PREVALENCE AND TREATMENT OF ANAEMIA IN HEART FAILURE PATIENTS IN TERTIARY CARE HOSPITAL

Pharm. D Project report

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DEDICATION

This is dedicated to my
beloved Parents, Teachers,
Friendsand Family.

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LIST OFABBREVIATIONS

ABBREVIATED FORM	FULL FORM
HF	Heart Failure
LV	Left Ventricular
EF	Ejection Fractioin
HFpEF	Heart Failure with the Preserved Ejection Fraction
HFrEF	Heart Failure with the Reduced Ejection Fraction
CV	cardiovascular
LVEF	Left Ventricular Ejection Fraction
DCM	Dilated Cardiomyopathy
SOLVD	Studies Of Left Ventricular Dysfunction
CABG	Coronary Artery Bypass Graft
PCI	Percutaneous Coronary Intervention
CHD	Coronary Heart Disease
CHF	Congestive Heart Failure
ECG	Electrocardiography
FIRST	Flolan International Randomized Survival Trial
NYHA	New York Heart Association
SOB	Shortness Of Breath
CBC	Complete Blood Count
TSH	Thyroid Stimulating Hormone
ICU	Intensive Care Unit
NIPPV	Noninvasive Positive Pressure Ventilation

ACEI	Angiotensin Converting Enzyme Inhibitor
ARB	Angiotensin Receptor Blocker
SGLT-2	Sodium Glucose Cotransporter-2
GLP	Glucagon Like Peptide
ICD	Implantable Cardioverter Defibrillator
PDE 3	Phosphodiesterase 3
ADHF	Acute Decompensated Heart Failure
IV	Intravenous


Introduction

INTRODUCTION

Background Information :

A normal heart is a powerful, muscular pump about the size of a fist. It continually circulates blood through the circulatory system.

The heart is divided into four chambers: upper two chambers refers to atria (right and left), and lower two chambers refers to ventricles (right and left).

The heart undergoes a sequence of highly organized contractions of the four chambers for Blood being pumped to the lungs along with all of the tissues of the body. For the heart to function properly, the four chambers must beat in a synchronized way.

The right atrium takes in deoxygenated blood from the remaining of the human body and sends it through the right ventricle where the blood becomes oxygenated in the lungs.

The lungs send oxygenated blood to the rest of the body through the left atrium, then onwards the left ventricle, which pumps it to the remainder of the body.[1]

Heart Failure (HF) is usually defined as a complex clinical syndrome in which cardiac dysfunction results in, or greater risk of, clinical symptoms and characterized by reduced cardiac output and/or pulmonary or systemic congestion at rest or with stress.[2]The cardinal manifestation includes structural and functional defects in the myocardium resulting in impairment of ventricular filling or the ejection of blood.[3]

Several compensating mechanisms, including the adrenergic nerve system, the renin-angiotensin system, and the cytokine system, are engaged as the heart's pumping capability declines. These

mechanisms can restore cardiovascular function to a normal homeostatic range for a short period. However, long term activation of these systems can lead to damage within the ventricle, with worsening LV remodelling and subsequent cardiac decompensation, patients eventually progress from asymptomatic to symptomatic heart failure.[4]

Mechanical disadvantages created by LV remodelling:

- Increased wall stress (afterload)
- Afterload mismatch
- Increased oxygen demand
- Worsening of compensatory mechanisms.[4]

The ejection fraction (EF) is a measurement of how much blood the left ventricle pumps out with each contraction, represented as a percentage. The healthy heart EF is between 50 and 70%.

A measurement under 40% may be an attestation of heart failure, cardiomyopathy.

A measurement above 75% may be an indication of hypertrophic cardiomyopathy.

The two scenarios of ejection fraction:

1. Preserved ejection fraction (HFpEF) – also signifies diastolic heart failure. The heart muscle normally contracts but the ventricles do not relax as they should during ventricular filling.
2. Reduced ejection fraction (HFrEF) – also signifies systolic heart failure. That myocardium is unable to contract adequately, so less oxygen-rich blood is pumped out to the body.[1] [5]

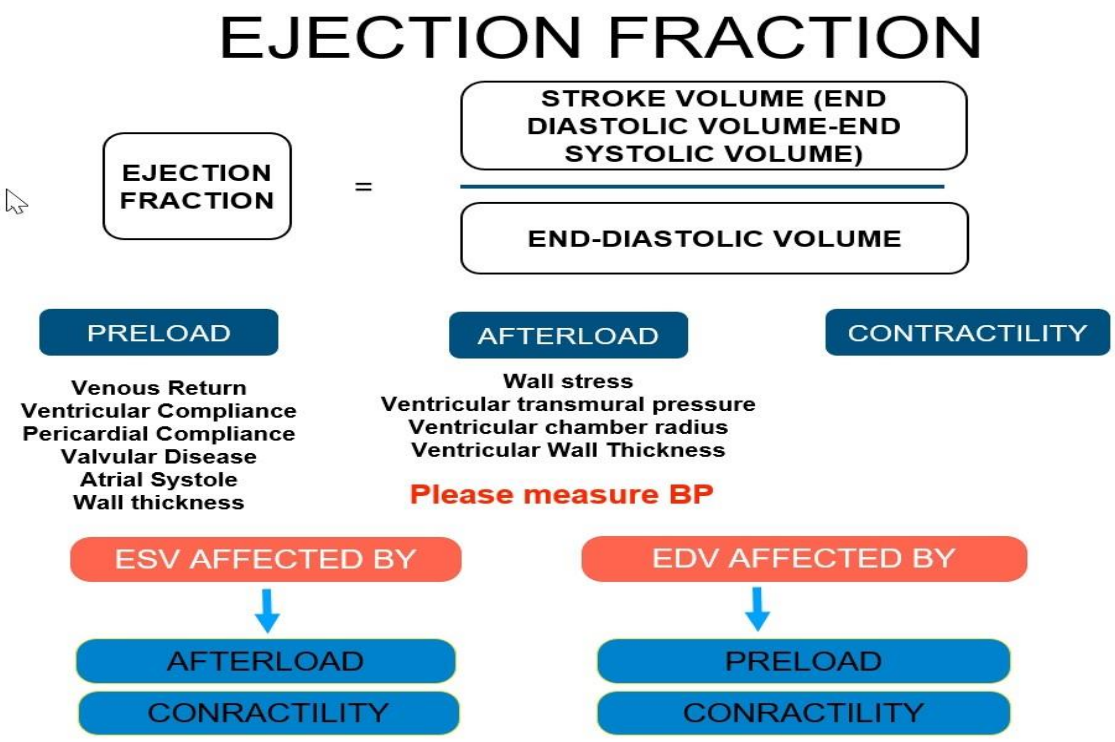

Fig:1 Ejection fraction

Figure courtesy: Baysan O, Akyıldız İZ. Looking beyond ejection fraction: what we have in echocardiography. Heart, Vessels and Transplantation

Epidemiology:

Cardiac failure is a serious clinical and public health problem affecting more than 40 million individuals worldwide (2015)[6]. HF is linked to significant patient distress and a costly burden on the worldwide health service as one of notable causes of morbidity, mortality, and hospitalizations, especially in the elderly[7]. Given changes in HF clinical outcomes over the

last few years, the overall prognostic value has remained low[7,8]. with survival estimates of ~50% after initial diagnosis [9,10]. The main distress is the increase in hospitalization in terms of age group 18-54 years for HF [9,11]. In summary, the annual incidence of HF ranges between 100 and 900 cases per 100,000 patients. [12]. Internationally, 17-45 percent of patients given a diagnosis with HF pass away within a year of being admitted to a hospital, and even the majority (majority) of patients suffering with HF die within five years after admission [13,14]. Fortunately, approximately 2-17% of deaths occur in the hospital as a result of HF[15,16]. The aging seem to be more susceptible to have heart failure..

Handful HF patients in Europe and Northern America are under the age of 50, and even the majority are over the age of 65. [17-20]. Every decade with existence, the prevalence of HF doubles. The prevalence is < 1 % for < 40 yrs of age and > 10% for greater than 80 yrs [21]. The HF Prevalence in modern nations generally varies from 1-2% of the adult population[22].

Mortality:

In accordance with Framingham Heart Study, the death rates after a diagnosis of HF in the United States was roughly 10% after 30 days, 20-30% after a year, and 45-60% after five years[23]. In contrast, the Rotterdam research, which included HF patients from all over Europe, observed decrease mortality, with mortality rates of 11% and 41% at 1 year and 5 years, respectively [24].

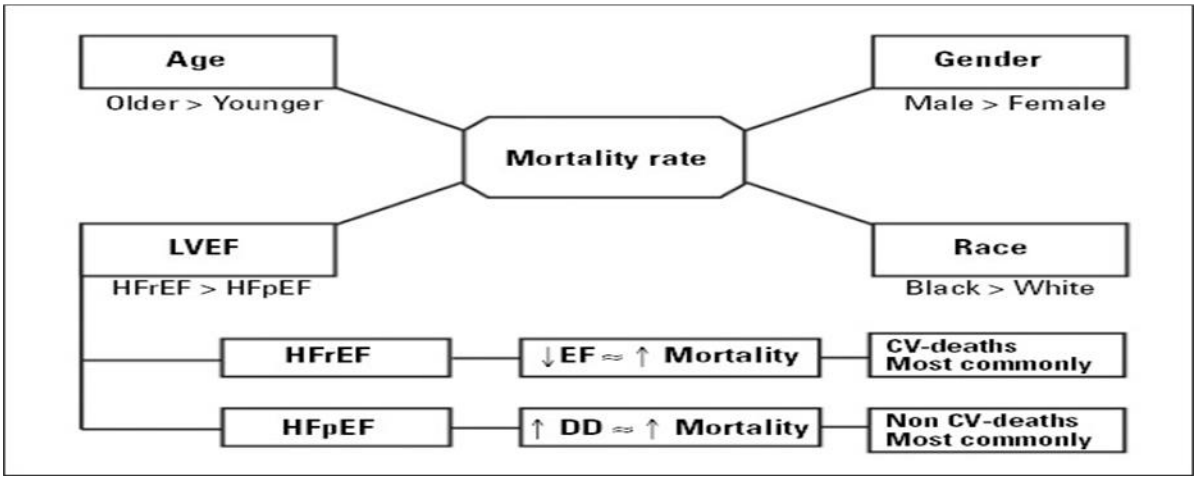

Fig: 2 Mortality Rate of HF

Figure courtesy Bytyçi I, Bajraktari G. Mortality in heart failure patients. Anatolian Journal of cardiology. 2015 Jan;15(1):63.

