ECG	Electrocardiogram
EF	Ejection fraction
EPO	Erythropoietin
ERFE	Erythroid factor erythroferrone
ESC	European Society of Cardiology
FC III	Functional class III
FCM	Ferric carboxymaltose
GI	Gastrointestinal
GUT	Gastrointestinal tract
Hb	Hemoglobin
HF	Heart failure
HFpEF	Heart failure with preserved ejection fraction
HFrEF	Heart failure with reduced ejection fraction
HIF-2α	Hypoxia-inducible factor 2α

HR	Hazard ratio
HRQoL	Health-related quality of life
ID	Iron deficiency
ID	Infectious dose
IDA	Iron deficiency anemia
IL	Interleukin
IQR	Interquartile range
IRIDA	Iron-refractory iron deficiency anemia
LV	Left ventricle
LVEF	Left ventricular ejection fraction
LVH	Left ventricular hypertrophy
LVSD	Left ventricular systolic dysfunction
MI	Myocardial infarction
MLHFQ	Minnesota Living with Heart Failure Questionnaire
NP	Natriuretic peptide
NT-proBNP	N-terminal pro-B-type natriuretic peptide
NYHA	New York heart association
PrEP	Pre-exposure prophylaxis
RAAS	Renin-angiotensin-aldosterone system
RBCs	Red blood cells
RDW	Red cell distribution width
RR	relative risk
RV	Residual volume
SD	Standard deviations
TIBC	Total iron-binding capacity
TNF	Tumor necrosis factor
TSAT	Transferrin saturation
WHO	World health organization

ABSTRACT

Background: Anemia is a common symptom of heart failure and a significant prognostic factor. We wanted to see if there was an iron deficit in heart failure patients and if was a relation for iron deficit and heart failure severity.

Methods: From January 2020 to May 2021, a cross-sectional study was undertaken in the department of General Medicine at Sri Devaraj URS Academy of Higher Education and Research, Tamaka, Kolar. Subjects who met the inclusion and exclusion requirements are recruited sequentially by convenient sampling until the sample size is attained, with the agreement of the institutional ethics committee.

Results: The final study included 89 patients with a mean age of 60.3511.47 years, with 65.2 percent of men and 34.8 percent of females. According to the NYHA classification, 31.5 percent of the patients in our study had severity grade IV, followed by 28.1 percent with severity grade I, 20.2 percent with severity grade II, and 20.2 percent with severity degree III. The prevalence of anemia in our study group was 76.4 percent, with all patients with grade II, III, and IV class failure having iron deficiency anemia, but only 16 percent of those with grade I class failure having iron deficiency.

Conclusion: There is a significant association found between anemia deficiency and NYHA grade heart failure with $p<0.001$. the present study showed significant relation of severity of heart failure with anemia.

Keywords: anemia; chronic heart failure, NYHA functional class, transferrin saturation.

INTRODUCTION

INTRODUCTION:

Heart failure is defined by the AHA and ACC as "a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood."[1] As cardiac output decreases because of stresses placed on the myocardium, galvanization of the sympathetic nervous and renin-angiotensin-aldosterone systems increases blood pressure (for tissue perfusion) and blood volume (enhancing preload, stroke volume, and cardiac output by the Frank-Starling mechanism). These compensatory mechanisms can also lead to further myocardial deterioration and worsening myocardial contractility. In failure, cardiac output is decreased directly through reduced left ventricular function. In diastolic heart failure, cardiac output is compromised by poor ventricular compliance, impaired relaxation, and worsened end-diastolic pressure.[1,2] Heart failure is usually divided into two manifestations: chronic heart failure (CHF) and acute heart failure (AHF). CHF describes those who have had an established diagnosis of HF or who have a more gradual onset of symptoms. NYHA system is a simple tool that divides subjects with failure into four classes according to their symptoms at rest and with activity, as follows: NYHA class I, patients with asymptomatic LV systolic dysfunction during routine physical activity; NYHA class II, mildly breathless on routine physical activity; NYHA class III, severely breathless on routine activity; and NYHA class IV, the patient is breathless even at rest and unable to perform any activity without symptoms.[3]

Heart failure has emerged as a major global health issue, with an estimated worldwide prevalence of >37.7 million.[4] The INDUS (India Ukieri Study) study estimated prevalence of HF in India is about 1% of the population or about 8–10 million individuals. The estimated mortality attributable to HF is about 0.1–0.16 million individuals per year.[5]

Subjects with heart failure (HF) have two common comorbidities one is anemia and the other is iron deficiency, both of which are linked to poor clinical outcomes. Anemia is due to a variety of factors, the most frequent of which is iron deficiency. Anemia is a known predictor of mortality and morbidity in people with HF. Even if anemia is not there, iron deficiency in systolic HF has been linked to higher mortality, more hospitalizations, and lower functional ability, and other life indicators.[6] Iron deficiency is a 'health-related condition in which iron availability is insufficient to meet the body's needs, and presence of anemia is not a rule.[7] The etiology of iron deficiency in CHF is not fully understood, but it is thought to be multifactorial and arising from: a general loss of appetite and poor nutrition; decreased gastrointestinal (GI) iron absorption due to edema; increased GI blood loss that may occur partially due to antiplatelet and anticoagulant drugs; and, importantly, as a consequence of the chronic inflammatory state of these patients.[8,9] Absolute or relative iron and/or erythropoietin (EPO) deficiency are involved in the pathogenesis of anemia in these patients, especially when some degree of chronic renal failure (CRF) is present.[10]

Patients with HF report significant impairment in their 'Health-related quality of life' (HRQoL) compared with patients with other long-term conditions and healthy people, [11] largely due to the physical limitations in daily living activities associated with HF.[12] NYHA functional class has consistently been shown to have an inverse relationship with iron status and strongly predicts the development of ID anaemia.[13–15] Hemoglobin levels were similar in all four NYHA-classes, but there were significantly more patients with anemia in NYHA-class III and IV compared with other classes ($P<0.05$).[16] When the association was examined after stratifying by NYHA class (NYHA I-II/NYHA III-IV), the incidence of death was 8.3%, and re-hospitalization was 34.8% in NYHA class I-II group, and 19.2% and 47.2% in NYHA class III-IV group, respectively. Anemia was an independent predictor of risk for

all-cause re-hospitalization (HR 1.32, 95% CI 1.07–1.65, p = 0.011) in patients with NYHA class III-IV, but not in patients with NYHA class I-II.[17]

Elevated NTpro-BNP and high-sensitive C-reactive protein levels have been shown to independently correlate with ID anemia in the chronic HF population.[13,14] Using several multivariable regression models, the combined impact of ID and anemia was investigated revealing that ID, but not anemia, was linked to poor HRQoL. ID has a poor impact on HRQoL in CHF patients, regardless of whether or not anemia is present.[18] Adults having HF frequently have anemia, with frequency varied depending on the demographic investigated. Anemia appears a risk factor for poor outcomes in patients with HF, according to a growing body of evidence from observational databases and clinical trials.[19] Iron deficiency is recognized as a co-morbidity in chronic heart failure, according to the 2016 European Society of Cardiology guidelines, which require iron status assessment in all newly diagnosed chronic heart failure patients.[20] The goal of this study is to find out how common iron deficiency in chronic HF patients is and how it relates to heart failure severity.

NEED OF THE STUDY:

Chronic heart failure (CHF) is a progressive illness that affects the patient's quality of life while also putting a financial strain on the healthcare system. Despite advanced remedies for cardiovascular disorders such as myocardial infarction (MI), the case load of CHF is on the rise. Anemia is a common complication of HF that is linked to a poor prognosis. Anemia is thought to occur in heart failure because of a complicated interaction between iron shortage, renal illness, and cytokine production; however, vitamin deficit and blood loss may also play a role. Anemia can decrease cardiac function because it increases cardiac stress through tachycardia and increased stroke volume, a reduction in renal blood flow, and fluid retention,

which puts the heart under even more strain. Despite numerous guidelines on iron deficiency and treatment in heart failure patients, it is frequently overlooked. In India, there are limited investigations on the prevalence of iron deficiency anemia in CHF subjects and its relationship to the severity of the condition.

AIMS & OBJECTIVES

AIMS AND OBJECTIVES:

1. To Determine iron deficiency in heart failure subjects.
2. To determine the severity of heart failure.
3. To correlate iron deficiency with the severity of heart failure.

REVIEW OF

LITERATURE

REVIEW OF LITERATURE:

Heart failure:

Heart failure is a problem where the heart is incompetent to provide enough blood flow to meet metabolic demands or accommodate a systemic venous return. Heart failure results from injury to the myocardium from a variety of causes, including ischemic heart disease, hypertension, and diabetes. Less common etiologies include cardiomyopathies, valvular disease, myocarditis, infections, systemic toxins, and cardiotoxic drugs.[21] The pathogenesis of heart failure has been described as a compromised systolic function of the heart followed by a low cardiac output state (systolic heart failure). Even if the systolic activity is retained, diastolic filling of the left ventricle is hampered by a variety of causes. Because of high left ventricular end-diastolic pressure and a decrease in cardiac output, this disease causes congestive heart failure. Diastolic heart failure is the name given to this type of pathology.[22,23] The contractility of the entire left ventricle is regarded normal in diastolic failure. However, in dual diastolic and systolic dysfunction, the contractile velocity in systole as determined by tissue Doppler reduced.[24] Furthermore, in diastolic heart failure, local contractility in the longitudinal direction is known to be diminished.[25] Recent research suggests that contractility in the myocardium declines even in diastolic cardiac failure. In systolic HF, however, the diastolic function is also reduced and shown to reduce exercise tolerance and be one of the drivers of prognosis.[26] As a result, both HFs are not regarded as discrete and distinct conditions.[21] Diastolic heart failure is now called heart failure with maintained ejection fraction (HFpEF), and systolic heart failure is called heart failure with reduced ejection fraction (HFrEF) (HFrEF). Because determining the pathogenesis and diagnosis of diastolic HF is difficult.[27]

Lowering of left ventricular ejection fraction is the definition of systolic heart failure. So, it is simple to diagnose. Diastolic heart failure, on the other hand, is difficult to diagnose because there are no straightforward and accurate criteria. When clinical symptoms and evidence of heart failure are present, and the reduction in left ventricular ejection fraction is none or minimal, diastolic HF can be clinically diagnosed.[27]

Diastolic HF is defined by the ACC Foundation and the AHA as a condition that has typical signs and symptoms of HF but has a normal left ventricular ejection fraction and no valve abnormalities on echocardiography.[28] Diastolic HF is defined by Vasan and Levy as (1) having congestive heart failure clinical symptoms, (2) having normal left ventricular systolic function during congestive heart failure (left ventricular ejection fraction of 45 to 50% and above), and (3) having left ventricular diastolic dysfunction.[29] Contractile dysfunction and left ventricular remodeling are the key variations between systolic and other heart failure. Progressive ventricular dilatation, also known as eccentric cardiac hypertrophy, can be found in systolic heart failure. Diastolic heart failure, on the other hand, is characterized by concentric ventricular remodeling without dilatation or concentric cardiac hypertrophy.[30]

Myocardial enlargement, myocardial cell death, and extracellular matrix rearrangement are all histological features of systolic heart failure. Diastolic heart failure, on the other hand, is characterized by severe myocardial fibrosis and cardiac hypertrophy. Increased stiffness is hypothesized to be caused by myocardial fibrosis.[30]

Chronic heart failure

The European Society of Cardiology (ESC) defines HF as a syndrome characterized by shortness of breath, persistent coughing or wheezing, ankle swelling, and fatigue, which may

be accompanied by signs such as jugular venous pressure, pulmonary crackles, increased heart rate, and peripheral oedema.[31] Chronic heart failure (CHF), also known as congestive heart failure, is a medical condition which is a primary cause of hospitalization and death in developed countries. HF is a condition that not only affects patients but also provides substantial problems to healthcare providers and systems. HF is no longer seen to be largely a problem with systolic function; instead, approximately half of HF patients have a maintained ejection fraction (HFpEF). Most critically, evidence suggests that HFpEF patients have a similar mortality risk as HF patients with a lower ejection percentage (HFrEF).[32]

Table 1: Framingham criterion for congestive heart failure.[33]

Major Criteria	Minor Criteria
Paroxysmal nocturnal dyspnea or orthopnea	
Neck-vein distention	Ankle edema
Rales	Night cough
Cardiomegaly	Dyspnea on exertion
Acute pulmonary edema	Hepatomegaly
S3 gallop	Pleural effusion
Increased venous pressure ->16 cm of water	Vital capacity ↓ ⅓ from maximum
Circulation time ≥25 sec	Tachycardia (rate of ≥ 120/min)
Hepatojugular reflux	

Major or Minor Criterion: Weight loss ≥4.5 kg in 5 days with treatment.

*For establishing a definite diagnosis of congestive heart failure in this study, 2 major or 1 major & 2 minor criteria had to be present concurrently.

Epidemiology:

People with HF is highly variable across the world, with the lowest in sub-Saharan Africa. People with HF risk factors also varies worldwide, with hypertension being most common in Latin America, the Caribbean, Eastern Europe, and sub-Saharan Africa. Ischemic heart disease is most prevalent in Europe and North America. Valvular heart disease is more

prevalent in East Asia and Asia-Pacific countries. The subjects with HF continue to rise over time, with the aging of the population. An estimated 6.2 million American adults ≥20 years of age had HF between 2013 and 2016, compared with an estimated 5.7 million between 2009 and 2012.[34] Based on disease-specific estimates of prevalence and incidence rates of HF, the subjects with HF in India due to coronary artery disease, hypertension, obesity, diabetes, and rheumatic heart disease is estimated to range from 1.3 to 4.6 million, with an annual incidence of 491 600–1.8 million.[35]

Classification:

Heart failure symptoms can occur with preserved or reduced ejection fraction (systolic or diastolic heart failure). The New York Heart Association classification system is the simplest and most widely used method to gauge symptom severity.[36] This system was a well-established predictor of mortality and can be used at diagnosis and to monitor treatment response.

Table 2: The classification system is a well-established predictor of mortality and can be used at diagnosis and to monitor treatment response.

Class	Description
I	No limitations of physical activity No heart failure symptoms
II	Mild limitation of physical activity Heart failure symptoms with significant exertion; comfortable at rest or with mild activity
III	Marked limitation of physical activity Heart failure symptoms with mild exertion; only comfortable at rest.
IV	Discomfort with any activity Heart failure symptoms occur at rest

Table 3: Indices or guidelines for diagnosis.

