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Impact of Iron Deficiency on Short-Term Clinical Outcomes in Patients Admitted With Acute Heart Failure at Benjamin Mkapa Hospital: A Prospective Cohort Study

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IMPACT OF IRON DEFICIENCY ON SHORT-TERM CLINICAL OUTCOMES IN PATIENTS ADMITTED WITH ACUTE HEART FAILURE AT BENJAMIN MKAPA HOSPITAL: A PROSPECTIVE COHORT STUDY

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ABSTRACT

Introduction: Iron deficiency is a common but under-recognized comorbidity in acute heart failure (AHF) and is associated with poor outcomes. However, data on its impact on short-term outcomes among AHF patients in Tanzania remain limited. This study assessed the association between absolute iron deficiency (AID) and short-term outcomes among patients admitted with AHF at Benjamin Mkapa Hospital (BMH).

Methods: A prospective cohort study was conducted among adults admitted with AHF at BMH between January 2025 and June 2026. AID was defined as serum ferritin <100 ng/mL. Participants were followed for 90 days. The primary outcome was a composite of all-cause mortality or hospital readmission. Secondary outcomes included quality of life (KCCQ-12 score), NYHA functional status, and length of hospital stay. Kaplan-Meier and Cox regression assessed the primary outcome; secondary outcomes were compared using parametric or non-parametric tests as appropriate.

Results: A total of 339 participants were enrolled, of whom 330 (97.3%) completed follow-up. The mean age was 61.5 ± 15.5 years, 176 (53.0%) were female and 175 (53.0%) participants had AID. During follow-up, 63 (19.0%) experienced the composite endpoint. Participants with AID had lower event-free survival than those without (72.5% vs. 90.3%, log-rank $p<0.001$). After adjustment, AID was independently associated with the composite endpoint (AHR 2.25, 95% CI 1.21–4.17; $p=0.010$). At 90 days, AID participants had poorer NYHA functional status, with more remaining in class IV (20.0% vs. 11.6%) and fewer reaching class II (28.0% vs. 37.4%; $\chi^2=21.20$, $p<0.001$). Participants with AID had a smaller improvement in KCCQ-12

scores (4.1 ± 9.8 vs. 9.2 ± 8.8 points; p<0.001), and hospital stay was longer (7.9 ± 2.5 vs. 6.8 ± 2.2 days; p<0.001).

Conclusion: AID is common among patients admitted with AHF and is independently associated with poorer short-term clinical outcomes. Larger multicentre studies with longer follow-up are needed to confirm these findings.

Keywords: Acute heart failure; absolute iron deficiency; clinical outcomes; quality of life; Tanzania.

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LIST OF ABBREVIATIONS AND ACRONYMS

ACC	American College of Cardiology
ADHF	Acute decompensated heart failure
AHF	Acute heart failure
AHA	American Heart Association
AID	Absolute iron deficiency
BMH	Benjamin Mkapa Hospital
CCU	Coronary Care Unit
CKD	Chronic kidney kidease
ESC	European Society of Cardiology
FCM	Ferric carboxymaltose
IDA	Iron deficiency anaemia
Hb	Haemoglobin
HF	Heart failure
HFrEF	Heart failure with reduced ejection fraction
HFpEF	Heart failure with preserved ejection fraction
KCCQ	Kansas City Cardiomyopathy Questionnaire
LVEF	Left ventricular ejection fraction
MOH	Ministry of Health
NCD	Non-communicable diseases
NYHA	New York Heart Association
TAPSE	Tricuspid Annular Plane Systolic Excursion
RVD	Right ventricular dysfunction
TaHeF	Tanzania Heart Failure Study

TMDA	Tanzania Medical and Medical Devices Authority
TSAT	Transferrin saturation
WHO	World Health Organization

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CHAPTER ONE

INTRODUCTION

1.1 Background Information

Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide, accounting for an estimated 20.5 million deaths annually and representing nearly one-third of all global deaths(1).

Among cardiovascular conditions, heart failure (HF) is a major and growing public health challenge due to its chronic nature, recurrent hospitalisations, poor prognosis, and substantial healthcare costs. Globally, approximately 64.3 million people are living with heart failure, making it a major contributor to morbidity, disability, reduced quality of life, and premature mortality(2). Despite significant advances in cardiovascular medicine, heart failure continues to be associated with poor long-term outcomes, with five-year mortality rates ranging between 42% and 60%(3).

The burden of HF is increasingly concentrated in low- and middle-income countries, where population ageing, urbanization, and the rising prevalence of hypertension, diabetes mellitus, obesity, and other cardiovascular risk factors are contributing to the growing burden of cardiovascular disease. Patients in these settings may also present

with more advanced disease because of delayed diagnosis, limited access to specialized cardiovascular care, and constrained healthcare resources(4).

Sub-Saharan Africa bears a disproportionately high burden of heart failure. The aetiological profile of HF in sub-Saharan Africa differs from that observed in many high-income settings where ischemic heart disease predominates; heart failure in Africa is commonly driven by uncontrolled hypertension, rheumatic heart disease and cardiomyopathies. Studies have reported annual mortality rates of approximately 34% among heart failure patients in Sub-Saharan Africa, which is more than double the global average of 16.5% (3).

Acute heart failure (AHF) refers to the rapid onset or worsening of heart failure signs and symptoms requiring urgent evaluation and, often hospitalisation. It represents one of the most severe manifestations of the heart failure. Management is primarily directed toward relieving congestion, correcting haemodynamic abnormalities, and treating precipitating factors. Although these interventions alleviate congestion and stabilize patients, patients remain at substantial risk of mortality and recurrent hospitalisation despite improvements in acute management(5,6). Furthermore, recurrent hospital admissions for acute heart failure impose a substantial burden on patients, families, and already overstretched healthcare systems.

In Tanzania, heart failure has become an increasingly important cause of cardiovascular morbidity and mortality. Additionally, patients hospitalised with heart failure experience significantly higher post-discharge mortality compared with individuals admitted for other medical illnesses. Studies conducted in tertiary hospitals have demonstrated poor outcomes among patients admitted with heart failure. Kingery et al (2017) , reported that more than half of heart failure patients died within one year following hospital discharge, highlighting the severe prognosis associated with the condition.

Consequently, there is growing interest in identifying comorbid conditions that may contribute to poor outcomes and could serve as potential therapeutic targets. Comorbid conditions are central to the natural history of acute heart failure, functioning simultaneously as risk factors for admission and as complications that worsen in-hospital and post-discharge prognosis (6).

Comorbidities are highly prevalent among patients with AHF and play an important role in disease progression, clinical deterioration, and prognosis(6). Data from the ESC Heart Failure Long-Term Registry demonstrate a high burden of both cardiovascular and non-cardiovascular comorbidities among hospitalised patients with HF, including hypertension, ischaemic heart disease, atrial fibrillation, diabetes mellitus, chronic kidney disease, and anaemia(8). Among these non-cardiac comorbidities, iron deficiency (ID) with or without accompanying anaemia has attracted increasing attention because of its high prevalence and potential effects on functional capacity and clinical outcomes.

Iron is the most common nutritional deficiency worldwide. Iron is also an essential micronutrient involved in oxygen transport, cellular metabolism, mitochondrial energy production, and skeletal muscle function(9). In patients with heart failure, ID arises from a combination of poor dietary intake, impaired gastrointestinal absorption, chronic low-grade inflammation, renal dysfunction, and increased metabolic demand(9). Rather than being merely a simple haematological abnormality, ID in heart failure independent of anaemia has been associated with reduced exercise tolerance, diminished quality of life, more frequent and prolonged hospitalisations, and higher mortality (10).

The prevalence of iron deficiency among patients with chronic heart failure ranges from approximately 35% to 55%, independent of the presence of anaemia. Importantly, its prevalence increases with worsening disease severity and higher New York Heart Association (NYHA) functional class (9). In patients admitted with acute heart failure, the prevalence is even higher, ranging from 50% to 80% in various studies(11).

Regional evidence demonstrates a similarly high burden. In Kenya, (12) reported iron deficiency in 56.7% of patients with chronic heart failure, while the Tanzania Heart Failure Study (TaHeF) reported a prevalence of approximately 49% among heart failure patients attending tertiary care facilities (13).

Because ID has been associated with adverse outcomes independently of haemoglobin level, intravenous iron replacement is now considered a modifiable therapeutic target rather than an incidental laboratory finding. Intravenous repletion has been shown to

improve functional status and quality of life and to reduce heart failure-related hospitalisations (14). In the acute hospitalised population setting, the AFFIRM-AHF trial, in which ferric carboxymaltose was given to iron-deficient patients stabilized after an ADHF episode reduced the risk of heart failure rehospitalisation over 52 weeks (15). However, evidence from therapeutic trials has largely been generated in high-income settings, where the epidemiological and aetiological profile of heart failure differs from that of many sub-Saharan African populations. The extent to which the prognostic significance of absolute iron deficiency observed in these settings applies to patients hospitalised with AHF in sub-Saharan Africa remains less well characterized.

Important gaps remain regarding its burden and prognostic significance among patients hospitalised with acute heart failure in Sub-Saharan Africa. In Tanzania specifically, iron status is not yet routinely assessed in the management of acute heart failure, and local evidence characterizing the relationship between absolute iron deficiency and short-term outcomes including mortality, hospital readmission, quality of life, functional status, and length of hospital stay remains scarce.

Therefore, this study was conducted to determine the impact of absolute iron deficiency on short-term clinical outcomes among patients admitted with acute heart failure at Benjamin Mkapa Hospital. Establishing this local evidence is an important step toward informing routine iron status screening and guiding future interventional research on iron repletion therapy in this population.

1.2 Statement of Problem

Acute heart failure (AHF) is a major cause of hospitalisation worldwide and is associated with substantial in-hospital morbidity and mortality. Patients hospitalised with AHF also remain at considerable risk of rehospitalisation and subsequent cardiovascular death, with approximately 25–30% of patients being readmitted within 30–90 days after discharge and mortality reaching about 10% within 60–90 days, a period increasingly recognized as a vulnerable phase following an acute heart failure episode(16,17).

This burden is also substantial in sub-Saharan Africa, where recent studies have reported mortality rates ranging from 3.7% to 19% among patients with heart failure,

with rehospitalisation remaining a frequent adverse outcome(18). In Tanzania, the burden is similarly concerning: among adults discharged after hospitalisation with heart failure, 57.9% died within one year, while a separate Tanzanian study reported a 30-day readmission rate of 25% among patients with previous heart failure admissions (7,19).

These persistently high rates of mortality and rehospitalisation highlight the need to identify comorbid conditions that may contribute to adverse outcomes and potentially provide opportunities for improved risk stratification and management. Among these, iron deficiency (ID) has emerged as an important and potentially modifiable comorbidity in patients with AHF and may occur with or without anaemia. Iron deficiency may adversely affect cellular energy metabolism and exercise capacity independently of its effects on haemoglobin, and has been associated with impaired functional capacity and adverse clinical outcomes in patients with heart failure (9,10,14).