Despite significant advances in pharmacological and non-pharmacological treatment of HF patients, which has unquestionably improved patient life, mortality remains high, especially among the elderly, males, and African Americans. Especially compared to individuals with HFpEF, HFrEF patients have a greater mortality rate, which is most frequently due to cardiovascular reasons [25].

Etiology of Heart failure:

The disorders that can cause HF are diverse, and early discovery is critical since it can alter diagnostic, therapeutic, and preventive strategies, as well as affect prognosis. As a result, a general diagnosis of "heart failure" inpatient reports is unacceptable; the type of structural cardiac defect, as well as the risk markers that contributed to it, must be included [26].

Heart failure can be mainspring of diseases of the pericardium, myocardium, endocardium, cardiac valves, vasculature, or metabolism, among other things. Idiopathic dilated cardiomyopathy (DCM), coronary heart disease (ischemic), hypertension, and valve disease are the most common causes of HF [27]. When all other etiological or risk factors were ruled out, such as hypertension and alcohol misuse, the rate of "idiopathic" dilated cardiomyopathy in EPICAL trials, was 11%. In the SOLVD trials, a similar approach was selected, with an 18% rate of dilated cardiomyopathy as a result [28].

Cause		Examples
Predisposing causes		
Etiological		Coronary artery disease, congenital heart disease
Probably etiological		AHT, diabetes, history of rheumatic fever
Non-etiological		Age, masculine sex, obesity, tobacco use
Determining causes		
Cardiomyopathy	Primary	Cardiomyopathy dilated, hypertrophic, and restrictive cardiomyopathy
	Secondary	Ischemic, infectious, toxic, and metabolic cardiomyopathy
Ventricular overload	Pressure	AHT, aortic/pulmonary stenosis, pulmonary hypertension
	Volume	Valve insufficiency, shunts
Altered ventricular filling		Ventricular hypertrophy, mitral/tricuspid stenosis, tumors, cardiac tamponade, constrictive pericarditis
Arrhythmias		Bradycardia, tachycardia, tachycardiomyopathy
Precipitant causes		
Cardiac		Arrhythmias, ischemic cardiomyopathy, negative inotropic drugs: calcium antagonists, beta-blockers, antiarrhythmics, others
Extracardiac		Infections, non-completion of treatment, pulmonary embolism, anemia, drugs (NSAIDs), surgery, effort, toxic substances

*AHT indicates arterial hypertension; NSAIDs, non-steroid anti-inflammatory drugs.

Table: 1 Etiology of HF.

Table adapted from Segovia Cubero J, et al. Heart Failure: Etiology and Approach to Diagnosis.

1. Valve disease:

On echocardiography, this group included all patients with notable aortic valve stenosis, severe aortic, mitral valve regurgitation. Patients with flailed or prolapsed leaflets on

echocardiography were diagnosed as having organic mitral valve regurgitation, whereas functional mitral regurgitation patients were diagnosed as having ischemic or dilated cardiomyopathy, depending on the severity of their symptoms[29].

2. **Ischemic heart disease**:

   All patients having a history of myocardial infarction or coronary intervention, either Coronary Artery Bypass Graft (CABG) surgery or Percutaneous Coronary Intervention (PCI), were included in this group (PCI). Patients having a history of chest pain who had pathologic Q waves on an ECG and/or dyskinetic regions on echocardiography were also included in this group[29].

3. **Hypertension:**

   In EPICAL, 44% of the CHD subgroup had either hypertension or history of hypertension, which was undifferentiated to the 44% of patients with CHF caused by Chronic Heart Disease. The high prevalence of hypertension in the EPICAL group matches that found in the Framingham Heart Study, SOLVD, and the Flolan International Randomized Survival Trial (FIRST) for CHF. In 13.8 % of EPICAL patients, hypertension was the sole cause of CHF, a relatively significant proportion when compared to that observed in white patients in SOLVD (7%)[28].

4. **Cardiomyopathy:**

   There are three patterns of primary myocardial changes that can cause HF:

   - **Idiopathic dilated cardiomyopathy**: Both male and female are affected by idiopathic dilated cardiomyopathy. However there may be dilation of the 4 heart chambers, this is

manifested by mainly LV systolic dysfunction. Where proper clinical testing (often by coronary angiography) is performed, no known aetiology is discovered, and endomyocardial biopsy reveals either normal myocardium or nonspecific abnormalities. The underlying pathogenic mechanisms are unknown, as the term implies[26]. Alcohol usage is a high-risk factor for idiopathic dilated cardiomyopathy, and alcoholic cardiomyopathy is a well-known diagnosis[28].

- **Hypertrophic cardiomyopathy**: Hypertrophic cardiomyopathy is a disorder characterised by LV hypertrophy without apparent explanation and has a known genetic origin in many cases (mutations in genes that encode sarcomere proteins). Autosomal dominant inheritance is present in half of the cases, and it is the common cause of sudden death in young adults, particularly sportsmen[26].
- **Restrictive cardiomyopathy:** A alteration in heart compliance, as well as fast early diastolic filling, characterises restrictive cardiomyopathy. This kind of cardiomyopathy is the least frequent of the three, and it usually has a poor prognosis[26]**.**

5. **Other etiologies:** This category included atrial fibrillation and a small percentage of HF patients with uncommon diseases such as infiltrative and storage myocardial illnesses. Despite the truth that this classification resulted in a heterogeneous group of etiologies, it was important to ensure a large enough group for statistical analyses[29].

Types of HF :

The heart can no longer pump enough blood around the body and resulting in heart failure. Either the cardiac muscle is too weak or it isn't elastic enough. Various regions of the heart may also impacted. The type of medication used to treat HF is determined by the type of heart failure a person has.

HF usually affects only one sided of the heart, although it can affect both. Accordingly, doctors distinguish three forms of heart failure:

- **Left-sided HF:** Left ventricle of heart no longer pumps enough blood across the body, resulting in left-sided heart failure. Blood builds up in the pulmonary veins as a result (the blood vessels that carries blood away from the lungs)[30]. The left ventricle is larger than the other chambers and crucial for appropriate cardiac function since it supplies the majority of the heart's pumping force. The left sided of the heart must work harder to pump the same amount of blood in left-sided or left ventricular (LV) heart failure[1]. Shortness of breath, difficulty breathing, or coughing are common symptoms, especially after strenuous exertion. The most prevalent type of heart failure is left-sided heart failure[30].

  Left-sided heart failure can be divided into two categories. The two types of drugs have different treatments.

  - **HfrEF :** Systolic failure, commonly known as HF with reduced ejection fraction (HFrEF). The ability of the left ventricle to contract regularly is lost. The heart can't push enough blood into circulation because it can't pump hard enough.

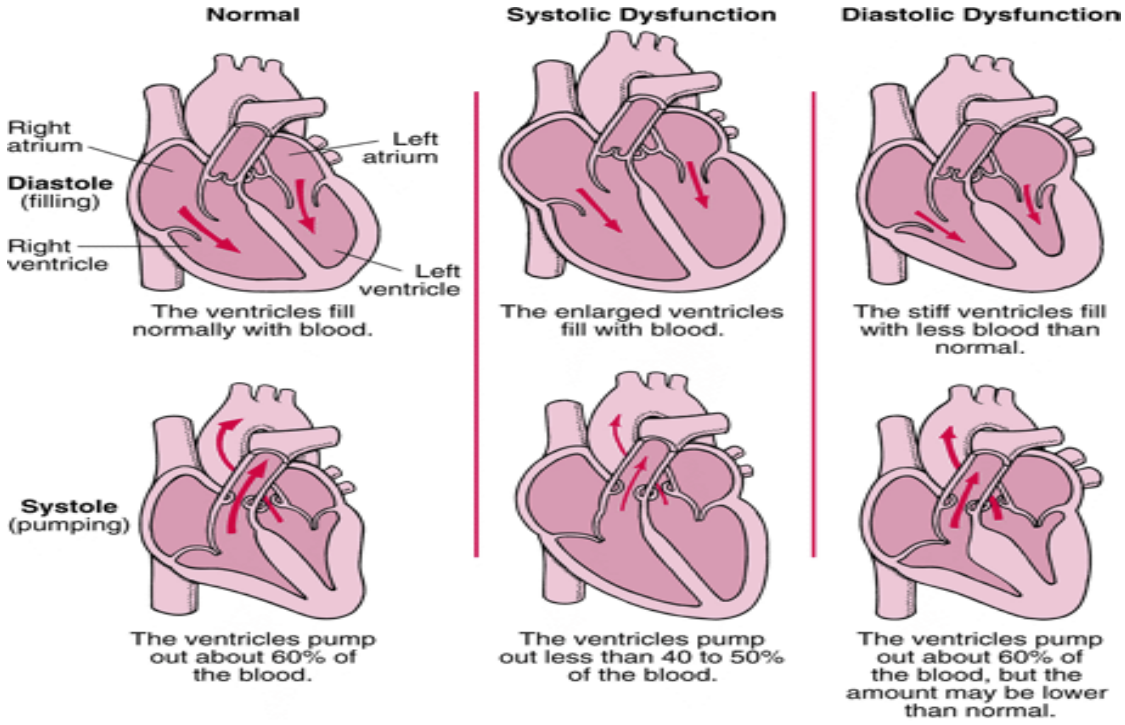

Fig : 3 Types of Heart failure. Figure adapted from https://www.aahfn.org

- **HfpEF :** Diastolic failure (or diastolic dysfunction), commonly known as HF with preserved ejection fraction (HFpEF): The ability of the left ventricle to relax normally is lost (because the muscle has become stiff). During the resting period between each beat, the heart is unable to properly fill with blood[1].

- **Right-sided HF:** The heart's right ventricle is too weak to pump sufficient blood to the lungs in this case. Blood builds up in the veins as a result of this (the blood vessels that carry blood from organs and tissue back to heart). Increased pressure inside the veins might cause fluid to leak out and into the surrounding tissue. This causes organs in the legs, belly or less usually in the genital area, to fill with fluid[30,1].