Definition	Advantages	Disadvantages
Framingham criteria Major and minor signs and symptoms Chest X-ray	Widely used and well-validated High specificity	Poor sensitivity, especially for early heart failure
2016 ESC criteria Signs and symptoms	Incorporate signs and symptoms with objective measures of cardiac dysfunction	Many patients with proven HFpEF have normal natriuretic peptide levels
Natriuretic peptides	Natriuretic peptides are easy to measure and widely available	Measurement variability of echocardiographic parameters may be high
Echocardiography or other cardiac imaging	EF and diastolic dysfunction can be readily measured with echocardiography	
Gothenburg criteria Symptoms and rales Atrial fibrillation on ECG	Easily applicable in primary care	Poor sensitivity
Boston criteria Signs and symptoms Chest X-ray	Predicts adverse outcomes	Heavily relies on dyspnoea, which is often absent in the elderly

ECG, electrocardiogram; EF, ejection fraction; HFpEF, heart failure with preserved ejection fraction; ESC, European Society of Cardiology.[37]

Etiology:

HF can be caused by a variety of heart problems, genetic abnormalities, and systemic disorders. Patients with HF might have a combination of aetiologies that are not mutually exclusive, and HF aetiologies differ significantly between high-income and low-income nations.[38,39] According to the Global Burden of Disease Study, there are 17 key aetiologies for HF.[40] Ischemic heart disease, chronic obstructive pulmonary disease, hypertensive heart disease, and rheumatic heart disease account for more than two-thirds of all cases of heart failure. Despite the fact that the Global Burden of Disease Study attempts to estimate the burden of right-sided HF from chronic obstructive pulmonary disease, studies measuring the prevalence of right-sided HF are sparse, necessitating further research.[40]

Risk factors:

Multiple cardiovascular conditions, ranging from arrhythmias to valvular heart disease, may ultimately lead to heart failure. Strict adherence to guideline-based management of these conditions is paramount in preventing heart failure. Advanced age is the most potent, albeit nonmodifiable, risk factor. Hypertension, which is easily diagnosed and treated, increases the failure risk 2- to 3-fold.[41] Incident risk factors for CAD, including diabetes and dyslipidemia, increase the probability of an MI, another important risk factor for heart failure.[42] Obesity, defined as a body mass index greater than 30 kg/m2, is increasingly being recognized as an individual risk factor for heart failure.[43] Genetics also play a role in many forms of heart failure.[44]

Pathophysiology:

Heart failure is a medical condition characterized by reduced cardiac output (CO) and increased venous pressure, associated with underlying molecular changes and subsequent damage to and death of cardiac muscle cells. The body has its own ways of increasing lowered CO, which together make up the neurohumoral response. This is composed of three basic elements: (1) a hemodynamic defense reaction which maintains perfusion pressure in the major organs by increasing circulating blood volume, inducing vasoconstriction, and stimulating the heart; (2) an inflammatory response (in which the body organs act as if they were facing an exogenous agent), in which inflammatory cytokines and reactive oxygen species play an important role; (3) a hypertrophic response and ventricular remodeling, with structural changes in cardiac muscle cells and in the shape of the ventricular chamber. Neurohumoral mechanisms are classified according to their effects: regulatory (increasing vasoconstriction, sodium retention, inotropism, and proliferation); and counter-regulatory (with the opposite effects). Ultimately, they are responsible for the failing heart.[45]

Diagnosis

The existence of HF symptoms and/or signs, as well as objective proof of heart failure, are required for confirming CHF. Breathlessness, tiredness, and ankle edoema are common symptoms. Symptoms and symptoms are insufficiently accurate to diagnose HF on their own, necessitating the use of diagnostic testing. Abnormalities such as AF, Q waves, LV hypertrophy (LVH), and a dilated QRS complex on an electrocardiogram (ECG) may raise the chance of a diagnosis of HF and may also guide therapy.[46] B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) measurements, as well as basic investigations like serum urea and electrolytes, creatinine, full blood count, liver, and thyroid function tests, are all recommended to distinguish HF from other conditions, provide prognostic information, and guide potential therapy. For evaluating LVEF, chamber size, eccentric or concentric LVH, regional wall motion abnormalities, RV function, pulmonary hypertension, valve function, and indicators of diastolic function, echocardiography is indicated as the primary inquiry.[47]

Management and prevention:

The first goal of treatment is to relieve symptoms, followed by preventing illness progression and hospitalization. Maintaining functional capacity and optimizing co-morbid conditions, the home environment, caregiver difficulties, and the emergency response system are all critical. In most cases, specialized care is required for difficult CHF patients. Stability for CHF is described as being able to walk at least one block without symptoms and having no limitations in routine daily activities. That can be achieved by maintaining a stable fluid balance, maintaining systolic blood pressure (BP) of less than 100 mmHg, and maintaining a heart rate of 60-85 beats per minute. Angina, diabetes mellitus (DM), chronic obstructive

pulmonary disease (COPD), anemia, and renal function all play key roles in CHF care, as does ensuring compliance with medical therapy and the absence of depression.[48]

Regular physical activity (exercising ≥5 d/wk) and maintaining a healthy body weight are key ingredients to preventing heart failure. Other healthy behaviors also lower the risk of developing heart failure: not smoking, eating fruits and vegetables (4 servings/d), and moderate alcohol intake (1 drink/d).[44] In systolic HF, dietary and lifestyle adjustments such as salt restriction to less than 2 g/d and fluid restriction to 1.5–2 L/d should be implemented. It is necessary to provide education on weight management and self-efficacy through the use of diuretics and other drugs. Low-intensity exercise is recommended. Who to contact and what to do if symptoms worsen should be clearly laid out to the patient and family.[49]

Iron-deficiency Anemia:

Iron deficiency is a condition in which there are no mobilizable iron stores and in which signs of a compromised supply of iron to tissues, including the erythron, are noted. The more severe stages of the iron deficit will have anemia. When iron-deficient erythropoiesis occurs, hemoglobin concentrations are reduced to below-optimal levels. Iron deficiency anemia is diagnosed when individual hemoglobin levels fall below two standard deviations (-2SD) of the distribution mean for hemoglobin in an otherwise healthy population of the same gender and age living at the same altitude. Anemia, a global public health crisis that troubles people of all ages in both developing and developed countries. Anemia is defined as hemoglobin (Hb) levels of 12.0 g/dL in women and 13.0 g/dL in males, according to the World Health Organization (WHO). However, normal Hb distribution varies not only with sex but also with ethnicity and physiological status.[50]

Epidemiology:

One-third of the world's population suffers from anemia, with IDA being the leading cause. Prevalence rates of up to 41.7 percent, 32.8 percent, and 40.1 percent, respectively, are found in preschool children (5 years), women of reproductive age, and pregnant women (2016 Global Health Observatory data).[51] In high-income nations, veganism, malabsorption disorders, and excessive menstrual bleeding are all high-risk categories, with roughly two-thirds of women with more menstrual bleed having ID/IDA.[52,53] IRIDA is likely to account for lesser than one percent of the instances of IDA seen in medical practice, despite the lack of precise estimates on the frequency of hereditary variants of IDA.[52]

Classification:

For numerous subtypes of ID, there is tremendous intricacy and a big store of terminology that is routinely employed interchangeably or in contradiction in the literature. Absolute ID refers to a low amount in total body iron reserves (mostly in macrophages and hepatocytes) that may or may not progress to IDA.[54] Absolute ID can arise when there is an increase in demand, a drop in intake, a reduction in or malabsorption of nutrients, or prolonged blood loss. Increased demand is normally physiologic and can be seen in infants, preschoolers, teenagers going through growth spurts, and pregnant women (mostly second and third trimesters).[52,54,55] Iron deficiency can be a direct result of poverty and hunger, as it is for many children and pregnant women in impoverished countries, or it can be linked to iron-deficient vegan or vegetarian diets.[52,54,55]

In the literature, the terms "functional" or "relative" ID (and consequent IDA) are used to characterize two main scenarios: for subjects having chronic kidney disease, chronic heart failure, inflammatory bowel disease, chronic pulmonary diseases, cancer, obesity, other

autoimmune diseases, and chronic infections, iron is hardly mobilized from stores to circulation and erythropoietic tissue due to chronic inflammation and elevated hepcidin levels.[52]

Indices/guidelines for diagnosis:

Anemia is defined as hemoglobin levels lower than 7.7 mmol/l or (13 g/dl) for men and 7.4 mmol/l or 12 g/dl for women, low serum iron (7.1 g/l), low serum ferritin (the storage form of iron) (30 ng/l), low transferrin saturation (15 percent), and a high total iron-binding capacity (>13.1 mol/l) according to the World Health Organization. A total blood cell count, reticulocyte count, peripheral smear, and serum iron indices are commonly used to determine the cause of anemia. The patient's hemoglobin or packed cell volume level determines the degree of anemia. Hypochromic, microcytic erythrocytes and low iron reserves indicate iron deficiency anaemia.[56]

Etiology:

Low iron bioavailability in food is the leading cause of IDA in underdeveloped nations.[57,58] In developed countries, however, poor iron absorption and blood loss were the more common causes of iron insufficiency. Atrophic gastritis or malabsorption disorders, particularly celiac disease, can cause decreased iron absorption. Iron deficiency anemia can be caused by postsurgical gastrectomy (partial or whole) and intestinal resection or bypass due to decreased iron absorption. The majority of causes of IDA are chronic blood loss from the genitourinary, gynecological, or gastrointestinal systems. Excessive menstruation is the leading cause of IDA in premenopausal women. Whether the bleeding is acute or persistent, gastrointestinal bleeding is a common cause of IDA. Patients may have maroon-colored stools or blood in

their stools with quick bleeding; however, blood loss of up to 100 mL/day from the GUT can be linked with normal-appearing stools.[59]

Pathophysiology:

To make iron available to plasma transferrin, the body recycles the majority of the needed iron from the breakdown of senescent erythrocytes by macrophages in the spleen. The hepatic hormone hepcidin controls iron intake into blood and recycling; however it can be readily destroyed, resulting in various types of ID and eventual anemia.[52,54] Hepcidin stops iron export from enterocytes and macrophages into the blood by binding to and degrading its receptor ferroprotein on the basolateral membrane of these cells. Hepcidin is inhibited in absolute ID, resulting in enhanced iron absorption from the gut as well as the release of recycled iron from splenic macrophages into the circulation.[60]

Additionally, tissue hypoxia in IDA increases levels of hypoxia-inducible factor 2α (HIF-2α), which stimulates erythropoietin production by the kidney leading to the expansion of erythropoiesis and release of hypochromic, microcytic erythrocytes. This increase in erythropoiesis during anemia further suppresses hepcidin through the erythroid factor erythroferrone (ERFE), released by erythroblasts.[61]

Chronic inflammation can generate moderate anemia through a variety of iron-unrelated pathways mediated by proinflammatory cytokines; this is known as anemia of chronic disease or anemia of inflammation, and it normally goes away after the underlying cause is addressed. In recent years, chronic inflammation is linked to iron imbalance.[62] The cytokines interleukin (IL)-6, IL-1, and IL-22 have been demonstrated to stimulate hepcidin production in intestinal enterocytes and macrophages, resulting in ferroportin breakdown and sequestration of iron away from the circulation (which is later lost through shedding). By

hepcidin-independent processes, stimulation of Toll-like receptors 2 and 6 in chronic inflammation lowers ferroportin expression in macrophages.[63]

Diagnosis:

The diagnosis of IDA can be readily made by assessing hemoglobin and serum ferritin levels. According to the World Health Organization (WHO), anemia is defined as a hemoglobin level <130 g L−1 in men, <120 g L−1 in nonpregnant women, and <110 g L−1 in pregnancy.[64] Serum ferritin level is the most specific and effective test to reflect total body iron stores and is universally available and standardized.[52] Although a value <12–15 μg L−1 is confirmatory for ID, a value of <30 μg L −1has higher sensitivity (92%) and similar specificity (98%) and is more widely used.[65,66]

Complications:

IDA will have reduced cognitive performance and delayed motor and cognitive development in children, decreased physical performance and quality of life in adults, especially women in the reproductive age group, and cognitive decline in the elderly. Although these symptoms remain nonspecific, they can be attributed to low delivery of oxygen to body tissues in IDA. They may also occur as a direct effect of ID, probably due to reduced iron levels in muscle or brain tissue and impact on energy production, myoglobin synthesis, and brain development.[67]

Management, prevention:

Efforts to increase access to and consumption of iron-rich foods should always be in place. Iron absorption enhancers (ascorbic acid) or inhibitors (calcium, phytates [cereals], tannins [tea and coffee]) should also be considered when supplying iron-rich meals. Enrichment of food (rice, maize flour, cornmeal) with iron is also practiced in some countries, such as in Asia, Africa, and Latin America, and recommended by the WHO.[65,68,69] The WHO

recommends iron supplementation to prevent ID/IDA in instances where the prevalence of anemia is 40% or higher: children 6–23 months (10–12.5 mg elemental iron daily – drops/syrups, three consecutive months in a year), 24–59 months (30 mg elemental iron daily – drops/syrups/tablets, three consecutive months in a year), 5–12 years (30–60 mg elemental iron daily – tablets/capsules, three consecutive months in a year). In malaria-endemic areas, the provision of iron supplementation in infants and children should be done in conjunction with public health measures to prevent, diagnose and treat malaria.[70]

Hepcidin-mediated reduced absorption may restrict the response to oral iron therapy in subjects having chronic inflammatory disorders. Over the course of four months, high-dose oral iron did not enhance exercise capacity in iron-deficient individuals with heart failure and a reduced ejection fraction.[71]

IDA in chronic HF:

According to the World Health Organization (WHO), anemia is defined as low hemoglobin levels (<12 g/dL in women and <13 g/dL in men).[72] The WHO criteria are used on a large scale to define anemia; however, age and race are considered. A ferritin level of <30 µg/L is usually suggestive of the presence of iron deficiency; it is classified as absolute (ferritin level <100 µg/L) or functional (ferritin level, 100-300 µg/L and transferrin saturation, <20%).