International observational studies have demonstrated associations between iron deficiency and adverse outcomes in patients with AHF, while clinical trials have investigated the effects of intravenous iron therapy in symptomatic patients with heart failure and iron deficiency(15,20–22). Accordingly, contemporary heart failure guidelines recommend assessment of iron status in appropriate patients with heart failure and provide recommendations for iron replacement in selected patients (23–25)

In Tanzania, the TAHEF study demonstrated that iron deficiency was common among patients with heart failure, affecting 49% of the study population. Iron deficiency was also associated with adverse prognosis, with iron deficiency anaemia associated with more than a two-fold higher risk of hospitalisation for heart failure or all-cause mortality (HR 2.67)(13).

However, important gaps remain regarding the prognostic significance of absolute iron deficiency among patients hospitalised with acute heart failure and its relationship with subsequent short-term clinical outcomes. In particular, local evidence remains limited regarding the association between absolute iron deficiency and mortality or hospital readmission, quality of life, functional status, and length of hospital stay following an acute heart failure admission.

Addressing these gaps is important because establishing the prognostic relevance of absolute iron deficiency among patients admitted with AHF could improve local risk stratification and provide a basis for future interventional research.

Locally generated evidence may therefore contribute to a better understanding of the clinical significance of absolute iron deficiency and inform future approaches to the assessment and management of patients with AHF in Tanzania.

Therefore, this study was conducted to determine the impact of absolute iron deficiency on short-term clinical outcomes among patients admitted with acute heart failure at Benjamin Mkapa Hospital.

1.3 Research Objectives

1.3.1 Broad objective

To determine the impact of absolute iron deficiency on short-term clinical outcomes among patients admitted with acute heart failure at Benjamin Mkapa Hospital.

1.3.2 Specific objectives

i. To assess the association between absolute iron deficiency and the composite endpoint of all-cause mortality or hospital readmission (whichever came first) during a 3-month follow-up period among patients admitted with acute heart failure at Benjamin Mkapa Hospital.

ii. To compare the quality of life (KCCQ score) in patients with and without absolute iron deficiency admitted with acute heart failure at Benjamin Mkapa hospital during a 3-month follow-up period.

iii. To compare the change in functional status (NYHA class) in patients with and without absolute iron deficiency admitted with acute heart failure at Benjamin Mkapa Hospital during a 3-month follow-up period

iv. To compare the length of hospital, stay between patients with and without absolute iron deficiency admitted with acute heart failure at Benjamin Mkapa Hospital.

1.4 Research Question

i. What is the association between absolute iron deficiency and the risk of the composite endpoint of all-cause mortality or hospital readmission within 3 months among patients admitted with acute heart failure at Benjamin Mkapa Hospital?
ii. Is there a difference in the change in quality of life, as measured by the KCCQ-12 score, between patients with and without absolute iron deficiency over 3 months following admission for acute heart failure at Benjamin Mkapa Hospital?
iii. Is there a difference in improvement in functional status, as assessed by NYHA functional class, between patients with and without absolute iron deficiency over 3 months following admission for acute heart failure at Benjamin Mkapa Hospital?
iv. Is there a difference in the length of hospital stay at admission between patients with and without absolute iron deficiency among patients admitted with acute heart failure at Benjamin Mkapa Hospital?

1.5 Rationale/Justification

This study was undertaken to address the limited evidence on absolute iron deficiency among patients hospitalised with acute heart failure in Tanzania. By prospectively evaluating the relationship between absolute iron deficiency and mortality or hospital readmission, quality of life, functional status, and length of hospital stay, the study provides context-specific evidence on the short-term clinical course of patients with acute heart failure.

The findings may assist clinicians in identifying patients with acute heart failure who have absolute iron deficiency and may be at greater risk of adverse short-term outcomes. The results may also inform consideration of iron status assessment within acute heart failure care and help identify priorities for future research, particularly interventional studies evaluating whether correction of iron deficiency can improve clinical outcomes. More broadly, the study contributes local evidence that may support improved risk assessment and inform future management strategies for acute heart failure within the context of Tanzania's growing cardiovascular disease burden.

1.6 Definition of Terms

Acute heart failure (AHF): In this study, acute heart failure (AHF) was defined as a sudden onset or rapid worsening of heart failure signs and symptoms that necessitate urgent hospitalisation. The term encompasses both de novo cases and acute exacerbations of chronic heart failure. Diagnosis was established by the attending physician using clinical criteria from the Framingham score, supported by relevant laboratory tests and imaging studies (23,25)

Hospital stay (Length of Stay): This was defined as the number of complete days a patient remains admitted in the hospital from the time of initial admission with AHF until the time of discharge, regardless of outcome. It reflects the burden of illness and the need for inpatient care (26)..

All-cause mortality: Refers to death from any cause occurring within 90 days of index admission for acute heart failure. Deaths may occur in-hospital or post-discharge and were included whether cardiovascular or non-cardiovascular(27)

Classification of heart failure according to left ventricular ejection fraction: Heart failure with reduced ejection fraction (HFrEF) was defined as heart failure with a left ventricular ejection fraction (LVEF) ≤40%. Heart failure with mildly reduced ejection fraction (HFmrEF) refers to heart failure with an LVEF of 41–49%, while heart failure with preserved ejection fraction (HFpEF) refers to heart failure with an LVEF ≥50%, together with evidence of increased left ventricular filling pressures or relevant structural/functional cardiac abnormalities. (25)

Hospital Readmission: This was defined as any unplanned readmission to a hospital within 90 days after discharge from the index hospitalisation for AHF, due to any cause(27)

Functional status: In this study, functional status was defined as the patient's capacity to carry out everyday activities, including walking, personal care, and household tasks. Functional status was evaluated using the New York Heart Association (NYHA) classification system (28)

Quality of life (QoL): In this study, quality of life refers to patients' perceived health-related quality of life in relation to heart failure, assessed using the 12-item Kansas City Cardiomyopathy Questionnaire (KCCQ-12). The KCCQ-12 assesses the impact of heart failure on symptoms, physical limitations, social limitations, and quality of life over a 2-week recall period**.** Scores range from 0 to 100**,** with higher scores indicating better health status and quality of life.(29).

CHAPTER TWO

LITERATURE REVIEW

2.0 Introduction

Iron deficiency (ID) is increasingly recognized as a common comorbidity in patients with heart failure (HF), significantly affecting morbidity and mortality. Despite advances in Heart failure treatment, ID remains underdiagnosed and undertreated, particularly in acute heart failure (AHF) settings. Iron status has been shown to influence clinical outcomes independently of haemoglobin (Hb) levels, with iron deficiency linked to decreased exercise tolerance, poorer quality of life, and a heightened risk of mortality and hospital admissions or readmissions. Clinical studies indicate that intravenous iron supplementation can improve symptoms, functional capacity, and quality of life**,** regardless of a patient's Hb concentration**.** These findings highlight the important physiological functions of iron that extend beyond red blood cell production(30) This review summarizes recent evidence on the epidemiology, pathophysiology, clinical consequences, and management of iron deficiency in acute heart failure, with emphasis on its global and regional burden, including data from Sub-Saharan Africa and Tanzania.

2.1 Global Burden of Iron Deficiency in Acute Heart Failure

Iron deficiency (ID) is common in patients with heart failure, occurring in an estimated 37–50% of those with chronic heart failure (CHF) and rising to 52–74% among individuals hospitalised with acute heart failure (AHF) (5).

2.2 Regional Perspective

The burden of iron deficiency in heart failure has been documented across multiple regions, though the populations studied, the outcomes measured, and the strength of the underlying evidence vary considerably. The following sections examine this regional evidence in turn, before drawing together what these differences mean for the present study.

2.2.1 United States

A large retrospective study based on the 2019 United States National Inpatient Sample (NIS) analyzed 112,864 hospital admissions for adult patients with heart failure and reported that iron deficiency anaemia (IDA) was present in approximately 7% of cases(31). In that study, the presence of IDA was associated with prolonged hospitalisation, with an average increase in length of stay of 1.31 days ($p < 0.01$).

In addition, patients with concomitant IDA demonstrated a higher burden of comorbidities, particularly complicated hypertension and diabetes mellitus, and incurred significantly greater inpatient costs, most notably among those with heart failure with reduced ejection fraction (HFrEF).

Furthermore, IDA was linked to an increased occurrence of acute inpatient complications, including atrial fibrillation and acute kidney injury, across both HFpEF and HFrEF phenotypes. Collectively, these findings suggest that iron deficiency in heart failure represents more than a coincidental comorbidity and may act as an independent contributor to unfavorable in-hospital outcomes. It is notable, however, that this figure of 7% is far lower than prevalence estimates reported elsewhere in this review a discrepancy that most plausibly reflects the study's reliance on administrative coding for iron deficiency anaemia rather than direct ferritin or transferrin saturation measurement, in contrast to the laboratory-based definitions used in most of the studies discussed below**.** In resource-limited settings such as Tanzania, where the burden of heart failure continues to rise amid constrained healthcare resources, these observations highlight the potential importance of routine iron deficiency screening and timely management as strategies to improve clinical outcomes and reduce preventable healthcare expenditures.

2.2.2 Europe

Recent European studies indicate that iron deficiency (ID) is substantially more common in patients with acute heart failure (AHF) than in those with chronic heart failure (CHF). Reported prevalence rates range from 74.8% to 79.9% among AHF patients, compared with 32.6% to 47.3% in individuals with CHF (32) and the rates are considerably closer to the laboratory-confirmed prevalence seen elsewhere in this review than to the 7% administrative estimate reported in the United States, reinforcing

that the US figure likely understates true prevalence rather than reflecting a genuinely lower regional burden.

More recently, the FERIC-RO registry, a multicentre Romanian study enrolling 163 patients hospitalised for worsening chronic heart failure across the full ejection fraction spectrum, reported an iron deficiency prevalence of 54.6% at discharge, with no significant change in prevalence between discharge and 30-day follow-up (54.6% vs 51.3%, p = 0.782)(22). Iron deficiency was independently associated with a more than two-fold higher adjusted hazard of 3-month rehospitalisation (HR, 2.165; 95% CI, 1.029–4.555; p = 0.042). Notably, only transferrin saturation and soluble transferrin receptor, rather than ferritin alone, were significantly associated with 90-day clinical outcomes in the multivariable analysis.

Building on this prevalence data, a separate study conducted at a tertiary referral centre in 2019 evaluated the prevalence and clinical significance of ID among patients admitted with acutely decompensated heart failure (ADHF), including both heart failure with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF). Among 503 patients, ID was identified in 54% of those with HFrEF and 56% of those with HFpEF, based on standard diagnostic criteria (absolute ID defined as ferritin <100 ng/mL and functional ID as ferritin 100–200 ng/mL with transferrin saturation <20%). Notably, in patients with HFpEF, iron deficiency was associated with a significantly longer duration of hospitalisation (mean length of stay 11 ± 7.7 days versus 9 ± 6 days in patients without ID; p = 0.036), and this association persisted after adjustment for age and comorbid conditions. In contrast, ID did not significantly influence hospital length of stay among patients with HFrEF(33). This phenotype-specific pattern, a length-of-stay effect confined to HFpEF is not something the US or subsequent Asian data (below) were positioned to detect, since neither study stratified by ejection fraction category; it remains an open question whether the same distinction holds in African cohorts, including the present study population.