- **Congestive HF:** Although the names are commonly used interchangeably, congestive heart failure (CHF) is a kind of heart failure that necessitates prompt medical intervention. The blood returning to the heart through the veins backs up as blood goes out of the heart decreases, causing congestion in the body's tissues. Edema (swelling) is frequently the outcome and seen in the legs and ankles, but it also occur in other regions of the body. Shortness of breath can occur when fluid gathers in the lungs and interferes with breathing, especially when a person is lying down. This is known as pulmonary edema, and it can induce respiratory difficulty if left untreated[1].

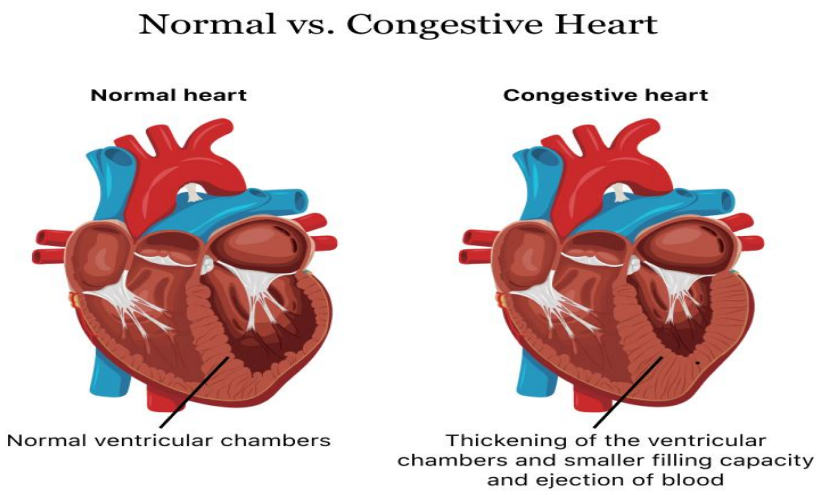

Fig: 4 Congestive HF Figure adopted from *JAMA Cardiology*

Classification of HF:

It is very important to understand the different stages of heart failure. HF symptoms and treatment may vary as HF progresses. The grouping system was developed by New York Heart Association (NYHA) are :

Class	Symptoms
I.	Symptomatically and Physically healthy at performing ordinary activities Example: Shortness of breath when physically active
II.	Symptomatically and Physically deprived during mild activity (mild SOB, and/or stable angina)
III.	Moderately limited during little or no physical activity (at rest) e.g. walking less than 100 meters
IV.	Extreme limitations even at rest (bedridden patients) with symptoms like unstable angina and shortness of breath

Table: 2 NYHA Classification [31]

The grouping system was also developed by the American Heart Association and American College of Cardiology :

- **Stage A:** High risk of heart failure but no structural heart disease or symptoms of heart failure (pre-heart failure)
- **Stage B:** Structural heart disease but no symptoms of heart failure (pre-heart failure)
- **Stage C:** Structural heart disease and symptoms of heart failure
- **Stage D:** Refractory heart failure requiring specialized interventions[32].

Comorbidities:

Diabetes (both type I and type II diabetes), obesity(defined as a body mass index above or equal to 30 kg/m^2), thyroid dysfunction (both hypo- and hyperthyroid disease), chronic kidney disease (CKD)(defined as an estimated glomerular filtration rates (eGFR) <60 mL/min/1.73 m^2) measured at baseline, a history of stroke, COPD, peripheral arterial disease (PAD), and anaemia (defined as haemoglobin below 12 g/dL in women and below 13 g/dL in men, measured at baseline) were all included as comorbidities.

CKD, anaemia, diabetes, and obesity were the most common non-cardiac comorbidities. Patients with HFpEF had the highest rate of comorbidities. While most comorbidities were related to a worse QoL in the whole population, this link was stronger in patients with HFrEF compared to patients with HfpEF.The majority of comorbidities were linked to a higher risk of death, however, the correlations with diabetes were only seen in patients with HFrEF rather thanHFpEF.

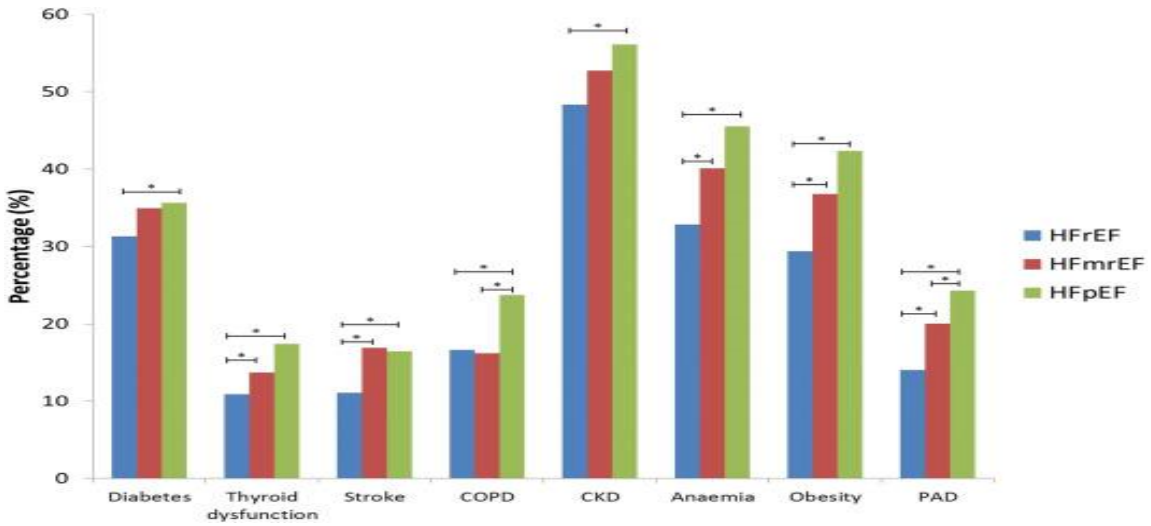

Fig: 5 Prevalence of non-cardiac comorbidities in HF groups[40].

Signs and Symptoms:

Heart failure patients have a wide range of symptoms, the majority of which are non-specific. Fatigue, dyspnoea, swelling ankles, and exercise intolerance are common symptoms of congestive heart failure, as well as symptoms related to the underlying cause. However, the accuracy of diagnosis based solely on clinical signs is frequently insufficient, especially in women and the elderly or obese[33].

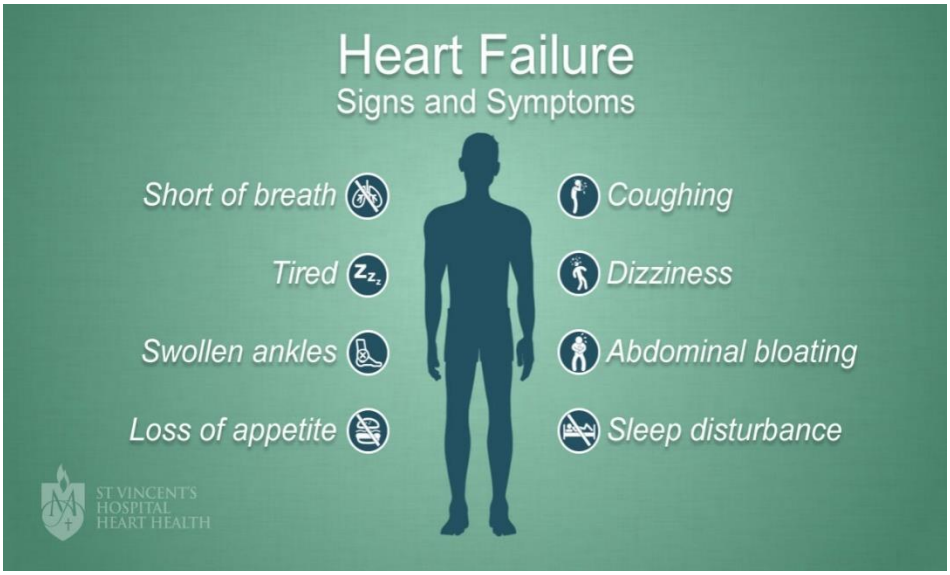

Fig: 6 Signs and Symptoms of HF

Figure adapted from https://www.svhhearthealth.com

The result, dyspnoea is somewhat sensitive but not very specific for the existence of heart failure. Although orthopnoea is a more specific symptom, it has limited sensitivity and thus minimal predictive value. Increased left ventricular filling pressures (owing to nocturnal fluid redistribution and increased renal reabsorption) cause paroxysmal nocturnal dyspnoea, which has a severe prognosis[33].

Characteristics features:

- The phenomenon of pulsus alternans is defined by equally spaced alternating strong and weak peripheral pulses.
- Apical impulse: a left ventricular enlargement is frequently indicated by a laterally displaced impulse past the midclavicular line.
- S3 gallop: a low-frequency, transient vibration that occurs in early diastole near the end of the right or left heart's quick diastolic filling cycle[33].

Diagnosis:

Your doctor will do the following during your **physical exam**:

- Take a reading of your heart rate, blood pressure, and weight.
- With a stethoscope, listen to your heart for sounds that indicate that it isn't performing up to mark.
- Listen for the sounds of fluid buildup in your lungs.
- Inspect your ankles, feet, legs, liver, and neck veins for edema[34]

Diagnostic tests and procedures[35,36,37] :

1. Complete blood count (CBC).
2. Iron Studies.
3. Urinalysis.
4. Electrolyte levels.
5. Renal and liver function studies.
6. Fasting blood glucose levels.

7. TSH Levels.
8. B Type natriuretic peptide and cardiac enzymes.
9. ECG.
10. Chest radiography.
11. Echocardiography.
12. Stress test.
13. Pulse oximetry and Arterial blood gas.
14. A Holter that you wear for 24 to 48 hours or longer while going about to normal activities.

Management:

Treatment for heart failure has two main goals:

1. Improve prognosis and minimise mortality,
2. Relieve symptoms and minimise morbidity by reversing or decreasing cardiac and peripheral dysfunction.

Other goals of therapy for in-hospital patients include

1. Reducing the length of stay and potential readmission
2. Preventing organ system damage,
3. Properly managing co-morbidities that may lead to poor prognosis[38].

In-patient HF management: It is recommended that the patient be admitted to a telemetry bed or the ICU, with treatment based on the following considerations.