Incidence:

Iron deficiency is estimated to affect between 37 and 61% of patients living with CHF, and its prevalence increases as CHF advances.[13,14] In a study of 751 stable chronic HF patients from a multi-ethnic Asian population, 61.4% were ID compared with 39.3% of controls from the general population.[73] In a study of 127 patients with stable chronic HF and an LVEF of <45%,

approximately one-third were ID (of whom three-quarters were not anemic).[74] In another report, involving 546 patients with chronic HF in Europe, 36% were found to be iron deficient, including 32% of the non-anemic patients.[15] The varying prevalence of ID depending on the definition is illustrated in a recent study where, firstly, 43% of 127 patients with HF were ID when defined using Tsat <20% alone, if ferritin levels were included in the definition 36% were ID but not anemic, and 23% had ID and anemia.[14]

Etiology:

Anemia can develop in people with HF for a variety of reasons, including a blunted erythropoietin response, dilutional anemia, and chronic illness anemia, with iron deficiency the leading cause.[10,75] There are two types of iron shortage: absolute iron deficit and functional iron deficiency. The storage iron in bone marrow, liver, and spleen is greatly diminished or nonexistent in absolute iron insufficiency. Normal or increasing total body iron reserves that are unavailable for integration into erythroid precursors for erythropoiesis indicate functional iron deficit.[76] Appetite loss, poor nutrition, decreased gut absorption of ferrium due to edema, and gastrointestinal blood loss due to the usage of anti-aggregants and anticoagulants can all contribute to an absolute iron shortage in HF.[8] Hepcidin, a peptide that restricts gut ferrium absorption and iron release from circulating macrophages, causes a functional iron shortage, also known as iron-restricted erythropoiesis, a kind of anemia caused by chronic inflammation.[60] Inflammation in HF can cause hepcidin expression independent of iron storage, limiting iron absorption improperly.

Pathophysiology:

The pathogenesis of low hemoglobin in HF is multifactorial. The major factors contributing to CHF-related anemia involve CKD, renin-angiotensin system, hematinic abnormalities,

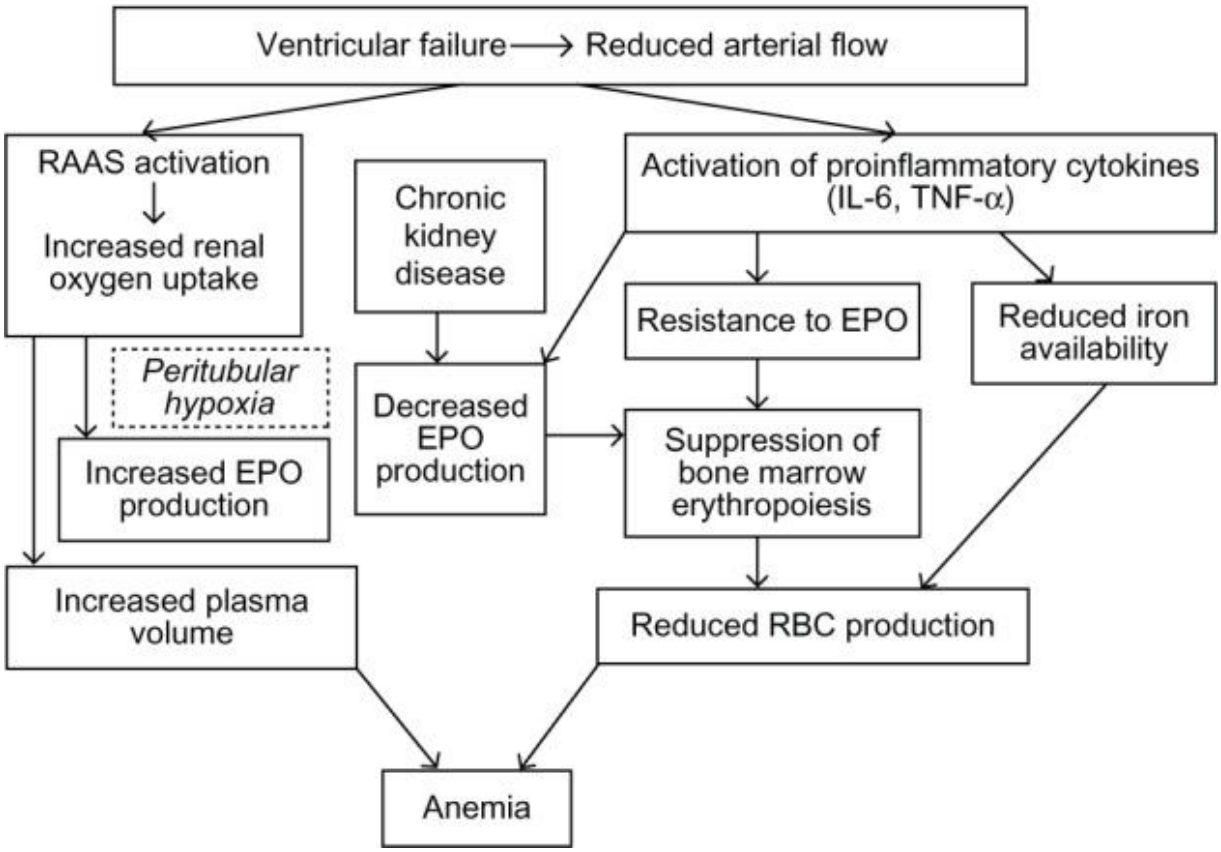
mainly iron deficiency, chronic inflammation, and hemodilution. A major factor contributing to anemia of CHF is kidney dysfunction, being associated with cardiac disorder.[77] Erythropoietin, which increases the generation of red blood cells (RBCs), is produced predominantly by specialized peritubular fibroblasts in the renal cortex and outer medulla and is frequently aberrant in HF. The primary stimulus for erythropoietin production is a low oxygen level. Renal impairment is common in people with heart failure, but structural renal illness, which might reduce erythropoietin production, is uncommon. However, an oxygen supply-demand mismatch induced by increased proximal tubular salt reabsorption due to decreased renal blood flow and glomerular filtration rate lowers renal Po2, activates hypoxia-inducible factor-1, and stimulates transcription of the erythropoietin gene.[78,79] As a result, erythropoietin levels are higher in proportion to the severity of HF but lower than expected for the degree of anemia, implying that erythropoietin production has been inhibited.[10,80]

Inflammation is a significant part of HF. TNF, interleukin-6, and numerous other proinflammatory cytokines, as well as C-reactive protein, are all elevated in HF and are inversely associated to hemoglobin levels. Interleukin-6 and tumour necrosis factor-activate transcription factors GATA binding protein 2 (which binds nucleotide consensus sequence GATA in target gene promoters) and nuclear factor light-chain enhancer of activated B cells attenuates erythropoietin response. These cytokines also stop erythroid progenitor cells from proliferating in the bone marrow. However, erythropoietin levels in some HF patients are abnormally high, and high erythropoietin levels are linked to poorer outcomes.[10,80–82]

Through numerous routes, the renin-angiotensin system is involved in erythropoietin pathology. Angiotensin II reduces Po2 by decreasing renal blood flow and increasing oxygen demand, which stimulates the formation of erythropoietin. With Angiotensin II induction in

bone marrow, there will be the formation of erythroid progenitor cells. Angiotensin receptor blockers and angiotensin-converting enzyme inhibitors reduce hemoglobin levels by inhibiting the breakdown of the hematopoiesis inhibitor N-acetyl-seryl-aspartyl-lysyl-proline and lowering the generation of erythropoietin and erythroid progenitors.[82,83] Finally, although clinically euvolemic individuals have normal plasma volume and hemoglobin measurement represents "real anemia" as measured by RBC volume in the great majority of anemic patients with HF, anemia may be attributed to hemodilution.[84]

Figure 1: Overlapping mechanisms of anemia in heart failure.[77]



Abbreviations: EPO, epoetin; IL-6, interleukin-6; RAAS, renin-angiotensin-aldosterone system; TNF-á, tumor necrosis alpha.

Diagnosis:

Anemia with poor iron reserve identifies the two most common types of anemia in subjects having HF, namely anemia of chronic disease (AOCD) and iron deficiency anemia, based on low transferrin saturation and significantly greater ferritin levels (IDA).[75] Diagnosing ID in daily practice is based on circulating biomarkers including ferritin, iron, and transferrin saturation (TSAT). Because ferritin is an acute phase reactant, levels tend to rise in inflammatory conditions.[62] As a result, ferritin levels of 100 g/L or 300 g/L if TSAT is 20% have been utilized to enrol patients with both absolute and functional ID in iron replacement trials in patients with HF.[84] TSAT is the percentage of transferrin saturated with iron and was calculated using serum iron and serum transferrin using the following formula: TSAT (%)=iron (μmol/L)/(transferrin [g/L]×25.2)×100.[85]

The major signs of CHF (fatigue, exercise intolerance) are identical of iron deficiency complicates the diagnosis of iron insufficiency in CHF. In CHF patients, fatigue is commonly connected to iron shortage and impaired activity and work ability.[7]

Morbidity and Mortality due to IDA in chronic heart failure:

The death rate due to of rehospitalization appears to be higher in individuals with HF-anemia as a co-morbidity. When compared to patients without anemia, patients with anemia have a 1.74 and 1.57 higher relative risk of death and re-admission episodes, respectively.[86] Iron deficiency can also negatively impact outcomes in CHF. Higher chances of death from iron deficiency in studies evaluating CHF patients ranges between 40 and 60%.[13,14] Hospitalizations have also been linked to iron deficiency in CHF patients, with one study finding that the risk of hospitalization was doubled in patients who were not treated for iron deficiency compared to those who were (relative risk [RR] 2.23, 95 percent confidence

interval [CI] 1.59–3.42, P 0.01).[87] The CONFIRM-HF research found that treating iron deficiency with ferric carboxymaltose gives a significant reduction in hospitalizations (hazard ratio [HR] 0.39, 95 percent confidence interval [CI] 0.19–0.82, P = 0.009).[88]

It was showed that the myocardium of subjects with HF has a lower iron concentration, suggesting that myocardial iron depletion may play a role in decreasing systolic performance.

Table 4: Several observational studies have looked into the link between iron deficiency and outcomes in heart failure patients.[13–15,89,90]

Parameter	Study design	N	Population	Definition of iron deficiency	Findings
Mortality	Prospective, two-centre.[15]	546	LVEF ≤45%, NYHA class I–IV	Ferritin <100 ng/mL or 100–300 ng/mL with TSAT <20%	Iron deficiency significantly related to mortality (HR 1.74, 95% CI 1.30–2.33, P < 0.001) on multivariate analysis
	Pooled cohort analysis (three countries).[13]	1506	NYHA class I–IV, reduced or preserved LVEF	Ferritin <100 ng/mL or 100–299 ng/mL with TSAT <20%	Iron deficiency significantly related to mortality (HR 1.42, 95% CI 1.14–1.77, P = 0.002) on multivariate analysis
	Retrospective, single-centre.[91]	274	LVEF ≤45%, NYHA class I–IV	Progression of iron deficiency was defined as increasing red cell distribution width with decreasing mean cell volume	Progression of iron deficiency significantly related to mortality (HR 2.78, 95% CI 1.64–4.73, P < 0.001)
	Community-based survey.[90]	574	Self-reported, community-dwelling heart failure patients	Ferritin <100 ng/mL or 100–299 ng/mL with TSAT <20%	No significant association between iron deficiency and all-cause or cardiovascular mortality on

				multivariate analysis
Prospective, two-centre.[14]	157	LVEF ≤45%, NYHA class I–IV	TSAT <20%	IDA will be with two-fold greater risk for death than iron deficiency without anaemia

CI, confidence interval; HR, hazard ratio; MLHFQ, Minnesota Living with Heart Failure Questionnaire; TSAT, transferrin saturation.

In most investigations, the iron deficiency revealed a substantial connection with mortality after controlling for confounding factors, regardless of whether or not patients had anemia or the severity of heart failure.[13–15,91] Iron deficiency was found to have an independent and linear relationship with submaximal exercise capacity as measured by the 6-minute walk (6MWD) test and symptomatic functional limitation as measured by the advanced NYHA functional class in a single-center cross-sectional study of 538 stable patients with chronic HF.[92]

In chronic heart failure, IDA is a negative prognostic factor linked to disease progression, poor quality of life, and an increase in cardiovascular mortality.[93] In comparison to patients without ID or those who receive iron replenishment, ID without anemia has been linked to higher fatigue, decreased exercise intolerance, decreased quality of life, increased hospitalization rates, and decreased mortality.[7,13–15,18,92]

Correlation of iron deficiency in iron deficiency anemia with the severity of chronic HF:

Iron deficiency is highly prevalent in patients with advanced heart failure (NYHA class III and IV), females, and patients with high levels of inflammatory markers (such as C-reactive protein) as well as increased levels of NT-proBNP; however, even in patients with lower risk,

such as those with NYHA class I or II, the prevalence remains >30 percent.[13,15,90] Patients with ID exhibit greater plasma NT-proBNP, and there is a borderline trend towards the more advanced NYHA class in these patients, according to a multivariable logistic regression model. Beyond the collection of clinical factors including or not the NYHA class or plasma NT-proBNP, it was shown that ID had a significant and independent input to the survival models in patients with CHF.[15]

Patients who are in the IV NYHA class, who are refractory to medication, associate anemia in 80% of cases.[94] Lower blood pressure reduces peripheral vascular resistance while also stimulating the sympathetic nervous system and the rennin-angiotensin-aldosterone pathway. The renin-angiotensin-aldosterone pathway is stimulated, which promotes salt and water retention. As a result, cardiac output rises while cardiac work rises at the same time.[86] Within six months, Anand et al.[95] discovered that every 1 g/dl rise in hemoglobin represents a 4,1 g/m2 drop in the left vertical mass index.

A cross-sectional retrospective study reported prevalence of anemia in NYHA Functional class III (FC III) was the most prevalent one (63.2%), followed by NYHA FC IV (31.3%).[96] In a prospective observational study, it was reported that ID was associated with female gender, lower body weight and hemoglobin, higher NYHA class, and natriuretic peptide (NP) levels (all $p < 0.05$).[97] In a study to assess the effects of intravenous iron therapy on clinical condition, upon comparing NYHA class after therapeutic approach showed a significant improvement in functional class. NYHA class III and IV before intervention was revealed in 60% and 16%, respectively, which reached to 36% and 8% respectively after intervention ($P = 0.017$).[98]

A prospective, parallel, 1:1 randomized controlled trial of intravenous ferric-carboxy maltose compared with standard of care in patients with heart failure showed that in the beginning, patients in the study were in a higher NYHA class (II, III) and at 12 weeks, none of them were in NYHA class III. This improvement was more marked in the FCM group than in the SOC group. Statistical analysis showed that at baseline, there was no difference in NYHA class ($p = 0.232$) but was significantly different at 12 weeks ($p = 0.027$), with benefit more marked in the FCM group.