2.2.3 Asia

While European evidence centres on length of stay and hospitalisation patterns, Asian data speak most directly to mortality. A five-year follow-up study found that iron deficiency (ID) is linked to a markedly higher risk of both cardiovascular and all-cause

mortality. In this cohort, 50.3% of participants were iron deficient; a prevalence broadly consistent with the European range above, despite the very different population and follow-up design. Individuals with severe ID had a 2.77-fold increased risk of cardiovascular death (95% CI: 1.28–5.99) and a 1.96-fold higher risk of all-cause mortality (95% CI: 1.26–3.04), even after controlling for confounding factors such as age, body mass index, blood pressure, glucose, and inflammatory markers. Furthermore, even mild iron deficiency was associated with an increased risk of all-cause mortality (RR: 1.63; 95% CI: 1.14–2.31) (34).

These findings underscore a dose-response relationship between ID severity and adverse outcomes, reinforcing its prognostic importance beyond anaemia alone. Taken together, the US, European, and Asian evidence point to a consistent picture: iron deficiency is prevalent across very different healthcare settings, and whether measured through length of stay, hospitalisation, or mortality it is repeatedly associated with worse outcomes. What none of these three regions can speak to, however, is whether the same holds true in Sub-Saharan Africa, where the demographic profile, disease etiology, and healthcare infrastructure differ substantially from all three settings above**.**

2.2.4 North Africa

A small single-centre Moroccan cohort of older adults with acute heart failure (n=50) reported an even higher iron deficiency prevalence of 82% though this estimate should be interpreted cautiously given the limited sample size.(35)

2.2.5 West Africa

A recent study in Nigeria, conducted at LAUTECH and Bowen University Teaching Hospitals in 2024, investigated the relationship between iron deficiency (ID) and right ventricular dysfunction (RVD) in 140 patients with heart failure (HF). Iron status was assessed using standardized definitions, and RVD was evaluated via echocardiography, with a TAPSE <20 mm indicating dysfunction. The study reported a high prevalence of ID, with a significantly greater proportion of patients with ID exhibiting RVD compared to those with normal iron levels (69.0% vs. 32.1%, $p<0.001$). Mean TAPSE was also lower among ID patients (14.4 ± 3.8 mm vs. 16.6 ± 4.5 mm, $p<0.05$), reflecting impaired right ventricular systolic function. Additionally,

pulmonary hypertension was more common in individuals with ID (33.3% vs. 25.9%, p=0.048)(36).

These findings highlight the prognostic implications of iron deficiency in African HF patients, linking it to structural cardiac complications beyond traditional morbidity metrics, and underscore the importance of routine iron status assessment in HF care in resource-limited African settings.

2.2.6 Sub-Saharan Africa

Moving from North &West to Southern and Eastern Africa, similarly high rates of iron deficiency have been documented. A study in South Africa reported absolute ID in 47.6% of patients with HFrEF, despite a relatively younger mean age and preserved haemoglobin in the majority, suggesting that ID may remain underdiagnosed when screening is based solely on anaemia(37). This observation that haemoglobin-based screening alone would miss a substantial proportion of iron-deficient patients recurs even more strongly in the East African evidence below.

2.2.6.1 East Africa

A study conducted in Kenya reported a high burden of iron deficiency among patients with heart failure, with an overall prevalence of 56.7%. Among individuals who were anemic, iron deficiency was identified in 86%, whereas a substantial proportion of non-anemic patients (43%) were also found to have depleted iron stores. In terms of iron deficiency subtypes, functional iron deficiency predominated, affecting 32.5% of patients, while absolute iron deficiency was observed in 24.4%. These findings emphasize that iron deficiency is common even in the absence of anaemia and underscore the importance of comprehensive iron assessment in patients with heart failure (12). This 43% non-anemic iron-deficiency rate in Kenya directly reinforces the South African finding above and is consistent with the broader pattern across every region reviewed so far: iron deficiency and anaemia overlap substantially but are not interchangeable, a distinction with direct implications for how absolute iron deficiency is operationalized in the present study.

2.2.6.2 Tanzania

A total of 401 patients with heart failure (HF) were enrolled in the Tanzania Heart Failure (TaHeF) study, with a median age of 56 years, and 51% female. Most patients were in NYHA class III–IV (80%), and 68% had reduced ejection fraction (LVEF <45%). The prevalence of anaemia was 57%, with ID present in 49% of the cohort. ID prevalence was markedly higher in patients with anaemia (69%) compared to those without (21%, $p<0.001$). Normocytic anaemia was the most common subtype, seen in 18% of all patients. Importantly, ID was significantly more prevalent in those with reduced LVEF (<45%), but did not significantly vary by sex or NYHA class(13). The 49% ID prevalence and the anaemia/ID overlap pattern reported here are consistent with the East and Southern African data above, suggesting that Tanzania's heart failure population is not pathophysiologically distinct from its regional neighbors in this respect. However, while that study provided the foundations and critical insights into the burden of ID in chronic heart failure, it did not explore the clinical impact of iron deficiency on short-term outcomes such as mortality or hospital readmissions, particularly in acute heart failure.

2.2.7 Synthesis of regional evidence.

Across every region reviewed from the United States and Europe through Asia to North, West, Southern, and East Africa, including Tanzania itself two patterns hold consistently: iron deficiency is prevalent regardless of setting (ranging from a likely underestimated 7% where administrative coding was used, to over 70% where ferritin and transferrin saturation were measured directly), and it is repeatedly associated with worse outcomes, whether measured as length of stay, mortality, or structural cardiac dysfunction. What differs across regions is not whether iron deficiency matters, but which outcome each study happened to examine: European data on length of stay, Asian data on mortality, West African data on right ventricular function, with no single setting examining all of these outcomes together, and none examining the specific 90-day composite of mortality and readmission that defines acute heart failure prognosis in the short term. Critically, the Tanzanian evidence available through the TAHEF study establishes that iron deficiency is common locally, but, like the South African and Kenyan data before it was conducted among stable or mixed heart failure populations rather than patients admitted with acute decompensation, and did not

follow patients forward to assess short-term clinical outcomes. This is precisely the gap the present study addresses.

2.3 Physiological Role and Regulation of Iron

Iron is an essential micronutrient required for oxygen transport (as a core component of haemoglobin and myoglobin), mitochondrial energy generation, cellular growth, and DNA synthesis (38). Its physiological role extends beyond oxygen transport to protein, lipid, and carbohydrate metabolism, with particularly high demand in metabolically active tissues such as cardiomyocytes, hepatocytes, and skeletal muscle, as well as in rapidly proliferating cells of the bone marrow and immune system; all of which are especially vulnerable to dysfunction when iron is deficient (30).

Because the body has no active mechanism for excreting excess iron, systemic iron balance is regulated almost entirely at the level of intestinal absorption rather than excretion. Minor losses occur through desquamation of intestinal and skin cells and, in women, menstrual bleeding, but most of the body's iron is continuously recycled from senescent red blood cells. As a result, an intake of only about 1–2 mg per day is sufficient to maintain the normal total body iron pool of 3–5 g (38).

2.4 Iron absorption and storage

Iron is absorbed mainly in the duodenum and upper jejunum, where dietary ferric iron is reduced to its ferrous form and taken up by enterocytes via the divalent metal-ion transporter 1 (DMT1) (30,39). Absorbed iron is either stored intracellularly as ferritin or exported into the circulation through ferroportin, the only known cellular iron exporter, after which it is oxidised and bound to transferrin for delivery to tissues via transferrin receptor-mediated uptake (40).

Systemic iron balance is governed centrally by hepcidin, a hepatocyte-derived peptide hormone that binds ferroportin and triggers its internalisation and degradation, thereby limiting intestinal iron absorption, macrophage iron recycling, and hepatic iron release into the circulation.(41)

2.5 Diagnosis of Iron Deficiency in Heart Failure

In otherwise healthy individuals, non-anemic iron deficiency is typically identified when serum ferritin drops below 30 ng/ml, while haemoglobin concentrations remain within normal ranges (≥12 g/dL in women and ≥13 g/dL in men(42,43). However, in the context of heart failure, the European Society of Cardiology (ESC) 2023 guidelines recommend higher ferritin thresholds. Specifically, iron deficiency in heart failure patients is defined either as an absolute deficiency, with ferritin below 100 ng/mL, or as a functional deficiency, with ferritin between 100 and 299 ng/mL accompanied by transferrin saturation (TSAT) under 20%(25). This distinction is now commonly referenced in international heart failure management guidelines.

While bone marrow iron staining remains the definitive reference method for assessing body iron stores, studies have shown that a substantial proportion of patients classified as iron deficient using conventional biochemical criteria do not exhibit true depletion of iron stores on bone marrow examination. This highlights the limitations of peripheral biomarkers in accurately reflecting tissue iron stores. In heart failure, this challenge is compounded by chronic inflammation, which may elevate serum ferritin despite impaired iron availability.(44,45).

2.6 Pathophysiological Links of Iron Deficiency and Heart Failure

In chronic conditions such as heart failure, proinflammatory cytokines can reduce iron availability by increasing intracellular sequestration through hepcidin-mediated inhibition of ferroportin, the sole known iron exporter in mammals. This mechanism results in functional iron deficiency, where total iron stores are sufficient but not readily accessible for cellular use(46).

Iron is essential for key processes in energy metabolism, including oxidative phosphorylation, the citric acid cycle, and respiratory chain enzyme function pathways particularly critical in cardiomyocytes due to their high energy demands for contraction. Evidence indicates that myocardial tissue from heart failure patients exhibits impaired mitochondrial respiration and reduced enzyme activity, suggesting that iron deficiency exacerbates pre-existing mitochondrial dysfunction. Additionally, iron deficiency compromises the electrochemical stability and contractility of

cardiomyocytes, potentially contributing to arrhythmias and worsening symptoms (46).

Chronic energy deficits in the myocardium mark stable heart failure (HF), AHF involves a sudden disruption of cardiac energy balance. In chronic HF, this "metabolic remodeling" is evident through impaired energy substrate use, reduced high-energy phosphate metabolism, and structural mitochondrial abnormalities, including decreased biogenesis. Though data on AHF are limited, experimental models (e.g., pacing-induced HF in dogs) show that even within weeks, early metabolic shifts occur favoring glucose metabolism over fatty acid oxidation**,** highlighting rapid energetic dysfunction during acute decompensation.(47).

2.7 Empirical Literature Review Based on Study Objectives

2.7.1 Iron deficiency and composite endpoint of all-cause mortality or hospital readmission

Ueda et al. (21) conducted a study among 615 patients hospitalised with acute decompensated heart failure and found that low serum iron was independently associated with adverse outcomes, including death and heart failure readmission. Although the study demonstrated the prognostic role of iron status, it was conducted outside Africa and assessed serum iron rather than focusing specifically on absolute iron deficiency.

