"ASSOCIATION OF IRON STUDIES WITH SERUM BRAIN NATRIURETIC PEPTIDE LEVEL IN HEART FAILURE PATIENTS- A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY."

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ENDORSEMENT

This is to certify that the dissertation entitled **"ASSOCIATION OF IRON STUDIES WITH SERUM BRAIN NATRIURETIC PEPTIDE LEVEL IN HEART FAILURE PATIENTS- A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY."** is a bonafide research work done by **REG NO. BG0115008.**

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LIST OF ABBREVIATIONS USED

%	-	PERCENTAGE
CHF	-	CHRONIC HEART FAILURE
CKD	-	CHRONIC KIDNEY DISEASE
EPO	-	ERTHROPOEITIN
HF	-	HEART FAILURE
BNP	-	BRAIN NATRIURETIC PEPTIDE
CGMP	-	CYCLIC GUANOSINE MONOPHOSPHATE
NT-PROBNP	-	N TERMINAL PRO NATRIURETIC PEPTIDE
EF	-	EJECTION FRACTION
HHF	-	HOSPITALIZED HEART FAILURE
YLL	-	YEARS OF LIFE LOST
YLD	-	YEARS LIVED WITH DISABILITY
HFREF	-	HEART FAILURE WITH REDUCED EJECTION FRACTION
HB	-	HAEMOGLOBIN
RHEPO	-	RECOMBINANT HUMAN ERYTHROPOEITIN
CRCL	-	CREATININE CLEARANCE
LVEF	-	LEFT VENTRICULAR EJECTION FRACTION
MLHFQ	-	MINNESOTA LIVING WITH HEART FAILURE QUESTIONNAIRE
6MW	-	6-MIN WALK
CRF	-	CHRONIC RENAL FAILURE
NYHA	-	NEW YORK HEART ASSOCIATION
QOL	-	QUALITY OF LIFE

CV	-	CARDIOVASCULAR
RD	-	RENAL DYSFUNCTION
EGFR	-	ESTIMATED GLOMERULAR FILTRATION RATE
PROANP	-	PRO ATRIAL NATRIURETIC PEPTIDE
ACHD	-	ADULT CONGENITAL HEART DISEASE
RDW	-	RED CELL DISTRIBUTION WIDTH
TSAT	-	TRANSFERRIN SATURATION
STFR	-	SOLUBLE TRANSFERRIN RECEPTOR
HSCRP	-	HIGH SENSITIVE C-REACTIVE PROTEIN
SD	-	STANDARD DEVIATION
IHD	-	ISCHEMIC HEART DISEASE
TIBC	-	TOTAL IRON BINDING CAPACITY

ABSTRACT

Background and Objectives

Iron deficiency plays a critical role in the anaemia of CHF, and it can contribute to EPO resistance, as the bone marrow will not respond to EPO unless adequate iron stores are present.

There is increasing volume of literature on high prevalence of anemia in heart failure patients and strong association between Iron metabolism and deterioration in heart function but studies linking Iron metabolism parameters with serum proBNP are scarce.

This study was conducted to find an association between iron studies and BNP levels in heart failure with reduced ejection fraction patients.

Methodology

A total of 93 consecutive patients presenting with Heart failure with reduced ejection fraction (HFrEF) were studied. Iron studies (Sr. Iron, Sr.TIBC, Sr. Ferritin, TSAT %), hemoglobin (Hb), serum creatinine, 2D echocardiography were done and then were compared with serum proBNP levels.

Results

Majority of the subjects with heart failure were aged between 61 to 70 years in the study, with male preponderance. Among the study population majority of 78.49% subjects had Iron deficiency (ID) .66.66% had ID with anemia and 11.82% had ID without anaemia. It was also noticed that serum proBNP had a significant linear negative correlation with Sr. Iron, moderate positive correlation with serum TIBC, a moderate negative correlation with TSAT% but a weak positive correlation with

Serum ferritin levels. We also noticed that patients who had left ventricular ejection fraction(LVEF) below ≤45% had a significant positive correlation with Hemoglobin, a moderate positive correlation with Serum iron but a weak positive correlation with Serum TIBC and weak negative correlation with serum Ferritin levels.

Conclusion

Our study showed that patients diagnosed with HFrEF for > 6 months had a 78.49% prevalence of iron deficiency with or without anaemia. Also iron deficiency had a statistically significant linear correlation with serum proBNP, Hb and LVEF.

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INTRODUCTION

Heart failure is considered an epidemic disease in the modern world affecting approximately 1% to 2% of adult population. It presents a multifactorial, systemic disease. Chronic heart failure (CHF) can result from a multitude of cardiac diseases in which after cardiac injury structural, neuro humoral, cellular, and molecular mechanisms are activated and act as a network to maintain physiological functioning.[1] Chronic heart failure (CHF) is increasingly viewed as a multi-system disease. Many recent studies have concluded that, beyond the impairment of cardiac function, CHF also affects the functional capacity of other organs such as the kidneys and skeletal muscle.[2]

Anaemia and chronic kidney disease(CKD) are reported be the most prevalent comorbidities in CHF[3]. They are reported to contribute to inadequate tissue oxygen supply and impaired oxygen use by the skeletal muscle, may underlie impaired exercise tolerance, beyond the hemodynamic dysfunction. Also, studies have reported that these co-morbidities can even worsen the prognosis of CHF patients.[4]

Anaemia in CHF can be the consequence of reduced glomerular filtration rate, reduced plasma flow, impaired erythropoietin (EPO) production, and haemodilution.[5] Iron deficiency plays a critical role in the anaemia of CHF, and it can contribute to EPO resistance, as the bonemarrow will not respond to EPO unless adequate iron stores are present.[6] An important point is that despite seemingly adequate iron stores assessed by serum iron and ferritin, up to 73% of patients with anaemia, normal kidney function, and advanced CHF had ID as assessed by bone marrow aspiration in a study by Nanas et al.[7]

Besides anaemia, iron deficiency (ID) in itself is recognized as an independent co-morbidity in patients with heart failure (HF) with serious consequences for patient well-being and outcomes.[8] The pivotal importance of iron is based on its essential role in oxygen transport, and its central role in processes maintaining cellular energy in high-energy demanding tissues like cardiac muscle.[9] Dependent on the various ID definitions, the prevalence of ID has been estimated between 13 and 34% with higher incidence rates among anaemic patients.[10]

Brain natriuretic peptide (BNP) is a 32 amino acid cardiac natriuretic peptide hormone originally isolated from porcine brain tissue. The human BNP gene is located on chromosome 1 and encodes the prohormone proBNP. The biologically active BNP and the remaining part of the prohormone, NT-proBNP (76 amino acids) can be measured by immunoassay in human blood. Cardiac myocytes constitute the major source of BNP related peptides. The main stimulus for peptide synthesis and secretion is myocyte stretch. Recently, cardiac fibroblasts have also been shown to produce BNP. Other neurohormones may stimulate cardiac BNP production in different cardiac cell types. In contrast to atrial natriuretic peptides (ANP/NT-proANP), which originate mainly from atrial tissue, BNP related peptides are produced mainly from ventricular myocytes. Ventricular (NT-pro)BNP production is strongly upregulated in cardiac failure and locally in the area surrounding a myocardial infarction. In peripheral organs, BNP binds to the natriuretic peptide receptor type A causing increased intracellular cGMP production. The biological effects include diuresis, vasodilatation, inhibition of renin and aldosterone production and of cardiac and vascular myocyte growth.[11]NT-proBNP has been recognized as marker of severity of cardiac dysfunction by many studies.[12]

Many recent studies conducted on subjects with heart failure have shown a strong positive association between, iron deficiency and elevated plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels in patients with heart failure.[13] This association was proved in various population groups and etiologies of heart failure.[14, 15] Some of the recent studies have also demonstrated that treatment of iron deficiency with intravenous iron preparations can reduce the pro- BNP levels and also positively impact the symptoms and mortality in patients with cardiac failure.[16] FAIR-HF trial by Gonzalez-Costello J et al has recommended a strong need for cardiologists to study the iron metabolism of patients with CHF with appropriate workup. It also strongly recommended initiation of treatment with IV iron if absolute or functional ID is found.

But there is very limited number of studies documenting the correlation between parameters of iron metabolism and pro- BNP levels in Indian patients. This kind of studies can enhance our understanding of the subjects and may pave the way for subsequent therapeutic trials on the subjects. Hence the present study has been conducted to enhance the available evidence on the association between iron parameters and pro BNP levels in Patients with CHF attending a tertiary care hospital.

AIMS & OBJECTIVES

Aim:

To study the association between iron studies and serum pro-BNP levels in heart failure patients.

Objectives:

1. To estimate the serum iron-related parameters (Serum ferritin, serum transferrin, and total iron binding capacity in patients presenting with heart failure to a tertiary care teaching hospital.

2. To estimate the serum pro-BNP (Brain natriuretic peptide levels in patients presenting with heart failure to a tertiary care teaching hospital.

3. To assess the correlation between the serum iron related parameters and serum pro-BNP levels in the study population.

REVIEW OF LITERATURE

Heart failure (HF) is a rapidly growing public health issue with an estimated prevalence of >37.7 million individuals globally. HF has numerous symptoms that affect the quality of life, including dyspnoea, fatigue, poor exercise tolerance, and fluid retention. Although the underlying causes of HF vary according to sex, age, ethnicity, comorbidities, and environment, the majority of cases remain preventable. HF is associated with increased morbidity and mortality and confers a substantial burden to the health-care system. HF is a leading cause of hospitalization among adults and the elderly. In the USA, the total medical costs for patients with HF are expected to rise from US$20.9 billion in 2012 to $53.1 billion by 2030. Improvements in the medical management of risk factors and HF have stabilized the incidence of this disease in many countries.[17]

Global Burden of heart failure

J.J.V McMurray and S Stewart have stated that chronic heart failure (CHF) imposes a heavy burden not only on patients and their families but also on society, through enormous use of health care resources. Prevalence of chronic heart failure was reported to be approximately 1–3%, rising to approximately 10% in the very elderly. Following a first hospital admission for heart failure, patients have a 5-year mortality of 75% — a survival rate worse than that for most forms of cancer. CHF impairs quality of life more than almost any other chronic medical problem. Over the past two decades, admissions of CHF have drastically increased. CHF was reported to account for about 5% of all medical admissions and approximately 2% of total healthcare expenditure. The authors came to a conclusion that, due to the increase in survival after acute myocardial infarction and aging of the population, there would be

a significant rise in the number of patients with CHF in most industrialized countries.[18]

Ambrosy, A. P et al., in their study have reported heart failure as a global pandemic which affected an estimated 26 million people worldwide and resulting in more than 1 million hospitalizations annually in both the United States and Europe. Although the outcomes for ambulatory heart failure patients with a reduced ejection fraction (EF) have improved with the discovery of multiple evidence-based drugs and device therapies, hospitalized heart failure (HHF) patients continue to experience unacceptably high post-discharge mortality and readmission rates that have not changed in the last 2 decades. In addition, the proportion of HHF patients classified as having a preserved EF continues to grow and may overtake HF with a reduced EF in the near future. However, the prognosis for HF with a preserved EF is similar and there are currently no available disease-modifying therapies. The authors have reviewed the global HHF registries to suggest the quality improvement initiatives, regional differences, and limitations from the available data.[19]

Cook.C et al, have carried out a study to estimate the global burden of heart failure as it imposed a direct cost to healthcare systems and indirect costs to society through morbidity. Authors have performed the estimations using World Bank data. The results have shown that the overall economic cost of HF in 2012 was estimated at $108 billion per annum. Direct costs accounted for ~60% ($65 billion) and indirect costs accounted for ~40% ($43 billion) of the overall spend. Heart failure spending varied widely between high-income and middle and low-income countries. High-income countries spend a greater proportion of direct costs: a pattern reversed for middle and low-income countries. Based on results, the authors have made

conclusions that heart failure imposes a huge economic burden, estimated at $108 billion per annum,which would continuously rise in the future.[20]

Salem Khal et al.,have carried out a study to describe both the direct (medical) and the indirect (morbidity and mortality) inpatient cost of congestive heart failure in a high-income non-Organization for Economic Cooperation and Development Middle Eastern country in relation to YLL (years of life lost) and YLD(years lived with disability).The authors have reported that cost of hospitalization, rehospitalization, and non-invasive and invasive procedures per 1000 HFrEF patients in US dollars (USD). Expressing results as per 1000 HFrEF capita revealed a DALY of 1480 +/- 1909 vs. 2177 +/- 2547 in women and men, respectively. The costs per HFrEF capita in USD were $909.00 +/- 676.1 for a single-day hospital stay, $7999 per single hospitalization, $12 311 +/- 13 840 for annual hospitalizations, $20 486 +/- 22 068 for all-cause hospitalizations, and $37 355 +/- 49 336 from the time of diagnosis until death or recovery. The authors have concluded that HFrEF imposed a substantial economic and disability burden on one non-Organization for Economic Cooperation and Development Middle Eastern country and men represented a higher economic burden than women.[21]

Stewart, S et al.,in their study to assess the future burden of heart failure in Scotland from contemporary epidemiological data have reported that there were currently estimated to be 40 000 men and 45 000 women aged ≥ 45 years with heart failure in Scotland. On the basis of population changes alone, these figures will rise in men and women by 12 300 (31%) and 7800 (17%) in the longer term (2020). On the same basis, the annual number of male and female GP visits is likely to rise by 35 200 (40%) and 17 300 (16%) by 2020. In the year 2000, about 3500 men and 4300 women

in Scotland had an incident hospital admission for heart failure. By the year 2020 these figures were likely to increase by 52% (1800 more) and 16% (717 more) in men and women, respectively. If recent trends in short-term case fatality rates continue to improve, the number of men who would survive this event will increase by 59% (1700 more). Overall, by 2020 the annual number of male and female hospital admissions associated with a principal diagnosis of heart failure is expected to increase by 34% (from 5500 to 7500) and by 12% (from 7800 to 8500), respectively. Based on the results the authors suggested that,unless rapid and major changes occur in the incidence of heart failure, the burden of this disorder will continue to increase and the increase is likely to occur in men. Future health service planning must take this into account.

Burden of heart failure in India

Vivek Chaturvedi et al.,conducted a study in India to determine the prevalence of heart failure in a rural community as well as tertiary hospital care setting.All adults (>20 years) with chronic breathlessness in six villages under a primary health care center in Northern India were identified and evaluated with astandardized questionnaire and physical examination by trained healthcare workers. For the systematic review, all published studies addressing HF or the burden of risk factors in India were identified. Out of the total study population the surveyed rural adult population of 10,163 patients, chronic breathlessness was present in 128 (1.3%). HF was present in 9% (n = 12), of which 67% (n = 8) had preserved left ventricular (LV) systolic function and 33% (n = 4) had LV systolic dysfunction. Therefore, the prevalence of HF in this general community was 1.2/1000. All patients with HF and preserved ejection fraction had poorly controlled hypertension. In the hospital study,

of 500 consecutive patients, 20.4% had HF. Rheumatic heart disease (52%) was the most common cause followed by ischemic heart disease (17%). The mean age of presentation was 39 ± 16 years. The prevalence of HF in the outpatient department patients was 22.5% below 30 years and 14.9% above 50 years, reflecting the young population of HF. The estimated prevalence of HF is about 1% of the total population or about 8–10 million individuals. The estimated mortality attributable to HF is about 0.1–0.16 million individuals per year. The results from the study demonstrated a low prevalence of symptomatic HF in the surveyed villages. And the authors have suggested that a significant proportion of this burden might be preventable with better screening and early and adequate treatment of the risk factors.[22]

Huffman et al.,in their study have stated that the incidence and prevalence rates of heart failure are rising due to population, epidemiological and health transitions. Based on disease-specific estimates of prevalence and incidence rates of heart failure, they conservatively estimated the prevalence of heart failure in India due to coronary heart disease, hypertension, obesity, diabetes and rheumatic heart disease to range from 1.3 to 4.6 million, with an annual incidence of 491 600-1.8 million. The double burden of rising cardiovascular risk factors and persistent 'pre-transition' diseases such as rheumatic heart disease, limited healthcare infrastructure, and social disparities contribute to these estimates. Staging of heart failure, introduced in 2005, provides a framework to target preventive strategies in patients at risk for heart failure (stage A), with structural disease alone (B), with heart failure symptoms (C) and with end-stage disease (D). Policy-level interventions, such as regulations to limit salt and tobacco consumption, are effective for primordial prevention and would have a wider impact on prevention of heart failure. Clinical preventive interventions and clinical quality improvement interventions, such as treatment of hypertension, atherosclerotic

disease, diabetes and acutely decompensated heart failure are effective for primary, secondary and even tertiary prevention.[23]

Iron and BNP:

Gary S. Francis in his study has stated that anaemia was common among patients with heart failure, probably occurring approximately in 20% of patients. Some anaemia was likely dilutional, but most was probably true anaemia due to chronic disease or iron deficiency. The degree of anaemia in patients with heart failure after acute myocardial infarction was associated with a poor prognosis, and anaemia in patients with chronic heart failure from any cause has repeatedly been demonstrated to predict a poor outcome. A consensus has seemingly emerged in the heart failure community that correction of a reduced hemoglobin (Hb) level is an attractive therapeutic target deserving of further study. Of interest, erythropoietin (EPO) levels were moderately elevated in patients with heart failure, more so in very severe heart failure (4). This was clearly a case where treatment precedes understanding of pathophysiology, a common occurrence throughout history.[24]

Schou, M et al.,have conducted a study to test their hypothesis that anaemia (World Health Organization criteria, hemoglobin levels <7.5 mmol/L for women and <8.0 mmol/L for men) and NT-pro-BNP were associated and evaluated how a possible association affects the prognostic value of each risk marker. They prospectively collected data from 345 patients who suffered from systolic heart failure at the baseline visit to the clinic (inclusion criterion left ventricular ejection fraction <0.45, no exclusion criteria). Follow-up was 30 months (median), and 70 events (mortality) occurred. Prevalence of anaemia was 27%. In a multivariate logistic regression model, the results showed that anaemia ($p = 0.041$) was closely associated

with NT-pro-BNP levels above the median (1,381 pg/ml) after adjustment for traditional confounders (left ventricular ejection fraction, age, body mass index, atrial fibrillation, chronic kidney disease). In an adjusted Cox proportional hazard model, the 2 parameters were associated with mortality after adjustment for traditional confounders (hazard ratio for anaemia 1.73, 95% confidence interval 1.06 to 2.83, p = 0.029; hazard ratio for NT-pro-BNP >1,381 pg/ml 2.68, 95% confidence interval 1.58 to 4.66, p <0.001). Patients with anaemia and high NT-pro-BNP levels had a fivefold increased risk for mortality (hazard ratio 4.77, 95% confidence interval 2.47 to 9.18, p <0.001). In conclusion, the authors have mentioned that anaemia was closely associated with NT-pro-BNP in patients with systolic heart failure, and anaemia and NT-pro-BNP carry independent prognostic information. Patients with anaemia and high levels of NT-pro-BNP have a markedly increased mortality risk.[25]

As Chronic heart failure and CRF associated with absolute or relative iron deficiency anaemia is a common problem,Toblli, J. E. et al., carried out a double-blind, randomized, placebo-controlled study to evaluate thepossible modifications in NT-pro-brain natriuretic peptide (NT-proBNP) and C-reactive protein (CRP) levels together with clinical and functional parameters, in a group of anaemic patients with chronic heart failure (CHF) and chronic renal failure (CRF) receiving intravenous iron therapy, without recombinant human erythropoietin (rhEPO), versus placebo.