1. Whether your PaO2 is 60 per cent or your SaO2 is 90 per cent, keep an eye on your oxygen levels.
2. Provide non-invasive positive pressure ventilation (NIPPV) for respiratory support in a few situations of respiratory distress to prevent intubation.
3. Depending on the triggering reasons and symptoms/signs of congestion, use the following pharmacological agents:
    - In patients with the present or past HF symptoms and lower LVEF, **diuretics** (thiazides, loop diuretics, and potassium-sparing) (to reduce edema by reducing blood volume and venous pressure) and salt restriction (to reduce fluid retention) are used to provide symptomatic relief.
    - **Angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers** (ARB) for neurohormonal alteration, vasodilation, and improvement in LVEF (in patients who do not respond to ACEIs or ARBs, substitute hydralazine and/or nitrates).
    - **Beta-adrenergic blockers** are used to treat neuro-hormonal disorders, improve symptoms and LVEF, enhance survival, avoid arrhythmias, and control ventricular contractions.
    - **Aldosterone antagonists** have been used as a supplement to other medicines for additive diuresis, heart failure symptom control, decreased ventricular arrhythmias, reduced cardiac workload, increased LVEF, and better survival.
    - **Digoxin** can result in a slight increase in cardiac output, improved heart failure symptoms, and a lower rate of heart failure hospitalization.

- If applicable, **Anticoagulants** reduce the risk of thromboembolism.
- To enhance cardiac output and diminish neuro-humoral activity**, Inotropic drugs** are used to restore organ perfusion and minimise congestion in patients with heart failure and a low ejection fraction[38].
- Aspirin and clopidogrel are the most commonly investigated and used antiplatelet drugs. Therefore, antiplatelet therapy may be beneficial if initiated in patients during an episode of HF[39].
- Newer medications. Sodium-glucose cotransporter-2 (SGLT-2) inhibitors and Glucagon-like peptide (GLP) agonists, two new classes of targeted therapies to lower blood sugar in diabetic patients, may help minimise heart failure hospitalizations.. Their use in treating heart failure is currently being studied[34].

Procedures and surgeries:

You may need one of the following medical devices if your HfrEF worsens:

- A biventricular pacemaker is a device that regulates the heart's rate (also called cardiac resynchronization therapy). This can assist reduce your symptoms by causing both sides of your heart to contract at the same time.
- A ventricular assist device or a whole artificial heart are examples of mechanical heart pump. The cardiac pump can be used until surgery or as a long-term treatment.
- A cardioverter defibrillator that can be implanted (ICD). An ICD monitors your heart rate and corrects abnormal heart rhythms that can lead to sudden cardiac arrest with electrical pulses[34].

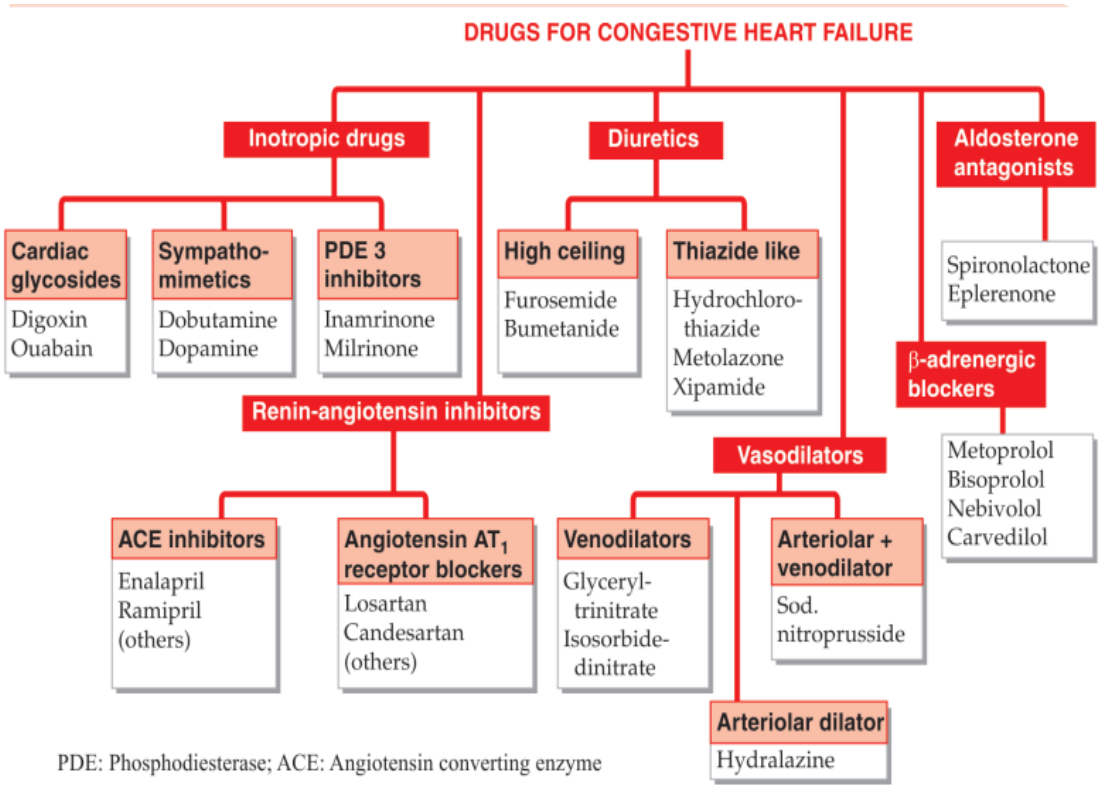

Fig: 7 Drugs classification of HF

Discharge Criteria for HF Patients:

When ADHF patients indulge the following requirements, they are ready to be discharged:

- Exacerbating issues have been identified and treated, and are now under control.
- The volume status has been improved.
- If needed for at least 24 hours, diuretic therapy has been effectively switched to oral medication, with IV vasodilator and inotropic therapy being discontinued.
- Oral therapy for chronic heart failure (HF) has been established with stable clinical status, including angiotensin-converting enzyme inhibitors (ACEIs) and beta-blockers (for patients with decreased LVEF).

- Complete patient and family education, as well as clear discharge instructions.
- Documented left ventricular ejection fraction (LVEF): The gold standard is echocardiography.
- Quitting smoking (if applicable).
- Within 3 days of discharge, a follow-up clinic appointment is planned, usually for seven to ten days[38].

SNO	DRUGS	DOSE
1.	Digoxin	0.25-0.5 mg/day
2.	Milirinone	50 mcg/kg iv bolus
3.	Dobutamine	0.5-1 mcg/kg/min iv infusion
4.	Inamrinone	0.5 mg/kg iv bolus
5.	Dopamine	1-5 mcg/kg/min iv
6.	Furosemide	40-80 mg iv
7.	Bumetanide	1 mg
8.	Hydrochlorothiazide	25-100 mg
9.	Metolazone	2.5-10 mg
10.	Spironolactone	25-100 mg
11.	Eplerenone	25 mg
12.	Metoprolol	12.5 mg
13.	Bisoprolol	1.25 mg
14.	Carvedilol	3.125 mg
15.	Sod. nitroprusside	0.3 mcg/kg/min
16.	Hydralazine	10-25 mg
17.	Glyceryl trinitrate	2.5-6.5 mg
18.	Isosorbide dinitrate	40 mg

19.	Losartan	50 mg
20.	Candesartan	4 mg
21.	Enalapril	2.5 mg
22.	Ramipril	2.5 mg
23.	Asprin	325 mg/day
24.	Dapagliflozin	10 mg/day
25.	Ivabradine	5 mg/day

Table : 3 Heart failure treatment w.r.t dose

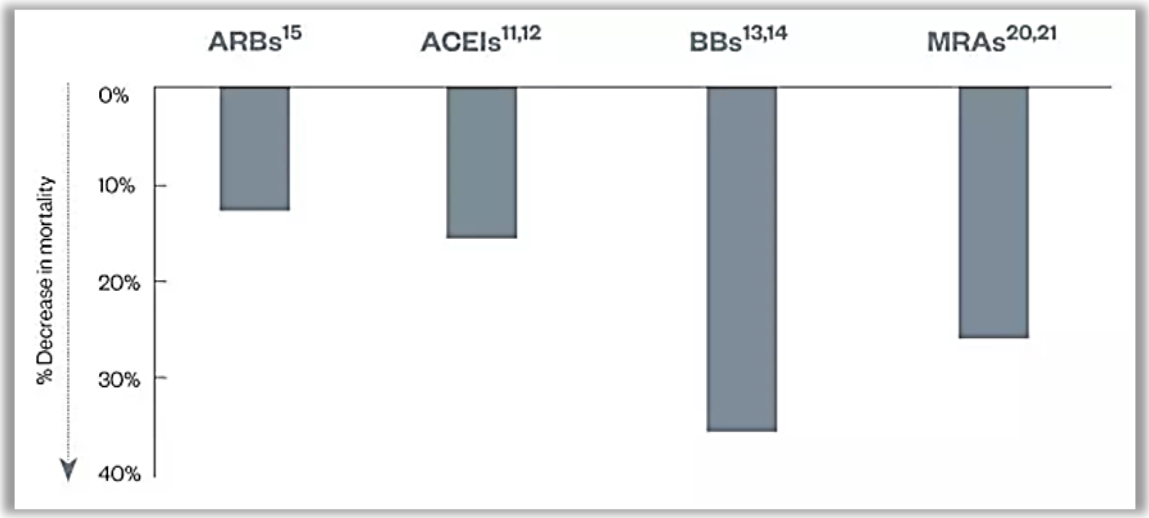

Fig 8: Drugs that reduce mortality in heart failure with a reduced ejection fraction

Figure adapted from https://pharmaceutical-journal.com

Anaemia in Heart Failure:

Anaemia, like a fever, is a symptom of a more serious underlying condition. Anaemia can be caused by a variety of diseases with different mechanisms. Anaemia affects a large number of people all over the world (especially in poor countries), leading to a major increase in the medical expenditure[41].Anemia was defined as hemoglobin (Hb) < 13 g/dl for males and <12 g/dl for female, based on WHO defination[42].Anaemia is a common comorbidity in stable HF patients, and it increases morbidity by increasing hospital admissions, impairing exercise ability, lowering QoL, and increasing mortality[43].HF is frequently linked to iron deficiency (ID) with or without anaemia. Although ID is the most common nutritional deficit in the world, affecting more than 1/3 rd of the population, its link to HF with or without anaemia is gaining attention[43].