Nunez et al. (20) studied 626 patients admitted with acute heart failure and reported that absolute iron deficiency was significantly associated with increased risk of early hospital readmission. However, the study was conducted in Europe, and the outcome was mainly readmission rather than a combined 90-day composite endpoint of death or readmission.

Palau et al. (48) analyzed 1,701 patients with acute decompensated heart failure and found that lower transferrin saturation was associated with increased short-term adverse outcomes. The study provided important evidence on iron markers, but it was registry-based and conducted in a high-income setting, limiting its applicability to Tanzanian patients.

Hsu et al. (34) reported that iron deficiency was associated with increased cardiovascular and all-cause mortality during follow-up. However, the study was not specific to patients admitted with acute heart failure and was conducted in an Asian population, creating both population and geographical gaps.

Makubi et al. (13) through the Tanzania Heart Failure Study, reported a high burden of iron deficiency and anaemia among patients with heart failure in Tanzania. However, the study mainly described prevalence and did not assess short-term outcomes such as 90-day mortality or readmission among patients with acute heart failure.

Therefore, although previous studies have shown that iron deficiency is associated with adverse outcomes, most were conducted outside Sub-Saharan Africa, used different populations, or focused on chronic heart failure. Limited Tanzanian evidence exists on whether absolute iron deficiency predicts the composite endpoint of all-cause mortality or hospital readmission within 90 days among patients admitted with acute heart failure.

2.7.2 Iron deficiency and quality of life among patients with acute heart failure

Klip et al. (10) demonstrated that iron deficiency was associated with poorer quality of life and reduced exercise capacity among patients with heart failure, independent of anaemia. However, the study was conducted among chronic heart failure patients and did not focus on acute heart failure admissions.

Sindone, Doehner and Comin-Colet et al. (49) reported that iron deficiency negatively affected health-related quality of life among patients with chronic heart failure. Although the study provided strong evidence on patient-reported outcomes, it was conducted in Europe and did not represent patients in low-resource African settings.

Anker et al. (50), in the FAIR-HF trial, found that intravenous ferric carboxymaltose improved symptoms, quality of life, and functional status among heart failure patients with iron deficiency. However, this was an interventional clinical trial mainly involving stable chronic heart failure patients rather than hospitalised acute heart failure patients.

Ponikowski et al. (51), through the CONFIRM-HF trial, also demonstrated improvement in quality of life and functional capacity following correction of iron deficiency. Nevertheless, the study population was predominantly European and did not address routine acute care settings in Tanzania.

Deichl and Edelmann (14) reviewed evidence showing that iron deficiency worsens physical performance, symptoms, and quality of life in heart failure patients. However, most studies reviewed were from high-income countries, and African data remained limited.

The gap remains that few studies have assessed quality of life among patients with acute heart failure and absolute iron deficiency in Sub-Saharan Africa. In Tanzania, no clear evidence exists on how absolute iron deficiency affects quality of life among patients admitted with acute heart failure at tertiary hospitals.

2.7.3 Iron deficiency and functional status among patients with acute heart failure

Rizzo et al. (9) reported that iron deficiency was more common among patients with worse New York Heart Association functional class, suggesting that iron deficiency increases with heart failure severity. However, the study largely focused on chronic heart failure and did not assess change in functional status during short-term follow-up.

Anker et al. (50)found that treatment of iron deficiency improved NYHA functional class among patients with heart failure. Although this showed the functional importance of iron deficiency, the trial was conducted in a controlled research setting and not among hospitalised acute heart failure patients in Tanzania.

Ponikowski et al. (51) also demonstrated improved functional capacity and symptoms after intravenous iron therapy. However, the study population was stable chronic heart failure patients, and the findings may not directly apply to acute heart failure patients admitted in low-resource settings.

Dhaliwal and Kalogeropoulos et al. (46) described how iron deficiency impairs mitochondrial function, skeletal muscle performance, and cardiac energy metabolism, thereby contributing to reduced functional capacity. However, this evidence was

mainly mechanistic and did not provide patient-level follow-up data in acute heart failure.

Omondi (12) reported a high prevalence of iron deficiency among heart failure patients in Kenya, including both anemic and non-anemic patients. However, the study mainly assessed burden and did not evaluate changes in NYHA functional class over time.

Therefore, available literature shows that iron deficiency is related to poor functional status, but most studies were conducted among chronic heart failure patients, outside Tanzania, or without short-term follow-up. This study addressed that gap by determining functional status among patients with absolute iron deficiency admitted with acute heart failure at Benjamin Mkapa Hospital.

2.7.4 Iron deficiency and length of hospital stay among patients with acute heart failure

Alharbi et al. (31) analyzed hospital admissions for heart failure in the United States and found that iron deficiency anaemia was associated with prolonged hospital stay and higher inpatient costs. However, the study focused on iron deficiency anaemia rather than absolute iron deficiency and was conducted in a high-income country.

Beale et al. (33) studied 503 patients admitted with acute decompensated heart failure and found that iron deficiency was associated with longer hospital stay, especially among patients with preserved ejection fraction. Although relevant, the study was conducted in a tertiary hospital outside Africa and may not reflect Tanzanian hospital settings.

Van Dalen et al. (5) reviewed acute heart failure and iron deficiency and reported that iron deficiency is common during acute admissions. However, their findings showed variability in hospital stay and were based on populations from developed settings.

Lanser et al. (32) reported that iron deficiency was highly prevalent among patients with acute heart failure and was associated with adverse clinical profiles. However, the evidence was European and may not reflect the demographic, nutritional, and healthcare system characteristics of Tanzania.

Núñez et al. (20) demonstrated that absolute iron deficiency predicted early readmission among acute heart failure patients, suggesting delayed recovery or instability after discharge. However, the study did not primarily evaluate length of hospital stay as the main outcome.

Thus, although previous studies suggest that iron deficiency may prolong hospitalisation, most were conducted in high-income countries, used retrospective or registry-based designs, or focused on iron deficiency anaemia rather than absolute iron deficiency. In Tanzania, limited evidence exists on the association between absolute iron deficiency at admission and length of hospital stay among patients admitted with acute heart failure. This study addressed this methodological, geographical, and population gap.

2.8 Conceptual Framework

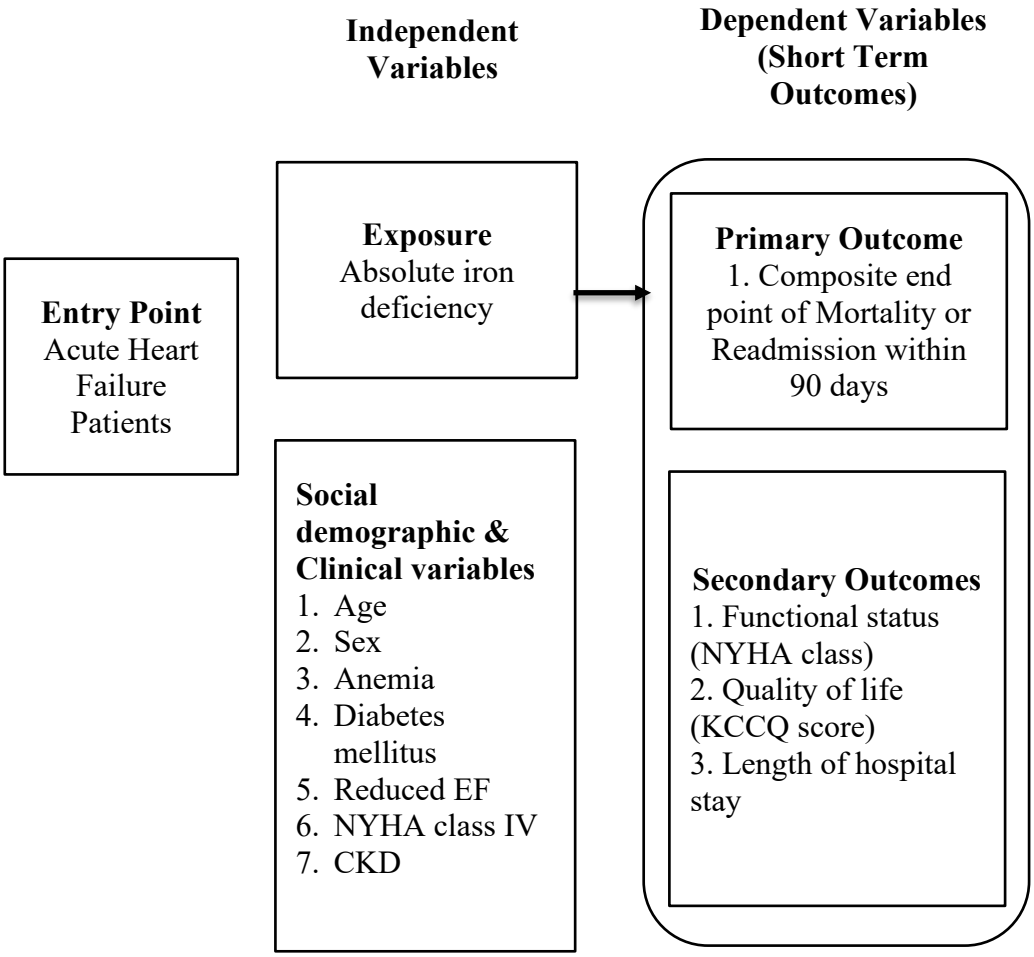


Figure 2.1: Conceptual Framework of the Impact of Absolute Iron Deficiency on Short-Term Clinical Outcomes in Patients Admitted with Acute Heart Failure

Key: NYHA, New York Heart Association; KCCQ, Kansas City Cardiomyopathy Questionnaire; CRP, C-reactive protein; Hb, haemoglobin.

The framework illustrates that absolute iron deficiency may lead to adverse short-term outcomes among patients with acute heart failure through various pathophysiological mechanisms. The relationship between absolute iron deficiency and outcomes may be influenced by demographic, clinical, and laboratory factors (confounders).

CHAPTER THREE

METHODOLOGY

3.1 Study Design and Duration

A prospective cohort study design was conducted over a six-month period from January to June 2026. Patients admitted with acute heart failure were enrolled at baseline and followed prospectively to assess clinical outcomes according to their iron deficiency status.

A prospective cohort study design was considered appropriate for this study because it enabled the assessment of the association between absolute iron deficiency and subsequent clinical outcomes among patients with acute heart failure. The design allowed exposure status (absolute iron deficiency) to be determined before the occurrence of outcomes, thereby establishing a temporal relationship between exposure and outcome. Furthermore, prospective data collection minimized recall bias and reduced the risk of exposure and outcome misclassification, thereby enhancing the validity and accuracy of the findings.

3.2 Study Area

The study was conducted at Benjamin Mkapa Hospital (BMH), a public tertiary referral and teaching hospital located in Dodoma City, Tanzania. As the Central Zonal Referral Hospital, BMH serves patients from Dodoma, Singida, Tabora, Iringa, Morogoro, and neighboring regions, providing both specialized and super-specialized healthcare services. The hospital has several key departments, including Cardiology, Internal Medicine, Nephrology, Paediatrics, Surgery, Obstetrics and Gynaecology, Emergency Medicine, Intensive Care, Radiology, and Laboratory Services.