Forty patients with hemoglobin (Hb) <12.5 g/dl, transferrin saturation <20%, ferritin <100 ng/ml, creatinine clearance (CrCl) <90 ml/min, and left ventricular ejection fraction (LVEF) < or =35% were randomized into 2 groups (n = 20 for each). For 5 weeks, group A received the isotonic saline solution and group B received iron sucrose complex, 200 mg weekly. Minnesota Living with Heart Failure Questionnaire

(MLHFQ) and 6-min walk (6MW) test were performed. NT-pro brain natriuretic peptide and CRP were evaluated throughout the study. No patients received erythroprotein any time. After a follow up for 6 months, group B showed better hematology values and CrCl ($p < 0.01$) and lower NT-proBNP (117.5 +/- 87.4 pg/ml vs. 450.9 +/- 248.8 pg/ml, $p < 0.01$) and CRP (2.3 +/- 0.8 mg/l vs. 6.5 +/- 3.7 mg/l, $p < 0.01$). There was a correlation initially ($p < 0.01$) between Hb and NT-proBNP (group A: $r = -0.94$ and group B: $r = -0.81$) and after 6 months only in group A: $r = -0.80$. Similar correlations were observed with Hb and CRP. Left ventricular ejection fraction percentage (35.7 +/- 4.7 vs. 28.8 +/- 2.4), MLHFQ score, and 6MW test were all improved in group B ($p < 0.01$). Additionally, group B had fewer hospitalizations: 0 of 20 versus group A, 5 of 20 ($p < 0.01$; relative risk = 2.33). Based on theresults,authors have come to a conclusion that Intravenous iron therapy without rhEPO substantially reduced NT-proBNP and inflammatory status in anaemic patients with CHF and moderate CRF. This situation was associated with an improvement in LVEF, NYHA functional class, exercise capacity, renal function, and better quality of life.[16]

In a cohort study by Henry.J et al.,they have reported that a low prevalence of ID and anaemia was observed in the SALIA cohort of healthy elderly women. Prohepcidin was not associated with the standard parameters of iron metabolism and BNP. Authors have confirmed an expected negative correlation between iron status measures and BNP.[15]

Avni, T.et al., have conducted a systematic review and meta-analysis of all randomized control trials that compared iron with no therapy for CHF patients with iron deficiency, whether or not they were anaemic. Authors have examined electronic

databases as well as haematology and cardiology conferences up to August 2011. The primary outcome was the effect of iron on QOL parameters such as New York Heart Association (NYHA) class and the Minnesota Living With Heart Failure Questionnaire (MLHWFQ). Secondary outcomes included all-cause mortality, mean ejection fraction; 6 min walk distance (6MWD), hospitalizations due to any cause, iron indices, C-reactive protein levels, and adverse events. Four trials performed fulfilled the inclusion criteria. A total of 370 patients were treated with i.v. iron, compared with 224 control patients. There was asignificant improvement in QOL in the iron arm according to the MLWHFQ score at 26 weeks, with a weighted mean difference of -18.00 (-22.54, -13.46, I(2) = 0%]. The point estimate for improvement in NYHA class was in favor of iron. Iron reduced the number of hospitalizations and C-reactive protein levels, and increased the 6MWD and mean ejection fraction. Iron indices were significantly improved without a change in hemoglobin levels. No increase in the rate of adverse events was found. Authors have concluded thatintravenous Iron therapy was associated with improved QOL parameters, reduction in hospitalizations, and increased 6MWD. Treatment with i.v. iron is safe, with no increased rate of adverse events.[26]

Bosselmann, H et al., carried out a study to assess whether the prognostic significance of cardiovascular (CV) biomarkers, were affected by renal dysfunction (RD) in systolic heart failure (HF). Clinical data and laboratory tests from 424 patients with systolic HF were collected prospectively. The patients were followed for 4.5 years (interquartile range: 2-7.7 years). CV biomarkers were analyzed on frozen plasma, and renal function was estimated by the Modification of Diet in Renal Disease (MDRD) formula. Cox proportional hazard models for mortality risk were constructed and tests for interaction between each CV biomarker and RD were

performed. Results from the study showed that estimated glomerular filtration rate (eGFR) was 68 ml/min/1.73 m^2 (18-157). A total of 252 patients died. All five biomarkers--log(NT-proBNP) (HR: 2.13, 95% CI: 1.57-2.87:, P<0.001), hsTNT (HR: 3.07, 95% CI: 1.90-4.96 P<0.001), proANP (HR: 1.02, 95% CI: 1.01-1.03, P<0.001), copeptin (HR: 1.02, 95% CI: 1.01-1.03, P=0.008) and proADM (HR: 2.37, 95% CI: 1.66-3.38, P<0.001) were associated with mortality risk, but not affected by RD (P>0.05 for all interactions). Authors have come to a conclusion that established and new CV biomarkers were closely associated with renal function in HF. However, their prognostic significance was not affected by RD, and all CV biomarkers can be used for risk stratification independently of renal function.[27]

In their study, Delaporta, P.et al., have prospectively evaluated plasma NT-proBNP levels in 187 adult patients aged 19-54 years with beta-thalassemia(TM). Possible correlations with the proposed recently cardiac Iron concentration based on an equation derived from heart T2* assessment by MRI: [Fe] = 45.0 x [T2*](-1.22) with [Fe] in milligrams per gram dry weight and T2* in milliseconds were explored. Authors have found that 143 patients had no cardiac hemosiderosis, defined as [Fe] < 1.1 mg/g dry weight, corresponding to T2* > 20 ms and 44 patients had cardiac hemosiderosis, defined as [Fe] > 1.2mg/g dry weight. The main results of the study showed that: a) NT-proBNP levels were markedly increased in thalassemic patients (152.2 +/- 190.1 pg/mL, ranged from 6.0 to 1336.0 pg/mL compared to normal control levels 40.1 +/- 19.7 pg/mL, p < 0.001, b) NT-proBNP levels were significantly higher in patients with cardiac hemosiderosis compared to patients without cardiac hemosiderosis (185.1 +/- 78.0 vs 128.9 +/- 20.2 pg/mL, p < 0.05), c) NT-proBNP levels correlated with [Fe] values (r = 0.387, p < 0.001). This correlation was significant in patients with cardiac hemosiderosis (r = 0.520, p < 0.001), but not

in patients without cardiac hemosiderosis ($p > 0.1$), and d) no significant correlation was found between NT-proBNP levels and left ventricular ejection fraction values, ($p > 0.3$). This study by Delaporta, P et al., has demonstrated for first time the significant association of NT-proBNP levels and cardiac iron concentration in patients with beta-thalassemia major linking blood chemistry and imaging techniques..[14]

Klip, I. T. et al., have studied the clinical associates of ID and its prognostic consequences in an international pooled cohort comprising 1,506 patients with chronic HF.Results from the study showed iron deficiency (defined as a ferritin level <100 mug/L or ferritin 100-299 mug/L with a transferrin saturation <20%) in 753 patients (50%). Anaemic patients were more often iron deficient than nonanaemic patients (61.2% vs 45.6%, $P < .001$). Other independent predictors of ID were higher New York Heart Association class, higher N-terminal pro-brain-type natriuretic peptide levels, lower mean corpuscular volume levels, and female sex (all $P < .05$). During follow-up (median 1.92 years, interquartile range 1.18-3.26 years), 440 patients died (29.2%). Kaplan-Meier survival analysis revealed ID as a strong predictor of mortality (log-rank chi(2) 10.2, $P = .001$). In multivariable hazard models, ID (but not anaemia) remained a strong and independent predictor of mortality (hazard ratio 1.42, 95% confidence interval 1.14-1.77, $P = .002$). Finally, the presence of ID significantly enhanced risk classification and integrated discrimination improvement when added to a prediction model with established risk factors. From the observations, the authors concluded that iron deficiency was common in patients with chronic HF, relates to disease severity, and is a strong and independent predictor of outcome and ID appears to have greater predictive power than anaemia.[28]

As iron deficiency anaemia is the most common single cause of anaemia worldwide, Martinez-Quintana, E.et al., have conducted a study on 278 patients to estimate the prevalence of anaemia in adult congenital heart disease (ACHD) patients, compare different hematology parameters between hypoxemic and non-hypoxemic ACHD patients, and determine which parameters are to be considered for detecting iron deficiency anaemia in hypoxemic ACHD patients. Out of the total study population, 60% of them were males. Two hundred forty-five patients were non-hypoxemic and 33 patients were hypoxemic. Hypoxemic ACHD patients had significant higher hemoglobin concentration (g/dL) (17.5 +/- 3.5 vs. 14.6 +/- 1.7, P <.001), red cell distribution width (RDW) (%) (17.0 +/- 3.3 vs. 14.1 +/- 7.6, P <.034), apoferritin (ng/mL) (19.8 [4.1-147.2] vs. 38.0 [6.7-191.2], P =.019), CRP (mg/dL) (0.50 [0.0-3.8] vs. 0.12 [0.0-1.4], P <.001), and NT-proBNP (pg/mL) (409.3 [33.3-9830.8] vs. 5.2 [0.0-1068.4], P <.001) levels than non-hypoxemic ACHD patients. Serum iron, total iron-binding capacity, and transferrin saturation index were not statistically significant between hypoxemic and non-hypoxemic ACHD patients. In the hypoxemic group, 15 (45%) patients had apoferritin levels <20 ng/mL and eight (24%) patients developed microcytosis and hypochromia. An RDW above the normal range (>14.5%) in hypoxemic ACHD patients allowed the detection of an apoferritin level <20 ng/mL with a sensitivity of 93%. Based on the results the authors came to a conclusion that RDW seems to be a useful and economical tool to detect low serum apoferritin levels in hypoxemic ACHD patients.[29]

IRON DEFICIENCY AND HEART FAILURE

As the management of ID is becoming an important therapeutic target in patients with CHF, Gonzalez-Costello, J. et al have reviewed iron metabolism in the context of anaemia and heart failure. They also focused on the importance of diagnosing and treating ID, preferably with IV iron preparations, in patients with CHF. Authors have concluded that after the positive findings of the FAIR-HF trial, there is a need for cardiologists to study the iron metabolism of patients with CHF, and it seems reasonable to undertake a workup evaluation if absolute or functional ID is found and start treatment with IV iron, although mortality and morbidity studies would help to further define the role of IV iron in CHF and its usefulness associated with ESA agents in patients with anaemia and CHF.[2]

In a study by Jankowska E. A.et al., they have investigated whether ID predicted exercise intolerance in patients with systolic chronic heart failure (CHF).As a part of the study,authors have prospectively studied 443 patients with stable systolic CHF (age 54 +/- 10 years, males 90%, ejection fraction 26 +/- 7%, New York Heart Association Class I/II/III/IV 49/188/180/26). ID was defined as serum ferritin <100 mug/L or serum ferritin 100-300 mug/L with serum transferrin saturation <20%. Exercise capacity was expressed as peak oxygen consumption (VO^2) and ventilatory response to exercise (VE-VCO^2 slope). ID was present in 35 +/- 4% (+/-95% confidence interval) of patients with systolic CHF. Those with ID had reduced peak VO^2 and increased VE-VCO^2 slope as compared to subjects without ID (peak VO^2: 13.3 +/- 4.0 versus 15.3 +/- 4.5 mL*min*kg, VE-VCO^2 slope: 50.9 +/- 15.8 versus 43.1 +/- 11.1, respectively, both $P < .001$, $P < .05$). In multivariable models, the presence of ID was associated with reduced peak (VO^2) (beta = -0.14, $P < .01$ $P <$

.05) and higher VE-VCO^2 slope (beta = 0.14, P < .01 P < .05), adjusted for demographics and clinical variables. Analogous associations were found between serum ferritin, and both peak VO^2 and VE-VCO^2 slope (P < .05). Finally, authors have concluded that ID independently predicts exercise intolerance in patients with systolic CHF, but the strength of these associations was relatively weak.[30]

Jankowska, E. A.et al.,have investigated iron status in a broad spectrum of patients with systolic HF in order to determine the changes in iron status in parallel with disease progression, and to associate iron status with long-term prognosis. Serum concentrations of ferritin, transferrin saturation (Tsat), soluble transferrin receptor (sTfR), and hepcidin were assessed as the biomarkers of iron status in 321 patients with chronic systolic HF [age: 61 +/- 11 years, men: 84%, left ventricular ejection fraction: 31 +/- 9%, New York Heart Association (NYHA) class: 72/144/87/18] at a tertiary cardiology centre and 66 age- and gender-matched healthy subjects. Compared with healthy subjects, asymptomatic HF patients had similar hematological status, but increased iron stores (evidenced by higher serum ferritin without distinct inflammation, P < 0.01) with markedly elevated serum hepcidin (P < 0.001). With increasing HF severity, patients in advanced NYHA classes had iron deficiency (ID) (reduced serum ferritin, low Tsat, high sTfR), Iron-restricted erythropoiesis (reduced haemoglobin, high red cell distribution width), and inflammation (high serum high-sensitivity-C-reactive protein and interleukin 6), which was accompanied by decreased circulating hepcidin (all P < 0.001). In multivariable Cox models, low hepcidin was independently associated with increased 3-year mortality among HF patients (P < 0.001). The results from the study have shown that increased level of circulating hepcidin characterizes an early stage of HF, and was not accompanied by

either anaemia or inflammation. The progression of HF was associated with the decline in circulating hepcidin and the development of ID.[31]

Jankowska, E. A.et al., in their study “Iron deficiency and heart failure: diagnostic dilemmas and therapeutic perspectives”,have stated that iron is a micronutrient essential for cellular energy and metabolism, necessary for maintaining body homeostasis. Iron deficiency is an important co-morbidity in patients with heart failure (HF). A major factor in the pathogenesis of anaemia, it is also a separate condition with serious clinical consequences (e.g. impaired exercise capacity) and poor prognosis in HF patients. Experimental evidence suggests that iron therapy in iron-deficient animals may activate molecular pathways that can be cardio-protective. Clinical studies have demonstrated favorable effects of i.v. iron on the functional status, quality of life, and exercise capacity in HF patients. It is hypothesized that i.v. iron supplementation may become a novel therapy in HF patients with iron deficiency.[32]

Beavers, C. J.et al., in their study have stated that ,despite advances in the management of heart failure (HF), quality of life and other outcomes remain suboptimal for many patients. Anaemia and iron deficiency are comorbidities associated with adverse outcomes, although their pathophysiology in the setting of HF is not entirely understood. Despite its many practical advantages, minimal evidence exists to support the use of oral iron supplementation in this setting. In contrast, intravenous iron has been the subject of several recent investigations, demonstrating improvements in both surrogate and clinical endpoints, although benefits seem to be the most substantial in patients with concomitant anaemia. Based on the currently available evidence, treatment of iron deficiency appears to confer benefit in patients

with HF, whereas strategies aimed at improving hemoglobin alone do not. Included is a review of the pathophysiology of these conditions in the setting of HF, clinical trials evaluating pharmacologic therapy, and recommendations for management.[33]

Cohen-Solal, A. et al.,have stated that, although iron deficiency is easily diagnosed with two biomarkers (serum ferritin and transferrin saturation), it is underdiagnosed in patients with HF. Iron is not only necessary for red blood cells, but also for cells in tissues with high-energy demands (heart, muscle, brain). Even before the onset of anaemia, HF patients with iron deficiency have decreased physical and cognitive performances and a poorer quality of life. Moreover, iron deficiency is a risk factor, independent of anaemia, of unfavorable outcome (death or heart transplantation) in patients with chronic HF. Several randomized controlled studies have shown improvement in exercise capacity, New York Heart Association functional class and quality of life after correction of iron deficiency. The results of these clinical trials, which are supported by European guidelines, suggest considering iron deficiency in HF as a possible therapeutic target.[34]