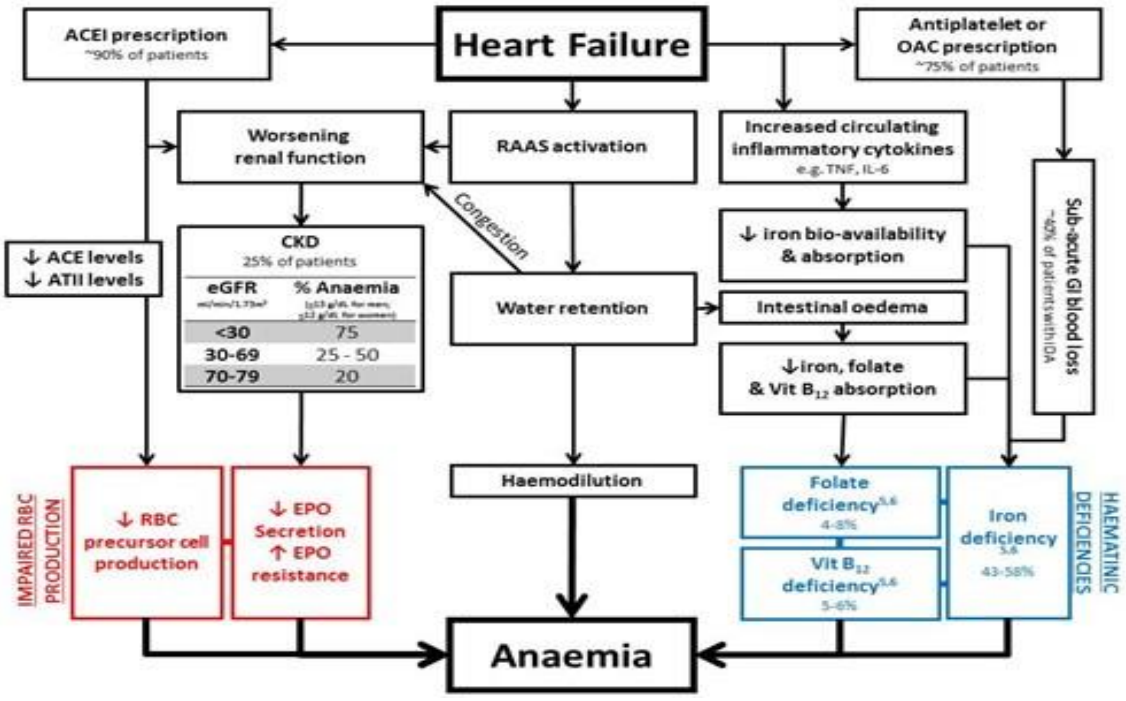

Fig: 9 Causes of anaemia in HF patients[46].

ID is an appealing therapeutic target because iron supplementation improves prognosis in patients with HF - a concept that has recently been verified in clinical research[44,45]. Although the exact cause of anaemia in heart failure is unspecified, the overwhelming evidence suggests that renal dysfunction, in combination with neurohormonal as well as proinflammatory cytokine enablement in heart failure, favours the further development of anaemia, with improper iron utilisation, erythropoietin consumption, and depressed bone marrow feature[47]. The processes through which anaemia affects heart failure are, linked to increased myocardial workload. Correcting anaemia could become an important and unique treatment focus to enhance long-term results in these individuals if anaemia is a mediator rather than just a marker of poor result[47]. Across both acute and chronic HF with LV dysfunction, anaemia and low Hgb have been found to be mutually correlated with an raised risk of mortality and readmission[48,49,50]. Patients with advanced age, more severe impairments in functional capability, and more extreme co-morbid CKD appear to have a higher prevalence of anaemia[50]. A study conducted in a multiethnic Asian community by Yeo et al. replicates our findings, indicating that HF patients of Indian ethnicity have the greatest prevalence of ID and anaemia [51]. Because anaemia is heavily associated with decline clinical status and mortality rate, it's only natural to wonder if treating anaemia can help. There are only a few options for improving Hgb[49]. A significant increase in Hgb was linked to lower diuretic doses and fewer admissions, along with improvements in NYHA functional class and LV ejection fraction[49]. Iron deficiency, either relative or absolute, is common in anaemic HF patients. Iron is required for erythropoiesis as well as various enzyme-dependent cellular metabolic activities in skeletal muscle and the Krebs cycle[4]. Chronic iron deficiency can diminish exercise capacity and create ultrastructural changes in cardiac myocyte.

LITERATURE REVIEW

- **Inder S. Anand, MD, FACC, FRCP, DPhil (OXON) Minneapolis, Minnesota, Anemia and Chronic Heart Failure Implications and Treatment Options**. In population with heart failure, anaemia is prevalent comorbidity that is very much linked to poor long-term results. Although the exact origin of anaemia in heart failure is unknown, the overwhelming evidence suggests that renal impairment, in combination with neurohormonal and proinflammatory cytokine trigger up in HF, promotes the development of chronic disease anaemia with poor iron utilisation, inappropriate erythropoietin production, and depressed bone marrow function. The processes through which anaemia affects heart failure outcomes are also uncertain, however, they may be linked to increased myocardial workload. Indeed, some modest trials have demonstrated that treating anaemia in HF population with recombinant erythropoietin and intravenous iron has a positive effect. However, the appropriate threshold at which therapy should be commenced, as well as the level of correction that is deemed safe and desirable in each particular patient with heart failure, must be determined.
- **W.H. Wilson Tang, MD, P.S. Daniel Yeo, MBBS, MRCP(UK), Epidemiology of Anemia in Heart Failure.** Anemia affects a large percentage of people with heart failure, generally in a moderate, normocytic form. The condition's links to comorbidities including diabetes and renal insufficiency point to common pathogenesis. Understanding epidemiologic data can help health care practitioners and researchers better understand the scope and repercussions of anaemia in the heart failure population, as well as the need to develop approaches to manage issues like patient selection and treatment options.

- **Qurat-ul-ain Jelani, MD, Philipp Attanasio, MD, Stuart D. Katz, MD, Stefan D. Anker, MD, PhD, Treatment with Iron of Patients with Heart Failure With and Without Anemia**. Short-term intravenous iron delivery has been associated with improved symptoms and QOL in individuals with HF, according to growing evidence. Functional iron deficiency may occur often in CHF patients, according to preliminary findings, and may exacerbate symptoms related to lower exercise ability. More research is must needed to better describe iron storage in the HF population, as well as to recognise the impact of benefit and long-term implications of supplemental iron therapy.
- **Sohan Kumar Sharma, Shalabh Kumar Agarwal, Kapil Bhargava, Mukesh Sharma, Karan Chopra, Gopinath Arumugam, Prevalence and spectrum of iron deficiency in heart failure patients in south Rajasthan**. The findings from our study highlight a remarkably high prevalence of ID in HF patients in the Indian population. ID is more prevalent in HF patients even without anaemia, which is an established poor prognostic factor. In our study, we found the prevalence of ID is 76%, which is significantly higher than these studies. This further emphasises the illness severity among HF patients in India. We discovered that ID was considerably greater in women with HF than in males in a sexual identity analysis. In this study, 76 per cent of patients had ID, and 51.3 per cent of those with ID also had anaemia. A large percentage of individuals (24.7 per cent) had an ID but no anaemia. As a result, if Hb levels are used in the workup of ID in HF patients, a major portion of the alleged iceberg will be overlooked. Functional ID accounts for a large portion of the mortality rate, with a prevalence of 27.3 per cent.

- **Mansour Rafie, Hooman Rahmani, Mahmood Sadr, Mohammad Forat, Zahra Behnamfar, Mohammad Hossein Ahmadieh and Reza Rafie, Prevalence and Treatment of Iron Deficiency Anemia in Patients with Chronic Heart Failure**. The prevalence of IDA was 10.7% in our patients, and 25.7 per cent of them had chronic condition anaemia. The anaemic group's mortality rate was 4.9 times greater than the normal haemoglobin group's mortality rate. There was a considerable increase in haemoglobin levels following therapy, which was more pronounced in the IDA group. Following therapy, EF rose in all groups, although it rose the most in the IDA group. Our findings suggest that treating IDA as part of CHF patient therapy improves the quality of life. Early recognition and diagnosis of anaemia can help individuals with CHF improve their EF.
- **James M Beattie, Rani Khatib, Ceri J Phillips, Simon G Williams, Iron deficiency in 78 805 people admitted with heart failure across England: a retrospective cohort study.** ID/IDA are substantial comorbidities and associated with unfavourable outcomes, both for affected individuals and the health economy, for adults admitted to hospitals in England, primarily with acute HF.
- **John G. F. Cleland, MD, FRCP, FESC; Jufen Zhang, PhD; Pierpaolo Pellicori, MD; Ben Dicken, MBBS, MRCP; Riet Dierckx, MD; Ahmad Shoaib, MBChB; Kenneth Wong, DM, FRCP, FESC; Alan Rigby, PhD; Kevin Goode, PhD; Andrew L. Clark, MA, MD, FRCP, Prevalence and Outcomes of Anemia and hematinic deficiencies in Patients with Chronic HF.** Anemia is frequent in people with HF, and it's commonly

linked to iron deficiency. Both anaemia and ID have been linked to an elevate in all-cause and CV mortality in this population and could be therapeutic targets.

- **Oren Zusmana, Osnat Itzhaki Ben Zadoka, Anat Gafter-Gvili, Management of Iron Deficiency in Heart Failure**. Anemia diagnostic workup is recommended for every patients with systolic HF, even if no particular aetiology is detected in many cases. The 2016 European Society of Cardiology (ESC) guidelines support this proposal. The ESC guidelines suggest that "IV FCM should be considered in symptomatic patients (serum ferritin 100 g/L or ferritin between 100–299 g/L with TSAT 20%) to reduce HF symptoms, raise exercise capacity, and enhance QoL." This is level A suggestion with a Class IIa recommendation."In patients with NYHA functional class II-III and iron deficiency (serum ferritin 100 g/L, or ferritin among 100–299 g/L if TSAT 20 per cent), IV iron might be reasonable to enhance the cognitive status and quality of life," according to the 2017 update of the American Heart Association (AHA) and American College of Cardiology (ACC) joint guidelines. The evidence level is IIb. There was no recommendation for a specific iron composition. We concur with these suggestions. We feel that existing data support using IV iron to treat HF patients with the iron deficit.