BMH serves approximately 1,000 patients daily and 36,000 patients monthly. The hospital was selected because it manages a high burden of acute heart failure cases, averaging 6–8 admissions per day (180–240 patients per month). It is equipped with advanced cardiovascular diagnostic and treatment facilities, including echocardiography services, comprehensive iron studies, a 10-bed Cardiac Care Unit (CCU), High Dependency Units (HDUs), and a 24-hour Cardiac Catheterization Laboratory (CATH-LAB). In addition, the presence of cardiology super-specialists, trained cardiology nurses, interventional radiologists, and internal medicine specialists provided the infrastructure required to conduct the study.

3.3 Study Population

Adult patients admitted with acute heart failure at Benjamin Mkapa Hospital during the study period constituted the study population. At admission, each eligible participant was screened for absolute iron deficiency and followed for three months to assess clinical outcomes.

3.3.1 Inclusion criteria

Participants qualified for enrolment if they met all of the following:

1. Aged 18 years or above and admitted to Benjamin Mkapa Hospital.
2. Diagnosed with acute heart failure based on clinical assessment.
3. Signed written informed consent to participate in the study.
4. Able and willing to be followed up for three months after hospital discharge.

3.3.2 Exclusion criteria

Participants were excluded from the study if they:

1. Had received intravenous iron or blood transfusion in the preceding three months.

2. Had active bleeding or a known hematological disorder that could affect iron status assessment.

3. Had severe cognitive impairment or any condition that prevented provision of informed consent or reliable participation in follow-up assessments.

4. Were pregnant or within six weeks postpartum.

3.4 Sampling Technique

Enrolment followed a non-probability, consecutive sampling approach: every eligible patient admitted with acute heart failure during the study window was recruited in sequence until the target sample size was reached. This method was selected because it was operationally practical and efficient in a busy, resource-constrained clinical environment characterized by high patient turnover and urgent acute admissions. In such a setting, more complex methods like random or stratified sampling would have been logistically difficult to implement.

Furthermore, consecutive sampling is widely accepted in hospital-based observational studies and aligns with previous research investigating iron deficiency and outcomes in acute heart failure (17,20,22). In addition, this approach was particularly suitable for the prospective cohort design, as it facilitated systematic and temporally consistent recruitment and follow-up. By enrolling every eligible patient sequentially, the method minimized investigator discretion and captured the natural variation in patient characteristics, clinical severity, and demographic backgrounds over time.

However, while consecutive sampling increases the likelihood that the sample represents the broader spectrum of acute heart failure admissions, it does not eliminate the risk of selection bias. To mitigate this residual selection bias, participants were enrolled prospectively at the exact point of hospital admission, strictly without regard

to their iron status or anticipated clinical outcomes. Furthermore, the established inclusion and exclusion criteria were rigidly and consistently applied to all potentially eligible participants throughout the study period.

3.5 Sample Size Calculation

Design rationale

The Schoenfeld event-driven formula for Cox proportional-hazards regression was used to derive the required sample size(52). This formula was chosen because it aligns directly with the study's planned primary analysis; Kaplan–Meier estimation and Cox regression applied to the composite endpoint. Power was set at 80%, with a two-sided α of 0.05.

Formula $$D = \frac{\left(Z_{\frac{\alpha}{2}} + Z_{\beta}\right)^2}{[\ln(HR)]^2 p(1-p)}$$

Where D = required number of events; Zα/2 = 1.96 (two-sided α=0.05); Zβ = 0.84 (80% power); HR = anticipated hazard ratio; p = anticipated proportion exposed (patients with absolute iron deficiency).

Assumption 1: Hazard ratio (HR = 2.0)

Previous heart failure cohorts have consistently reported an association between iron deficiency or iron deficiency-related phenotypes and adverse clinical outcomes, with reported hazard ratios ranging from 1.47 to 2.67 (13,20,53). Specifically, Núñez et al. (20) reported an HR of 1.72 (95% CI 1.13–2.60) for absolute iron deficiency and 30-day readmission following acute heart failure hospitalisation; Makubi et al. (13) reported an HR of 2.67 (95% CI 1.39–5.07) for iron deficiency anaemia and hospitalisation or death; and Grote Beverborg et al. (53)reported an HR of 1.47 (95% CI 1.26–1.71) for low iron stores and mortality or heart-failure hospitalisation.

An HR of 2.0 was prespecified as a clinically meaningful effect size lying within the range of associations previously reported (1.47–2.67).

Assumption 2: Anticipated event rate (23%)

Previous studies of patients with acute heart failure have reported 90-day readmission or mortality rates of approximately 23%–28%(54–56). The lower bound of this range (23%) was adopted as the anticipated event rate to provide a conservative sample-size estimate, as a lower anticipated event rate requires a larger sample for a given number of required events.

Assumption 3: Exposure proportion (p = 0.50)

Makubi et al. (13) reported an overall ID prevalence of 49% in a Tanzanian HF cohort approximated as p=0.50, which also maximizes p(1−p) and is therefore the statistically conservative choice.

Calculation:

$$\mathrm{D} = \frac{(1.96 + 0.84)^2}{[\backslash \ln(2.0)]^2 (0.5)(0.5)}$$

$$\mathrm{D} = \frac{2.8^2}{(0.6931)^{2(0.25)}}$$

= 66 events were required.

Converting required events to participants required ***n,***

Where ***n***= D/event rate;

66/0.23= 287 participants.

Adjusted for 10% anticipated loss to follow-up: ***n*** = 287 / 0.90 ≈ 318.88 rounded upwards to 319 participants.

Thus, 319 participants as minimum sample size target.

A total of **339** participants were ultimately enrolled, exceeding the calculated target and 9 participants were lost to follow-up**,** leaving 330 for analysis.

3.6 Study Variables

3.6.1 Independent variables

- Absolute iron Deficiency (exposure status) as measured by serum ferritin.

- Demographic variables: Age, sex, socioeconomic status, residence.
- Clinical variables: History of heart failure hospitalisations, NYHA class IV, Comorbidities such as CKD, DM, Chronic liver diseases, HIV/AIDS, Other cardiovascular diseases.
- Laboratory variables.

3.6.2 Dependent variables (outcomes)

1. Primary Composite Outcome:

- Composite endpoint of All-cause mortality or Hospital readmission within 90 days.

2. Secondary Outcomes:

- Change in NYHA functional status.
- Change in quality-of-life scores via the Kansas City Cardiomyopathy Questionnaire (KCCQ-12) score.

3.6.3 Follow-up and outcome assessment

All participants were followed up for 90 days following hospital discharge. Follow-up information was obtained through scheduled clinic visits and telephone interviews conducted at predefined intervals. During each follow-up contact, information on survival status, hospital readmissions, quality of life, and functional status was collected and documented using a standardized data collection tool.

Participants who could not be contacted during the 90-day follow-up period despite repeated attempts to ascertain their clinical outcomes were considered lost to follow-up. Of the 339 participants enrolled, 9 (2.7%) were lost to follow-up and their 90-day outcomes could not be ascertained. These participants were excluded from the final outcome analysis, resulting in 330 participants available for analysis. Participants who completed the 90-day follow-up without experiencing the composite outcome were considered event-free and were appropriately censored at 90 days in the time-to-event analyses.

3.7 Data Collection

Data were collected by the principal investigator and trained research assistants through patient interviews, review of clinical records, and laboratory investigations. Face-to-face interviews were conducted using a structured data collection tool to obtain demographic characteristics, clinical history, and other relevant information. Additional clinical and medical history data were extracted from patients' medical records.

The principal investigator supervised all data collection activities to ensure adherence to the study protocol, ethical standards, and data quality requirements. Confidentiality was maintained by assigning unique identification numbers to participants instead of using personal identifiers. Written informed consent was obtained from all participants before enrollment, and all collected information was handled in a confidential manner throughout the study.

3.7.1 Patient interviews

Information collected through patient interviews included:

Demographic characteristics: Age, sex, residence, education level, occupation, and socioeconomic status.

Clinical history: Duration and severity of heart failure symptoms, number of heart failure decompensations within the previous 12 months, date of the most recent decompensation, symptoms suggestive of iron deficiency, comorbidities, and previous hospitalisations.

Lifestyle and dietary habits: Dietary history, smoking status, and alcohol consumption.

Medication history: Use of chronic heart failure medications before admission and other medications that could influence iron status, including iron supplementation.

NYHA functional classification: Functional status was assessed during at admission and at 90 days using the New York Heart Association (NYHA) functional classification system. Patients were classified as NYHA class I, II, III, or IV according

to the degree of limitation of physical activity attributable to cardiac symptoms. The NYHA classification is an established measure of functional status in patients with cardiovascular disease and has demonstrated evidence of validity; however, its assignment involves clinical judgment and may be affected by inter-rater variability NYHA functional class was assigned by trained study clinicians using the standard NYHA criteria. Prior to data collection, the study team reviewed the classification criteria to promote consistency in assessment. Formal inter-rater reliability assessment was not performed (28).

Quality of life: Quality of life was assessed using the 12-item Kansas City Cardiomyopathy Questionnaire (KCCQ-12), a validated, heart-failure-specific patient-reported outcome measure derived from the original 23-item KCCQ. The KCCQ-12 assesses the impact of heart failure on symptom frequency, physical limitations, social limitations, and quality of life over a 2-week recall period. The questionnaire generates a KCCQ-12 overall summary score ranging from 0 to 100, with higher scores indicating better health status. For interpretation, scores of 0–24 represent very poor to poor health status, 25–49 poor to fair, 50–74 fair to good, and 75–100 good to excellent health status. The KCCQ-12 was administered at baseline during the index hospitalisation and repeated at the 3-month follow-up. Change in KCCQ-12 score was calculated as the 3-month score minus the baseline score, with positive values indicating improvement in health status. The KCCQ-12 was selected as the measure of health-related quality of life because it is a validated heart-failure-specific patient-reported outcome measure and has been used to assess quality of life in patients with acute heart failure and iron deficiency.(29,36)

3.7.2 Clinical records

The review of patient medical records was primarily conducted to verify information obtained during patient interviews and to collect additional clinical data not captured during the interview process. Information extracted from medical records included:

Vital signs and anthropometric measurements: Blood pressure, heart rate, respiratory rate, oxygen saturation, weight, height, and body mass index (BMI).

Previous clinical history and cardiac assessment: Previous hospitalisations, admission diagnosis, and echocardiographic findings, as well as verification of information obtained during patient interviews.

Cause of heart failure decompensation: Documented precipitating factors for the current episode of acute heart failure among patients with chronic heart failure and causes of presentation among patients with de novo heart failure.

Medication history: Current and previous medications prescribed for heart failure management, including iron supplementation, blood transfusions, and other treatments that could influence iron status.

3.7.3 Laboratory Investigations

Blood samples were collected by the principal investigator or trained research assistants within 24 hours of hospital admission. All samples were labelled using unique participant identification numbers and handled according to standard operating procedures (SOPs) for specimen collection, transportation, processing, and storage. Laboratory investigations were performed to determine absolute iron deficiency status and assess other clinical parameters relevant to heart failure. The results were subsequently used to evaluate their association with clinical outcomes.