Von Haehling, S. et al, has reported that anaemia and iron deficiency were frequent co-morbidities in patients with chronic heart failure. Both are bound to worsen an already reduced exercise capacity in these patients. The authors have stated that two clinical entities should be differentiated in this context: absolute and functional iron deficiency, the first being an absolute deficiency of iron, the second representing a disturbed mobilization capacity. The FAIR-HF study has shown that intravenous iron administration can improve quality of life and exercise capacity in affected patients. A correct diagnosis can easily be arrived at using parameters such as serum ferritin and transferrin saturation. Replenishing iron stores is most useful using

the intravenous route, and administered doses need to be adjusted to individual needs.[35]

Yeo, T. J.et al., have carried out a study to assess the prevalence, clinical correlates, functional significance and prognosis of ID in HF patients, compared with community-based controls in a multi-ethnic Southeast Asian population. Iron status was assessed in 751 HF patients (age 62.0 +/- 12.2 years, 75.5% men, 64.7% Chinese, 23.9% Malay, 10.2% Indian) and 601 controls (age 56.9 +/- 10.4 years, 49.8% men, 70.9% Chinese, 21.5% Malay, 7.2% Indian). ID, defined as ferritin <100 microg/L or ferritin 100-300 microg/L and transferrin saturation (Tsat) <20%, was present in 39.3% of controls and 61.4% of HF [odds ratio (OR) 3.5, 95% confidence interval (CI) 2.5-4.9, adjusting for clinical covariates]. Independent correlates of ID in HF were Indian ethnicity (OR 2.4 vs. Chinese, 95% CI 1.2-5.0), female gender (OR 2.8, 95% CI 1.7-4.8), larger body mass index (OR 1.05/unit increase, 95% CI 1.01-1.1) and decreased left ventricular ejection fraction (OR 1.03/unit decrease, 95% CI 1.01-1.04). In a subset of 48 HF patients undergoing cardiopulmonary exercise testing, Tsat correlated with peak oxygen consumption (rho = 0.53, P < 0.01), independent of baseline characteristics. The HF patients with Tsat<20% as well as anaemia showed the poorest event-free survival after adjusting for clinical covariates. Based on the results,authors have concluded that iron deficiency was highly prevalent and independently related to functional capacity and outcomes in the study cohort and have suggested a pathophysiological role of ID in HF and support its importance as a therapeutic target in Southeast Asian patients with HF[36]

To identify the prevalence of ID in an HF clinic and evaluate whether ID is associated with increased plasma concentrations of different cardiovascular

biomarkers that carry a poor prognosis, Schou, M. et al., have carried out a prospective study among including149 patients with systolic HF referred to an outpatients HF clinic. ID was defined as ferritin<100 mug/L or ferritin 100-300 mug/L and Tranferin-saturation<0.20. Five different cardiovascular biomarkers were analyzed on the frozen plasma. Results showed that patients had a median age of 70 (Interquartile range: 64-75) years, 25% were females, 29% were in functional class III-IV and LVEF was 32 (27-39) %. The prevalence of ID was 45% (95%-confidence interval (CI): 37-53%). In multivariate analyses, ID was not associated with plasma concentrations of troponin I, NT-proBNP, MR-proANP, chromogranin An or copeptin (P>0.05 for all) but with plasma concentrations of hs-CRP (odds ratio: 2.03, 95%-CI: 1.02-4.02, P=0.043). Authors have concluded that ID was frequent in an outpatient HF clinic. ID was not associated with cardiovascular biomarkers after adjustment for traditional confounders. Inflammation, but not neurohormonal activation is associated with ID in systolic HF.[37]

Silverberg, D. S. et al., in their study “Is Correction of Iron Deficiency a New Addition to the Treatment of the Heart Failure?” has reported that anaemia was present in about 40% of heart failure (HF) patients. Iron deficiency (ID) was present in about 60% of the patients with anaemia (about 24% of all HF patients) and in about 40% of patients without anaemia (about 24% of all HF patients). Thus ID was present in about half the patients with HF. The ID in HF was associated with reduced iron stores in the bone marrow and the heart. ID is an independent risk factor for severity and worsening of the HF. Correction of ID with intravenous (IV) iron usually corrects both the anaemia and the ID. Currently used IV iron preparations are very safe and effective in treating the ID in HF whereas little information was available on the effectiveness of oral iron. In HF IV iron correction of ID is associated with

improvement in functional status, exercise capacity, quality of life and, in some studies, improvement in therate of hospitalization for HF, cardiac structure, and function, and renal function. Authors have recommended large long-term adequately-controlled intervention studies to clarify the effect of IV iron in HF. Several heart associations suggested that ID should be routinely sought for in all HF patients and corrected if present.[38]

Ebner, N. et al., have conducted a study to assess the impact of iron deficiency and anaemia on exercise capacity and outcomes in patients with chronic heart failure.Theyhave enrolled 331 out-patients with stable chronic HF (mean age: 64 +/- 11 years, 17% female, left ventricular ejection fraction [LVEF] 35 +/- 13%, body mass index [BMI] 28.5 +/- 5.2 kg/m(2), New York Heart Association [NYHA] class 2.2 +/- 0.7, chronic kidney disease 35%, glomerular filtration rate 61.7 +/- 20.1 mL/min). Anaemia was defined according to World Health Organization criteria (haemoglobin [Hb] < 13 g/dL in men, < 12 g/dL in women). ID was defined as serum ferritin < 100 mug/L or ferritin < 300 mug/L with transferrin saturation (TSAT) < 20%. Exercise capacity was assessed as peak oxygen consumption (peak VO^2) by spiroergometry and 6-minute walk test (6MWT). A total of 91 (27%) patients died from any cause during a mean follow-up of 18 months. At baseline, 98 (30%) patients presented with anaemia and 149 (45%) patients presented with ID. A significant reduction in exercise capacity was seen in parallel to decreasing Hb levels ($r = 0.24$, $p < 0.001$). In patients with anaemia and ID (n = 63, 19%), exercise capacity was significantly lower than in patients with ID or anaemia only. Cox regression analysis showed that after adjusting for NYHA, age, hsCRP and creatinine anaemia is an independent predictor of mortality in patients with HF (hazard ratio [HR]: 0.56, 95% confidence interval [CI]: 0.33-0.97, p = 0.04).From the results, authors have

concluded that the impact of anaemia on reduced exercise capacity and on mortality is stronger than that of ID.[39]

As iron deficiency (ID) has been identified as an important co-morbidity in patients with heart failure (HF), intravenous iron therapy reduced symptoms and re-hospitalizations of iron-deficient patients with HF in randomized trials. Wienbergen, H. et al carried out a multicenter study to investigate the actual ongoing management of iron status in patients with HF. Consecutive patients with HF and ejection fraction <40% were recruited and analyzed from December 2010 to October 2015 by 11 centers in Germany and Switzerland. Of 1,484 patients with HF, iron status was determined in only 923 patients (62.2%), despite the participation of the centers in a registry focusing on ID and despite guideline recommendation to determine iron status. In patients with determined iron status, a prevalence of 54.7% (505 patients) for ID was observed. Iron therapy was performed in only 8.5% of the iron-deficient patients with HF; 2.6% were treated with intravenous iron therapy. The patients with iron therapy were characterized by a high rate of symptomatic HF and anaemia. In conclusion, the authors have mentioned that despite strong evidence of beneficial effects of iron therapy on symptoms and re-hospitalizations, diagnostic and therapeutic efforts on ID in HF are low in the actual clinical practice, and they suggested that the awareness to diagnose and treat ID in HF should be strongly enforced.[40]

Doehner, W. et al., in their review, have suggested a diagnostic algorithm for ID. Confounding factors for diagnosis and adequate treatment of ID in HF were explained. Iron deficiency (ID) occurs in up to 50% of patients with heart failure (HF). Even without the presence of anaemia ID contributes to more severe symptoms,

increased hospitalization, and mortality. A number of randomized controlled trials demonstrated the clinical benefit of replenishment of iron stores with the improvement of symptoms and fewer hospitalizations. Assessment of iron status should, therefore, become routine assessment in newly diagnosed and in symptomatic patients with HF. The ID can be identified with simple and straightforward diagnostic steps. Assessment of Ferritin (indicating iron stores) and transferrin saturation (TSAT, indication capability to mobilize internal iron stores) are sufficient to detect ID.The authors have suggested that regular workups for iron deficiency parameters may benefit patients with heart failure by providing symptomatic improvements and fewer hospitalizations.[41]

In their paper, Drozd, M.et al.,have provided information on how to diagnose ID in HF and have discussed pros and cons of different iron preparations and their results of major trials implementing iron supplementation in HF patients, in order to provide practical guidance for clinicians on how to manage ID in patients with HF. In patients with heart failure (HF), iron deficiency (ID) correlates with decreased exercise capacity and poor health-related quality of life and predicts worse outcomes. Both absolute (depleted iron stores) and functional (where iron is unavailable for dedicated tissues) ID can be easily evaluated in patients with HF using standard laboratory tests (assessment of serum ferritin and transferrin saturation). Intravenous iron therapy in iron-deficient patients with HF and reduced ejection fraction has been shown to alleviate HF symptoms and improve exercise capacity and quality of life.[42]

As heart failure (HF) is a common, costly, disabling, and deadly clinical syndrome and often associated with one or several co-morbidities complicating its treatment or worsening its symptoms. During the last decade, iron deficiency (ID) got

recognized as a frequent, debilitating yet easily treatable co-morbidity in HF. Van Aelst, L. N. L.et al., in their review have focused on new evidence that emerged during the last 5 years and discusses the epidemiology, the causes, and the clinical consequences of ID in HF. Recent findings have shown that, apart from replenishing iron stores, intravenous iron improves patient's symptoms, perceived quality of life (QoL), exercise capacity, and hospitalization rates. These beneficial effects cannot be attributed to oral iron, as increased hepcidin levels, typical in inflammatory states such as HF, preclude resorption of iron from the gut. Intravenous iron is the only valid treatment option for ID in HF.[43]

Anand et al. conducted a study to investigate the relationship between anaemia, the severity of CHF, and clinical outcomes. Hemoglobin concentration (Hb) was measured in 912 subjects with CHF enrolled in the Randomized Etanercept North American Strategy to Study Antagonism of Cytokines trial. In a subgroup of 69 subjects, cardiac MRI was performed at randomization and 24 weeks later. Anaemia (Hb ≤12.0 g/dL) was present in 12% of subjects. Cox regression analysis indicated that for every 1-g/dL-higher baseline Hb, the risk of mortality was 15.8% lower (P=0.0009) and the risk of mortality or hospitalization for heart failure was 14.2% lower (P<0.0001). Greater CHF severity was associated with significantly lower Hb concentrations. An increase in Hb over time was associated with a decrease in left ventricular mass and lower mortality, whereas a decrease in Hb over time was associated with an increase in left ventricular mass and higher mortality. In multivariate analysis, anaemia remained a significant, independent predictor of death or hospitalization for heart failure, with both outcomes being significantly higher in all NYHA classes. Based on the results, authors have concluded that anaemia was frequently present in patients with CHF. Lower Hb was associated with greater

disease severity, a greater left ventricular mass index, and higher hospitalization and mortality rates.[44]

Mikhail Kosiborod MD et al. carried out a study to determine the prognostic value of hematocrit level in a cohort of elderly patients hospitalized with heart failure.Authors have studied a consecutive sample of 2281 patients aged 65 years or older who had been admitted with a principal discharge diagnosis of heart failure. The mean (± SD) age of the patients was 79 ± 8 years; 58% (n = 1324) were women. Their median hematocrit was 38% (25th to 75th percentile, 33% to 42%). Lower hematocrits were associated with a higher mortality. After adjusting for demographic and clinical factors, each 1% lower hematocrit was associated with a 2% greater 1-year mortality (*P* = 0.007). Compared with patients with a hematocrit >42%, those with a hematocrit ≤27% had a 40% greater 1-year mortality (hazard ratio [HR] = 1.40; 95% confidence interval [CI]: 1.02 to 1.92; *P* = 0.04). This increased risk was similar to that conferred by traditional risk factors, including a left ventricular ejection fraction ≤20% (HR = 1.50; 95% CI: 1.20 to 1.86). Lower hematocrits were also associated with a greater risk of hospital readmission. Based on the results, authors have come to a conclusion that anaemia was associated with an increased risk of death and re-hospitalization in older patients with heart failure but whether anaemia is a direct cause of worse outcomes or a marker for other causal factors, was not known.[45]

MATERIAL & METHODS

Study site: The study was conducted in KLES Dr.Prabhakar Kore Hospital, Belgaum.

Study population: The study population included patients admitted in the wards and ICU of General Medicine at the study setting with congestive heart failure

Study design: The study was a cross sectional study.

Sample size: Considering the estimated frequency of an outcome in study population as 37%, 10% absolute precision and 95% confidence level, the total number of subjects required in the final analysis would be 90. To account for non-participation and loss to follow up of about 5% it was decided to sample 94 subjects into the study population at the time of planning the study. The final analysis included 93 subjects.

The sample size is calculated by the following formula:

N= 4PQ/D2

Where N=Sample size

P = Prevalence of the disease Q= 100- P

D = Absolute error taken as 10%

(P = 37; Q = 63; D=10)

Sampling method: The study subjects were selected using purposive sampling technique.

Study duration: The data collection/n for the study was carried out 1STJanuary 2016 to 31ST December 2017

Inclusion Criteria:

1. A documented history of CHF of≥6 months
2. LVEF ≤45% as assessed by Echocardiography
3. Clinical stability and unchanged medications for ≥ 1 months

Exclusion criteria:

1. Acute coronary syndromes, coronary revascularization or any major surgery within the 3 months preceding study.
2. Any acute/chronic illness that might influence iron metabolisms such as known malignancy, infection, renal diseases requiring dialysis, and hematological diseases.
3. Any anaemia or/and ID treatment in the past 12 months.
4. Blood transfusions in the past 3 months, erythropoietin therapy, intravenous iron infusions, and also any nutritional supplements potentially containing iron.
5. Pregnancy- Iron deficiency anaemia occurs in many pregnant women because their iron stores need to serve their own increased blood volume as well as be a source of hemoglobin for the growing fetus, and for placental development.

Study methodology:

- A detailed history and clinical examination were done of all Heart failure patients.

- Anaemia was defined as hemoglobin level<12 g/dL in women and<13 g/dL in men.

- The following blood biomarkers reflecting iron metabolism were assessed directly: serum concentrations of iron (mg/L), ferritin (mg/L), and total iron-binding capacity (TIBC, mg/L). Transferrin saturation (Tsat) was calculated as a ratio serum iron (mg/L) and TIBC (mg/L), multiplied by 100 and expressed in percent. Iron deficiency was defined prospectively as serum ferritin <100 mg/L, or serum ferritin ≥100 mg/L and ≤300 mg/L with Tsat, <20%.

- Plasma concentration of N-terminal pro-type Brain natriuretic peptide (NT-proBNP) was measured by using the *Elecsys® NT-proBNP* immunochemistry assay from Roche Diagnostics Limited. Sample material used was patient's serum (50µL). The measuring range of serum nT-proBNP was from 5 - 35,000 ng/L.

Ethical considerations:

Approval of the institute Human Ethics committee was obtained. Informed written consent was obtained from all the participants, after explaining the objectives of the study, risks, and benefits involved and voluntary nature of their participation. The personal details of the patients were kept confidential throughout the study.

Statistical Methods:

Serum iron metabolism-related parameters and the proBNP values were considered as primary variables of interest. Demographic parameters like age, gender, clinical parameters like etiology of heart failure, echocardiographic parameters etc. were considered as other variables of interest.

Descriptive analysis: Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables. Data was represented using appropriate diagrams like bar diagram, pie diagram, and box plots.

The association between categorical explanatory variables and quantitative outcomes was assessed by comparing the mean values. The mean differences along with their 95% CI were presented. Independent sample t-test/ ANOVA was used to assess statistical significance. Association between quantitative explanatory and outcome variables was assessed by calculating person correlation coefficient and the data was represented in a scatter diagram.