NEED OF STUDY

NEED OF STUDY

- Heart Failure (HF) affects a vast number of people not only in India but around the world, causing a slew of difficulties in patients and raising the mobility and death rates of those who suffer from it.
- As hypertension is a key risk factor and a prevailing symptom among HF patients, it has a significant impact on the disease's course.
- Even though hypertension is treated with various antihypertensives, control and maintenance of blood pressure are unlikely to be noticed. As a result, we must pay more attention to blood pressure maintenance and control in HF patients in order to achieve the target BP goals.
- In stable HF patients, anaemia is prevalent comorbidity that increases morbidity by increasing hospital admissions, reducing exercise ability, reducing QoL, and increasing mortality.
- The contemporary international prevalence of HF is 64.34 million cases (8.52 per 1,000 people), resulting in 9.91 million years lost due to disability (YLDs) and a cost of $346.17 billion US dollars. Men do have a rather higher YLD value.
- With the severity of HF, the frequency of iron deficiencies rises. For a long time, the repercussion of iron deficiencies was overlooked, particularly in view of worsening of cardiovascular disorders and the development of anaemia.
- In recent years, investigations involving intravenous iron agents in patients with iron deficiency and HF have shown fresh insights on iron therapy improvement.

AIMS AND OBJECTIVE

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AIM: To study the prevalence and treatment of anemia in HF patients in a tertiary hospital.

PRIMARY OBJECTIVE:

- To observe the prevalence of Anaemia in heart failure patients.
- To observe the management of Anaemia in heart failure patients.

SECONDARY OBJECTIVE:

- To observe the common risk factors for Anaemia in heart failure patients.


STUDY PLAN

PLAN OF WORK

- ✓ A survey of relevant literature
- ✓ Patient information is gathered from medical records in tertiary care hospitals' cardiology branch.
- ✓ All of the case sheets will indeed be examined, and those that satisfy the exclusion and inclusion criteria will be chosen.
- ✓ Receiving approval from the ethical committee.
- ✓ The patient's demographic characteristics, such as age, gender, prior medical history, prior medication history, social history, and blood pressure levels, are recorded on a **PROFORMA**.
- ✓ The information gathered will be analysed.


Methodology

METHODOLOGY

MATERIALS AND METHODS:

- **STUDY SITE:**

  The Study Will Be Conducted in The Cardiology branch at Care Tertiary Hospital, Located at Banjara Hills Road No.1 &10, Hyderabad, Telangana.

- **STUDY APPROVAL:**

  The study protocol will be submitted to the institutional Ethical Committee (IEC) for approval.

- **STUDY TYPE:**

  A Prospective and Observational study.

- **STUDY DURATION:**

  4 Months.

- **SAMPLE SIZE:**

  43 Patients.

- **STUDY CRITERIA:** It involves inclusion criteria and exclusion criteria.

  - **INCLUSION CRITERIA:**

    - Patients irrespective of gender.
    - Patients above 18 years old.
    - Heart failure patients.
    - Patients with Hb < 10 g/dl are observed for iron studies

- **EXCLUSION CRITERIA:**
  - Patients who are on iron supplements.
  - Patients who are not willing to cooperate.
  - Patients below 18 years old.
  - Pregnant women.


RESULTS

RESULTS

1. DISTRIBUTION OF PATIENTS ACCORDING TO GENDER:

There are 55 males and 25 females in a total of 80 cases. Patient age range of 31 to 98 years.

GENDER	COUNT OF GENDER	PERCENTAGE %
Male	55	68.75%
Female	25	31.25%

Table: 4DISTRIBUTION OF PATIENTS ACCORDING TO GENDER

Fig: 10 DISTRIBUTION OF PATIENTS ACCORDING TO GENDER

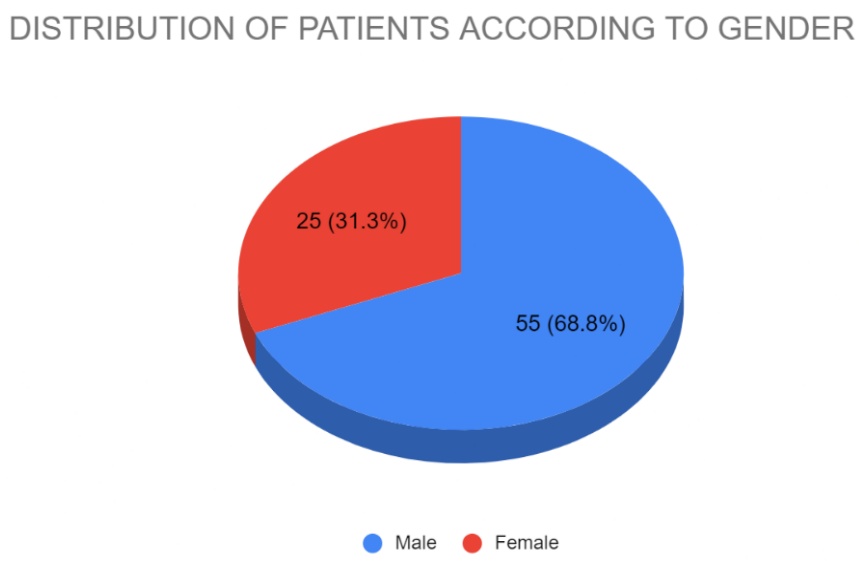


Illustration: Among the 80 patients, 68.8% are male patients and 31.3% are female patients. Fig 10 shows that the male population are more affected in our study when compared to female population.

2. DISTRIBUTION OF PATIENTS ACCORDING TO AGE:

The patients are divided according to their age, to identify which age group of patients are more affected.

AGE	NO OF PATIENTS	PERCENTAGE
30 – 40	1	1.25%
40 – 50	1	1.25%
50 – 60	17	21.25%
60 – 70	30	37.5%
70 – 80	22	27.5%
80 – 90	8	10%
90 – 100	1	1.25%

Table: 5 DISTRIBUTION OF PATIENTS ACCORDING TO AGE

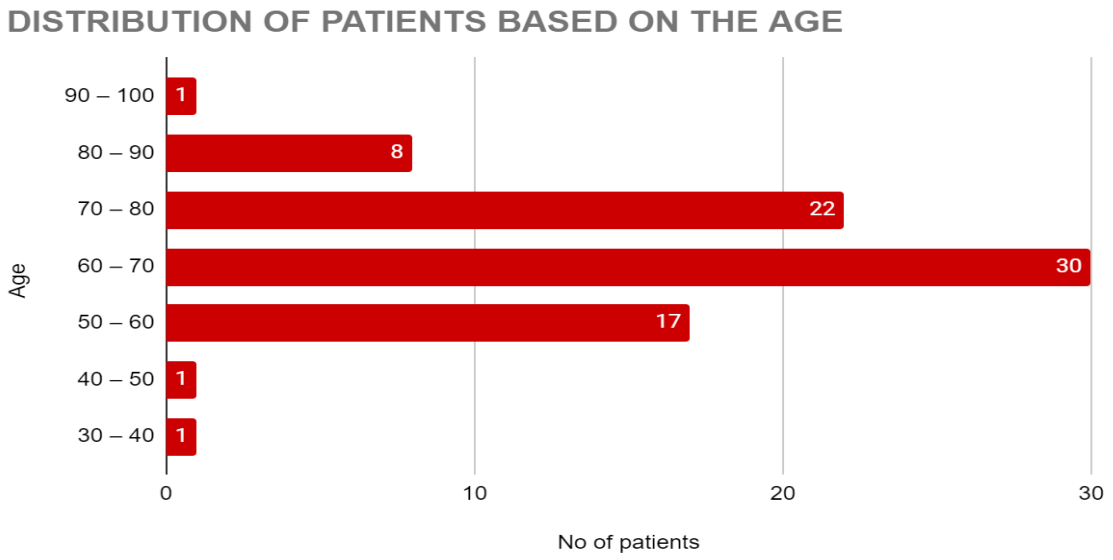


Fig: 11 DISTRIBUTION OF PATIENTS ACCORDING TO AGE

Illustration: As fig.11 shows out of 80 patients 30 are under 60-70 age group, 17 patients are under 50-60 age group, 22 patients are under 70- 80 age group, 1 patient is under the 40-50age group, 8 patients are under 80-90 age group, 1 patient is under 30-40 age group and 1 patient is under 90-100 age group. 60-70 age group is highly affected in our study.

3. DISTRIBUTION OF PATIENTS BASED ON THE NYHA CLASSIFICATION:

The patients are divided according to their symptoms and characteristics features, to identify which NYHA class is more distributed.

NYHA CLASSIFICATION	NO OF PATIENTS	PERCENTAGE
CLASS I	03	3.75%
CLASS II	22	27.5%
CLASS III	27	33.75%
CLASS IV	28	35%

Table: 6 DISTRIBUTION OF PATIENTS BASED ON THE NYHA CLASSIFICATION

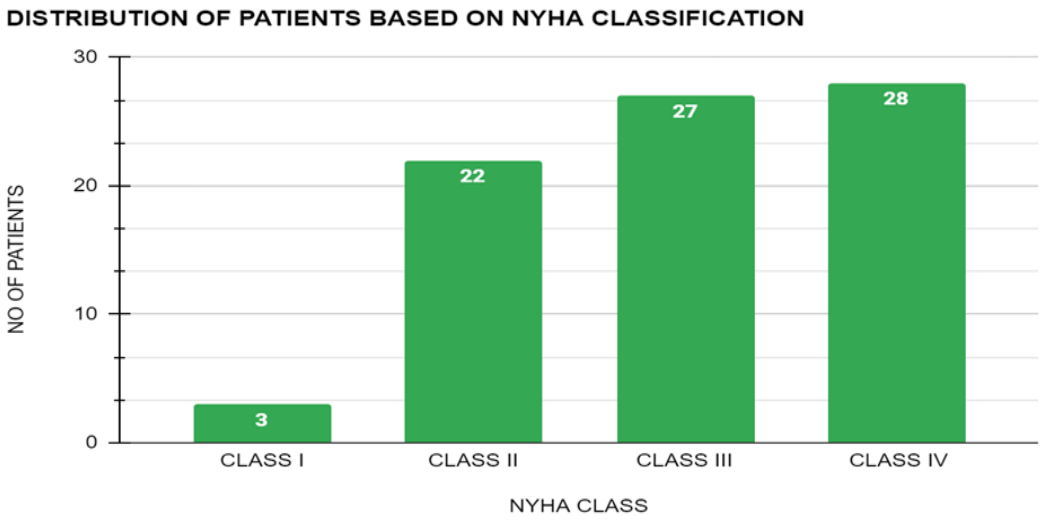


Fig: 12 DISTRIBUTION OF PATIENTS BASED ON THE NYHA CLASSIFICATION

Illustration: As the table.6, fig.12 shows out of 80 patients 22 patients are presented with NYHA class II symptoms, 27 patients are presented with NYHA class III symptoms, 28 patients are presented to NYHA class IV symptoms and 03 patients are presented to NYHA class I symptoms. Maximum patients (35%) are presented with NYHA class IV symptoms.