The following laboratory tests were performed:

- **Serum ferritin:** The primary marker used to assess iron stores. Absolute iron deficiency was defined as serum ferritin levels **<100 ng/mL**. Absolute iron deficiency was defined as a serum ferritin concentration <100 ng/mL. This threshold was selected based on its established use in contemporary heart failure guidelines and evidence from previous studies(20,33,57).

- **Transferrin saturation (TSAT):** Used to assess iron availability and characterize iron deficiency status.

- **Full blood picture (FBP):** Performed to assess haemoglobin levels and other hematological parameters.
- **C-reactive protein (CRP):** Measured to assess the presence of systemic inflammation.

- **Kidney function tests:** Serum creatinine and blood urea nitrogen (BUN) were measured to evaluate renal function.
- **Serum electrolytes:** Sodium, potassium, magnesium, chloride, phosphate, and calcium levels were assessed.
- **HIV testing:** Provider-Initiated Testing and Counselling (PITC) was offered in accordance with national guidelines.
- **Liver function tests:** Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were measured.
- **Additional investigations:** N-terminal pro-B-type natriuretic peptide (NT-proBNP) was measured where resources and laboratory capacity permitted.

3.8 Data Management and Statistical Analysis

Data were entered, cleaned, and validated using Microsoft Excel before being exported to IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA) for analysis. Data quality checks were performed regularly to identify and correct inconsistencies, missing values, and data entry errors. Baseline data were checked for completeness prior to statistical analysis. There were no missing values for the variables included in the primary analysis; therefore, no imputation was required, and all eligible participants with ascertainable 90-day outcomes were included in the relevant analyses. All statistical tests were two-sided, and statistical significance was determined at a p-value of less than 0.05. Results were presented with corresponding 95% confidence intervals (CIs) where appropriate.

3.8.1 Descriptive analysis

Categorical variables such as sex, residence, New York Heart Association (NYHA) functional class, comorbidities, and iron deficiency status were summarized using frequencies and percentages. Continuous variables such as age, haemoglobin level, body mass index, left ventricular ejection fraction, and Kansas City Cardiomyopathy Questionnaire (KCCQ-12) score were summarized using means and standard deviations for normally distributed data, or medians and interquartile ranges (IQRs) for skewed data.

3.8.2 Determination of the prevalence of absolute iron deficiency

The prevalence of absolute iron deficiency among patients admitted with acute heart failure was calculated as the proportion of participants diagnosed with absolute iron deficiency at baseline divided by the total number of participants enrolled in the study and expressed as a percentage.

3.8.3 Analysis of the primary outcome

The primary outcome was the composite endpoint of all-cause mortality or hospital readmission within 90 days following hospital discharge. Baseline characteristics between participants with and without absolute iron deficiency were compared using the Chi-square test or Fisher's exact test for categorical variables and the Student's t-test or Mann–Whitney U test for continuous variables, as appropriate.

Time-to-event analyses were performed using Kaplan–Meier survival curves to compare the cumulative incidence of the composite outcome, all-cause mortality, and hospital readmission between participants with and without absolute iron deficiency. Differences in survival distributions were assessed using the log-rank test.

Cox proportional hazards regression models were used to determine the association between absolute iron deficiency and clinical outcomes. Potential confounding variables were identified a priori based on clinical relevance, existing literature, and their potential association with both iron deficiency and the clinical outcomes. Variables considered included demographic characteristics, heart failure severity, anaemia and comorbidities. These variables were assessed in multivariable Cox proportional hazards regression to determine whether the association between iron deficiency and the composite outcome persisted after adjustment for measured confounders. A parsimonious model was used, taking into consideration the number of observed outcome events. Covariates with clinical relevance or a p-value less than 0.20 in univariable analysis were included in multivariable models to estimate the association between absolute iron deficiency and the 90-day composite outcome of all-cause mortality or hospital readmission after adjustment for measured potential confounders. Results were reported as crude hazard ratios (CHR) and adjusted hazard ratios (AHR) with corresponding 95% confidence intervals. Considering the study was

observational, adjustment was intended to reduce confounding by measured covariates and was not considered sufficient to establish a causal relationship.

3.8.4 Assessment and management of multicollinearity

Multicollinearity among candidate explanatory variables was assessed before multivariable Cox regression using variance inflation factors (VIF) and tolerance statistics. A VIF >10 or tolerance <0.10 was considered indicative of potentially problematic multicollinearity. Variables demonstrating substantial conceptual overlap were not entered simultaneously into the same mode.

3.8.5 Methods addendum

Because absolute iron deficiency exhibited complete separation in the mortality model (all deaths occurred among iron-deficient participants), Firth's penalized partial likelihood regression was applied post hoc to the mortality Cox models to obtain finite, bias-corrected hazard ratio estimates(58). This method was not part of the original pre-specified analysis plan but was adopted after the standard maximum partial likelihood estimator failed to converge for this variable.

3.8.6 Analysis of secondary outcomes

Changes in NYHA functional class between admission and 90-day follow-up were assessed using the Wilcoxon signed-rank test. Differences in NYHA functional status between participants with and without iron deficiency were evaluated using the Chi-square test.

Quality of life was assessed using the Kansas City Cardiomyopathy Questionnaire (KCCQ-12). Mean KCCQ scores were compared between participants with and without absolute iron deficiency using the independent-samples t-test or Mann–Whitney U test, as appropriate.

Length of hospital stay was summarized using measures of central tendency and dispersion. Differences between groups were assessed using the independent-samples t-test or Mann–Whitney U test depending on data distribution. Multivariable linear regression was performed to evaluate the association between absolute iron deficiency and length of hospital stay while controlling for potential confounders.

3.9 Data presentation

Results were presented using tables, figures, and graphs. Kaplan–Meier survival curves were used to illustrate time-to-event outcomes, while appropriate tables were used to summarize descriptive statistics and regression analyses.

3.10 Ethical Considerations

This study received ethical clearance from the University of Dodoma Institutional Research Review Ethics Committee (UDOM-IRREC) under reference **MA.84/261/98/4**, granted on 5 January 2026, before data collection began. Institutional permission to conduct the study at the study site followed shortly after, granted by Benjamin Mkapa Hospital under reference **AB.150/293/01/'B'/283** on 6 January 2026. Conduct of the study adhered to the principles of the Declaration of Helsinki alongside the National Institute for Medical Research (NIMR) research guidelines applicable in Tanzania.

Written informed consent was obtained from every participant prior to enrolment. Participants were given a full explanation of the study's objectives, procedures, expected duration, potential risks, and anticipated benefits, in a language they understood. It was explicitly clarified to participants that enrolment in the study did not constitute enrolment in treatment, and that participation was independent of, and would not influence, the clinical care they received at the hospital. Participants were also informed of their right to withdraw at any stage without penalty and without any effect on their ongoing access to medical care.

As an observational study, this research did not direct, restrict, or withhold clinical management at any point; participants received whatever care existed within the standard hospital system, and the researchers' role was confined to observation and data recording.

Participant confidentiality was preserved throughout the study. Each participant was assigned a unique study identification number in place of personal identifiers, and this code, rather than any personal information, was used on data collection tools and in the study database. Hard-copy records were kept in locked cabinets accessible only to the principal investigator and authorised research staff, while electronic data were

stored on password-protected devices with access restricted to the research team. No personal identifying information was included in any report, presentation, or publication arising from this study.

Blood samples were obtained by trained healthcare personnel using standard aseptic technique in accordance with hospital infection prevention and safety protocols. Only the volume of blood required for the planned laboratory analyses was collected, and any adverse events arising from specimen collection would have been managed according to standard hospital procedure; none were recorded during the study period.

Selection of participants was governed by predefined inclusion and exclusion criteria applied consistently to minimise selection bias. Participation was entirely voluntary; no participant was subjected to coercion, inducement, or undue influence to take part, and refusal to participate carried no consequence for the care an individual received. In the event of any study-related harm, participants would have been entitled to appropriate medical attention at no cost to them, as provided through the hospital's standard clinical care pathways.

The study received no external funding that could be considered a source of conflict of interest, and the researchers declare no competing interests in relation to the conduct, analysis, or reporting of this study. Findings arising from this research will be disseminated to relevant academic, institutional, and clinical stakeholders while preserving participant confidentiality and anonymity at every stage.

CHAPTER FOUR

RESULTS AND DISCUSSION

4.1 Results

4.1.1 Participant enrollment

During the study period, a total of 377 patients admitted with acute heart failure at Benjamin Mkapa Hospital were screened for eligibility. Thirty-eight participants were excluded due to refusal to participate, severe concurrent illnesses affecting iron metabolism, IV iron therapy or blood transfusion within 3 months, active bleeding or hematological disorder and being pregnant or within 6 weeks postpartum. A total of 339 participants fulfilled the inclusion criteria, were enrolled, and 330 were included in the final analysis as 9 patients were lost to follow-up. Among the analyzed participants, 175 (53%) had absolute iron deficiency while 155 (47%) had no evidence of absolute iron deficiency. All enrolled participants were followed for 90 days from the date of recruitment. Participants who did not experience death or readmission during follow-up were censored at 90 days. Therefore, survival analysis was performed using time-to-event and event indicator variables for the composite endpoint, mortality alone, and readmission alone.