MOST RELEVANT STUDIES:

Iosebashvili et al.[97] **(2021**) to study prevalence and clinical impact of ID and anemia in HF patients. ID was present in 78(58.6%) patients. 70(52.6%) patients from 133 presented with anemia. There was a highly significant association between hemoglobin and serum ferritin in patients with ID, but in patients without ID, this association was only of borderline significance. The presence of anemia, ID, or both were associated with significantly higher NYHA class.

Dhoot et al.[99] **(2020)** conducted a prospective, parallel, 1:1 randomized controlled trial of intravenous ferric-carboxy maltose compared with standard of care in subjects with heart failure. Post 12 weeks, there were improvements noticed in peak VO2, NYHA functional classification, 6-min walk test distance covered, and reduction in Minnesota Living with Heart Failure Questionnaire score in the ferric-carboxy maltose as compared with standard of care group. However, no improvement in ejection fraction was noticed.

Jin et al.[17] **(2019)** analyzed clinical data from HFpEF patients with and without anemia who were registered in the China National Heart Failure Registration Study (CN-HF) to see how

anemia affected all-cause mortality and all-cause re-hospitalization. In patients with NYHA class III-IV, anemia was linked to an increase in all-cause re-hospitalization. Except for all-cause re-hospitalization in patients with NYHA class III-IV, the study indicated that anemia was more in subjects with HFpEF from the CN-HF registry, but it was not an independent predictor of all-cause mortality and all-cause re-hospitalization.

The goal of Negi et al.[3] **(2018)** was known the prevalence, risk factors, and clinical importance of iron deficiency and anemia in nonischemic HF patients with decreasing ejection fraction (HFrEF). Iron deficiency and anemia were found in 58.8% (52.2 percent–65.1 percent) and 35.8% (29.8 percent–42.3 percent) of patients, respectively. Comorbidities associated with HFrEF include iron insufficiency and anemia. Low hemoglobin and transferrin saturation are both linked to progressive heart failure. The findings have significant implications for heart failure management.

Mirdamadi et al.[98] **(2018)** wanted to see how intravenous iron therapy affected subjects with chronic HF and iron deficiency's clinical condition, left ventricular function, and quality of life. After the therapeutic method, the NYHA class demonstrated considerable improvement. The rate of hospitalization was lowered significantly from 42 percent to 16 percent (P 0.001). Furthermore, the mean 6-minute walk test (6MWT) was raised from 155.18 to 187.40 metres (P 0.001). The study concluded that treating iron deficiency improves functional status, ejection fraction, and quality of life in patients with chronic HF, as well as reducing the need for re-hospitalization. However, renal function deteriorated, necessitating greater attention to renal function.

Abebe et al.[100] **(2017)** performed a retrospective cohort study to assess the prevalence of anemia in subjects with HF, as well as to compare baseline clinical characteristics and

outcomes of severe HF patients having and not having anemia. The researchers discovered that HF patients with anemia are older, had lower hemoglobin and salt levels, and have a higher creatinine level. Furthermore, there was a substantial difference in prognosis between research groups, with anemic patients having a poorer prognosis. Despite the fact that anemia is a significant risk factor, it was not found to be an independent predictor of mortality in this investigation.

Von Haehling et al.[101] **(2017)** conducted a prospective, observational study to find the prevalence and clinical impact of ID and anemia in HF outpatients attending cardiology practices in Germany. ID was associated with female gender, lower body weight and hemoglobin, higher NYHA class, and natriuretic peptide (NP) levels (all $p < 0.05$). ID was also more common in anemic than non-anemic patients ($p < 0.0001$), and 9.8% of PrEP-participants had both ID and anemia. Despite the high prevalence, ID was previously unknown in all PrEP-participants, and anemia was often unappreciated.

Cleland et al.[93] **(2016)** studied the prevalence of anemia and iron deficiency in a diverse group of patients with suspected HF who were referred to a cardiology clinic. Anemia was found in 27.8% of the patients, with a higher prevalence of 33.3 percent in those who satisfied the criteria for HF with or without LVSD. Iron deficiency was found in 43.2 percent to 68.0 percent of patients with anemia and 14.7 percent to 35.3 percent of individuals without anemia, depending on the definition used. Anemia is frequent in HF patients, and it's commonly linked to iron deficiency. Both iron deficiency and anemia are linked to a high all-cause and cardiovascular mortality in this population and could be therapeutic targets.

Berry et al.[102] **(2016)** used a large multinational pooled dataset of prospectively enrolled HF patients to assess the predictive value of anemia, with the specific goal of determining the prognostic role of anemia in HF with preserved and lowered ejection fraction (HF-PEF and HF-REF, respectively). Subjects having anemia were older, more likely to have diabetes, ischemic aetiology, NYHA class IV symptoms, a lower estimated glomerular filtration rate, and were more likely to be on a diuretic and less likely to be on a beta-blocker than patients with normal Hb values. Independent of the EF group, patients with anemia had higher all-cause mortality (aHR 1.38, 95 percent confidence interval [CI] 1.25–1.51): aHR 1.67 (1.39–1.99) in HF-PEF and aHR 2.49 (2.13–2.90) in HF-REF. Anemia is an unfavorable prognostic factor in HF regardless of EF, according to the study. Anemia stands out as the most important prognostic factor in patients with HF-REF.

Enjuanes et al.[92] **(2016)** investigated the impact of iron deficiency and anemia on submaximal exercise capacity in chronic HF patients. Increased levels of soluble transferrin receptor, indicating impaired iron status, were independently linked with advanced NYHA class (P.05) in multivariate logistic regression analysis. Iron deficiency, but not anemia, was linked to reduced submaximal exercise capacity and symptomatic functional limitations in subjects having chronic HF.

Cavalini et al.[96] **(2016)** did a cross-sectional investigation to determine the prevalence of anemia in subjects having HF, characterize the morphology, and investigate the relationship between the morphology and the NYHA functional class. The prevalence of anemia in this population was 41.0 percent, with the majority (38.2%) of cases being mild to moderate. Functional class III (FC III) was the most common (63.2%), followed by FC IV (43.2%). (31.3 percent). The normocytic and hypochromic morphological characteristics were detected

in 49.1% of the cases. Anemia was found to have a p=0.008 correlation with increasing age (>60 years). According to the findings, the prevalence of anemia in HF patients was higher in older age groups, in FC III and IV, and the primary morphological characteristic was normocytic and hypochromic anemia.

In a cross-sectional study with prospective data collection, **Ikama et al.**[103] **(2015)** aimed to identify the prevalence of anemia in patients with HF and analyze its impact on their prognosis. Anemia was shown to be common in subjects having heart failure in this exploratory investigation, and it had a detrimental impact on their prognosis.

Ponikowski et al.[88] **(2015)** conducted CONFIRM-HF, a multi-center, double-blind, placebo-controlled trial to assess the benefits and safety of long-term intravenous iron treatment in iron-deficient heart failure patients (HF). Over a one-year period, treating symptomatic, iron-deficient HF patients with i.e., Iron in the form of ferric carboxymaltose (FCM) resulted in sustained improvements in functional ability, symptoms, and QoL and may be linked to a lower likelihood of hospitalization for worsening HF.

In an international cohort of 1278 patients with CHF, **Enjuanes et al.**[18] **(2014)** evaluated the influence of ID on HRQoL and the association with anemia status, iron status, clinical baseline information, and HRQoL, measured using the Minnesota Living with Heart Failure questionnaire (MLHFQ). Unadjusted global MLHFQ scores were lower in ID and anaemic patients (ID +: 42 25 vs. ID: 37 25; p-value = 0.001 and A+: 46 25 vs. A: 37 25; p-value 0.001). Using several multivariable regression models, the combined impact of ID and anemia was investigated, revealing that ID, but not anemia, was linked to poor HRQoL. ID has a poor impact on HRQoL in CHF patients, regardless of whether or not anemia is present

Klip et al.[13] **(2013)** investigated the clinical correlates of ID and their prognostic implications in a global pooled population of 1,506 chronic HF patients. 753 patients had iron deficiency (defined as ferritin levels of less than 100 g/L or ferritin levels of 100-299 g/L with a transferrin saturation of less than 20%). (50 percent). More likely anemic was more than nonanemic patients to be iron deficient (61.2 percent versus 45.6 percent, P.001). ID was found to be a strong predictor of mortality in a Kaplan-Meier survival analysis (log-rank 2 10.2, P =.001). ID (but not anemia) remained a strong and independent predictor of mortality in multivariable hazard models (hazard ratio 1.42, 95 percent confidence interval 1.14-1.77, P =.002). They came to the conclusion that iron deficiency is widespread in subjects with chronic HF, that it is linked to disease severity, and that it is a powerful and independent predictor of prognosis. The ID appears to have greater predictive power than an anemia in this study.

In patients with chronic HF, **Comin-Colet et al.**[12] **(2013)** investigated the impact of iron deficiency (ID) and/or anemia on health-related quality of life (HRQoL) (CHF). When other characteristics associated with HRQoL were controlled for, ID was linked with worse overall summary (P = 0.008) and physical dimension scores (P = 0.002) on the Minnesota Living with HF questionnaire, although anemia was not (both P > 0.05). Increased soluble transferrin receptor levels were similarly linked to poor HRQoL (P 0.001). After adjusting for hemoglobin and C-reactive protein, ID was shown to be more evident in anemia patients than in those without (P 0.001). The researchers concluded that in subjects with CHF, ID, but not anemia, was linked to a lower HRQoL, which they attributed to physical factors.

In patients with CHF, **Aung et al.**[91] **(2013)** wanted to see if temporal variations in red cell distribution width (RDW) and developing ID had any bearing on survival. Evolving ID was

also linked to a higher risk of death (HR 2.78, 95 percent CI 1.64 to 4.73, P 0.001) and associated with a worse prognosis than growing RDW alone (P 0.005). Patients with evolving ID who kept their Hb levels stable throughout time had a 2-fold higher chance of dying than those whose Hb levels dropped without evolving ID. The researchers discovered that an increasing RDW and growing iron deficit over time indicate a more chances of death in CHF patients and that these factors should be used for risk stratification and/or treatment targeting to enhance outcomes.

Okonko and colleagues et al.[14] **(2011)** The goal of this study was to thoroughly examine iron metabolism and its implications in CHF patients. Iron homeostasis problems were linked to worsening inflammation and disease severity, and lower hemoglobin levels were strongly predicted by age, sex, erythrocyte sedimentation rate, NYHA functional class, and creatinine levels, regardless of age, sex, erythrocyte sedimentation rate, NYHA functional class, and creatinine. The causes of anemia varied based on the severity of the disease, with an iron-deficient substrate (chronic disease anemia and/or iron-deficiency anemia) present in 16 percent, 72 percent, and 100 percent of anemic NYHA functional classes I or II, III, and IV patients, respectively. In patients with CHF, abnormal iron homeostasis is linked to decreased exercise capacity and survival, and it appears to be more dangerous than anemia from a prognosis standpoint.

In 574 persons with self-reported heart failure, **Parikh et al.**[90] **(2011)** looked at the links between iron deficiency, hemoglobin, C-reactive protein (CRP), and all-cause and cardiovascular death. Hemoglobin, CRP, and transferrin saturation, but not an iron deficiency, were substantially related with all-cause and cardiovascular death in age- and sex-adjusted Cox proportional hazards models. Hemoglobin was an individual predictor of cardiovascular

mortality in multivariate models, while CRP was an individual predictor of both all-cause and cardiovascular death.

In a prospective observational trial, **Jankowska et al.**[15] **(2010)** sought to investigate the connection between ID and survival in subjects having systolic CHF. Among the whole CHF population, the prevalence of ID was 37.4% [95 percent confidence intervals (CI)] (32.4% vs. 57.1% —in persons without vs. with anemia defined as hemoglobin level of 12 g/dL in women and 13 g/dL in males, P 0.001). ID was more common in women in the advanced NYHA class, who had greater plasma N-terminal pro-type B natriuretic peptide and serum high-sensitivity C-reactive protein (all P 0.05) in a multiple logistic model. The researchers concluded that ID is frequent in subjects having systolic CHF and is a strong, independent predictor of poor outcomes.

LACUNAE OF LITERATURE:

In individuals having chronic HF, anemia is linked to higher death and hospitalization rates. Anemia prevalence varies greatly among chronic HF patients, depending on ethnicity and socioeconomic status. Indians are genetically susceptible to heart disease; hence research into the prevalence of anemia among Indian patients with chronic HF is needed.

MATERIALS & METHODS

MATERIALS AND METHODS:

Study site: This study was conducted in the department of General Medicine at Sri Devaraj URS Academy of Higher Education and Research, Tamaka, Kolar-563101

Study population: All the eligible admitted patients to medicine in RLJH with a diagnosis of chronic heart failure in the department of General Medicine at Sri Devaraj URS Academy of Higher Education and Research were considered as the study population.

Study design: The current study was a cross-sectional study

Sample size:

Sample size: Sample size was calculated assuming the proportion of iron deficiency among the heart failure patients as 41% as per the study by Jankowska EA **e**t al.[15] The other parameters considered for sample size calculation was 11% absolute precision and 95% confidence level. The following formula was used for sample size as per the study by Daniel WW et al.[104]

$$N = \frac{Z^2 P(1-P)}{d^2}$$

Where *n* = Sample size

Z= Z statistic for a level of confidence level= 1.960

P = Expected prevalence/proportion of outcome= 0.50

d = Precision= 0.11

The required sample size as per the above-mentioned calculation was 77. To account for a non-participation rate of about 15%, another 12 subjects were added to the sample size. Hence the final required sample size would be 89.

Sampling method: All the eligible subjects were recruited into the study consecutively by convenient sampling till the sample size is reached.

Study duration: The data collection for the study was done between January 2020 to May 2021 for a period of 1 year 5 months.

Inclusion Criteria:

All patients aged above 18 years diagnosed with based HF on Framingham criteria and 2D echocardiography.

Exclusion criteria:

Patients with associated co morbities, which increase iron deficiency such as

1. Chronic kidney disease
2. Chronic liver disease
3. Bleeding disorder
4. Inflammatory bowel disease
5. Pregnancy
6. Bowel cancers and
7. Other chronic inflammatory conditions.

Method of collecting data:

- This is a cross-sectional study which includes the patients who fulfill the inclusion and exclusion criteria.
- The severity of heart failure is assessed in terms of NYHA Grading, and it is correlated to the levels of iron deficiency.
- Framingham diagnostic criteria for heart failure.[105]

Table 5: Heart failure is diagnosed when two major or one major and two minor criteria are met.