P value < 0.05 will be considered statistically significant. IBM SPSS version 22 was be used for statistical analysis.[46]

RESULTS

Table 1: Descriptive analysis for Age in study population (N= 93)

Parameter	Mean ±STD	Median	Min	Max	95% C.I. for EXP(B)	
					Lower	Upper
Age	62.43 ± 9.92	63.00	41.00	88.00	60.39	64.47

The mean age was 62.43 ± 9.92 in the study population. Youngest participant was 41 years and oldest participant was 88 years in the study group (table 1)

Table 2: Descriptive analysis of Age Group in study population (N=93)

Age Group	Frequency	Percentage
Up to 50	12	12.90%
51 to 60	27	29.03%
61 to 70	36	38.71%
71 and above	18	19.35%

Among the study population, 12 (12.90%) participants were aged below 50 years, 27 (29.03%) were aged 51 to 60 years, 36 (38.71%) were aged 61 to 70 years, 18 (19.35%) were above 71 years. (Table 2)

Figure 1: Pie chart of Age Group distribution in study population (N=93)

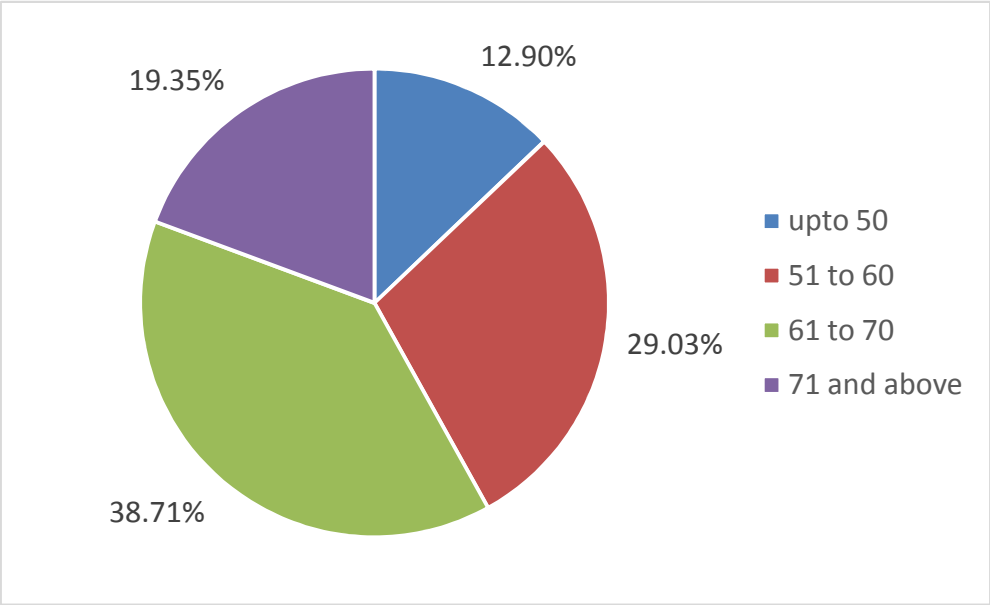


Table 3: Descriptive analysis of Gender in study population (N=93)

Gender	Frequency	Percentage
Male	75	80.65%
Female	18	19.35%

Among the study population, male participants were 75(80.65%)and remaining 18 (19.35%) were female participants. (Table 3)

Figure 2: Pie chart of gender distribution in study population (N=93)

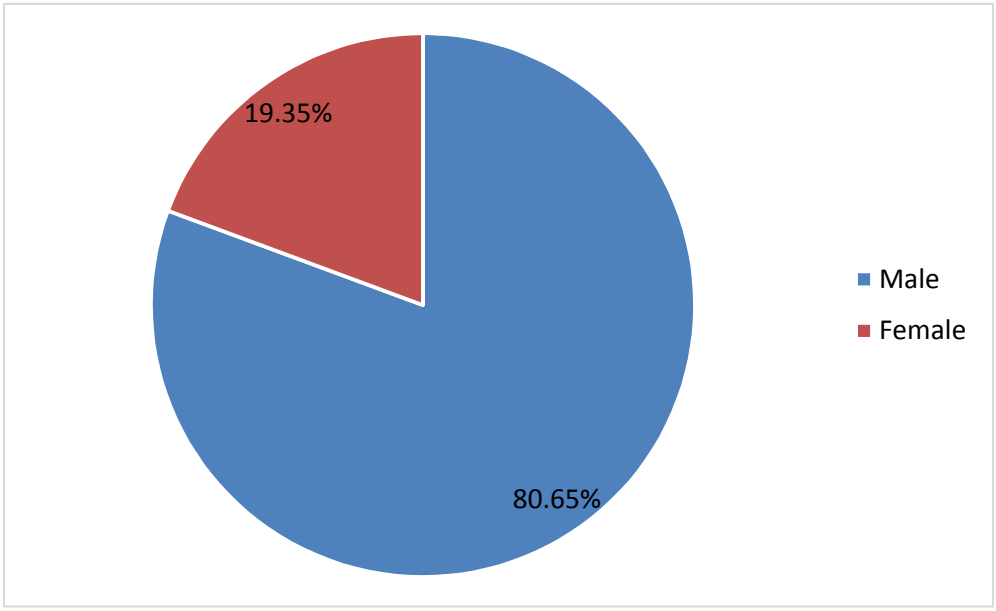


Table 4: Descriptive analysis of Diagnosis in study population (N=93)

Diagnosis	Frequency	Percentage
Hypertension	63	67.7 %
Type 2 Diabetes Mellitus	43	46.2 %

Out of 93 subjects, the most common co-morbidity was hypertension seen in 63 (67.7%) followed by Type 2 Diabetes Mellitus was seen in 43 (46.2%) subjects. (Table 4).

Table 5: Descriptive analysis for Serum pro BNP in study population (n= 93)

Parameter	Mean ±STD	Median	Min	Max	95% C.I. for EXP(B)	
					Lower	Upper
Serum pro BNP	7640.28 ± 7381.74	5465.0	66.4	33447.0	6120.03	9160.54

The mean serum pro BNP level was 7640.28±7381.74 in the study population. Lowest level was 66.4 and highest level was 33447.0 in the study group (table 5)

Table 6: Descriptive analysis of serum pro BNP in study population (n=93)

Pro BNP	Frequency	Percentage
Normal(<1800ng/L)	23	24.73%
High(>1800ng/L)	70	75.27%

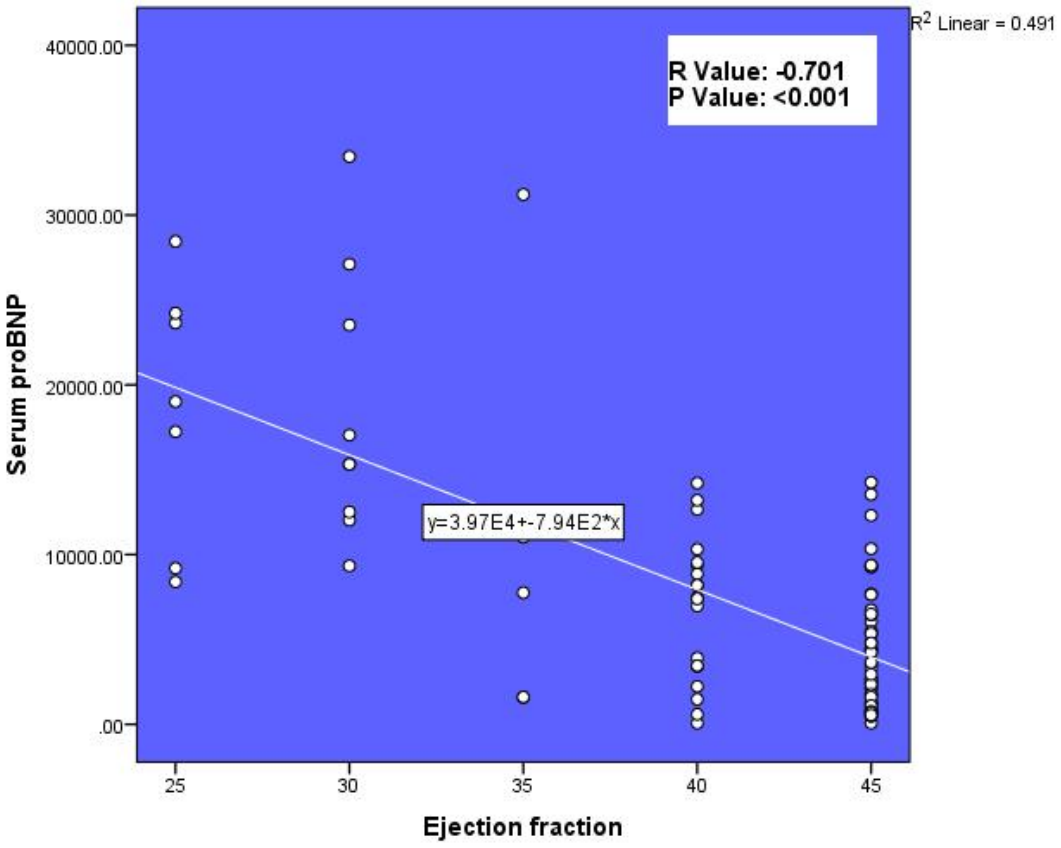
Majority of subjects (75.27%) reported as high proBNP level remaining (24.73%) subjects reported normal level (table 6)

Table 7: Descriptive analysis for Ejection fraction(%) in study population (n= 93)

Parameter	Mean ±STD	Median	Min	Max	95% C.I. for EXP(B)	
					Lower	Upper
Ejection fraction(%)	40.38 ± 6.52	45.00	25.00	45.00	39.03	41.72

The mean ejection fraction level(%) was 40.38 ± 6.52 in the study population. Lowest level was 25% and highest level was 45% in the study group (table 7)

Figure 8: Correlation between ejection fraction and Serum proBNP in the study population (N= 93)



There was a strong and statistically significant negative correlation between ejection fractionand serum proBNP (R Value: -0.701, P value: <0.001)

Table 8: Descriptive analysis of Regional wall motion abnormality in study population (n=93)

Regional wall motion abnormality	Frequency	Percent
Hypokinesia of anterior wall	12	12.90%
Hypokinesia of anteroseptal wall	23	24.73%
Hypokinesia of anterolateral wall	23	24.73%
Hypokinesia of inferior wall	4	4.30%
Akinesia of anterior wall	6	6.45%
Akinesia of anteroseptal wall	6	6.45%
Akinesia of anterolateral wall	1	1.08%
Akinesia of inferior wall	1	1.08%
Global hypokinesia	17	18.28%

Out of 93 subjects, echocardiography showed hypokinesia of anterior wall in 12 (12.90%) subjects, hypokinesia of anteroseptal wall and hypokonesia of anterolateral wall, present in 23 (24.73%) subjects, Hypokinesia of inferior wall in 4(4.30%) subjects, Akinesia of anterior wall in 6(6.45%) subjects, Akinesia of anteroseptal wall 6(6.45%) subjects, Akinesia of anterolateral wall in 1(1.08%) subjects, Akinesia of inferior wall in 1 (1.08%) subject and Global hypokinesia in 17 (18.28%). (Table 8)

Figure 4: Bar chart of Regional wall motion abnormality distribution in study population (n=93)

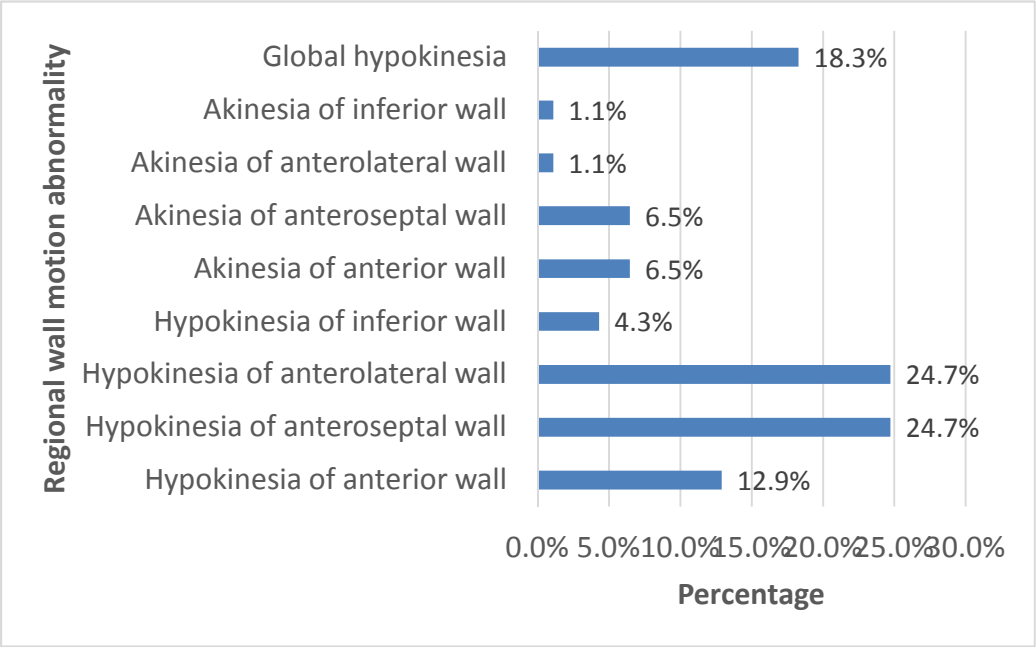


Table 9: Descriptive analysis for Iron parameters in study population (n= 93)

Parameter	Mean ±STD	Median	Min	Max	95% C.I. for EXP(B)	
					Lower	Upper
Haemoglobin	11.15 ± 1.89	11.30	6.80	14.50	10.76	11.54
Serum Iron	39.94 ± 29.47	34.00	10.00	190.00	33.87	46.00
Serum TIBC	276.21 ± 104.89	256.00	43.00	521.00	254.21	297.82
Serum Ferritin	298.54 ± 144.66	312.00	20.30	739.00	268.74	328.33
TSAT	18.31 ± 17.09	13.54	2.48	85.71	14.79	21.84

The mean hemoglobin was 11.15 ±1.89 g/dL in the study population. The lowest level was 6.8µg/dL highest level was 14.5 g/dL in the study population. The mean Serum Iron was 39.94 ± 29.47µg/dL in the study population. The lowest level was 10.0 µg/dL highest level was 190.0 g/dL in the study population. The mean Serum TIBC was 276.21± 104.89 µg/dL in the study population. The lowest level was 43.0 µg/dL highest level was 521.0µg/dL in the study population. The mean Serum ferritin was 298.54± 144.66mg/Lin the study population. The lowest level was 20.3mg/L highest level was 739 mg/L in the study population. The mean TSAT was 18.31% ± 17.09% in the study population. The lowest level was 2.48% highest level was 85.71% in the study population. (Table 9)

Table 10: Descriptive analysis of TSAT in study population (n=93)

TSAT(%)	Frequency	Percentages
Decreased(<20%)	62	66.67%
Normal(20-50%)	25	26.88%
Overload(>50%)	6	6.45%

Among the study population, 62 (66.67%) participants were had decreased TSAT, 25 (26.88%) were had normal transferrin saturation, 6 (6.45%) were had increased transferrin saturation. (Table 10)

Figure 5: Pie chart of TSAT distribution in study population (n=93)

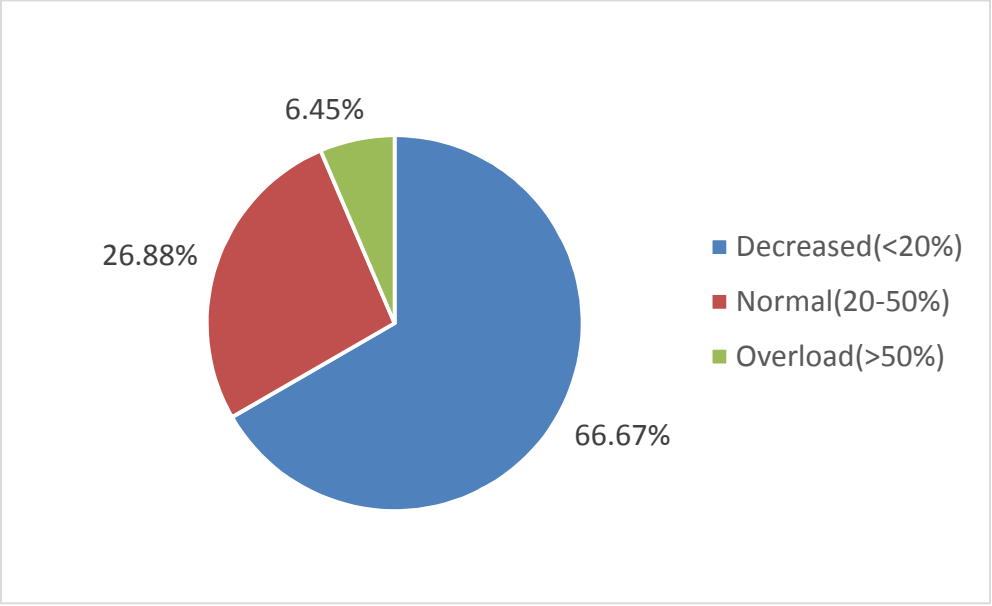


Table 11: Descriptive analysis of Peripheral smear in study population (N=93)

Peripheral smear	Frequency	Percentages
Normocytic normochromic	14	15.05%
Normocytic hypochromic	38	40.86%
Microcytic hypochromic.	41	44.09%

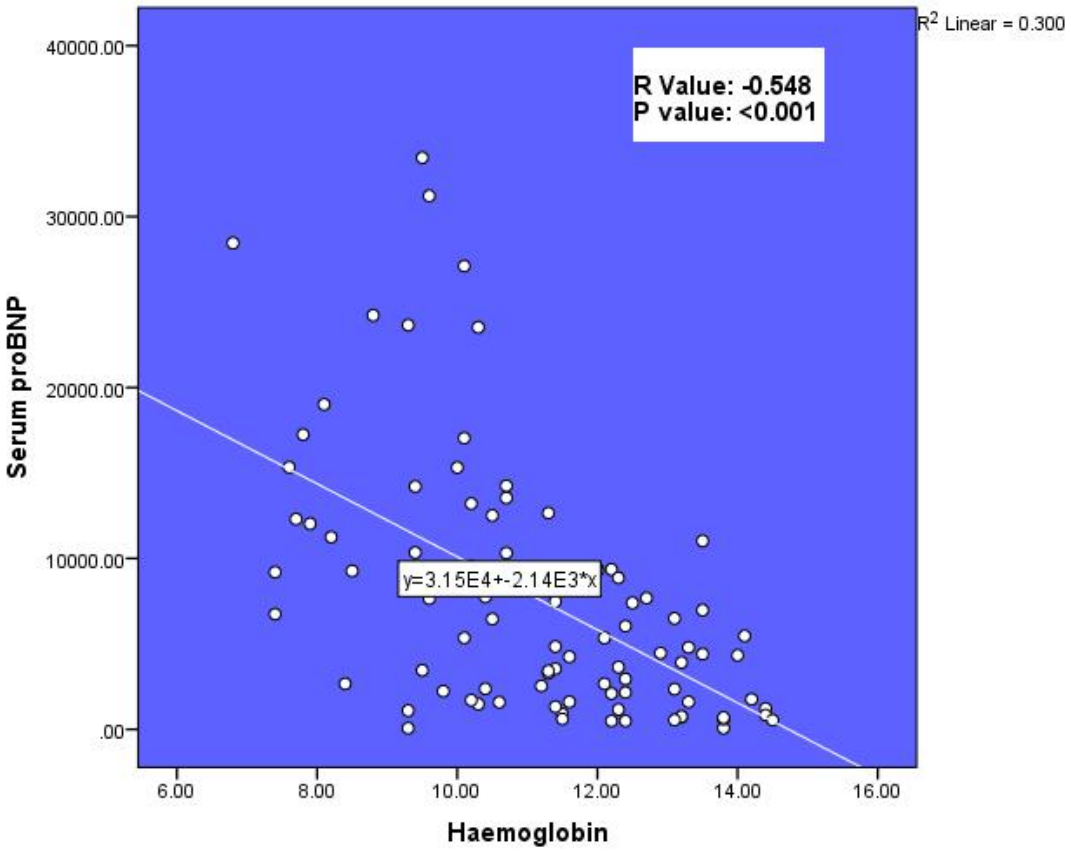
Out of 93 subjects, 14 (15.05%) subjects had normocytic normochromic in thePeripheral smear. The normocytic hypochromic picture was seen in 38(40.86%) subjects and 41(44.09%) subjects had microcytic hypochromic in the study population. (table 11)