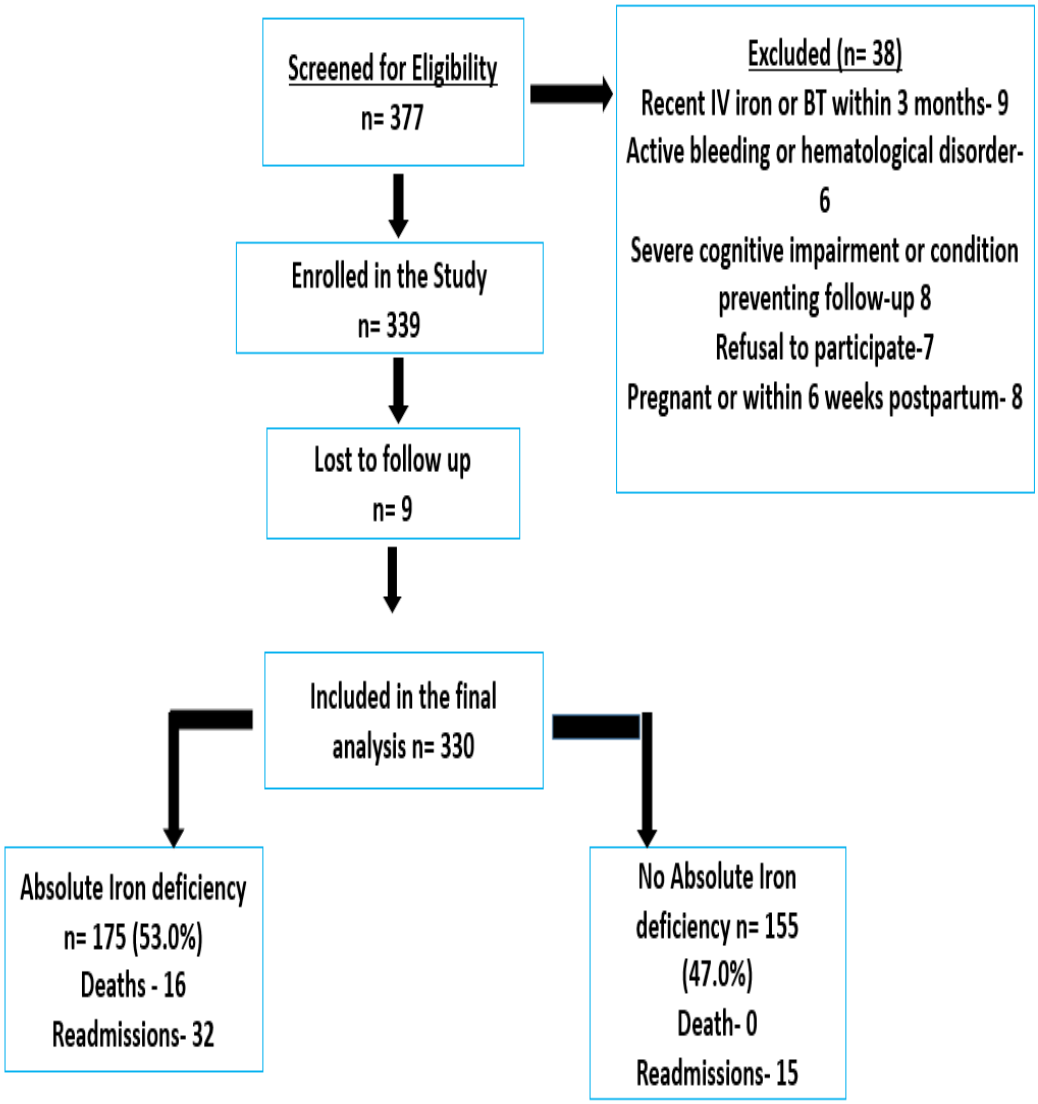


Figure 4.1: Participant Enrollment Flow Diagram

4.1.2 Follow-up characteristics and outcome status at 90 days

Table 4.1 compares 90-day clinical outcomes according to absolute iron deficiency status. During follow-up, **16 (9.1%)** patients with absolute iron deficiency died, whereas no deaths occurred among patients without absolute iron deficiency (**$p < 0.001$**). Similarly, hospital readmission was significantly more frequent among patients with absolute iron deficiency than among those without iron deficiency (**18.3% vs. 9.7%, $p = 0.024$**). Overall, the composite endpoint of all-cause mortality or hospital readmission occurred in **48 (27.4%)** patients with absolute iron deficiency compared with **15 (9.7%)** patients without absolute iron deficiency (**$p < 0.001$**),

indicating a higher incidence of the composite endpoint among participants with absolute iron deficiency during the 90-day follow-up period.

Table 4.1: Comparison of 90-Day Clinical Outcomes between Patients with and without Absolute Iron Deficiency among Patients Admitted with Acute Heart Failure (n = 330)

Outcome	Absolute Iron Deficiency (n =175)	No Absolute Iron Deficiency (n=155)	p-value
Deaths/Mortality	16 (9.1%)	0 (0.0%)	<0.001
Readmission	32 (18.3%)	15 (9.7%)	0.024
Composite Endpoint*	48 (27.4%)	15 (9.7%)	<0.001

4.1.3 Sociodemographic characteristics of the study participants

Table 4.2 presents the baseline sociodemographic characteristics of participants according to absolute iron deficiency status. There was no statistically significant difference in age distribution between participants with and without absolute iron deficiency, with 57.1% and 56.1% of participants aged less than 65 years, respectively ($\chi^2 = 0.03$, $p = 0.861$). Similarly, the proportion of female participants was comparable between the two groups (54.3% vs. 52.3%; $\chi^2 = 0.07$, $p = 0.796$).

The distribution of place of residence did not differ significantly between participants with and without absolute iron deficiency, with the majority residing in rural areas (58.3% vs. 54.2%; $\chi^2 = 0.41$, $p = 0.524$). Likewise, marital status was comparable across the two groups ($\chi^2 = 1.42$, $p = 0.702$), with more than half of participants in each group being married or cohabiting. There was also no significant difference in educational attainment between participants with and without absolute iron deficiency ($\chi^2 = 3.88$, $p = 0.274$). Primary education was the most common level attained in both groups (42.3% and 36.8%, respectively), followed by secondary education.

Similarly, smoking status ($\chi^2 = 0.61$, $p = 0.435$), alcohol use ($\chi^2 = 0.01$, $p = 0.907$), and medication adherence ($\chi^2 = 0.63$, $p = 0.428$) did not differ significantly between the two groups. Overall, participants with and without absolute iron deficiency were comparable with respect to their baseline sociodemographic and lifestyle

characteristics, indicating that there were no significant differences in these variables at study enrolment.

Table 4.2: Sociodemographic Characteristics of Participants by Iron Deficiency Status among Patients Admitted with Acute Heart Failure (n= 330)

Variable	Category	Absolute Iron Deficiency (n =175)	No Absolute Iron Deficiency (n=155)	χ^2	p-value
Age group (years)	<65	**100 (57.1)**	**87 (56.1)**	0.03	0.861
	≥65	**75 (42.9)**	**68 (43.9)**		
Sex	Female	95 (54.3)	81 (52.3)	0.07	0.796
	Male	80 (45.7)	74 (47.7)		
Residence	Rural	102 (58.3)	84 (54.2)	0.41	0.524
	Urban	73 (41.7)	71 (45.8)		
Marital status	Married/cohabiting	100 (57.1)	84 (54.2)	1.42	0.702
	Widowed	44 (25.1)	47 (30.3)		
	Divorced/Separated	16 (9.1)	14 (9.0)		
	Single	15 (8.6)	10 (6.5)		
Education level	Primary	74 (42.3)	57 (36.8)	3.88	0.274
	Secondary	53 (30.3)	43 (27.7)		
	Tertiary	26 (14.9)	36 (23.2)		
	Informal	22 (12.6)	19 (12.3)		
Smoking status	No	146 (83.4)	135 (87.1)	0.61	0.435
	Yes	29 (16.6)	20 (12.9)		
Alcohol use	No	152 (86.9)	133 (85.8)	0.01	0.907
	Yes	23 (13.1)	22 (14.2)		
Medication adherence	Regular	90 (51.4)	72 (46.5)	0.63	0.428
	Irregular	85 (48.6)	83 (53.5)		

4.1.4 Clinical Characteristics of Participants

Table 4.3 compares the baseline clinical characteristics of participants according to absolute iron deficiency status. Participants with absolute iron deficiency had a significantly different distribution of NYHA functional class compared with those without absolute iron deficiency ($\chi^2 = 6.40$, $p = 0.041$). Specifically, a higher proportion of participants with absolute iron deficiency presented with NYHA class IV (30.3% vs. 18.7%), whereas participants without absolute iron deficiency were more likely to present with NYHA class II (23.2% vs. 17.1%).

The prevalence of hypertension was similar between the two groups (50.3% vs. 51.0%; $\chi^2 = 0.00$, $p = 0.989$). Likewise, no statistically significant differences were observed in the prevalence of diabetes mellitus (18.3% vs. 15.5%; $\chi^2 = 0.28$, $p = 0.596$), dyslipidaemia (33.1% vs. 28.4%; $\chi^2 = 0.66$, $p = 0.416$), HIV infection (4.0% vs. 7.7%; $\chi^2 = 1.49$, $p = 0.223$), or chronic kidney disease (18.3% vs. 16.8%; $\chi^2 = 0.05$, $p = 0.830$) between participants with and without absolute iron deficiency.

Similarly, the distribution of ejection fraction categories did not differ significantly between the two groups ($\chi^2 = 0.52$, $p = 0.772$). However, anaemia was significantly more common among participants with absolute iron deficiency than among those without absolute iron deficiency (85.1% vs. 54.2%; $\chi^2 = 36.46$, $p < 0.001$). Overall, apart from NYHA functional class and anaemia, the two groups were comparable with respect to their baseline clinical characteristics.

Table 4.3: Clinical Characteristics of Participants by Absolute Iron Deficiency Status Among Patients Admitted with Acute Heart Failure (n = 330)

Variable	Category	Absolute Iron Deficiency (n=175)	No Absolute Iron Deficiency (n=155)	χ^2	p-value
NYHA functional class	II	30 (17.1)	36 (23.2)	6.4	0.041
	III	92 (52.6)	90 (58.1)		
	IV	53 (30.3)	29 (18.7)		

Variable	Category	Absolute Iron Deficiency (n=175)	No Absolute Iron Deficiency (n=155)	χ^2	p-value
Hypertension	Yes	88 (50.3)	79 (51.0)	0	0.989
	No	87 (49.7)	76 (49.0)		
Diabetes mellitus	Yes	32 (18.3)	24 (15.5)	0.28	0.596
	No	143 (81.7)	131 (84.5)		
Dyslipidaemia	Yes	58 (33.1)	44 (28.4)	0.66	0.416
	No	117 (66.9)	111 (71.6)		
HIV infection	Yes	7 (4.0)	12 (7.7)	1.49	0.223
	No	168 (96.0)	143 (92.3)		
Chronic kidney disease	Yes	32 (18.3)	26 (16.8)	0.05	0.83
	No	143 (81.7)	129 (83.2)		
Ejection fraction category	HFrEF (≤40%)	102 (58.3)	86 (55.5)	0.52	0.772
	HFmrEF (41–49%)	35 (20.0)	36 (23.2)		
	HFpEF (≥50%)	38 (21.7)	33 (21.3)		
Anaemia	Yes	149 (85.1)	84 (54.2)	36.46	<0.001
	No	26 (14.9)	71 (45.8)		

4.1.5 Baseline clinical and laboratory parameters

Table 4.4 presents the baseline overall demographic and clinical characteristics of the study participants. The mean age of participants was 61.6 ± 15.5 years. The mean body mass index (BMI) was 26.0 ± 5.2 kg/m², indicating that the study population was within the overweight range. The mean systolic and diastolic blood pressures were 131.3 ± 25.1 mmHg and 82.6 ± 13.1 mmHg, respectively, while the mean heart rate was 92.8 ± 17.8 beats per minute.

The mean haemoglobin level was 11.5 ± 1.8 g/dL; anaemia was present in 233 (70.6%) participants. The mean serum ferritin level was 112.2 ± 67.9 ng/mL, and the mean

transferrin saturation was 19.4 ± 7.4%. The mean serum creatinine level was 123.8 ± 44.2 µmol/L.

The mean ejection fraction was 40.3 ± 11.2%, indicating impaired cardiac function among many participants. In addition, the mean baseline KCCQ-12 score was 45.7 ± 15.6, suggesting reduced health-related quality of life at admission. The mean length of hospital stay was 7.4 ± 2.5 days.