Major criteria	Minor criteria
Acute pulmonary oedema	Ankle oedema
Cardiomegaly	Dyspnea
Hepatojugular reflex	Pedal oedema
Neck vein distention	Hepatomegaly
Paroxysmal nocturnal dyspnea	Nocturnal cough
Rales	Pleural effusion
Third heart sound gallop	Tachycardia >120 beats

New York Heart Association classification:[106]

- Class I: Symptoms only on levels of activity that would produce symptoms in normal individuals; Ordinary physical activity does not cause dyspnea or fatigue.
- Class II: Symptoms on ordinary exertion resulting in mild limitation of physical activity.
- Class III: Symptoms on less than ordinary exertion, resulting in marked limitation of physical activity.
- Class IV: Symptoms at rest or minimal exertion, resulting in an inability to carry on any physical activity without discomfort.

Investigations required were:

1. 2D echo
2. Serum ferritin
3. Transferrin saturation
4. Serum iron levels
5. CBC with peripheral smear

6. N terminal pro BNP levels.

Ethical considerations: Institutional human ethics committee approved the study. All the study participants gave informed written consent, and only those participants willing to sign the informed consent were there in the study. The risks and benefits involved in the study and the voluntary nature of participation were explained to the participants before obtaining consent. The confidentiality of the study participants was maintained.

Data collection tools: All the relevant parameters were documented in a structured study proforma.

STATISTICAL ANALYSIS:

Transferrin saturation percentage was considered as the outcome variable. The severity of HF was considered as an explanatory variable.

Descriptive statistics of the study population was carried out by mean and standard deviation for continuous variable whereas frequency and percentage for categorical variable. Descriptive statistics of the outcome measures were carried out by median and interquartile range (IQR) since they were not normally distributed. Shapiro Wilk's test was used to test the normality of the outcome measures. Kruskal Wallis test was used to compare continuous outcome variables between different categories of the explanatory variable. Multiple pairwise comparisons were used as a post-hoc test to compare continuous outcome variables of each category of the explanatory variable with one another. The Chi-square test was used to see the association between categorical outcome and explanatory variable. P-value <0.05 was considered statistically significant. RStudio Version 1.2.1093 was used for statistical analysis. *(Reference: **RStudio** Team (2020). **RStudio**: Integrated Development for R. **RStudio**, PBC, Boston, MA URL http://www.**rstudio**.com/.)*

OBSERVATIONS AND RESULTS

RESULTS:

Table 6: Background characteristics of the study population (N=89)

Characteristics	Descriptive statistics
Age (Mean (±SD))	60.35 (±11.47)
Sex, N (%)	
Male	58 (65.2%)
Female	31 (34.8%)

A total of 89 patients were included in the analysis. The mean age of the study population was 60.35(±11.47) years. The majority (65.2%) of the study population were males, whereas 34.8% were females. (Table 6)

Table 7: Descriptive statistics of the outcome measures in the study population (N=89)

Outcome measures	Median (IQR)
Serum ferritin (ng. dl.)	17 (15.0-76.0)
Serum transferrin (mg. dl.)	181 (161-200)
Serum iron (mcg. dl.)	37 (33.0-43.0)
Transferrin saturation percentage	8.60 (6.4-12.6)
N terminal pro BNP (pg. ml.)	350 (247.0-669.0)
TIBC mcg. dl.	397 (291.0-506.0)

The median serum ferritin in the study population was 17 ng. dl. with IQR 15 to 76 ng. dl.; median serum transferrin was 181 mg. dl. with IQR 161 to 200 mg. dl.; median serum iron was 37 mcg. dl. with IQR 33 to 43 mcg. dl.; median transferrin saturation percentage was 8.60% with IQR 6.4% to 12.6%; median N terminal pro BNP was 350 pg. ml. with IQR 247 to 669 pg. ml.; median TIBC was 397 mcg. dl. with IQR 291 to 506 mcg. dl. (Table 7)

Table 8: Severity of the heart failure in the study population (N=89)

NYHA GRADE	N (%)
I	25 (28.1%)
II	18 (20.2%)
III	18 (20.2%)
IV	28 (31.5%)

The severity of HF was graded based on NYHA classification. The higher the grade, the higher was the severity. The majority of the patients (31.5%) were graded IV, followed by grade I (28.1%), grade II (20.2%), and grade III (20.2%). (Table 8)

Table 9: Comparison of transferrin saturation percentage according to severity of heart failure using Kruskal Wallis test (N=89)

NYHA grade	Transferrin saturation percentage Median (IQR))	P-value
I	16.2 (15.5-16.6)	<0.001
II	10.9 (10.5-11.8)	
III	7.6 (7.3-8.1)	
IV	6.2 (5.8-6.6)	

Since $p<0.001$, there was a statistically significant difference of median transferrin saturation percentage between the different grades of heart failure. It can be seen in the above table that median transferrin saturation percentage decreased with the increase in the NYHA grade. (Table 9)

Table 10: Multiple pairwise comparison of transferrin saturation percentage between group levels (N=89)

Comparison	NYHA grade	Transferrin saturation percentage Median (IQR)	P-value
I vs II	I	16.2 (15.5-16.6)	<0.001
	II	10.9 (10.5-11.8)	
I vs III	I	16.2 (15.5-16.6)	<0.001
	III	7.6 (7.3-8.1)	
I vs IV	I	16.2 (15.5-16.6)	<0.001
	IV	6.2 (5.8-6.6)	
II vs. III	II	10.9 (10.5-11.8)	<0.001
	III	7.6 (7.3-8.1)	
II vs IV	II	10.9 (10.5-11.8)	<0.001
	IV	6.2 (5.8-6.6)	
III vs. IV	III	7.6 (7.3-8.1)	<0.001
	IV	6.2 (5.8-6.6)	

The median transferrin saturation percentage was statistically significantly higher in Grade I as compared to Grade II, Grade III, and Grade IV, respectively ($p<0.001$). The median transferrin saturation percentage of Grade II was statistically significantly higher than Grade III and Grade IV ($p<0.001$). The median transferrin saturation percentage of Grade II was statistically significantly higher than Grade III and Grade IV ($p<0.001$). The median transferrin saturation percentage of Grade III was statistically significantly higher than Grade IV ($p<0.001$). (Table 10 & Figure 2)

Figure 2: Box plot showing transferrin saturation percentage according to different grade (N=89)

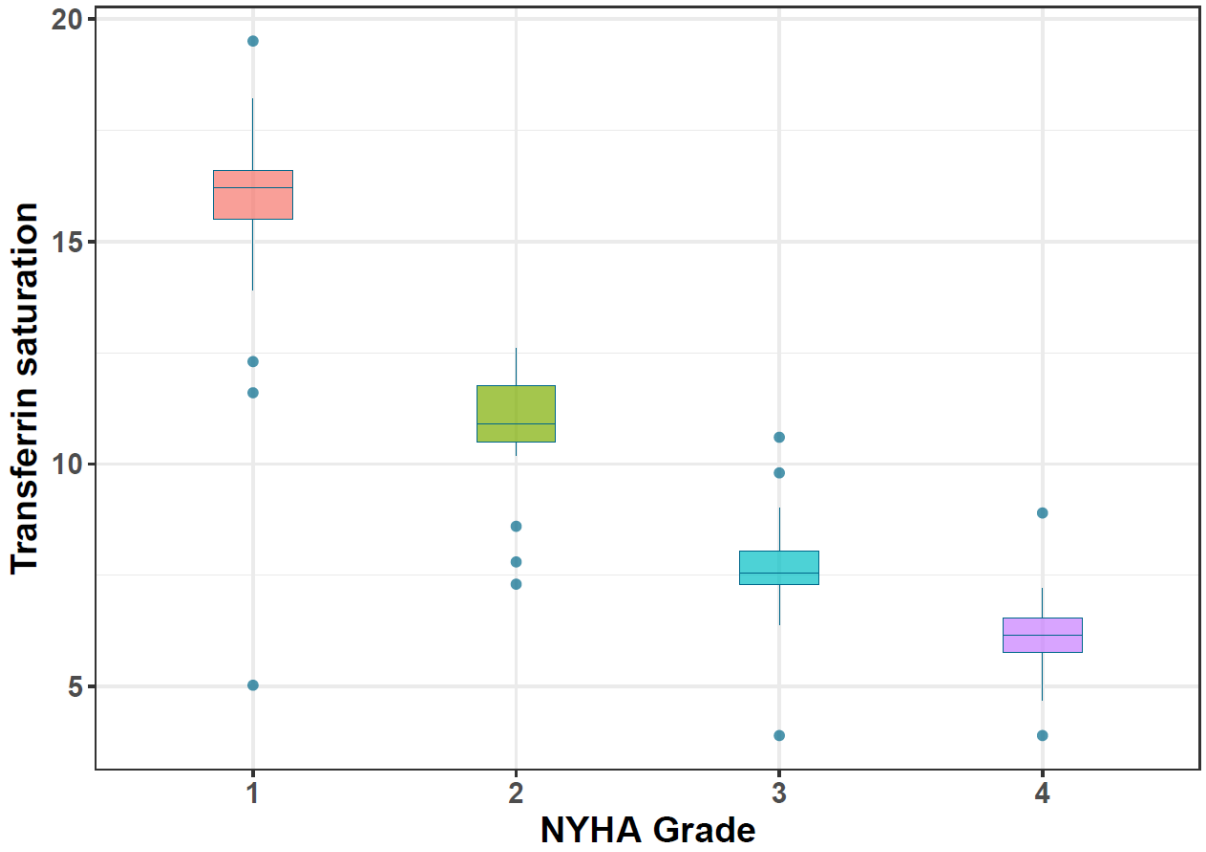


Table 11: Association between iron deficiency and NYHA grade (N=89)

NYHA grade	Iron deficiency		P-value
	Yes	No	
I	4 (16%)	21 (84%)	<0.001
II	18 (100%)	0 (0%)	
III	18 (100%)	0 (0%)	
IV	28 (100%)	0 (0%)	

Note: Simulated p-value was used

When the transferrin saturation percentage was less than 15%, it was considered to be iron deficiency. There was a significant association found between iron deficiency and NYHA grade ($p<0.001$). Only 16% of the graded I patients had iron deficiency. All the patients of grade II, grade III, and grade IV had iron deficiency. (Table 11)

DISCUSSION

DISCUSSION:

Anemia is a common complication of HF that is linked to a poor prognosis. Anemia is thought to occur in HF as a result of a complicated interaction between iron shortage, renal illness, and cytokine production; however, vitamin deficit and blood loss may also play a role.[107] Anemia, which was once said to be a side effect of heart failure, is being recognized as a critical and potentially modifiable aspect in therapy strategy for patients with chronic HF. In spite of the vast range of definitions for anemia, it affects about one-fifth to one-third of HF subjects at any given moment. In severe heart failure, the prevalence can rise to more than 50% of patients, and it varies depending on the context.[108] The true prevalence of anemia in patients with chronic HF is impacted not only by the terminology used but also depends on patient demographics in which anemia is evaluated. The current study is done to estimate the determine iron deficiency in chronic heart failure subjects and to correlate the iron deficiency with the severity of heart failure. The severity of HF is assessed in terms of NYHA grading, and anemia is determined using serum ferritin and less than 15% of transferrin saturation percentage. Transferrin saturation percentage is the outcome variable, and severity of HF is the explanatory variable.

A total of 89 patients meeting the inclusion and exclusion criteria are there in the study. The mean age of the study population is 60.35±11.47 years consisting of 65.2% males and 34.8% females. Jin et al.[17] study had a much older population with a mean age of 74.3 ± 11.3, and they noted that the anemic group was much older with a mean age of 76.9 ± 10.2 compared to the non-anemic in their study. Negi et al.[3] study had a similar age group to our study with a mean age of 58.2 ± 14.1 but a greater proportion of females with 44.2% males and 55.8% females. Similar age group was noted in Mirdamadi et al.[98] study with a mean age of 59.88 ± 18.05 years, and 40% of them were male. In Abebe et al.[101] study they had older age in the low hemoglobin group with a mean age of 56.47 ± 17.76 with 52.99 ± 17.15 in the non-

anemic group. The study population was much older in von Haehling's study with a mean age of 69.0 ± 10.6 years, and they had a male preponderance with only 25.7% females, and Cavalini et al.[96] study had 52.8% men with the mean age of study population being 67.8±13.8.

Table 12: Mean age and gender distribution across studies.

Study	Study type	Mean age (years)	% Of males	% Of females
Current study	Cross-sectional	60.35±11.47	65.2%	34.8%
Jin et al.[17]	Multicenter, prospective registry	74.3 ± 11.3	53.1%	46.9%
Negi et al.[3]	single-center prospective registry	58.2 ± 14.1	44.2%	55.8%
Mirdamadi et al.[98]	Clinical trial	59.88 ± 18.05 years and of them were male	40%	60%
Berry et al.[102]	multinational prospective	68 ± (12)	64%	36 %

The severity of HF is graded based on NYHA classification, and the majority of the patients in our study are found to have grade IV severity at 31.5%, followed by 28.1% with grade I, 20.2% grade II and grade III. Jin et al.[17] study had the highest subjects with grade II heart failure at 43.6%, followed by 42.6% with grade III, 10.3% with grade IV, and 3.6% with grade I severity. Negi et al.[3] study had most of the subjects with 58.4% with grade II NYHA heart failure, 37.6% with grade III, and 4.0% with grade IV severity. Mirdamadi et al.[98] in a clinical trial where they treated anemia with IV iron in chronic HF patients, had the majority of patients in grade III NYHA heart failure at 60%, grade II 24%, and grade IV 16% before IV iron treatment after which there was an improvement in the severity of HF with 56% having NYHA grade II, 36% grade III and 8% grade IV. Berry et al.[102] study had maximum with grade II failure at 43%, followed by 29% with grade III, 17% with grade I, and 11% with grade IV failure. Cavalini et al.[96] study group consisted of 63.2% with grade III, 31.3% with grade IV, 4.9% with grade II and 0.7% with grade I failure.

Table 13: Populations according to NYHA functional class across studies.