Table 12: Descriptive analysis for Serum Creatinine in study population (N= 93)

Parameter	Mean ±STD	Median	Min	Max	95% C.I. for EXP(B)	
					Lower	Upper
Serum Creatinine	1.08 ± 0.19	1.00	0.60	1.80	1.04	1.12

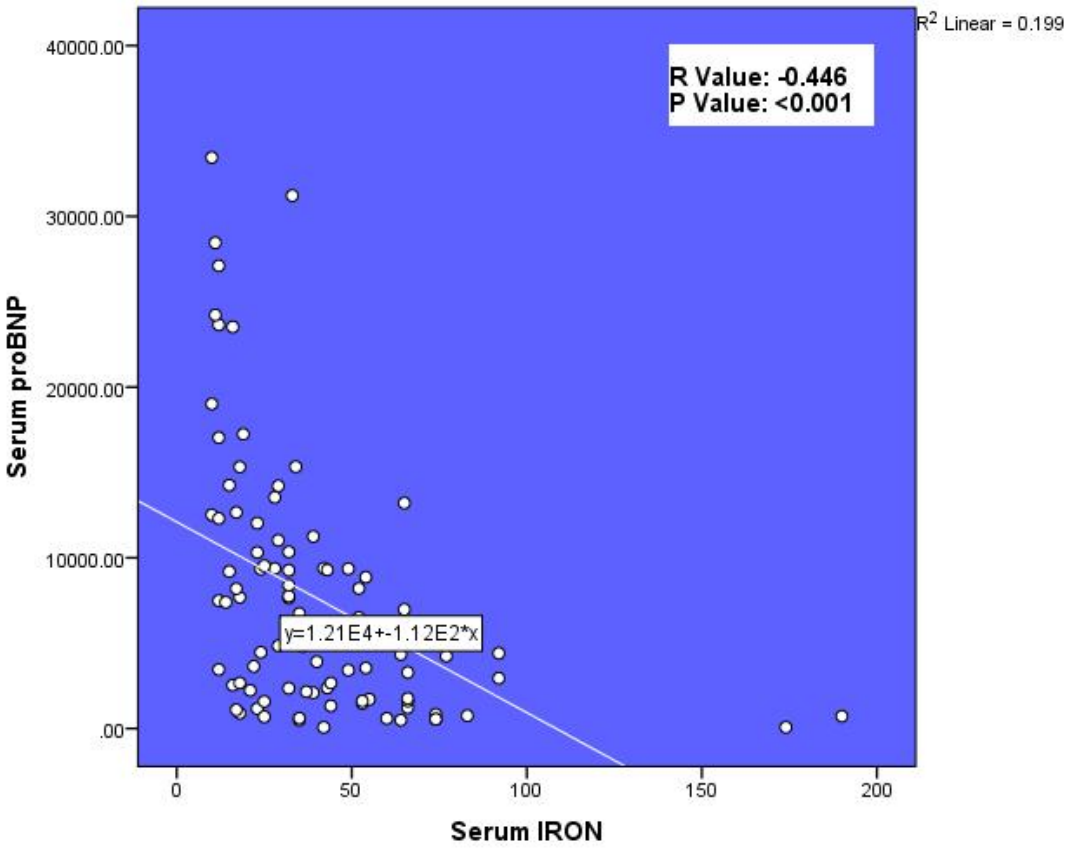
The mean Serum creatinine was 1.08±0.19mg/dL in the study population. Lowest level was 0.60 mg/dL highest level was 1.80mg/dL in the study population.(table 12)

Figure 6: Correlation between hemoglobin and Serum pro BNP in the study population (N= 93)



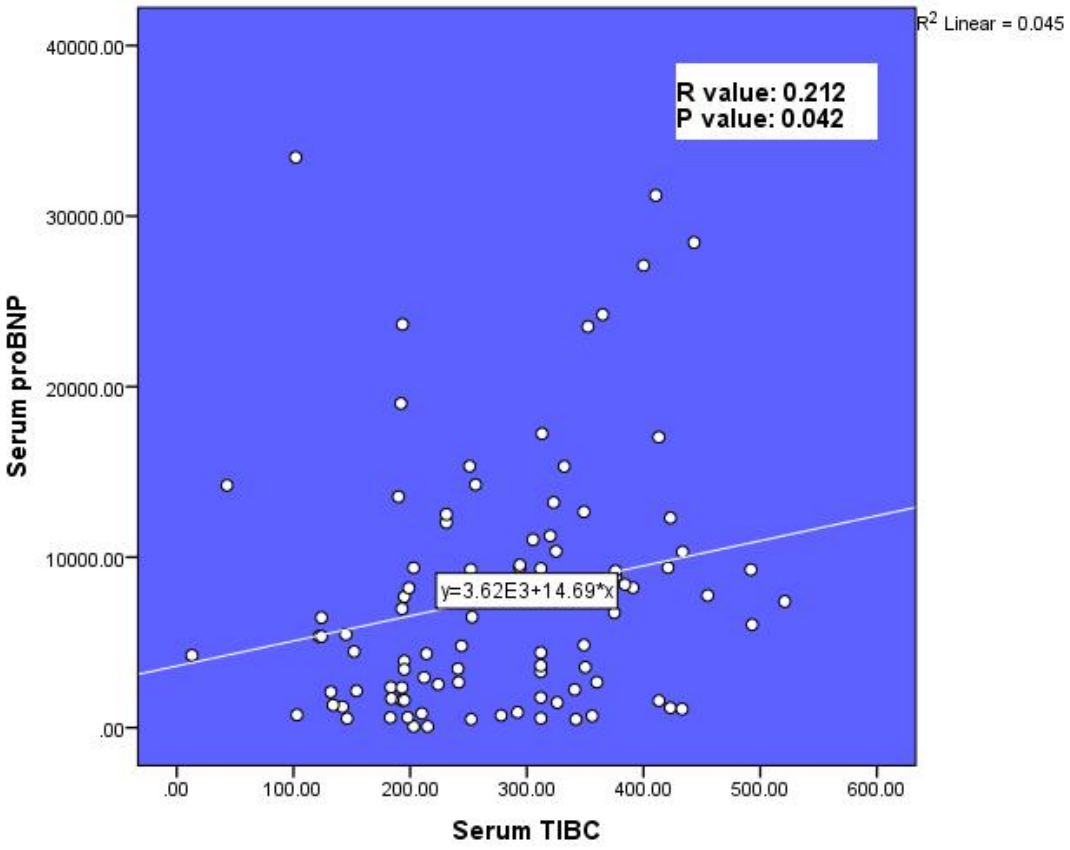
There was a moderate and statistically significant negative correlation between hemoglobin and serum proBNP (R Value: -0.548, P value: <0.001)

Figure 7: Correlation between Serum Iron and Serum pro BNP in the study population (N= 93)



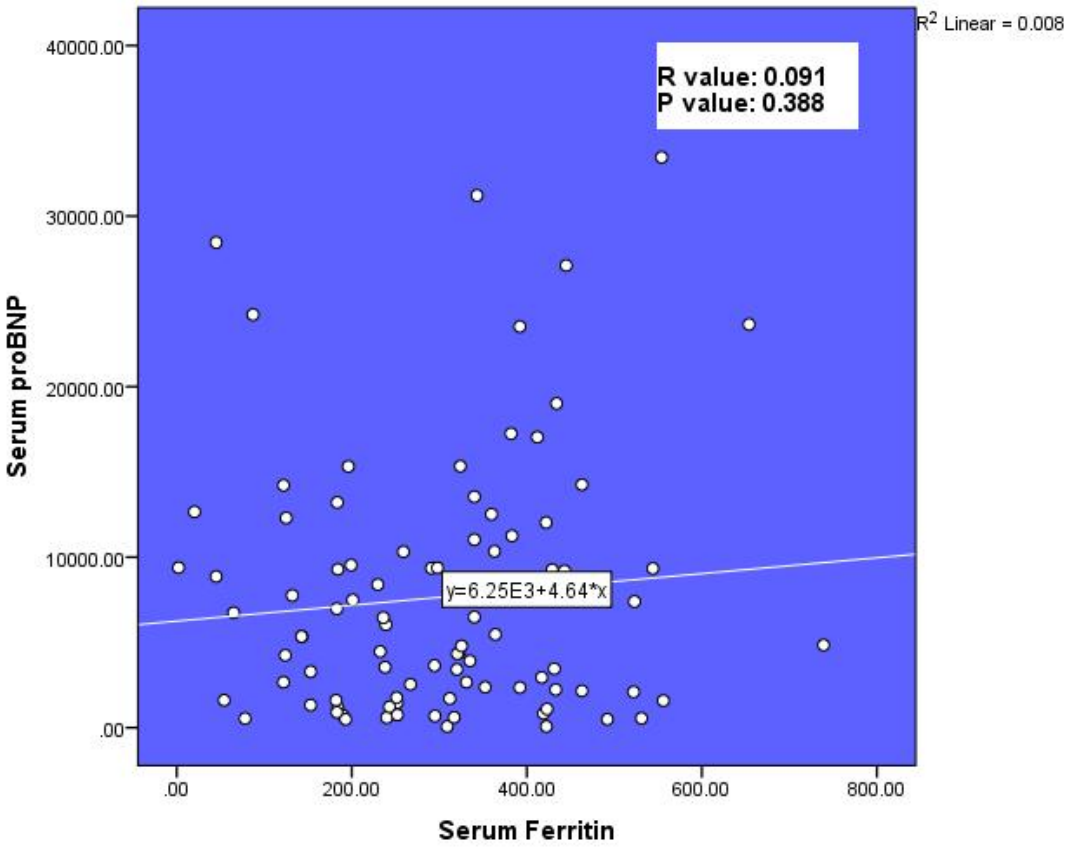
There was statistically significant negative correlation between Serum Iron and serum proBNP (R Value: -0.446, P value: <0.001)

Figure 8: Correlation between Serum TIBC and Serum pro BNP in the study population (N= 93)



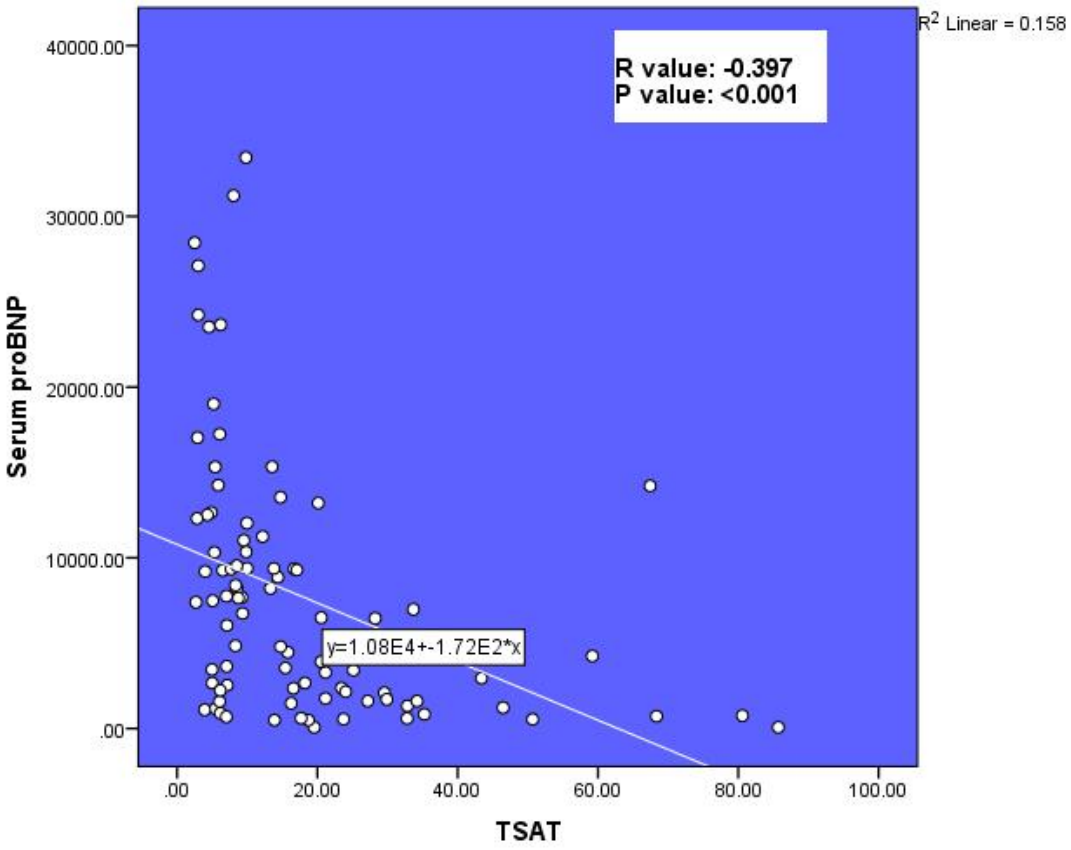
There was a moderate and statistically significant positive correlation between Serum TIBC and serum proBNP (R Value: 0.212, P value: 0.042)

Figure 9: Correlation between Serum Ferritin and Serum pro BNP in the study population (N= 93)



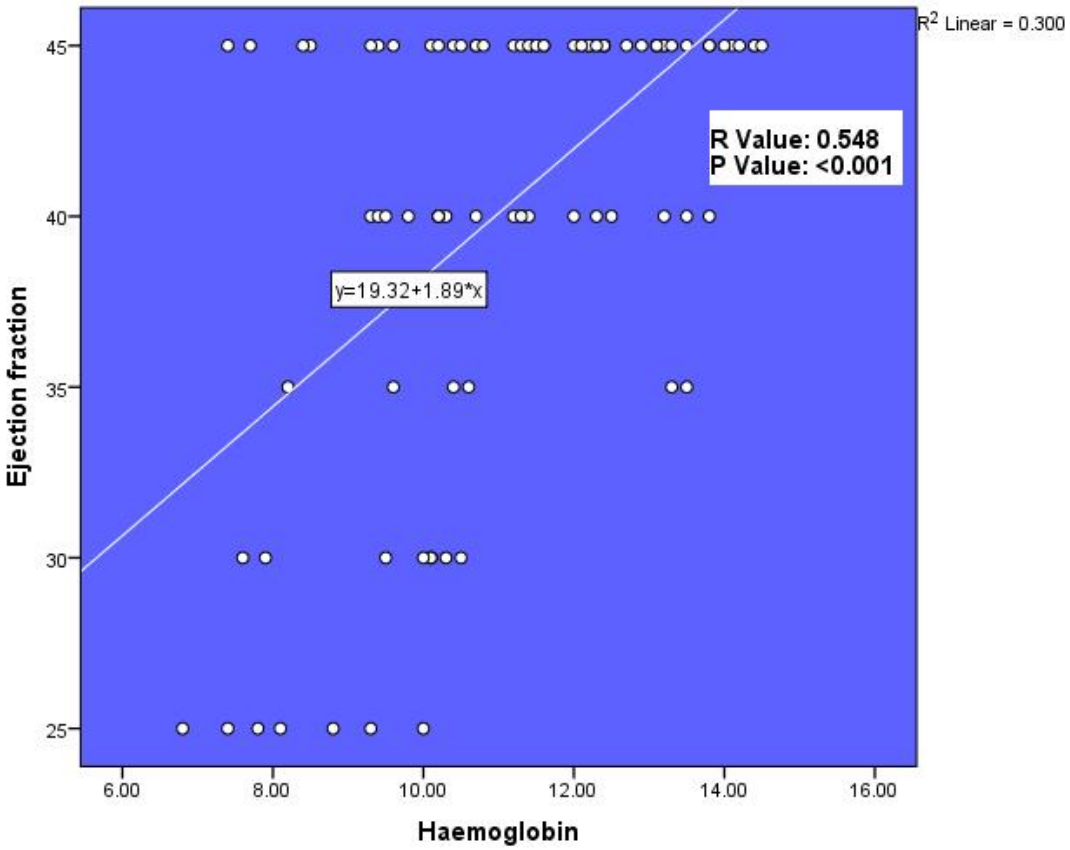
There was a moderate positive correlation between Serum ferritin and serum proBNP (R Value: 0.091, P value: 0.388), but this association was statistically not significant.