4. DISTRIBUTION OF PATIENTS BASED ON THE LVEF:

The patients were splitup according to ejection fraction (%), to deterimne the LV dysfunction, based on 2D echography. LVEF values are adopted from https://www.acc.org.

EJECTION FRACTION	NO OF PATIENTS	PERCENTAGE
Normal function	4	5%
Mild dysfunction	11	13.75%
Moderate dysfunction	30	37.5%
Severe dysfunction	35	43.75%

Table: 7 DISTRIBUTION OF PATIENTS BASED ON THE LVEF

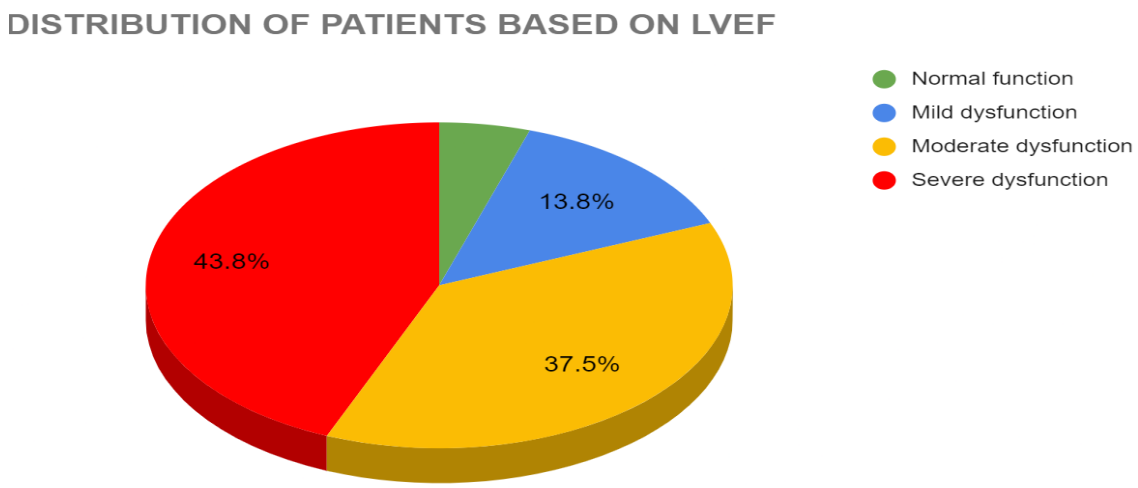


Fig: 13 DISTRIBUTION OF PATIENTS BASED ON THE LVEF

Illustration: As the table.7, fig.13 shows out of 80 patients 30 are affected with moderate dysfunction, 35 are affected with severe dysfunction, 11 are affected with mild dysfunction and 04 are presented with normal function. Maximum patients (43.75%) are patients are affected with severe LV dysfunction.

5. DISTRIBUTION OF PATIENTS BASED ON PAST MEDICAL HISTORY:

The patients were distributed according to specific type of disease. To determine the comorbidities of HF:

COMORBIDITY	NO OF PATIENTS
Hypertension	62
Diabetes mellitus Type 2	51
Hypothyroidism	09
Anemia	05
Chronic kidney disease	25
Obesity	17
Pulmonary arterial hypertension	1
Atrial fibrillation	06

Table: 8 DISTRIBUTION OF PATIENTS BASED ON PAST MEDICAL HISTORY

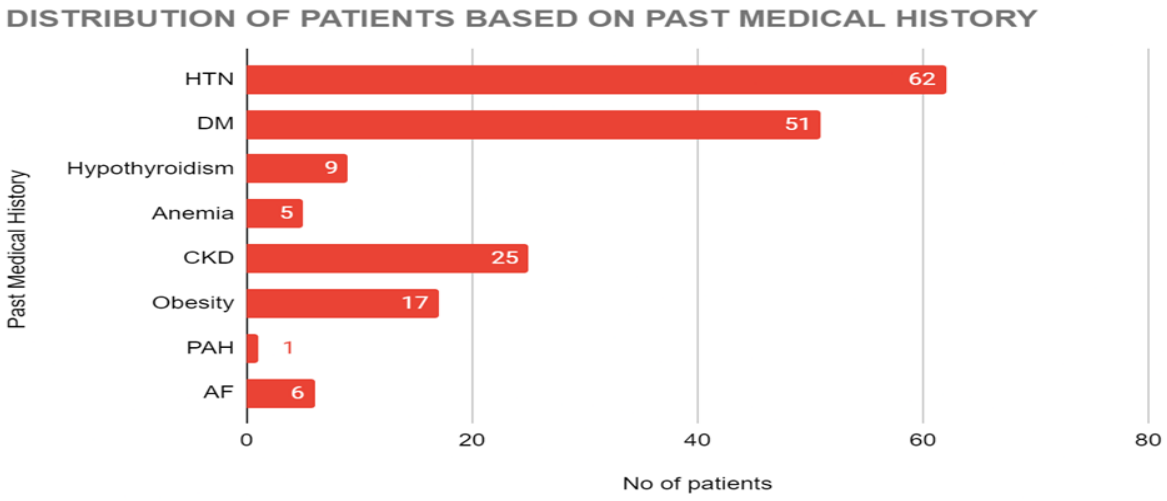


Fig:14 DISTRIBUTION OF PATIENTS BASED ON PAST MEDICAL HISTORY

Illustration: As the table.8, fig.14 shows that maximum patients (62) are primarily affected with hypertension, 51 patients are affected with diabetes mellitus, 25 patients have a history of CKD, 17 patients are having a history of obesity, 06 patients are primarily diagnosed with AF, 09 patients are affected with hypothyroidism, 05 patients are primarily affected with anemia and 01 patient is affected with PAH. From our study hypertension is the most common comorbidity.

6. DISTRIBUTION OF PATIENTS BASED ON TYPE OF DRUG ADMINISTERED:

The anemic patients are distributed are according to type of drug administered. The data follows:

DRUG ADMINISTERED	NO OF PATIENTS	PERCENTAGE
Ferrous ascorbate	09	16.66%
Ferric carboxymaltose	19	35.1%

Table: 9DISTRIBUTION OF PATIENTS BASED ON TYPE OF DRUG ADMINISTERED

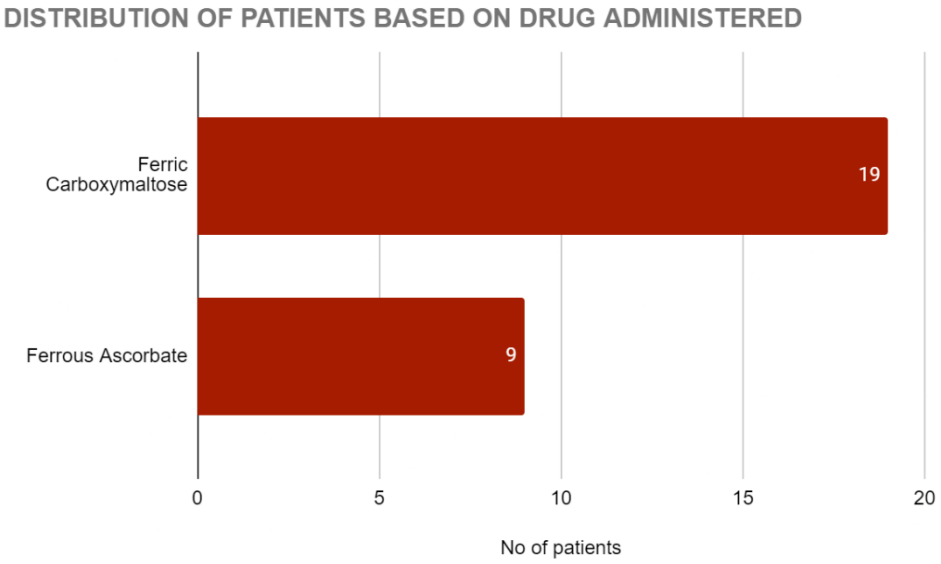


Fig: 15 DISTRIBUTION OF PATIENTS BASED ON TYPE OF DRUG ADMINISTERED

Illustration: As the table.9, fig.15 shows that out of 80 patients in our population 54 are anemic. Out of 54 patients, 09 are administered with the Ferrous ascorbate and 19 are administered with the Ferric carboxymaltose (FCM).