Study	NYHA class I	NYHA class II	NYHA class III	NYHA class IV
Current	28.1%	20.2%	20.2%	31.5%
Cavalini et al.[96]	0.7%	4.9%	63.2%	31.3%
Berry et al.[102]	17%	43%	29%	11%
Mirdamdi et al.[98]		24%	60%	16%
Negi et al.[3]		58.4%	37.6%	4.0%
Jin et al.[17]	3.6%	43.6%	42.6%	10.3%

We defined iron deficiency anemia as transferrin saturation percentage less than 15%, and at this cut-off value, there is a significant association found between iron deficiency and NYHA grade heart failure with $p<0.001$. In our study group, the prevalence of anemia is 76.4%, with all the patients having grade II, III, and IV class failure had iron deficiency anemia, but only 16% of the grade I class had iron deficiency. The median transferrin saturation percentage decreased with the increase in the NYHA grade. Our finding was higher than in previous studies. This was attributable to patients' characteristics such as gender, age, use of inconsistent definitions for anemia in subjects with HF[17,3] and inclusion of severely anemic patients in the study, unlike other studies where severe anemia is an exclusion criterion.

In accordance with our observation, the presence of anemia, iron deficiency, or both was associated with significantly higher NYHA class in Iosebashvili et al.[97] study. In Jin et al.[17] study, 51.0% of the patients were diagnosed with anemia, and they also noted that patients with anemia were older and had higher NYHA classes. The association between transferrin saturation and advanced heart failure was statistically significant in Negi et al.[3] study. Iron deficiency and anemia were prevalent in 58.8% (52.2%–65.1%) and 35.8% (29.8%–42.3%) of patients, respectively. They found that a one-unit increase in transferrin saturation odds of advanced heart failure was decreased by 2% (1%–4%); however, its association with the

ferritin level was not statistically significant. Due to decreased intake and impaired absorption due to decreased appetite and a clogged stomach as a symptom of congestive HF, heart failure may contribute to iron deficiency. As a result, iron deficiency may play a role in the evolution of heart failure.[3]

The NYHA class showed a significant improvement after IV iron treatment in Mirdamadi et al.[98] clinical trial. Comparing NYHA class after therapeutic approach before that showed a significant improvement in functional class, so NYHA class III and IV before intervention was revealed in 60% and 16% respectively, which reached to 36% and 8% respectively after intervention ($p = 0.017$). Disease severity, assessed by NYHA functional class and NT-proBNP levels, proved to be powerful and independent predictors of disordered iron status in Klip et al.[13] study. The maximum number of subjects with anemia were in NYHA grade III disease.

Table 14: Prevalence of anemia in subjects with HF across studies:

Study	Prevalence
Current study	76.4%
Jin et al.[17]	51.0%
Cavalini et al.[96]	40.97%
Abebe et al.[100]	41.90%
Negi et al.[3]	35.8%

Cavalini et al.[96] used the WHO criteria for defining anemia, men with hemoglobin <13.0 g/dL and women hemoglobin <12.0 g/dL and the percentage of people having anemia in hospitalized patients with HF found in their study was 40.97%, with 31.3% having NYHA functional class IV failure and 63.2% in NYHA III. In concordance with our study, on univariable analysis, the presence of anemia was associated with significantly higher NYHA

class in von Haehling et al.[101] study. Abebe et al.[100] study reported a prevalence of anemia around 41.90% in heart failure patients. Contrary to our study, they found no significant disparity among HF subjects with and without anemia based on NYHA class in their study. Iron deficiency was present in 61% of patients in the total cohort in Enjuanes et al.[92] study. Advanced NYHA functional class (III or IV) was more common in subjects having iron deficiency and anemia. Multivariate logistic regression analyses showed that increased levels of soluble transferrin receptor indicating abnormal iron status were individually associated with advanced NYHA class ($P < 0.05$). The current study reported a significant association of advanced heart failure with anemia. Anemia may be a marker of the severity of HF and/or a mediator of the progression of heart failure.

SUMMARY

SUMMARY:

Chronic HF is the severe and end-stage of many cardiovascular diseases, anemia, and renal dysfunction are common comorbidities of heart failure.[20] Anemia is a growing problem in people with chronic HF, and it may be a target for treatment. This cross-sectional study is conducted in the department of General Medicine at Sri Devaraj URS Academy of Higher Education and Research, Tamaka, Kolar. A total of 89 eligible patients admitted with a diagnosis of chronic heart failure from January 2020 to May 2021 are included in the study. The objective of the study is to determine the amount of people having anemia in heart failure patients and to correlate it with the severity of heart failure. The severity of heart failure is graded based on NYHA classification, and the majority of the patients in our study are found to have grade IV severity at 31.5%, followed by 28.1% with grade I, 20.2% grade II and grade III. In our study group, the prevalence of anemia is 76.4%, with all the patients having grade II, III, and IV class failure had iron deficiency anemia, but only 16% of the grade I class had iron deficiency. The current study reported a significant association of severity of heart failure with anemia ($p<0.001$).

CONCLUSIONS

CONCLUSIONS:

- A total of 89 patients meeting the exclusion and inclusion criteria were used in the study. The mean age of the study population is 60.35±11.47 years consisting of 65.2% males and 34.8% females.
- The severity of HF is graded based on NYHA classification, and the majority of the patients in our study are found to have grade IV severity at 31.5%, followed by 28.1% with grade I, 20.2% grade II and grade III.
- We defined iron deficiency anemia as transferrin saturation percentage less than 15%, and at this cut-off value, there is a significant association found between iron deficiency and NYHA grade heart failure with $p<0.001$.
- In our study group, the prevalence of anemia is 76.4%, with all the patients having grade II, III, and IV class failure had iron deficiency anemia, but only 16% of the grade I class had iron deficiency.
- The present study gave a significant association of the severity of HF with anemia.

LIMITATIONS:

This study's conclusions are based on single-center data, which has an inherent element of selection bias and may not provide an accurate assessment of anemia prevalence in the general population. Larger multicenter studies are needed to better determine the prevalence of anemia in individuals with chronic HF.

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ANNEXURES

STUDY OF IRON DEFICIENCY IN CHRONIC HEART FAILURE SUBJECTS

PROFORMA

Name:

Age/Sex:

Residential Address:

Mobile No:

Case History:

Other Known Illness:

BP: Pulse Rate:

CVS:

RS:

P/A:

CNS:

Outcome Measures:

Serum ferritin	
Serum Transferrin	
Serum Iron	
Transferrin saturation	
N Terminal Pro BNP	
NYHA GRADE	

Signature

PATIENT INFORMATION SHEET

Study Title: Study of IRON DEFECIENCY in chronic heart failure subjects

Study Site: R L Jalappa hospital, Tamaka, Kolar.

- One of the important co-morbidities in heart failure is iron deficiency.
- For a long time, the influence of Iron deficiency was underestimated especially in terms of worsening of cardiovascular diseases and of developing anaemia.

  The 2016 European society of Cardiology guidelines for the diagnosis and treatment of acute and chronic heart failure recognize iron deficiency as a co-morbidity in chronic heart failure and recommend iron status screening in all newly diagnosed patients with heart failure.

Aim: To study the iron deficiency in chronic heart failure subjects.

Blood samples will be taken for iron profile, CBC and N Terminal pro BNP. This information is intended to give you the general background of the study. Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for publication. Principal investigator will be paying for iron profile, CBC and N terminal pro BNP.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the institutional ethics committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For any further clarification you can contact the study investigator:

Dr A DHEERAJ

Mobile: 9492300660

Email: dheer818@gmail.com

CONCENT FORM

I _____participant, hereby give consent to participate in the study entitled "**Study of iron deficiency in chronic heart failure subject"**

I have been explained that;

1. I would have to provide a blood sample for the study purpose
2. I have to answer the questionnaires related to project
3. I do not have to incur any additional expenditure on my inclusion into the study
4. The data generated from my clinical examination and laboratory tests and other reports will be used in the study (which maybe subsequently published) without revealing my identity in any manner.

I affirm that I have been given full information about the purpose of the study and the procedures involved and have been given ample opportunity to clarify my doubts in my mother tongue. In giving my consent, I have not faced any coercion. I have been informed that, not withstanding this consent in given, I can withdraw from the study at any stage.

For any further clarification you can contact the study investigator:

Dr A DHEERAJ

Mobile: 9492300660

Email: dheer818@gmail.com

Signature of Participant:

NAME OF PARTICIPANT:

ಸಮ್ಮತಿ ಪತ್ರ:

ಈ ಕೆಳಗೆ ಸಹಿ ಮಾಡಿರುವ ---------- ಆದ ನಾನು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವ ಸಲುವಾಗಿ ವೈದ್ಯಕೀಯ ಪ್ರಯೋಗ ಪರೀಕ್ಷೆಗೆ ಒಳಪಡಲು ನನ್ನ ವೈಯ್ಯಕ್ತಿಕ ವಿವರಗಳನ್ನು ನೀಡಲು ಸಮ್ಮತಿಸಿರುತ್ತೇನೆ.

ಈ ಅಧ್ಯಯನದ ಉದ್ದೇಶ, ಅಧ್ಯಯನದ ಸಂದರ್ಭದಲ್ಲಿ ನೀಡುವ ಮತ್ತು ಸಂಗ್ರಹಿಸುವ ಮಾಹಿತಿಯ ಗೋಪ್ಯತೆಯ ಬಗ್ಗೆ ನನಗೆ ನನ್ನ ಸ್ಥಳೀಯ ಭಾಷೆಯಲ್ಲಿ ಓದಿ ಹೇಳಲಾಗಿದೆ/ವಿವರಿಸಲಾಗಿದೆ ಮತ್ತು ನಾನು ಇದನ್ನು ಅರ್ಥ ಮಾಡಿಕೊಂಡಿರುತ್ತೇನೆ. ಈ ಅಧ್ಯಯನದ ವಿವಿಧ ಅಂಶಗಳ ಬಗ್ಗೆ ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳುವ ಅವಕಾಶವನ್ನು ನನಗೆ ನೀಡಲಾಗಿದೆ ಮತ್ತು ನನ್ನ ಪ್ರಶ್ನೆಗಳಿಗೆ ತೃಪ್ತಿಕರವಾದ ಉತ್ತರಗಳು ದೊರೆತಿರುತವೆ. ಈ ಅಧ್ಯಯನದ ಮೂಲಕ ಸಂಗ್ರಹಿಸಿರುವ ಮಾಹಿತಿಯನ್ನು ಸಂಶೋಧನೆಯ ಉದ್ದೇಶಕ್ಕೆ ಮಾತ್ರ ಬಳಸತಕ್ಕದ್ದು.

ಈ ಅಧ್ಯಯನದಿಂದ ಯಾವುದೇ ಸಂದರ್ಭದಲ್ಲಿ ಹಿಂದೆ ಸರಿಯುವ ಸ್ವಾತಂತ್ರ್ಯ ನನಗಿದೆ ಎಂಬುದನ್ನೂ, ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವುದರಿಂದ ನನಗೆ ಯಾವುದೇ ಹೆಚ್ಚುವರಿ ವೆಚ್ಚ ತಗಲುವುದಿಲ್ಲವೆಂಬುದನ್ನು ತಿಳಿದಿರುತ್ತೇನೆ.

ಪರೀಕ್ಷಾರ್ಥಿಯ ಹೆಸರು ಮತ್ತು ಸಹಿ/ಹೆಬ್ಬೆಟ್ಟಿನ ಗುರುತು

ಸಾಕ್ಷಿಗಳ ಹೆಸರು ಮತ್ತು ಸಹಿ

1. ದಿನಾಂಕ:

2. ದಿನಾಂಕ:

ಸಂದರ್ಶಕರ ಹೆಸರು ಮತ್ತು ಸಹಿ

ಪ್ರಧಾನ ಪರೀಕ್ಷಕರ ಹೆಸರು ಮತ್ತು ಸಹಿ

ದಿನಾಂಕ:

ದಿನಾಂಕ:

ಮಾಹಿತಿಯುಕ್ತ ಸಮ್ಮತಿ

ಮುಖ್ಯ ಸಂಶೋಧಕರು: ಡಾ||ದೀರಜ್

ನಾನು ಡಾ|| ದೀರಜ್ ದೇವರಾಜ್ ಅರಸ್ ಮೆಡಿಕಲ್ ಕಾಲೇಜಿನ ಮೆಡಿಸಿನ್ ವಿಭಾಗದ ಸ್ನಾತಕೋತ್ತರ ವಿದ್ಯಾರ್ಥಿ ಹೃದಯ ವೈಫಲ್ಯದ ವಿಷಯಗಳಲ್ಲಿ ಐರನ್ ಕೊರತೆಯ ಅಧ್ಯಯನ ಎಂಬ

ನನ್ನ ಮಹಾಪ್ರಬಂಧಕ್ಕಾಗಿ ಡಾ||ಶ್ರೀ ನಿವಾಸ್ ಎಸ್.ವಿ , ಪ್ರೊಫೆಸರ್, ಮೆಡಿಸಿನ್ ವಿಭಾಗ ಮಾರ್ಗದರ್ಶನದಲ್ಲಿ ಮಾಡುತ್ತೇನೆ.

ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿದಲ್ಲಿ ನಾವು ನಿಮ್ಮ ಆಸ್ಪತ್ರೆಯ ದಾಖಲೆಗಳಿಂದ ನಿಮ್ಮ ಬಗ್ಗೆ ಸಂಬಂಧಿಸಿದ ವಿವರಗಳನ್ನು ಸಂಗ್ರಹಿಸುತ್ತೇವೆ. ಸಂಗ್ರಹಿಸಿದ ಮಾಹಿತಿಯನ್ನು ಮಾತ್ರ ಸಂಶೋಧನೆಯ ಉದ್ದೇಶಕ್ಕಾಗಿ ಬಳಸಲಾಗುತ್ತದೆ. ಈ ಅಧ್ಯಯನವು ಸ್ಥಳೀಯ ನೈತಿಕ ಬೋರ್ಡ್ ವಿಮರ್ಶೆ ಮಾಡುತ್ತದೆ ಮತ್ತು ಕೇವಲ ಅವರ ಔಪಚಾರಿಕ ಅನುಮೋದನೆ ನಂತರ ಪ್ರಾರಂಭಿಸಲಾಗುವುದು. ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪುತ್ತೀರಿ ಮಾತ್ರ / ಹೆಬ್ಬೆಟ್ಟಿನ ಗುರುತು ಸೈನ್ ಅಗತ್ಯವಿದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಯಾವುದೇ ವೆಚ್ಚದಲ್ಲಿ ಒಳಗೊಳ್ಳುವಂತಿಲ್ಲ.