Figure 10: Correlation between TSAT and Serum pro BNP in the study population (N= 93)



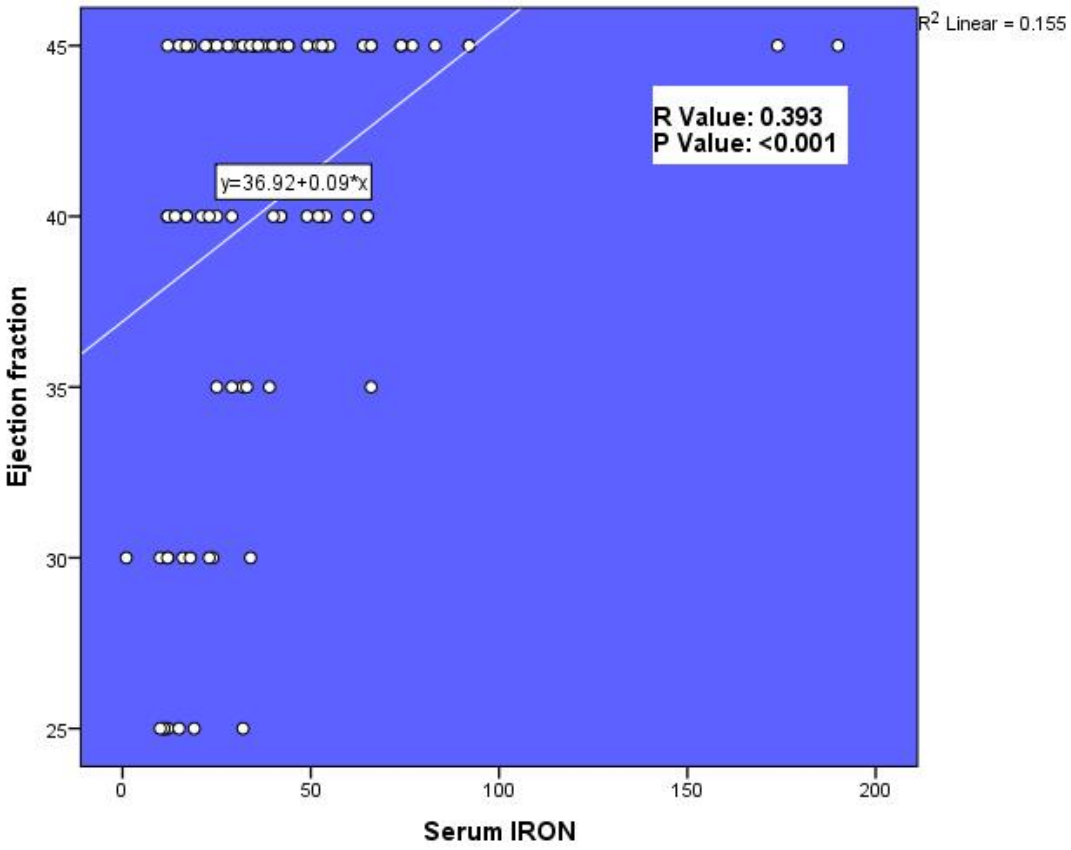
There was a moderate and statistically significant negative correlation between TSAT and serum proBNP (R Value: -0.397, P value: <0.001)

Figure 11: Correlation between hemoglobin and Ejection fraction in the study population (N= 93)



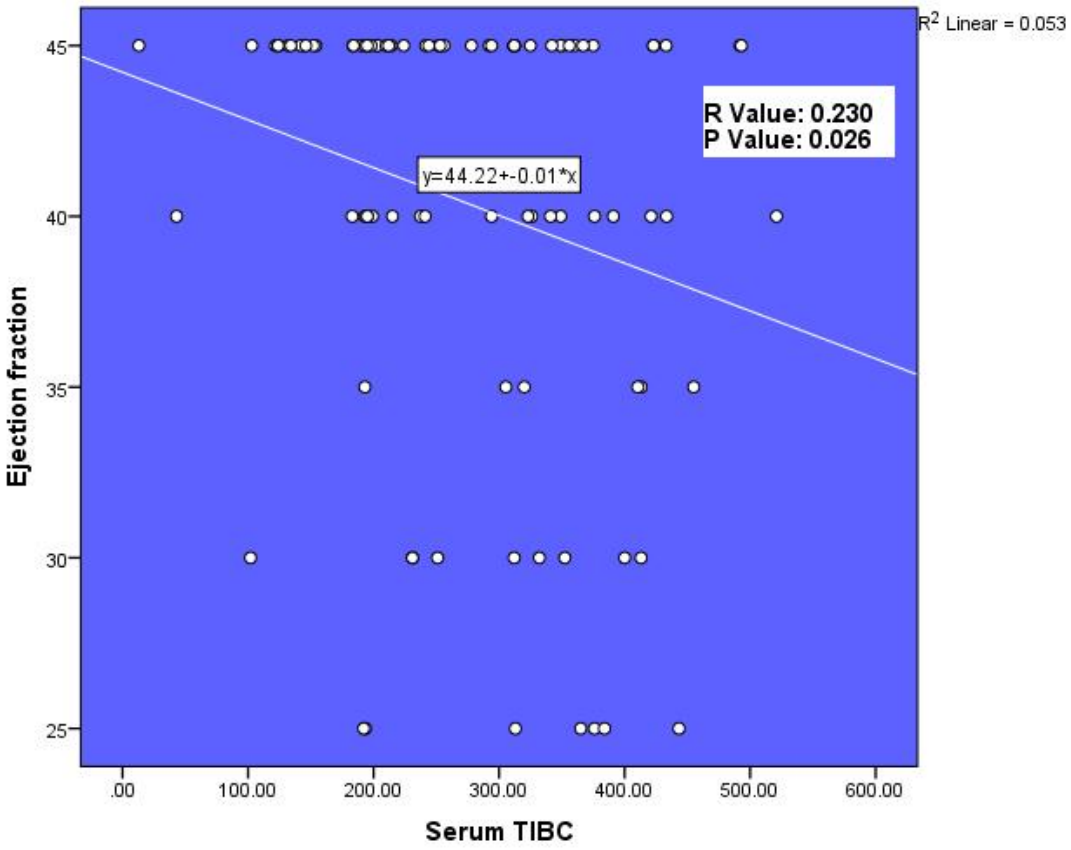
There was a moderate and statistically significant positive correlation between Hemoglobin and ejection fraction (R Value: 0.548, P value: <0.001)

Figure 12: Correlation between Serum Iron and Serum Ejection fraction in the study population (N= 93)



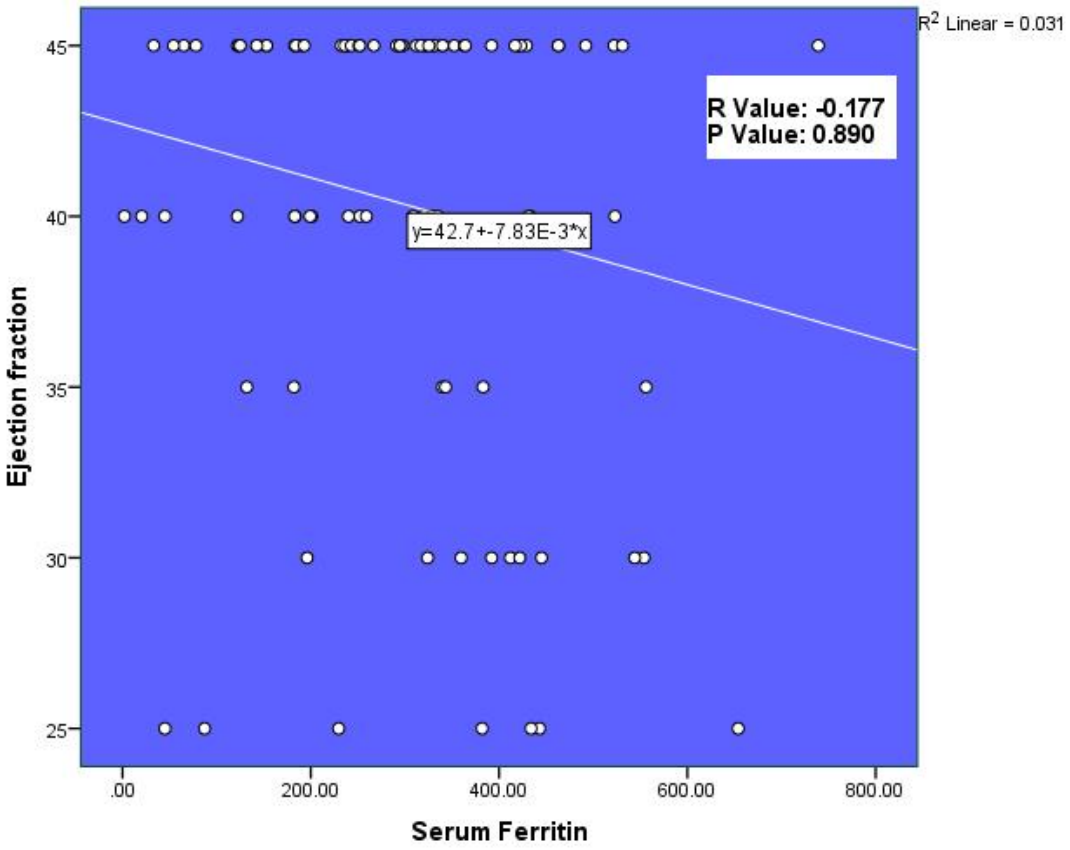
There was a moderate and statistically significant positive correlation between serum Iron and ejection fraction (R Value: 0.393, P value: <0.001)

figure 13: Correlation between Serum TIBC and Ejection fraction in the study population (N= 93)



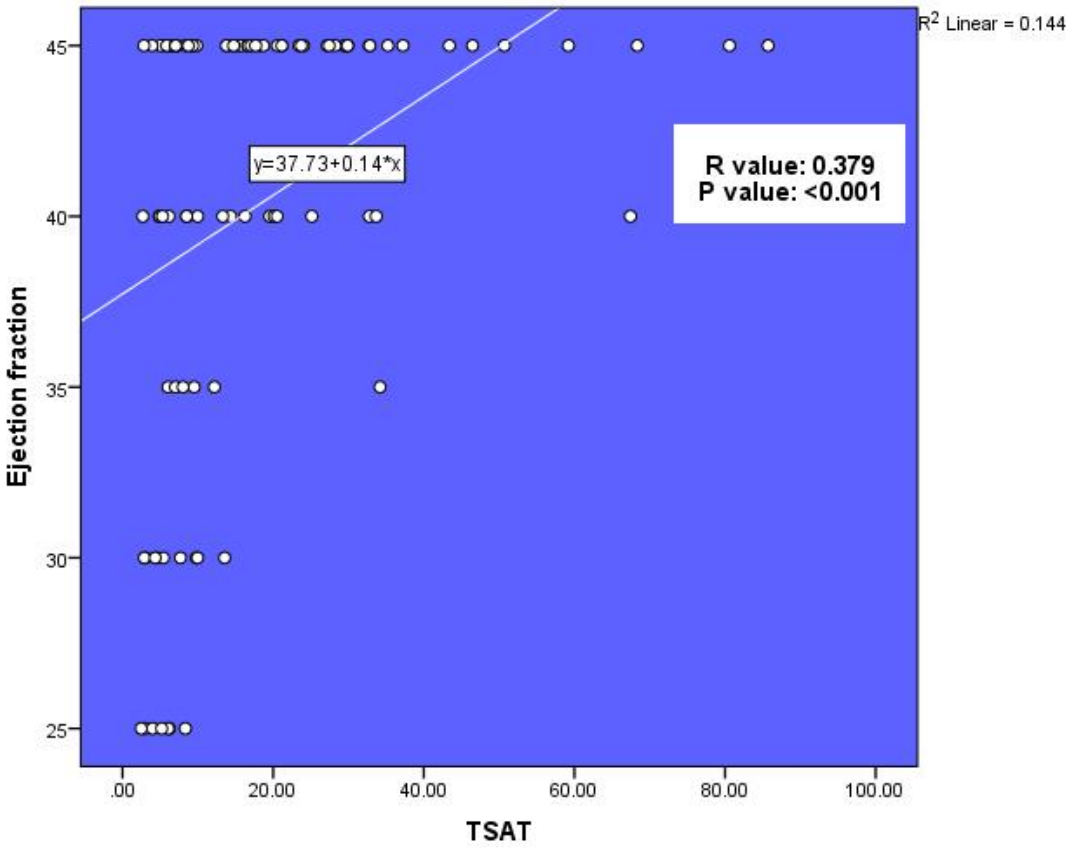
There was a statistically significant negative correlation between Serum TIBC and ejection fraction (R Value: 0.230, P value: 0.026)

Figure 14: Correlation Between Serum Ferritin and Ejection fraction in the study population (N= 93)



There was a weak negative correlation between serum ferritin and ejection fraction (R Value: -0.177, P value: 0.890), which was statistically not significant.

Figure 15: Correlation Between TSAT and Ejection fraction in the study population (N= 93)



There was a moderate positive correlation between TSAT and ejection fraction (R Value: 0.379, P value:<0.001), which was statistically significant.

Table 13: Descriptive analysis of Serum Iron(ug/dL) in study population (N=93)

Serum Iron (ug/dL)	**Frequency**	**Percentage**
Low (in male <55 , in female <40)	71	76.34%
Normal	22	23.66%

Among the study population majority (76.34%) subjects had low serum Iron and only 22(23.66%) subjects had a normal level.

Table 14: Descriptive analysis of Serum Ferritin(mg/L) in study population (N=93)

Serum Ferritin (mg/L)	**Frequency**	**Percentages**
Low (Up to 99)	8	8.60%
Normal (100 to 299)	37	39.78%
High (Above 300)	48	51.61%

Among the study population, in serum ferritin8 (8.60%) subjects had a low level. The proportion of normal and high level was 39.78% and 51.61% respectively.

Table 15: Descriptive analysis of TSAT (%) in study population (N=93)

Transferrin saturation (%)	Frequency	Percentage
Low (below 20)	62	66.67%
Normal (20 and above)	31	33.33%

Among the study population majority (66.67%) subjects had low transferrin saturation and 31(33.33%) subjects had anormal level.

Table 16: Descriptive analysis of Iron deficiency in study population (N=93)

Iron	Frequency	Percentage
Deficiency	73	78.49%
No deficiency	20	21.51%

Among the study population 73 (78.49%) subjects had Iron deficiency.

62 subjects (66.66%) had iron deficiency with anemia and 11 subjects (11.82%) had iron deficiency without anaemia.

Table 17: Comparison of mean Serum proBNP (ng/L)between normal and Iron deficiency group (N=93)

Iron deficiency	Serum pro BNP (ng/L) Mean± STD	Mean difference	95% CI		P value
			Lower	Upper	
Deficiency	8873.08 ± 7716.74	5732.48	2208.14	9256.81	**0.002**
No deficiency	3140.6 ± 3322.51				

The mean serum pro BNP in Iron deficiency group was 8873.08 ng/L and in no iron deficiency group was 3140.6 ng/L. The difference between two groups was statistically significant (P value <0.002)

Table 18: Association of proBNP with Iron deficiency of study population (N= 93)

Iron deficiency	proBNP		Chi square	P-value
	Normal	High		
Deficiency	12 (16.44%)	61 (83.56%)	12.541	**<0.001**
No deficiency	11 (55%)	9 (45%)		

Among the study population, subjects who had an iron deficiency, the subjects with normal proBNP levels were 12(16.44%) and 61(83.56%) had high proBNP levels. There were 11(55%) subjects who had no iron deficiency in subjects with normal proBNP level. There were 9(45%)subjects who had no iron deficiency in

subjects with high proBNP level. The difference in the proportion between Iron deficiency and proBNP levels was statistically significant (P value <0.001)

Table 19: Association between pro BNP and serum Iron (ug/dL) (n=93)

Pro BNP	Serum Iron (ug/dL) Mean± STD	Mean difference	95% CI		P value
			Lower	Upper	
Normal	61.57 ± 42.89	28.74	15.92	41.55	***<0.001***
High	32.83 ± 19.08				

The mean serum iron in the normal proBNP group was 61.57ug/dL and in the high proBNP group was 32.83ug/dL. The difference between two groups was statistically significant (P value <0.001)

Table 20: Association between proBNP and Serum Ferritin (mg/L) (N=93)

proBNP	Serum Ferritin (mg/L) Mean± STD	Mean difference	95% CI		P value
			Lower	Upper	
Normal	283.98 ± 135.59	-19.34	-88.66	49.98	0.581
High	303.32 ± 148.14				

The mean serum ferritin in the normal proBNP group was 283.98 mg/L and in thehigh proBNP group was303.32mg/L. The difference between two groups was statistically not significant (P value 0.581)

Table 21: Association between pro BNP and serum TIBC (µg/dL) (N=93)

Pro BNP	Serum TIBC (µg/dL) Mean± STD	Mean difference	95% CI		P value
			Lower	Upper	
Normal	254.15 ± 96.71	-29.31	-79.30	20.66	0.247
High	283.4 ± 107.11				

The mean serum TIBC in the normal pro BNP group was 254.15 µg/dL and in the high proBNP group was 283.4µg/dL. The difference between two groups was not statistically significant (P value 0.247)

DISCUSSION

Multiple studies in the literature have documented derangements in iron metabolism to be a common phenomenon observed in heart failure patients proBNP is a cardiac neurohormone secreted from the ventricles into the plasma in response to ventricular volume expansion and pressure overload[47]. It has previously been demonstrated that the determination of proBNP levels provides a straightforward method for the early detection of HF, the assessment of HF severity and the effectiveness of treatment[48].

A total of 93 subjects were included in the study. The mean age was 62.43 ± 9.92 in the study population. The youngest participant was 41 years old and oldest participant was 88 years old in the study group. Among the study population, 12 (12.90%) participants were aged below 50 years, 27 (29.03%) were aged 51 to 60 years, 36 (38.71%) were aged 61 to 70 years, 18 (19.35%) were above 71 years. Male participants 75(80.65%) were predominant over the female participants 18 (19.35%). Among 93 patients with HFrEF, 63(67.7%) patients were hypertensives and 43(46.2%) were type 2 DM patients. Mean serum proBNP level was 7640.28±7381.74 in the study population. Lowest and the highest proBNP levels recorded were 66.4 and 33447.0 respectively.