7. PREVALENCE OF ANEMIA IN HF PATIENTS :

To determine prevalence of the anemia in the total study population, as data follows:

TYPE	NO OF PATIENTS
Total study population	80
Anemia patients	54

Table: 11 PREVALENCE OF ANEMIA IN HF PATIENTS

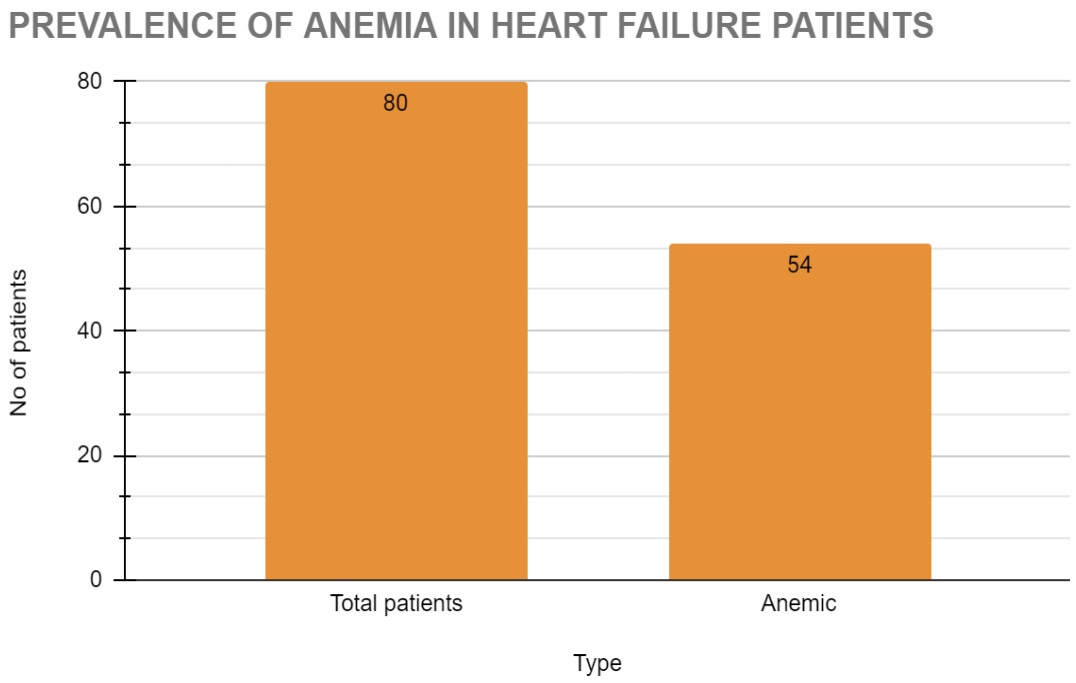


Fig: 17PREVALENCE OF ANEMIA IN HF PATIENTS

Illustration: As table.11, fig.17 shows that out of 80 patients 54 patients are found to be anemic.

Anemia (Hb < 13g% for males and < 12g% for females) was present in 54 (67.5%) patients. Thus the prevalence of anemia is found to have be 67.5% in HF patients of our study population.

8. PREVALENCE OF IDA IN HF PATIENTS

To determine the prevalence of iron deficiency anemia (IDA) in the total anemia population, as data follows:

TYPE	NO OF PATIENTS
Total anemic patients	54
IDA patients	26

Table: 10 PREVALENCE OF IDA IN HF PATIENTS

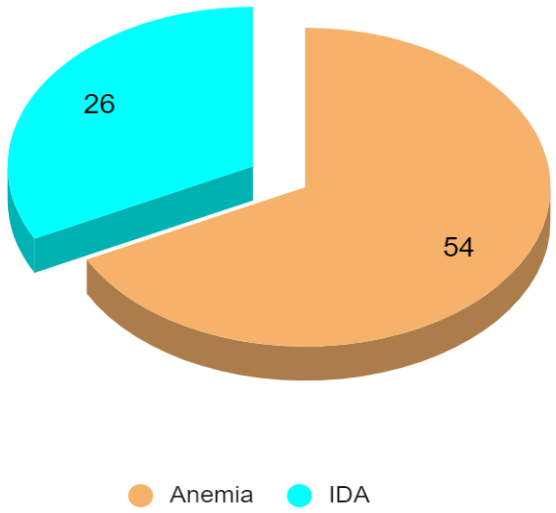


Fig: 16 PREVALENCE OF IDA IN HF PATIENTS

Illustration: As table.10, fig.16 shows that out of 54 anemic patients 26 patients are found to be (IDA) Iron deficiency anemic. 26 (48.1%) patients are found to be Iron deficiency and prevalence of iron deficiency is found to be 48.1%.

DISCUSSION

DISCUSSION

The collected data reveal a very high prevalence of anaemia in HF patients in Indian community. Anemia is common in HF patients, however it is already a known bad prognostic factor. In recent time, there has been a growing understanding of the gravity of anaemia in HF patients. Heart failure refers to the heart's failing to drive enough blood to meet the body's metabolic requisite. HF can be caused by any cardiogenic disease affecting the pericardium, epicardium, endocardium, or any blood vessel.HF affects 40 million people around the world; males are the most impacted ones.

Starting from sexuality analysis, we found that anemia was significantly overhead in male with HF as compared to female.

The ESC advised Iron deficiency testing in HF patients based on ferritin and TSAT assessments in the 2012 ESC Guidelines for the diagnosis and management of acute and chronic HF.

The significance to assess and treat ID and anaemia in individuals with advanced HF is being incorporated into global recommendations. As our research shows, ID and anaemia are a prevalent but underappreciated burden in Indian HF patients, necessitating the inclusion of more routine diagnostics in future Indian guidelines.

The patients enrollment was also lower than in these large-scale investigations because it was a single-centre study. Furthermore, because this was an observational analysis, the effect of iron supplementation on NYHA class improvement could not be determined.


CONCLUSION

CONCLUSION

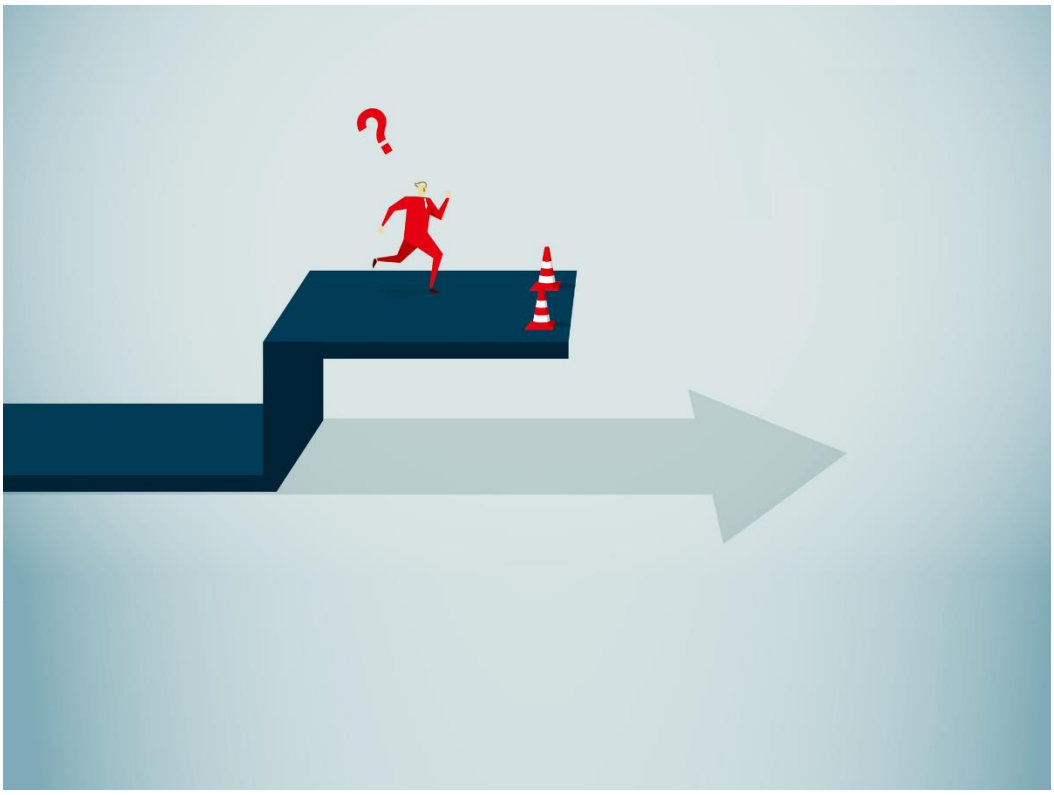
Anemia is a recurrent comorbidity among HF patients, according to the findings.

The importance of assessing and treating ID and anaemia among people with advanced HF is being integrated into worldwide guidelines.

ID and anaemia are a common but underrated burden in Indian HF patients, as evidenced by our research, justifying the inclusion of more routine tests in future Indian guidelines.

The overwhelming evidence suggests that managing anemia in HF can decrease hospital readmission.

LIMITATIONS



LIMITATIONS

This is a prospective study, and the information gathered was based only on the patient records that were accessible.

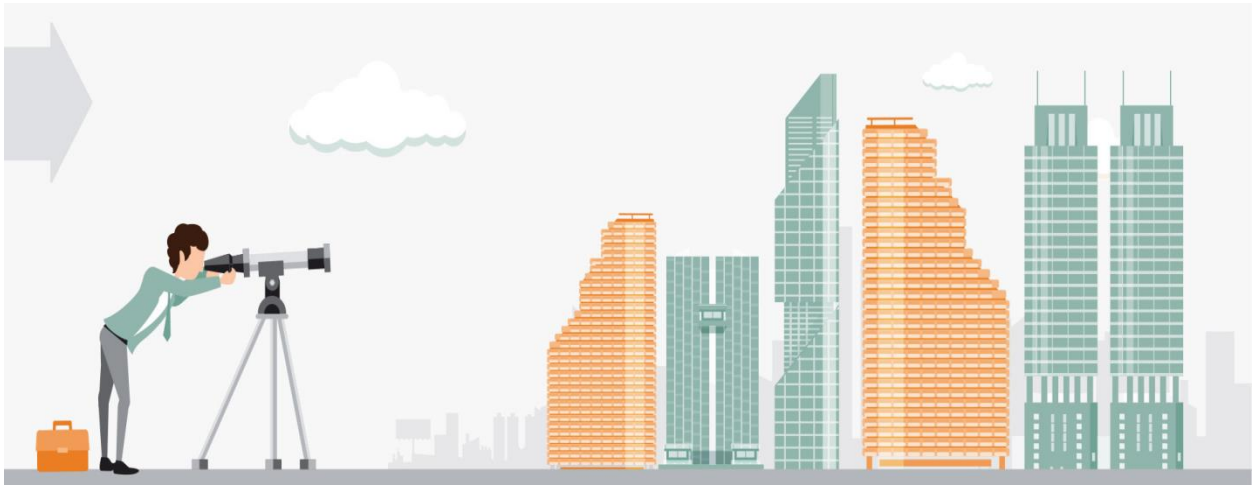
Because the sample size was insufficient, the results could not be fully generalised.

Because the study was conducted in tertiary care hospitals, the results may not be applicable to the general community.

The duration of our study is also short.

The study involved a small group of people with HF who were not farther segmented into HFrEF, HFpEF, and HFmrEF groups.

FUTURE OUTLOOK



FUTURE OUTLOOK

Because blood pressure is one of the key causes of HF and also worsens the condition of patients, it is critical to keep blood pressure under control so that HF patients' quality of life improves.

Because our study had a small sample size, more research is needed to determine the prevalence of anaemia in different subgroups of the population.

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