ಸಂಪರ್ಕ ವಿವರಗಳು:

ಡಾ|| ದೀರಜ್

ದೂರವಾಣಿ: 9492300660

S.No	AGE	AGE GROUP	GENDER	SERUM FERRITIN	SERUM TRANSFERRIN	SERUM IRON	TRANSFERRIN SATURATION	N TERMINAL PRO BNP	TIBC (mcg/dl)	NYHA GRADE
1	77	GT65	M	16	191	41	16.1	450	256	I
2	52	51 to 65	M	18	190	43	16.4	139	262	I
3	54	51 to 65	M	17	163	36	10.2	250	352	II
4	45	20 to 50	M	18	144	36	7.4	254	484	III
5	41	20 to 50	M	22	139	30	6	453	500	IV
6	80	GT65	M	15	140	30	6.07	453	494	IV
7	53	51 to 65	M	14	164	37	10.9	259	337	II
8	27	20 to 50	M	17	205	39	15	151	260	I
9	43	20 to 50	M	18	200	35	11.3	247	309	II
10	67	GT65	M	15	192	40	16	143	250	I
11	45	20 to 50	F	18	142	29	4.9	283	594	IV
12	65	51 to 65	M	1000	139.46	29	11.6	153	248	I
13	20	20 to 50	M	15	142	32	5.8	31277	550	IV
14	55	51 to 65	M	17	201	49	19.5	145	251	I
15	63	51 to 65	F	202	159.31	14	3.9	280	356	III
16	70	GT65	F	17	200.1	37	10.5	369	350	II
17	85	GT65	M	15	190	39	7.9	450	488	III
18	60	51 to 65	M	16	206	41	15.1	133	261	I
19	80	GT65	F	12	144	33	6.7	550	490	IV
20	52	51 to 65	F	1000	167.41	32	6.1	690	523	IV
21	55	51 to 65	F	454	202	45	18.1	149	248	I
22	70	GT65	M	1569	147	39	9.8	1000	397	III
23	60	51 to 65	M	159	219.5	251	7.3	400	342	III
24	75	GT65	M	23	310.86	46	8.9	289	512	IV
25	52	51 to 65	M	596	85.68	22	3.9	551	564	IV
26	64	51 to 65	M	450	191	39	7.8	159	496	II
27	58	51 to 65	M	464	206	42	16.3	136	258	I
28	65	51 to 65	F	400	160	37	7.3	247	510	II
29	54	51 to 65	M	66	200	45	15.5	155	290	I
30	69	GT65	F	460	168	44	12.4	380	353	II
31	64	51 to 65	M	400	206	49	12.3	151	397	I
32	57	51 to 65	M	715	181	36	7.2	1000	498	IV
33	76	GT65	F	550	417	40	8.1	369	492	III

34	56	51 to 65	F	15	181	33	6.1	692	533	IV
35	68	GT65	M	56	148	35	7.1	334	489	III
36	70	GT65	F	76	205	48	17.4	156	275	I
37	65	51 to 65	M	17	195	44	16.2	154	271	I
38	57	51 to 65	F	474	204	39	10.9	258	357	II
39	56	51 to 65	F	789	187	38	6.4	789	593	IV
40	75	GT65	M	19	256	38	10.5	350	359	II
41	65	51 to 65	M	19	207	46	15.7	159	292	I
42	75	GT65	F	47	200	33	8.6	259	380	II
43	47	20 to 50	F	39	166	44	11.1	198	396	II
44	69	GT65	M	59	188	33	6.3	584	518	IV
45	70	GT65	F	17	234	48	16.9	155	283	I
46	65	51 to 65	M	14	159	36	7.3	335	488	III
47	63	51 to 65	M	19	199	40	13.9	255	291	I
48	71	GT65	M	48	144	31	6.4	358	484	III
49	68	GT65	M	16	144	36	7.1	669	506	IV
50	64	51 to 65	M	10	177	30	5.7	789	519	IV
51	71	GT65	F	14	189	37	7.6	350	486	III
52	65	51 to 65	F	18	204	42	15.7	148	267	I
53	69	GT65	M	474	178	44	12.4	225	354	II
54	45	20 to 50	M	10	165	33	5.4	1560	601	IV
55	56	51 to 65	F	14	180	32	5.6	1120	566	IV
56	63	51 to 65	M	11	146	34	6.2	1000	546	IV
57	40	20 to 50	F	17	199	49	16.4	150	268	I
58	66	GT65	M	14	179	38	10.9	256	346	II
59	47	20 to 50	M	16	198	44	12.6	456	349	II
60	50	20 to 50	M	14	188	39	10.6	400	367	III
61	60	51 to 65	M	10	157	33	6.2	1458	526	IV
62	67	GT65	M	15	202	46	15.9	258	289	I
63	80	GT65	F	13	177	34	6.7	1785	509	IV
64	55	51 to 65	M	11	166	37	10.8	369	341	II
65	49	20 to 50	F	17	199	17	5.03	155	278	I
66	53	51 to 65	M	13	175	37	7.5	459	488	III
67	64	51 to 65	M	16	198	44	16.4	250	267	I
68	77	GT65	M	11	166	31	6.1	1456	502	IV
69	67	GT65	F	15	185	37	7.7	459	477	III
70	56	51 to 65	F	86	206	46	16.6	155	277	I
71	A 61	51 to 65	M	559	180	35	7.02	1569	498	III

72	52	51 to 65	M	173	196	44	12.6	256	348	II
73	46	20 to 50	M	641	172	33	6.3	1258	520	IV
74	72	GT65	F	14	144	36	9	351	400	III
75	58	51 to 65	M	17	201	47	16.5	256	284	I
76	66	GT65	F	16	167	35	11.9	255	292	II
77	59	51 to 65	M	10	146	31	5.9	1456	521	IV
78	50	20 to 50	F	54	147	30	4.7	1235	630	IV
79	62	51 to 65	M	13	156	35	8.7	409	400	III
80	67	GT65	M	17	206	49	18.2	366	268	I
81	56	51 to 65	M	19	189	39	7.8	336	498	III
82	60	51 to 65	M	9	184	35	6.8	789	509	IV
83	68	GT65	F	58	176	34	5.6	1587	606	IV
84	55	51 to 65	M	11	161	37	7.5	559	491	III
85	45	20 to 50	M	10	177	35	6.7	1008	517	IV
86	68	GT65	F	700	169	33	6.5	1111	506	IV
87	51	51 to 65	F	20	204	49	17.8	151	274	I
88	48	20 to 50	M	48	179	36	11.2	258	319	II
89	70	GT65	F	15	158	32	6.2	1156	512	IV

S.No	2D ECHO
1	BASAL INFERIOR WALL HYPOKINETIC , CONCENTRIC LVH, MYXOMATOUS MV WITH MILD MR, MILD AR/TR , GRADE 1 LV DIASTOLIC DYSFUNCTION ,LV EF=55%
2	BASAL AND MILD INFERIOR WALL HYOKINETIC,MILD MR/AR,TRIVIAL TR, PASP=25mmHg,LV EF=55%
3	BASAL AND MILD INFERIOR WALL HYPOKINETIC, MILD SYSTOLIC DYSFUNCTION, MILD MR/AR, TRIVIAL RVSP =25mmHg,LV EF= 45%
4	BASAL AND MILD APICAL SEGMENTS OF APEX AND ANTERIOR WALL , LATERAL WALLS ARE HYPOKINETIC, MILD MR/AR,MILD TR,PASP=25mmHg MODERATE LV SYSTOLIC DYSFUCTION,LV EF =30%
5	TOTAL ANTERIOR WALL AND LATERAL WALLS ARE SEVERELY HYPOKINETIC , GRADE I MR,GRADE II TR, MILD PAH, MILD AR/PR, MODERATE LV SYSTOLIC DYSFUNCTION ,LV EF=30%
6	TOTAL ANTERIOR WALL AND LATERAL WALLS AE SEVERELY HYPOKINETIC , AV SCLEROTIC WITH MILD AR , GRADE II MR ,MILD TR,MILD PAH GRADE III LV DIASTOLIC DYSFUNCTION ,SEVERE LV SYSTOLIC DYSFUNCTION , LV EF= 25%
7	BASAL AND MID APICAL SEGMENTS OF APEX AND ANTERIOR WALL AND LATERAL WALLS ARE HYPOKINETIC ,MILD MR, TRIVIAL AR, MILD TR, MILD LV SYSTOLIC DYSFUNCTION ,LV EF=40-45%
8	MILD CONCENTERIC LVH, TRIVIAL MR, TRIVIAL AR, TRIVIAL TR , LV EF=60%
9	BASAL AMD MID INFERIOR WALL HYPOKINETIC, MID CONCENTERIC LVH, MILD MR, TRIVIAL AR/TR, MILD LV SYSTOLIC DYSFUNCTION , LV EF 45%
10	BASAL AND MID INFERIOR WALL HYPOKINETIC, MILD MR/AR, TRIVIAL TR, PASP=25mmHg, GRADE I LV DIASTOLIC DYSFUNCTION ,LV EF=50%
11	GLOBAL HYPOKINESIA OF LV, DILATED ALL CARDIA CHAMBERS, MODERATE TO SEVERE MR, MILD AR, SEVERETR WITH SEVERE PAH, SEVERE LV SYSTOLIC DYSFUNCTION, LV EF=20%
12	CONCENTERIC LVH MILD MR, MILD AR/TR, GRADE I LV DIASTOLIC DYSFUNCTION ,LV EF=60%
13	DILATED LEFT SIDED CHAMBERS REDUCED BIVENTRICULAR FUNCTION ,MILD MR TR,MODERATE PULMONARY HYPERTENSION LV EF=32%
14	THICKNED AND CALCIFIED AV SEVERE AS WITH GRADE 1 AR,CONCENTERIC LVH,MILD MR/TR,MILD PAH,SMALL PE+, LV EF=55%
	BASAL AND MILD APICAL SEGMENTS OF APEX AND ANTERIOR WALL , LATERAL WALLS ARE HYPOKINETIC, MILD

15	MR/AR,MILD TR,PASP=25mmHg MODERATE LV SYSTOLIC DYSFUCTION,LV EF =30%
16	BASAL AND MID APICAL SEGMENTS OF APEX AND ANTEROSEPTUM AND ANTERIOR WALL AND LATERAL WALLS ARE HYPOKINETIC , AV SCLEROTIC WITH MILD AR , GRADE 2 MR/MILD TR , MILD PAH, MODERATE LV SYSTOLIC DYSFUNCTION ,LV EF =35-40%
17	BASAL AND MILD APICAL SEGMENTS OF APEX AND ANTERIOR WALL , LATERAL WALLS ARE HYPOKINETIC, MILD MR/AR,MILD TR,PASP=25mmHg MODERATE LV SYSTOLIC DYSFUCTION,LV EF =30%
18	BASAL AND MILD INFERIOR WALL HYOKINETIC,MILD MR/AR,TRIVIAL TR, PASP=25mmHg,LV EF=55%
19	TOTAL ANTERIOR WALL AND LATERAL WALLS AE SEVERELY HYPOKINETIC , AV SCLEROTIC WITH MILD AR , GRADE II MR ,MILD TR,MILD PAH GRADE III LV DIASTOLIC DYSFUNCTION ,SEVERE LV SYSTOLIC DYSFUNCTION , LV EF= 25%
20	TOTAL ANTERIOR WALL AND LATERAL WALLS ARE SEVERELY HYPOKINETIC , GRADE I MR,GRADE II TR, MILD PAH, MILD AR/PR, MODERATE LV SYSTOLIC DYSFUNCTION ,LV EF=20%
21	BASAL INFERIOR WALL HYPOKINETIC CONCENTRIC LVH, MYXOMATOUS MV ,WITH MILD MR, MILD AR/TR LV DIASTOLIC DYSFUNCTION ,LV EF=60%
22	BASAL AND MILD APICAL SEGMENTS OF APEX AND ANTERIOR WALL , LATERAL WALLS ARE HYPOKINETIC, MILD MR/AR,MILD TR,PASP=25mmHg MODERATE LV SYSTOLIC DYSFUCTION,LV EF =35%
23	BASAL AND MILD APICAL SEGMENTS OF APEX AND ANTERIOR WALL , LATERAL WALLS ARE HYPOKINETIC, MILD MR/AR,MILD TR,PASP=25mmHg MODERATE LV SYSTOLIC DYSFUCTION,LV EF =30%
24	BASAL AND MILD APICAL SEGMENTS IHD, LATERAL WALL HYPOKINETIC, DILATED CARDIA CHAMBERS,MODERATE MR, MILD AR,SEVERE LV SYSTOLIC DYSFUNCTION,LVEF=25%
25	BASAL AND MID APICAL SEGMENTS OF APEX AND ANTERIOR WALL AND LATERAL WALLS ARE HYPOKINETIC ,MILD MR, TRIVIAL AR, MILD TR,

	PASP=25mmHg,MODERATE LV SYSTOLIC DYSFUNCTION ,LV EF=25%
26	BASAL AMD MID INFERIOR WALL HYPOKINETIC, MID CONCENTERIC LVH, MILD MR, TRIVIAL AR/TR, MILD LV SYSTOLIC DYSFUNCTION , LV EF 45%
27	BASAL AND MID INFERIOR WALL HYPOKINETIC, MILD MR/AR, TRIVIAL TR, PASP=25mmHg, GRADE I LV DIASTOLIC DYSFUNCTION ,LV EF=50%
28	BASAL AND MILD INFERIOR WALL HYPOKINETIC MILD SYSTOLIC DYSFUNCTION, MILD MR/AR, TRIVIAL RVSP =25mmHg,LV EF= 45%
29	BASAL AND MID INFERIOR WALL HYPOKINETIC, MILD MR/AR, TRIVIAL TR, PASP=25mmHg, GRADE I LV DIASTOLIC DYSFUNCTION ,LV EF=50%
30	BASAL AND MILD INFERIOR WALL HYOKINETIC,MILD MR/AR,TRIVIAL TR, PASP=25mmHg,LV EF=40%
31	MILD CONCENTERIC LVH, TRIVIAL MR, TRIVIAL AR, TRIVIAL TR , LV EF=60%
32	TOTAL ANTERIOR WALL AND LATERAL WALLS ARE SEVERELY HYPOKINETIC , GRADE I MR,GRADE II TR, MILD PAH, MILD AR/PR, MODERATE LV SYSTOLIC DYSFUNCTION ,LV EF=20%
33	BASAL AND MILD APICAL SEGMENTS OF APEX AND ANTERIOR WALL , LATERAL WALLS ARE HYPOKINETIC, MILD MR/AR,MILD TR,PASP=25mmHg MODERATE LV SYSTOLIC DYSFUCTION,LV EF =30%
34	GLOBAL HYPOKINESIA OF LV, DILATED ALL CARDIA CHAMBERS, MODERATE TO SEVERE MR, MILD AR, SEVERETR WITH SEVERE PAH, SEVERE LV SYSTOLIC DYSFUNCTION, LV EF=20%
35	BASAL AND MILD APICAL SEGMENTS OF APEX AND ANTERIOR WALL , LATERAL WALLS ARE HYPOKINETIC, MILD MR/AR,MILD TR,PASP=25mmHg MODERATE LV SYSTOLIC DYSFUCTION,LV EF =30%
36	THICKNED AND CALCIFIED AV SEVERE AS WITH GRADE 1 AR,CONCENTERIC LVH,MILD MR/TR,MILD PAH,SMALL PE+, LV EF=55%
37	BASAL INFERIOR WALL HYPOKINETIC , CONCENTRIC LVH, MYXOMATOUS MV WITH MILD MR, MILD AR/TR , GRADE 1 LV DIASTOLIC DYSFUNCTION ,LV EF=55%
38	BASAL AMD MID INFERIOR WALL HYPOKINETIC, MID CONCENTERIC LVH, MILD MR, TRIVIAL AR/TR, MILD LV SYSTOLIC DYSFUNCTION , LV EF 45%
39	THICKNED AND CALCIFIED AV SEVERE AS WITH GRADE 1 AR,CONCENTERIC LVH,MILD MR/TR,MILD PAH,SMALL PE+, LV EF=25%
	MAC+WITH MILD MR,