There was a significant negative correlation between Serum TIBC and serum proBNP (RValue: -0.701, P value: <0.001) levels.

The mean ejection fraction level was 40.38 ± 6.52 in the study population. The lowest level was 25% and the highest level was 45% in the study group. Out of 93 subjects, echocardiography showed hypokinesia of anterior wall in 12 (12.90%)

subjects, hypokinesia of anteroseptal wall and hypokonesia of anterolateral wallin 23 (24.73%) subjects, Hypokinesia of inferior wall in 4(4.30%) subjects, Akinesia of anterior wall in 6(6.45%) subjects, akinesia of anteroseptal wall in 6(6.45%) subjects, Akinesia of anterolateral wall in 1(1.08%) subjects, akinesia of inferior wall in 1 (1.08%) subject and Global hypokinesia in 17 (18.28%).

The mean hemoglobin was 11.15 ±1.89 g/dL in the study population. The lowest level was 6.8µg/dL highest level was 14.5 g/dL in the study population. The mean Serum iron was 39.94 ± 29.47µg/dL in the study population. The lowest level was 10.0 µg/dL highest level was 190.0 g/dL in the study population. The mean serum TIBC was 276.21 ± 104.89 µg/dL in the study population. The mean Serum ferritin was 298.54± 144.66 mg/L in the study population. The mean TSAT was 18.31% ± 17.09% in the study population

Out of 93 subjects, 14 (15.05%) subjects had normocytic normochromic in peripheral smear. The normocytic hypochromic picture was seen in 38(40.86%) subjects and 41(44.09%) subjects had microcytic hypochromic in the study population. The mean Serum creatinine was 1.08±0.19mg/dL in the study population. Lowest level was 0.60 mg/dL highest level was 1.80mg/dL in the study population.

There was a moderate negative correlation between hemoglobin and serum proBNP (R Value: -0.548, P value : <0.001)in our study. In a similar study by Knudsen et al[49]., they reported similar results on the correlation between the parameters (R-value: −0.30; P value < 0.0001). Whereas in contrast to these reports, Desai,A.S et al[50] showed a linear relationship between the two parameters.

Among the study population, 62 (66.67%) participants had<20% TSAT, 25 (26.88%) had TSAT between 20-50% normal transferrin saturation, 6 (6.45%) were had above normal transferrin saturation ie. >50%.

The serum pro-BNP levels had a moderate negative correlation between Serum Iron (R Value: -0.446, P value:<0.001), moderate positive correlation with serum TIBC (R Value: 0.212, P value: 0.042), moderate positive correlation with Serum ferritin (R Value: 0.091, P value: 0.388) and a moderate negative correlation with TSAT(R Value: -0.153, P value: 0.143) in our study.

The Ejection Fraction (EF) had a moderate positive correlation with Hemoglobin (R Value: 0.548, P value: <0.001), a moderate positive correlation with Serum Iron (R Value: 0.393, P value:<0.001), a weak positive correlation with Serum TIBC (R Value: 0.230, P value: 0.026), a weak negative correlation with serum ferritin (R Value: -0.177, P value: 0.890) and moderate positive correlation with TSAT (R Value: 0.379, P value: <0.001)

There have been many recent studies of the correlations between BNP level and cardiac function. Kim et al.[51]and Takayoshi et al.[52] reported that the concentration of serum BNP was inversely correlated with left ventricle ejection fraction similar to our study.

Among the study population majority of 71 (76.34%) subjects had low serum iron. The mean serum proBNP in iron deficiency subjects was 8873.08 ng/L and in people with no iron deficiency was 3140.6 ng/L. The difference between two groups was statistically significant (P value 0.002). According to Gary S. Francis et al[24] anaemia is common among patients with heart failure, probably occurring approximately in 20% of patients. The authors have proposed a correction of a

reduced hemoglobin (Hb) level as an attractive therapeutic target deserving of further study. Of interest, erythropoietin (EPO) levels were moderately elevated in patients with heart failure, more so in very severe heart failure.Yeo, T. J.et al., [36] in their case control study to assess prevalence and factors influencing anaemia in heart failure patients have defined iron Deficiency (ID), as ferritin <100 microg/L or ferritin 100-300 microg/L and transferrin saturation (Tsat) <20%, was present in 39.3% of controls and 61.4% of HF. The proportion of anaemia reported by this study was comparable with the findings of the current study.Schou, M. et al., [37]have reported a prevalence of ID as 45% (95%-confidence interval (CI): 37-53%). In patients with heart failure.

The mean serum iron levels observed in subjects with normal proBNP levels was 61.57ug/dL and high proBNP levels was 32.83ug/dL. The difference between two groups was statistically significant (P value <0.001). Study by Martinez-Quintana, E.et al have documented a NT-proBNP (pg/mL) (409.3 [33.3-9830.8] vs. 5.2 [0.0-1068.4], P <.001) levels than non-hypoxemic acynotic heart disease (ACHD) patients. Serum iron, total iron-binding capacity, and transferrin saturation index were not statistically significant between hypoxemic and non-hypoxemic ACHD patients. In the hypoxemic group, 15 (45%) patients had apoferritin levels <20 ng/mL and eight (24%) patients developed microcytosis and hypochromia. An RDW above the normal range (>14.5%) in hypoxemic ACHD patients allowed the detection of an apoferritin level <20 ng/mL with a sensitivity of 93%. Based on the results the authors came to a conclusion that**,** RDW seems to be a useful and economical tool to detect low serum apoferritin levels in hypoxemic ACHD patients.[29] Schou, M et al. [25]have demonstrated prevalence of anaemia was 27% in heart failure patients. In a multivariate logistic regression model, the results showed that anaemia (p = 0.041)

was closely associated with NT-pro-BNP levels above the median (1,381 pg/ml) after adjustment for traditional confounders (left ventricular ejection fraction, age, body mass index, atrial fibrillation, chronic kidney disease). In an adjusted Cox proportional hazard model, the 2 parameters were associated with mortality after adjustment for traditional confounders (hazard ratio for anaemia 1.73, 95% confidence interval 1.06 to 2.83, p = 0.029; hazard ratio for NT-pro-BNP >1,381 pg/ml 2.68, 95% confidence interval 1.58 to 4.66, p <0.001). Patients with anaemia and high NT-pro-BNP levels had a fivefold increased risk for mortality (hazard ratio 4.77, 95% confidence interval 2.47 to 9.18, p <0.001.have reported a prevalence of ID as 45% (95%-confidence interval (CI): 37-53%). In multivariate analyses of patients with heart failure, ID was not associated with plasma concentrations of troponin I, NT-proBNP, MR-proANP, chromogranin A or copeptin (P>0.05 for all) but with plasma concentrations of hs-CRP (odds ratio: 2.03, 95%-CI: 1.02-4.02, P=0.043).

There is not much uncertainty regarding the association of heart failure with iron deficiency. Even though the reported prevalence of heart failure varied widely across the studies, bulk of the literature has documented a positive association between heart failure and anaemia. But the debated aspect of this association was the casual relationship between the two factors and role of anaemia in progression and outcomes of heart failure. Even though proBNP has been documented to be independently associated with iron deficiency, there are few studies contradicting this finding. Before making any meaningful conclusions, the methodological quality, the extent of the potential confounding variables considered and adjusted in the analysis etc. have to be considered.

In patients with heart failure, iron deficiency is frequent but overlooked, with a prevalence of 30%-50%. Iron deficiency emerges as a new comorbidity and a therapeutic target of heart failure in addition to chronic renal insufficiency, anaemia and diabetes.

The 2013 ACCF/AHA Guideline for the Management of Heart Failure provided no specific recommendations, neither for the evaluation of iron status nor for potential repletion of iron deficiency in patients with HF who demonstrate iron deficiency.

However the 2017 ACC/AHA/HFSA Focused Update of 2013 ACCF/AHA Guidelines for management of Heart Failure has mentioned a Class IIb recommendation for assessment of anaemia in heart failure patients and intravenous iron replacement in NYHA class II and III HF patients for improvement of functional status and Quality of Life.

CONCLUSIONS

1. Majority of the subjects with heart failure were aged between 61 to70years in the study, with high male preponderance with Male to female ratio of about 4:1

2. In all the subjects heart failure was secondary to Ischemic Heart Disease (IHD). Hypertension and Diabetes mellitus were the most common comorbidity observed seen in 67.7% and 46.2% of the subjects respectively.

3. The mean serum pro BNP level was 7640.28±7381.74 gm/dl. The mean hemoglobin was 11.15 ±1.89 g/dL, the mean serum iron was 39.94 ± 29.47µg/dL. The mean Serum TIBC was 274.96 ± 107.35 µg/dL, the mean Serum ferritin was 298.54 ± 144.66µg/dL and the mean TSAT was 24.05 ± 61.82 in the study population.

4. Among the study population majority of 73 (78.49%) subjects had iron deficiency. 62 subjects (66.66%) had iron deficiency with anemia and 11 subjects(11.82%) had iron deficiency without anaemia.The mean serum proBNP of iron deficiency was 8873.08 ng/L and in subjects with no iron deficiency proBNP level was 3140.6 ng/L. The difference between two groups was statistically significant (P value 0.002).

5. The mean left ventricular ejection fraction was 40.38%± 6.52% in the study population. Lowest level was 25% and highest level was 45% in the study group.

6. The most common echocardiography finding observed was hypokinesia of anteroseptal and anterolateral wall, in 24.73% subjects, global hypokinesia in 18.28% followed by hypokinesia of anterior wall in 12.90% subjects.

7. In the study, proBNP had a strong and statistically significant negative correlation with serum proBNP levels and ejection fraction (R Value: -0.701, P value: <0.001).

8. Among iron parameters serum proBNP had statistically significant negative correlation with hemoglobin (R Value: -0.548, P value: <0.001), Serum iron (R Value: -0.446, P value: <0.001) and TSAT (R Value: -0.397, P value: <0.001) . Serum proBNP also had a positive correlation with Serum TIBC (R Value: 0.212, P value: 0.042)

9. There was a moderate and statistically significant positive correlation between Hemoglobin and ejection fraction (R Value: 0.548, P value: <0.001). EF also had statistically significant positive correlation with serum iron (R Value: 0.393, P value: <0.001) and Serum TIBC (R Value: 0.230, P value: 0.026)

SUMMARY

This cross sectional study has assessed the correlation between serum iron parameters and serum proBNP level in heart failure with reduced ejection fraction patients. Among the study population majority of 73 (78.49%) subjects had iron deficiency. 62 subjects (66.66%) had iron deficiency with anemia and 11 subjects (11.82%) had iron deficiency without anaemia. The mean serum proBNP in iron deficiency and normal groups was 8873.08 ng/L and 3140.6 ng/L (P value 0.002). Among the iron parameters, serum proBNP had statistically significant negative correlation with serum iron (R Value: -0.446, P value: <0.001) and TSAT (R Value: -0.397, P value: <0.001) and a positive correlation with Serum TIBC (R Value: 0.212, P value: 0.042).

Hence this study emphasizes the need to conduct further studies to understand role of iron metabolism in progression of heart failure and its therapeutic implications.

LIMITATIONS

1. Considering a smaller sample size, multivariate analysis could not be carried out to assess the role confounding by various factors in the association between parameters of iron metabolism and serum proBNP

2. Considering cross sectional nature of the study temporal relationship of impaired iron metabolism and elevation in serum proBNP levels could not be established.

3. Generalizability of the study findings to other causes of heart failure is limited as all the cases in the current study were secondary to Ischemic heart disease

RECOMMENDATIONS:

1. There is a strong need for large-scale prospective studies on the subjects, to study the exact nature of association between parameters or iron metabolism and serum pro-BNP levels, independent of potential confounders.

2. The therapeutic implications of correcting the iron deficiency also need to be studied by appropriate intervention studies to guide clinical practice.

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ANNEXURE-I

PATIENT INFORMATION SHEET (PIS) &

INFORMED CONSENT FORM (ICF)

Title Of Research Study:

ASSOCIATION OF Iron STUDIES WITH SERUM BNP LEVELS IN HEART FAILURE PATIENTS- A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY.

Principal Investigator:-

Dr. _____

Post Graduate Student,

Department Of General Medicine,

JNMC, Belgaum.

Guide:-

Dr. _____

Professor and Vice-Principal,

Department of General Medicine,

JNMC, Belgaum.

Introduction and Purpose:-

He/She is a well-recognized case of Heart Failure and the presence and prompt identification of well-defined precipitating factors is extremely important in diagnosis and treatment of this fatal condition. Heart Failure is the reason for at least 20% of all hospital admissions among persons older than 65.

Procedure:

If you agree to be part of the research study, you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood and urine samples for the necessary investigations.

Risk and Benefits:

The only risk and possible discomfort you might get is while taking blood from your arm for the investigations. It may cause swelling, pain, redness (rarely happens) at the site from where the blood is drawn.

You may not be benefitted by these investigations but you will be part of this study which is going to be useful to others in the future.

Alternatives:

Taking part in this study is voluntary. You may choose not to take part in this study.

If you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study at any time. If you choose not to take part in the study, you will receive the standard treatment for patients with your condition.

Privacy and Confidentiality:

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you

in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy:

Does not apply to this research

Financial incentives for participation:

You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results:

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

In case of the queries during study or in future you may contact following persons,

Dr. GANGA PILLI MD
Professor, Dept. Of Pathology, Chairman,
JNMC Institutional Ethics Commitee,
J.N. Medical College,
K.L.E. University, Belgaum - 10

CONSENT FORM

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read this consent form, or it has been read to me and has been explained to me in my vernacular language and all my questions have been answered. I will be given a copy of this consent form.

Signature / Left Thumb print of the Participant or legally authorized representative

Participant's name :……...

Signature / Left thumb impression :……...

of the participant

Name of the legally authorized :……...

representative / guardian

Signature / Left thumb impression :……...

Witness' name :……...

Signature / Left thumb impression :……...

Investigator's name and signature :……...

Date:

Place:

ANNEXURE II – PROFORMA

ASSOCIATION OF Iron STUDIES WITH SERUM BRAIN NATRIURETIC PEPTIDE LEVEL IN HEART FAILURE PATIENTS- A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY.

IP NO.:

NAME:

AGE/SEX:

IP NO.:

ADDRESS:

DIAGNOSIS:

TREATMENT HISTORY:

INVESTIGATIONS:

HB:

SR. CREATININE:

PERIPHERAL SMEAR FOR BLOOD PICTURE:

Iron STUDIES:

1. **SERUM Iron:**
2. **SERUM FERRITIN:**
3. **TIBC:**
4. **TSAT(%)**

SERUM BNP:

2DECHO:

SNO	Name	Age	Gender	ID_no	IHD	HTN	T2DM	Pro_BNP	Ejectionfraction	RWMA	HB	Sr_iron	TIBC	Serum Ferritin	Peripheral smear	Sr_Creatinine	Age_GRP	TSAT	TSAT_CAT	proBNP	IRON_ID	Ferritin_Group	Tsat_group_ID	Iron_Deficiency
1	KASTURI H	66	2	813,258	1	1	2	2,536.00	45	2	11.20	16	224.00	267.00	3	1.00	3.00	7.14	1.00	2.00	1.00	2.00	1.00	1.00
2	LAKSHMI	61	2	811,324	1	1	1	27,105.00	30	2	10.10	12	400.00	445.00	3	1.10	3.00	3.00	1.00	2.00	1.00	3.00	1.00	1.00
3	MAHADEV	55	1	812,300	1	1	2	13,542.00	45	1	10.70	28	190.00	340.00	2	0.90	2.00	14.74	1.00	2.00	1.00	3.00	1.00	1.00
4	RAMESH	68	1	813,104	1	2	1	7,683.00	45	1	12.70	18	195.00	331.00	2	1.30	3.00	9.23	1.00	2.00	1.00	3.00	1.00	1.00
5	RAMU DODDANNAVAR	56	1	811,815	1	2	1	33,447.00	30	9	9.50	10	102.00	554.00	3	1.40	2.00	9.80	1.00	2.00	1.00	3.00	1.00	1.00
6	SARVAMANGALA	73	2	813,282	1	1	1	12,656.00	40	2	11.30	17	349.00	20.30	2	0.80	4.00	4.87	1.00	2.00	1.00	1.00	1.00	1.00
7	SUBHASH	68	1	812,173	1	1	1	3,548.00	45	2	11.40	54	350.00	238.00	1	1.00	3.00	15.43	1.00	2.00	1.00	2.00	1.00	1.00
8	HUSSAIN	46	1	813,332	1	1	2	722.00	45	2	13.20	190	278.00	190.00	1	0.60	1.00	68.35	3.00	1.00	2.00	2.00	2.00	2.00
9	MAYAPPA	52	1	812,480	1	1	2	1,161.00	45	2	12.30	23	423.00	184.00	3	1.20	2.00	5.44	1.00	1.00	1.00	2.00	1.00	1.00
10	BALASAHEB KORE	61	1	813,080	1	1	1	73.30	45	4	13.80	174	203.00	422.30	1	1.20	3.00	85.71	3.00	1.00	2.00	3.00	2.00	2.00
11	SUBHASH P	48	1	813,053	1	1	1	2,096.00	45	1	12.20	39	132.00	522.00	3	1.20	1.00	29.55	2.00	2.00	1.00	3.00	2.00	1.00
12	CHANNABASAPPA	69	1	812,238	1	1	2	1,474.00	40	8	10.30	53	326.00	252.00	3	1.40	3.00	16.26	1.00	1.00	1.00	2.00	1.00	1.00
13	RAYAPPA P	60	1	812,818	1	1	1	2,376.00	45	3	10.40	43	183.50	352.30	3	1.00	2.00	23.43	2.00	2.00	1.00	3.00	2.00	1.00
14	RAYAPPA	54	1	812,903	1	1	2	1,582.00	35	9	10.60	25	413.20	556.00	2	1.00	2.00	6.05	1.00	1.00	1.00	3.00	1.00	1.00
15	ANANDI	67	2	799,219	1	1	1	66.40	40	2	9.30	42	215.00	309.00	2	1.20	3.00	19.53	1.00	1.00	2.00	3.00	1.00	2.00
16	DANAPPA	72	1	813,084	1	1	2	587.00	40	4	13.80	60	183.00	240.00	3	0.90	4.00	32.79	2.00	1.00	2.00	2.00	2.00	2.00
17	CHANDRASHEKHAR	63	1	788,491	1	1	1	9,266.00	45	3	8.50	32	492.00	429.00	3	0.90	3.00	6.50	1.00	2.00	1.00	3.00	1.00	1.00
18	KENCHAPPA	69	1	811,509	1	1	2	8,192.00	40	1	10.20	17	199.00	330.00	3	1.20	3.00	8.54	1.00	2.00	1.00	3.00	1.00	1.00
19	SAIRAM	50	1	812,246	1	1	1	23,649.00	25	9	9.30	12	193.40	654.00	3	1.40	1.00	6.20	1.00	2.00	1.00	3.00	1.00	1.00
20	SUMITRA	65	2	#NULL!	1	1	1	2,665.00	45	3	8.40	18	360.00	122.00	3	1.00	3.00	5.00	1.00	2.00	1.00	2.00	1.00	1.00
21	MALLIKARJUN	59	1	810,493	1	1	2	2,665.00	45	1	12.10	44	241.50	331.00	2	1.00	2.00	18.22	1.00	2.00	1.00	3.00	1.00	1.00