40	AORTIC VALVE SCLEROTIC WITH MILD AR , MILD TR WITH MILD PAH,GRADE 1 LV DIASTOLIC DYSFUNCTION,PERSERVED LV SYSTOLIC DYSFUNCTION,LV EF=50%
41	AORTIC VALVE SCLEROTIC WITH MILD AR,NORMAL CHAMBER DIMENSIONS,MILD MR,MILD AR,MILD TR WITH MILD PAH,GRADE 1 LV DIASTOLIC DYSFUNCTION ,PERSERVED LV SYSTOLIC FUNCTION,LV EF =50%
42	NORMAL DIMENSIONS, THIN IAS SEPTUM,MILD MR/AV SCLEROTIC WITH MILD AR,MILD TR WITH MILD PAH, GRADE 1 LV DIASTOLIC DYSFUNCTION ,NORMAL LV SYSTOLIC FUNCTION ,MILD B/L PLEURAL EFFUSSION ,LV EF=60%
43	RHD:THICKENED &DOMING MV MILD TO MODERATE MS WITH MILD MR, DILATED LA,DILATED RA&RV ,SEVERE TR WITH SEVERE PAH,PERSERVED LV SYSTOLIC FUNCTION ,LV EF=55%
44	GLOBAL HYPOKINESIA OF LV , NORMAL DIMENSIONS,MILD MR,TRIVIAL AR,TRIVIAL TR,MODERATE LV SYSTOLIC DYSFUNCTION LV EF= 30%
45	CONCENTERIC LVH, AORTIC VALVE SCLEROTIC WITH MILD AR,MILD MR,MILD TR WITH MILD PAH,GRADE 1 LV DIASTOLIC DYSFUNCTION,PERSERVED LV SYSTOLIC FUNCTION,LV EF=55%
46	IHD: BASAL INFERIOR WALL HYPOKINETIC ,AV SCLEROTIC WITH MILD AR, GRADE 1MR/GRADE 1 TR, MILD PAH,LV EF=50%
47	CONCENTERIC LVH,MILD MR,MILD AR ,MILD TR WITH PAH,GRADE 1 LV DIASTOLIC DYSFUNCTION,LV EF=55%
48	MAC+WITH MILD MR, DILATED RA&RV MILD TR ,GRADE 2 TR WITH MODERATE PAH,GRADE LV DIASTOLIC DYSFUNCTION,PERSERVED LV SYSTOLIC DYSFUNCTION,LV EF=50%
49	MAC+WITH MILD MR, AORTIC VALVE SCLEROTIC WITH MILD AR , MILD TR WITH MILD PAH,GRADE 1 LV DIASTOLIC DYSFUNCTION,PERSERVED LV SYSTOLIC DYSFUNCTION,LV EF=30%
50	RHD:THICKENED &DOMING MV MILD TO MODERATE MS WITH MILD MR, DILATED LA,DILATED RA&RV ,SEVERE TR WITH SEVERE PAH,PERSERVED LV SYSTOLIC FUNCTION ,LV EF=25%
	IHD: BASAL INFERIOR WALL HYPOKINETIC ,AV SCLEROTIC WITH MILD AR, GRADE 1MR/GRADE 1 TR, MILD PAH,LV EF=40%

51	
52	BASAL INFERIOR WALL HYPOKINETIC , CONCENTRIC LVH, MYXOMATOUS MV WITH MILD MR, MILD AR/TR , GRADE 1 LV DIASTOLIC DYSFUNCTION ,LV EF=55%
53	BASAL AND MID INFERIOR WALL HYPOKINETIC, MID CONCENTERIC LVH, GRADE 2 MR, TRIVIAL AR/TR,MILD PAH, MILD LV SYSTOLIC DYSFUNCTION , LV EF 45%
54	BASAL AND MILD APICAL SEGMENTS IHD, GLOBAL HYPOKINESIA, DILATED CARDIA CHAMBERS,MODERATE MR, MILD AR,SEVERE LV SYSTOLIC DYSFUNCTION,LVEF=25%
55	TOTAL ANTERIOR WALL AND LATERAL WALLS ARE SEVERELY HYPOKINETIC , GRADE I MR,GRADE II TR, MILD PAH, MILD AR/PR, MODERATE LV SYSTOLIC DYSFUNCTION ,LV EF=20%
56	THICKNED AND CALCIFIED AV SEVERE AS WITH GRADE 1 AR,CONCENTERIC LVH,MILD MR/TR,MILD PAH,SMALL PE+, LV EF=25%
57	MILD CONCENTERIC LVH, TRIVIAL MR, TRIVIAL AR, TRIVIAL TR , MILD SYSTOLIC DYSFUNCTION, LV EF=60%
58	WITH MILD MR, AORTIC VALVE SCLEROTIC WITH MILD AR , MILD TR WITH MILD PAH,GRADE 1 LV DIASTOLIC DYSFUNCTION,PERSERVED LV SYSTOLIC DYSFUNCTION,LV EF=40%
59	IHD:BASAL AND MID INFERIOR WALLS ARE HYPOKINETIC,MILD MR/AR,TRIVIAL TR,RVSP-25mmHg,MILD SYSLOTIC DYSFUNCTION LV EF=45%
60	IHD: BASAL AND MID INFERIOR WALL POSTRIOR WALLS ARE SEVERELY HYPOKINETIC ,DILATED LV,GRADE 1 MR,TR,MODERATE LV SYSTOLIC DYSFUNCTION LV EF=30%
61	IHD:TOTAL INFERIOR WALL AND LATERAL WALLA ARE HYPOKINETIC,MODERATE MR,MILD AR,SEVERE TR WITH SEVERE PAH,MILD PR,SEVERE LV SYSTOLIC DYSFUNCTION LV EF =25%
62	CONCENTERIC LVH,MILD MR,MILD AR CONCENTERIV LVH,MILD MR,TRIVIAL TR WITH PAH, NORMAL LV SYSLOTIC FUNCTION,LV EF=55%
63	THICKNED AND CALCIFIED AV SEVERE AS WITH GRADE 1 AR,CONCENTERIC LVH,MILD MR/TR,MILD PAH,SMALL PE+, LV EF=20%
	MAC+WITH MILD MR,

64	AORTIC VALVE SCLEROTIC WITH MILD AR , MILD TR WITH MILD PAH,GRADE 1 LV DIASTOLIC DYSFUNCTION,PERSERVED LV SYSTOLIC DYSFUNCTION,LV EF=40%
65	CONCENTERIC LVH, AORTIC VALVE SCLEROTIC WITH MILD AR,MILD MR,MILD TR WITH MILD PAH,GRADE 1 LV DIASTOLIC DYSFUNCTION,PERSERVED LV SYSTOLIC FUNCTION,LV EF=55%
66	BASAL AND MILD APICAL SEGMENTS OF APEX AND ANTERIOR WALL , LATERAL WALLS ARE HYPOKINETIC, MILD MR/AR,MILD TR,PASP=25mmHg MODERATE LV SYSTOLIC DYSFUCTION,LV EF =30%
67	CONCENTERIC LVH,MILD MR,MILD AR CONCENTERIV LVH,MILD MR,TRIVIAL TR WITH PAH GRADE 1 LV DIASTOLIC DYSFUNCTION,PERSERVED LV SYSTOLIC DYSFUNCTION,LV EF=50%
68	CONCENTERIC LVH, AORTIC VALVE SCLEROTIC WITH MILD AR,MILD MR,MILD TR WITH MILD PAH,GRADE 1 LV DIASTOLIC DYSFUNCTION, LV SYSTOLIC DYSFUNCTION,LV EF=35%
69	BASAL INFERIOR WALL HYPOKINETIC , CONCENTRIC LVH, MYXOMATOUS MV WITH MILD MR, MILD AR/TR , GRADE 1 LV DIASTOLIC DYSFUNCTION ,LV EF=40%
70	NORMAL DIMENSIONS, THIN IAS SEPTUM,MILD MR/AV SCLEROTIC WITH MILD AR,MILD TR WITH MILD PAH, GRADE 1 LV DIASTOLIC DYSFUNCTION ,NORMAL LV SYSTOLIC FUNCTION ,MILD B/L PLEURAL EFFUSSION ,LV EF=60%
71	BASAL AND MID INFERIOR WALL HYPOKINETIC, MID CONCENTERIC LVH, GRADE 2 MR, TRIVIAL AR/TR,MILD PAH, MILD LV SYSTOLIC DYSFUNCTION , LV EF 40%
72	AORTIC VALVE SCLEROTIC WITH MILD AR,NORMAL CHAMBER DIMENSIONS,MILD MR,MILD AR,MILD TR WITH MILD PAH,GRADE 1 LV DIASTOLIC DYSFUNCTION ,PERSERVED LV SYSTOLIC FUNCTION,LV EF =45%
73	TOTAL ANTERIOR WALL AND LATERAL WALLS ARE SEVERELY HYPOKINETIC , GRADE I MR,GRADE II TR, MILD PAH, MILD AR/PR, MODERATE LV SYSTOLIC DYSFUNCTION ,LV EF=20%
74	BASAL AND MID INFERIOR WALL HYPOKINETIC, MILD MR/AR, TRIVIAL TR, PASP=25mmHg, GRADE I LV DIASTOLIC DYSFUNCTION ,LV EF=40%

75	RHD:THICKENED &DOMING MV MILD TO MODERATE MS WITH MILD MR, DILATED LA,DILATED RA&RV ,SEVERE TR WITH SEVERE PAH,PERSERVED LV SYSTOLIC FUNCTION ,LV EF=55%
76	BASAL AND MILD APICAL SEGMENTS OF APEX AND ANTERIOR WALL , LATERAL WALLS ARE HYPOKINETIC, MILD MR/AR,MILD TR,PASP=25mmHg MODERATE LV SYSTOLIC DYSFUCTION,LV EF =45%
77	GLOBAL HYPOKINESIA OF LV, DILATED ALL CARDIA CHAMBERS, MODERATE TO SEVERE MR, MILD AR, SEVERETR WITH SEVERE PAH, SEVERE LV SYSTOLIC DYSFUNCTION, LV EF=20%
78	BASAL AND MILD APICAL SEGMENTS IHD, GLOBAL HYPOKINESIA, DILATED CARDIA CHAMBERS,MODERATE MR, MILD AR,SEVERE LV SYSTOLIC DYSFUNCTION,LVEF=25%
79	BASAL AMD MID INFERIOR WALL HYPOKINETIC, MID CONCENTERIC LVH, MILD MR, TRIVIAL AR/TR, MILD LV SYSTOLIC DYSFUNCTION , LV EF 40%
80	BASAL AND MILD INFERIOR WALL HYPOKINETIC MILD SYSTOLIC DYSFUNCTION, MILD MR/AR, TRIVIAL RVSP =25mmHg,LV EF= 45%
81	TOTAL ANTERIOR WALL AND LATERAL WALLS ARE SEVERELY HYPOKINETIC , GRADE I MR,GRADE II TR, MILD PAH, MILD AR/PR, MODERATE LV SYSTOLIC DYSFUNCTION ,LV EF=35%
82	RHD:THICKENED &DOMING MV MILD TO MODERATE MS WITH MILD MR, DILATED LA,DILATED RA&RV ,SEVERE TR WITH SEVERE PAH,PERSERVED LV SYSTOLIC FUNCTION ,LV EF=25%
83	BASAL AND MILD APICAL SEGMENTS OF APEX AND ANTERIOR WALL , LATERAL WALLS ARE HYPOKINETIC, MILD MR/AR,MILD TR,PASP=25mmHg MODERATE LV SYSTOLIC DYSFUCTION,LV EF =30%
84	BASAL AND MID APICAL SEGMENTS OF APEX AND ANTERIOR WALL AND LATERAL WALLS ARE HYPOKINETIC , MILD MR/AR,MILD TR,PASP=25mmHg LV EF =35%

85	BASAL AND MID INFERIOR WALL HYPOKINETIC, MILD MR/AR, TRIVIAL TR, PASP=25mmHg, GRADE I LV DIASTOLIC DYSFUNCTION ,LV EF=20%
86	THICKNED AND CALCIFIED AV SEVERE AS WITH GRADE 1 AR,CONCENTERIC LVH,MILD MR/TR,MILD PAH,SMALL PE+, LV EF=25%
87	IHD: BASAL INFERIOR WALL HYPOKINETIC ,AV SCLEROTIC WITH MILD AR, GRADE 1MR/GRADE 1 TR, MILD PAH,LV EF=50% IHD: BASAL INFERIOR WALL HYPOKINETIC ,AV SCLEROTIC WITH MILD AR, GRADE 1MR/GRADE 1 TR, MILD PAH,LV EF=50%
88	BASAL AND MID INFERIOR WALL HYPOKINETIC, MILD MR/AR, TRIVIAL TR, PASP=25mmHg, GRADE I LV DIASTOLIC DYSFUNCTION ,LV EF=40%
89	BASAL AND MILD APICAL SEGMENTS IHD, GLOBAL HYPOKINESIA, DILATED CARDIA CHAMBERS,MODERATE MR, MILD AR,SEVERE LV SYSTOLIC DYSFUNCTION,LVEF=25%