ANNEXURE-III -MASTERCHART

22	SALIM	58	1	812,031	1	1	2	2,153.00	45	3	12.40	37	154.00	463.00	2	1.00	2.00	24.03	2.00	2.00	1.00	3.00	2.00	1.00
23	HANAMANTA	56	1	812,938	1	1	1	4,839.00	45	2	11.40	29	349.00	739.00	2	0.90	2.00	8.31	1.00	2.00	1.00	3.00	1.00	1.00
24	TATYASAHEB K	70	1	4,445,719	1	1	1	4,404.00	45	3	13.50	92	312.00	323.00	2	1.20	3.00	29.49	2.00	2.00	2.00	3.00	2.00	2.00
25	TUKARAM L	66	1	4,371,929	1	1	1	23,521.00	30	9	10.30	16	352.40	392.00	2	1.20	3.00	4.54	1.00	2.00	1.00	3.00	1.00	1.00
26	SWATI KRISHNA	49	2	3,471,106	1	1	1	6,040.00	45	1	12.40	35	493.00	239.00	2	1.00	1.00	7.10	1.00	2.00	1.00	2.00	1.00	1.00
27	RAMESH KHOT	53	1	4,445,743	1	1	1	9,383.00	40	2	12.00	42	421.00	200.00	2	0.90	2.00	9.98	1.00	2.00	1.00	2.00	1.00	1.00
28	BIKASH SWAIN	54	1	4,445,376	1	1	1	10,344.00	45	3	9.40	32	325.00	363.00	2	1.00	2.00	9.85	1.00	2.00	1.00	3.00	1.00	1.00
29	PARIKHITA P	55	2	4,445,365	1	1	2	4,464.10	45	3	12.90	24	152.00	232.40	3	1.00	2.00	15.79	1.00	2.00	1.00	2.00	1.00	1.00
30	RAMU YADAGE	72	1	4,441,076	1	2	1	2,353.00	45	1	13.10	32	193.00	392.00	2	1.20	4.00	16.58	1.00	2.00	1.00	3.00	1.00	1.00
31	BABU CHOUGULA	72	1	4,440,568	1	1	2	492.50	45	1	12.20	35	252.30	492.00	2	0.80	4.00	13.87	1.00	1.00	1.00	3.00	1.00	1.00
32	SANTOSH PRABHU	56	1	4,432,196	1	1	1	7,483.00	40	3	11.40	12	237.40	201.00	2	1.00	2.00	5.05	1.00	2.00	1.00	2.00	1.00	1.00
33	MARIA D	55	2	4,432,324	1	1	1	5,350.00	45	2	10.10	40	122.00	143.00	3	0.80	2.00	32.79	2.00	2.00	2.00	2.00	2.00	2.00
34	SANTOSH CHITLE	55	1	4,443,275	1	1	2	11,249.00	35	9	8.20	39	320.00	383.00	3	1.00	2.00	12.19	1.00	2.00	1.00	3.00	1.00	1.00
35	SURYAN DSOUZA	68	1	4,432,465	1	1	1	13,203.00	40	3	10.20	65	323.00	183.40	3	1.00	3.00	20.12	2.00	2.00	2.00	2.00	2.00	2.00
36	ALAGASWAMY V	62	1	4,453,490	1	1	1	6,973.60	40	2	13.50	65	193.00	182.90	1	1.20	3.00	33.68	2.00	2.00	2.00	2.00	2.00	2.00
37	URMILA M	67	2	4,433,087	1	2	2	894.10	45	2	11.50	18	292.00	183.00	3	1.00	3.00	6.16	1.00	1.00	1.00	2.00	1.00	1.00
38	SIDDHALINGAPPA B	70	1	4,432,656	1	1	2	9,354.00	45	1	12.20	49	294.00	291.00	2	1.00	3.00	16.67	1.00	2.00	1.00	2.00	1.00	1.00
39	APPASAHEB DHARMANNAVAR	62	1	4,452,697	1	1	2	2,231.00	40	3	9.80	21	341.00	433.00	2	1.00	3.00	6.16	1.00	2.00	1.00	3.00	1.00	1.00
40	BASAPPA BASARGII	64	1	4,532,442	1	2	1	9,284.00	45	2	12.00	43	252.00	184.00	2	1.00	3.00	17.06	1.00	2.00	1.00	2.00	1.00	1.00
41	SAROJINI PATIL	48	2	4,442,356	1	2	1	14,252.00	45	2	10.70	15	256.00	463.00	2	1.00	1.00	5.86	1.00	2.00	1.00	3.00	1.00	1.00
42	SUDAN CHADLA	84	1	4,440,472	1	1	2	9,335.00	30	9	10.10	24	312.00	544.00	3	1.40	4.00	7.69	1.00	2.00	1.00	3.00	1.00	1.00
43	MAHANTESH KAMATE	63	1	4,430,861	1	1	2	5,465.00	45	2	14.10	54	145.00	364.00	1	1.20	3.00	37.24	2.00	2.00	1.00	3.00	2.00	1.00
44	MAHAVEER SATAPPA	64	1	4,629,406	1	2	1	6,453.00	45	3	10.50	35	124.00	236.00	3	1.80	3.00	28.23	2.00	2.00	1.00	2.00	2.00	1.00
45	RAJU PAWAE	70	1	4,356,269	1	1	2	17,039.00	30	9	10.10	12	413.10	412.00	3	1.00	3.00	2.90	1.00	2.00	1.00	3.00	1.00	1.00
46	AVAKKA H	42	2	4,373,979	1	1	1	6,743.50	45	2	7.40	35	375.00	65.00	3	1.00	1.00	9.33	1.00	2.00	1.00	1.00	1.00	1.00
47	BASAVARAJ P	53	1	4,368,243	1	1	1	7,640.28	45	2	9.60	32	367.00	33.00	3	1.20	2.00	8.72	1.00	2.00	1.00	1.00	1.00	1.00
48	GIRISH MANDI	54	1	4,410,426	1	2	2	15,334.00	30	9	7.60	34	251.00	324.00	2	1.00	2.00	13.55	1.00	2.00	1.00	3.00	1.00	1.00
49	SHIVAJI TIGADALLI	68	1	4,388,410	1	1	2	24,221.00	25	9	8.80	11	365.00	87.10	3	1.50	3.00	3.01	1.00	2.00	1.00	1.00	1.00	1.00
50	SIDDHESHWAR BHOSALE	74	1	4,136,936	1	1	2	3,282.00	45	2	11.30	66	312.00	153.00	2	1.20	4.00	21.15	2.00	2.00	2.00	2.00	2.00	2.00
51	USHA SHIVAKUMAR	60	2	4,410,645	1	1	1	14,210.00	40	2	9.40	29	43.00	122.00	3	1.00	2.00	67.44	3.00	2.00	1.00	2.00	2.00	1.00
52	AKHTAR SALIM	59	1	4,351,710	1	2	1	8,864.00	40	4	12.30	54	376.00	45.00	2	1.00	2.00	14.36	1.00	2.00	1.00	1.00	1.00	1.00

53	NANDA MIRAJKAR	85	1	4,409,440	1	1	2	15,320.00	30	9	10.00	18	332.00	196.00	3	1.00	4.00	5.42	1.00	2.00	1.00	2.00	1.00	1.00
54	IRAPPA I	59	1	4,409,218	1	1	2	1,220.00	45	3	14.40	66	142.00	243.00	1	1.00	2.00	46.48	2.00	1.00	2.00	2.00	2.00	2.00
55	DATTATREY VERNEKAR	66	1	1,316,740	1	1	1	3,910.00	40	1	13.20	40	195.00	335.00	2	1.00	3.00	20.51	2.00	2.00	1.00	3.00	2.00	1.00
56	KARSHAN PATEL	50	1	4,343,346	1	2	1	4,333.00	45	3	14.00	64	214.00	320.60	1	1.00	1.00	29.91	2.00	2.00	2.00	3.00	2.00	2.00
57	ASHOK GAUDE	67	1	4,408,653	1	2	2	4,242.00	45	4	11.60	77	130.00	124.00	3	1.20	3.00	59.20	3.00	2.00	2.00	2.00	2.00	2.00
58	ASHOK PATIL	64	1	4,249,040	1	1	1	9,192.00	25	9	7.40	15	376.00	443.00	3	1.20	3.00	3.99	1.00	2.00	1.00	3.00	1.00	1.00
59	PANDURANG PARULEKAR	88	1	4,426,534	1	1	2	1,323.40	45	2	11.40	44	134.00	153.00	2	1.20	4.00	32.84	2.00	1.00	1.00	2.00	2.00	1.00
60	RAMESH W	41	1	4,431,201	1	1	2	1,707.00	45	3	10.20	55	184.00	312.00	2	1.00	1.00	29.89	2.00	1.00	2.00	3.00	2.00	2.00
61	BHUJANGONDRAY	63	2	4,204,829	1	1	2	8,204.00	40	3	11.20	52	391.00	323.00	2	0.80	3.00	13.30	1.00	2.00	2.00	3.00	1.00	2.00
62	SUMAN SANKALP	57	2	4,344,991	1	2	1	12,030.00	30	9	7.90	23	231.00	422.00	3	1.40	2.00	9.96	1.00	2.00	1.00	3.00	1.00	1.00
63	PANDURANG BHOSALE	72	1	4,428,331	1	2	2	1,606.00	35	3	13.30	66	193.00	182.00	2	1.10	4.00	34.20	2.00	1.00	2.00	2.00	2.00	2.00
64	RAMLAL AGARWAL	52	1	4,433,920	1	2	1	7,753.00	35	9	10.40	32	455.00	132.00	3	1.10	2.00	7.03	1.00	2.00	1.00	2.00	1.00	1.00
65	BANU LAKENDI	65	1	819,703	1	1	2	3,413.00	40	6	11.30	49	195.00	320.00	2	1.00	3.00	25.13	2.00	2.00	1.00	3.00	2.00	1.00
66	HANUMANT	51	1	818,905	1	2	2	6,493.00	45	3	13.10	52	253.00	340.00	1	0.80	2.00	20.55	2.00	2.00	1.00	3.00	2.00	1.00
67	MALLIKARJUN	68	1	819,786	1	1	2	3,453.60	40	3	9.50	12	241.00	431.40	3	1.10	3.00	4.98	1.00	2.00	1.00	3.00	1.00	1.00
68	SALIM KHAN	73	1	818,916	1	1	2	17,239.30	25	9	7.80	19	313.00	382.00	3	1.30	4.00	6.07	1.00	2.00	1.00	3.00	1.00	1.00
69	JAYALAKSHMI PRABHU	56	2	818,545	1	2	1	9,372.50	45	7	10.80	28	203.00	298.00	3	1.40	2.00	13.79	1.00	2.00	1.00	2.00	1.00	1.00
70	KAMALAVVA	62	2	819,943	1	2	2	492.00	45	3	12.40	64	342.00	193.00	1	1.00	3.00	18.71	1.00	1.00	2.00	2.00	1.00	1.00
71	MUBARAK	56	1	818,745	1	2	2	1,765.00	45	6	14.20	66	312.00	251.20	1	1.10	2.00	21.15	2.00	1.00	2.00	2.00	2.00	2.00
72	YAMANAPPA	78	1	819,403	1	2	2	604.20	45	1	11.50	35	198.00	316.90	2	1.00	4.00	17.68	1.00	1.00	1.00	3.00	1.00	1.00
73	ADAMSAB	64	1	819,186	1	2	2	832.30	45	6	14.40	74	210.00	419.00	1	1.00	3.00	35.24	2.00	1.00	2.00	3.00	2.00	2.00
74	REVANSIDDA	70	1	816,782	1	2	1	28,451.00	25	9	6.80	11	443.30	45.00	3	1.30	3.00	2.48	1.00	2.00	1.00	1.00	1.00	1.00
75	PARASHURAM	50	1	819,114	1	1	2	1,608.00	45	3	11.60	53	195.00	54.10	2	1.00	1.00	27.18	2.00	1.00	1.00	1.00	2.00	1.00
76	MUDDASAR	57	1	818,274	1	2	2	1,093.00	45	2	9.30	17	433.00	423.00	3	1.10	2.00	3.93	1.00	1.00	1.00	3.00	1.00	1.00
77	ABDUL KADAR	68	1	289,329	1	1	1	11,023.00	35	5	13.50	29	305.30	340.00	2	1.10	3.00	9.50	1.00	2.00	1.00	3.00	1.00	1.00
78	ACHYUT KULKARNI	48	1	822,445	1	1	1	7,393.00	40	3	12.50	14	521.00	523.00	2	1.00	1.00	2.69	1.00	2.00	1.00	3.00	1.00	1.00
79	RAMESH WANJLE	75	1	809,476	1	1	2	12,513.30	30	5	10.50	10	231.00	359.60	3	1.00	4.00	4.33	1.00	2.00	1.00	3.00	1.00	1.00
80	SATRAM	48	1	811,324	1	2	2	538.90	45	2	14.50	74	146.00	78.00	1	1.10	1.00	50.68	3.00	1.00	2.00	1.00	2.00	1.00
81	LAXMINARAYAN	75	1	720,440	1	1	1	19,013.10	25	9	8.10	10	192.10	434.00	3	1.00	4.00	5.21	1.00	2.00	1.00	3.00	1.00	1.00
82	VIJAY TAMBE	63	1	813,080	1	2	2	752.10	45	5	13.20	83	103.00	252.00	1	1.00	3.00	80.58	3.00	1.00	2.00	2.00	2.00	2.00
83	RAYAPPA	51	1	766,784	1	2	2	5,345.00	45	1	12.10	34	124.00	142.50	2	1.00	2.00	27.42	2.00	2.00	1.00	2.00	2.00	1.00

84	SUMITRA	62	2	729,932	1	2	1	9,534.00	40	5	10.20	25	294.00	199.20	2	1.00	3.00	8.50	1.00	2.00	1.00	2.00	1.00	1.00
85	UDAY P	48	1	753,992	1	2	2	2,943.90	45	3	12.40	92	212.00	417.00	2	0.70	1.00	43.40	2.00	2.00	2.00	3.00	2.00	2.00
86	BHIMAPPA	64	1	794,469	1	2	2	688.40	45	5	13.80	25	356.00	295.00	3	1.00	3.00	7.02	1.00	1.00	1.00	2.00	1.00	1.00
87	MANOHAR H	73	1	844,234	1	2	1	10,312.80	40	6	10.70	23	433.40	259.00	3	1.00	4.00	5.31	1.00	2.00	1.00	2.00	1.00	1.00
88	BALASAHEB PATIL	88	1	812,355	1	1	2	31,210.00	35	6	9.60	33	410.50	343.10	3	1.30	4.00	8.04	1.00	2.00	1.00	3.00	1.00	1.00
89	KENCHAPPA	72	1	811,509	1	1	2	8,394.00	25	9	10.00	32	384.00	229.60	3	0.80	4.00	8.33	1.00	2.00	1.00	2.00	1.00	1.00
90	FAIZAL AHMED	58	1	4,445,863	1	1	2	545.40	45	3	13.10	74	312.00	531.00	2	1.50	2.00	23.72	2.00	1.00	2.00	3.00	2.00	2.00
91	LAKSHMI M	76	2	810,394	1	2	1	12,302.00	45	6	7.70	12	423.00	125.00	3	1.20	4.00	2.84	1.00	2.00	1.00	2.00	1.00	1.00
92	BASAVARAJ PATIL	62	1	799,424	1	1	2	3,640.50	45	5	12.30	22	312.00	294.50	2	1.10	3.00	7.05	1.00	2.00	1.00	2.00	1.00	1.00
93	TATYASAHEB P	76	1	801,323	1	1	2	4,794.00	45	2	13.30	36	244.00	325.40	1	1.20	4.00	14.75	1.00	2.00	1.00	3.00	1.00	1.00