Table 4.4: Baseline Clinical and Laboratory Parameters

Variable	Mean ± SD	Unit
Age	61.6 ± 15.5	years
BMI	26.0 ± 5.2	kg/m²
Systolic blood pressure	131.3 ± 25.1	mmHg
Diastolic blood pressure	82.6 ± 13.1	mmHg
Heart rate	92.8 ± 17.8	beats/minute
Haemoglobin	11.5 ± 1.8	g/dL
Serum ferritin	112.2 ± 67.9	ng/mL
Transferrin saturation	19.4 ± 7.4	%
Serum creatinine	123.8 ± 44.2	µmol/L
Ejection fraction	40.3 ± 11.2	%
Baseline KCCQ-12 score	45.7 ± 15.6	score
Length of hospital stay	7.4 ± 2.5	days

4.1.6 Prevalence of absolute iron deficiency

The prevalence of absolute iron deficiency among patients admitted with acute heart failure was 53.0% (95% CI: 47.6–58.4). As illustrated in Figure 4.2, more than half of the study participants met the criteria for absolute iron deficiency, while 47.0% had no evidence of absolute iron deficiency.

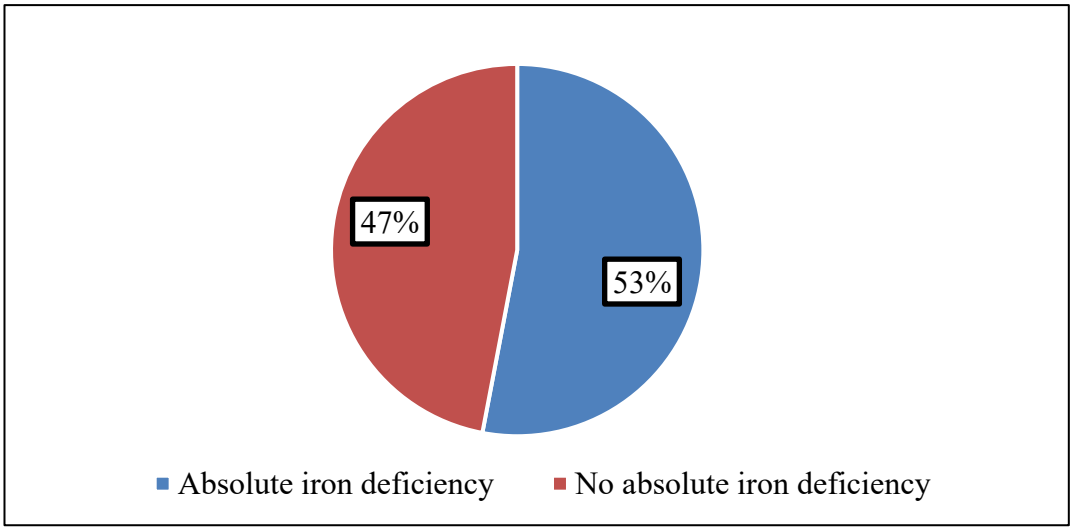


Figure 4.2: Prevalence of Absolute Iron Deficiency Among Patients with Acute Heart Failure

4.1.7 Kaplan-Meier analysis for composite endpoint

Kaplan-Meier analysis showed that participants with absolute iron deficiency had lower event-free survival over the 90-day follow-up period compared with participants without absolute iron deficiency. The 90-day event-free probability was 72.5% among participants with absolute iron deficiency compared with 90.3% among participants without absolute iron deficiency. The difference between the survival curves was statistically significant using the log-rank test ($\chi^2 = 10.89$, $p = <0.001$). Median event-free survival was not reached in either group because more than 50% of participants remained event-free at 90 days.

Table 4.5: Kaplan-Meier Summary for Composite Endpoint

Group	N	Events	90-day event-free probability	Median event-free time
Absolute iron deficiency	175	48	72.50%	Not reached
No absolute iron deficiency	155	15	90.30%	Not reached

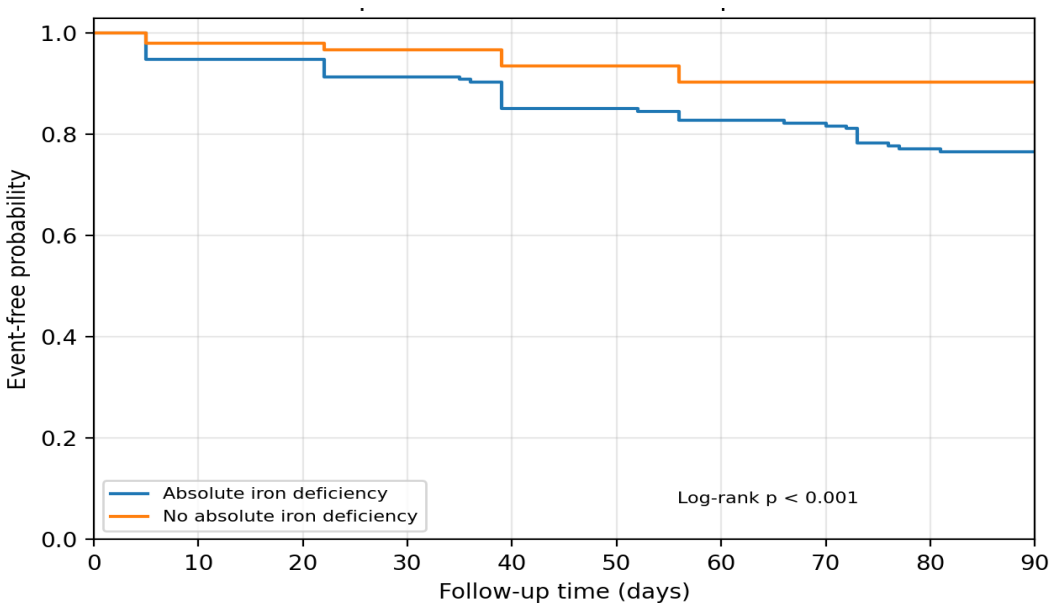


Figure 4.3: Kaplan–Meier Curve Showing Event-Free Survival for the Composite Endpoint by Absolute Iron Deficiency Status Among Patients with Acute Heart Failure

4.1.8 Assessment of Multicollinearity

Multicollinearity among the candidate variables considered for the multivariable Cox proportional hazards models was assessed using variance inflation factors (VIF) and tolerance statistics. A VIF >10 or tolerance <0.10 was considered indicative of potentially problematic multicollinearity.

The VIF values ranged from 1.02 to 1.62, with a mean VIF of 1.19. The highest VIF was observed for HFrEF (VIF = 1.62), followed by serum creatinine (VIF = 1.33). Tolerance values ranged from 0.618 to 0.983, and all were above 0.10. Overall, the results indicated no evidence of problematic multicollinearity among the variables included in the assessment.

Variables were subsequently selected for multivariable Cox regression based on the prespecified criteria described in methodology section, including the univariable significance threshold and clinical relevance**.**

Table 4.6: Assessment of multicollinearity among variables considered for the multivariable Cox proportional hazards model.

Variable	VIF	Tolerance (1/VIF)	Interpretation
Absolute iron deficiency (exposure)	1.15	0.872	No multicollinearity
Age	1.07	0.933	No multicollinearity
Sex	1.02	0.983	No multicollinearity
Hypertension	1.05	0.951	No multicollinearity
Diabetes mellitus	1.04	0.964	No multicollinearity
Chronic kidney disease	1.32	0.759	No multicollinearity
Serum creatinine	1.33	0.75	No multicollinearity
NYHA class	1.09	0.914	No multicollinearity
Anaemia	1.17	0.855	No multicollinearity
Ejection fraction category – HFrEF	1.62	0.618	No multicollinearity
Mean VIF	1.19	—	Acceptable

4.1.9 Predictors of composite endpoint:

Multivariable Cox proportional hazards regression analysis was performed to identify independent predictors of the composite endpoint of death or readmission within 90 days. After adjusting for age, sex, diabetes mellitus, chronic kidney disease, NYHA functional class, ejection fraction category, and anaemia, absolute iron deficiency remained independently associated with an increased hazard of the composite endpoint (AHR 2.25, 95% CI 1.21–4.17; p=0.010). Participants with NYHA class IV heart failure also had a significantly increased hazard of adverse outcomes (AHR 1.85, 95% CI 1.08–3.17; p=0.026). Anaemia was associated with a higher hazard of the composite endpoint on univariable analysis (CHR 2.05, 95% CI 1.03–4.06; p=0.040), but this association did not persist after multivariable adjustment (AHR 1.40, 95% CI 0.69–2.87; p=0.353). Age ≥65 years, male sex, diabetes mellitus, chronic kidney disease, and HFrEF were not independently associated with the composite endpoint (p>0.05).

Table 4.7: Univariable and Multivariable Cox Regression Analysis for the Composite Endpoint

Variable	CHR (95% CI)	p-value	AHR (95% CI)	p-value
Absolute iron deficiency	2.60 (1.44–4.70)	0.002	2.25 (1.21–4.17)	0.010
Age ≥65 years	0.99 (0.58–1.68)	0.963	1.00 (0.58–1.71)	0.990
Male sex	0.72 (0.42–1.23)	0.230	0.70 (0.41–1.20)	0.190
Diabetes mellitus	1.23 (0.63–2.37)	0.544	1.20 (0.61–2.35)	0.592
CK	1.35 (0.71–2.56)	0.353	1.26 (0.66–2.42)	0.487
HIV infection	1.68 (0.67–4.22)	0.267	—[b]	—
NYHA class IV	2.05 (1.20–3.51)	0.009	1.85 (1.08–3.17)	0.026
HFrEF	1.28 (0.74–2.20)	0.373	1.23 (0.72–2.12)	0.446
Anaemia	2.05 (1.03–4.06)	0.040	1.40 (0.69–2.87)	0.353
Irregular adherence	1.19 (0.71–2.02)	0.508	—[b]	—

[b] Not carried forward into the multivariable model, as it did not meet the pre-specified criterion of p<0.20 on univariable analysis.

4.1.10 Mortality within 90 Days

Mortality within 90 days occurred only among participants with absolute iron deficiency. The 90-day survival probability was 90.9% among participants with absolute iron deficiency and 100.0% among participants without absolute iron deficiency. The difference in survival curves was statistically significant using the log-rank test ($\chi^2 = 14.81$, p = <0.001).

Table 4.8: Kaplan-Meier Summary for Mortality

Group	N	Deaths	90-day survival probability	Median survival time
Absolute iron deficiency	175	16	90.9%	Not reached
No absolute iron deficiency	155	0	100.0%	Not reached

Figure 4.4 presents the Kaplan–Meier survival curves comparing 90-day mortality among patients with and without absolute iron deficiency. Participants with absolute

iron deficiency demonstrated lower survival probabilities throughout the follow-up period compared with those without absolute iron deficiency. Mortality events occurred exclusively among participants with absolute iron deficiency, while no deaths were observed among participants without absolute iron deficiency during the 90-day follow-up period.

The estimated 90-day survival probability was 90.9% among participants with absolute iron deficiency compared with 100.0% among those without absolute iron deficiency. The difference in survival between the two groups was statistically significant according to the log-rank test ($p < 0.001$), indicating that absolute iron deficiency was associated with an increased risk of mortality among patients admitted with acute heart failure.

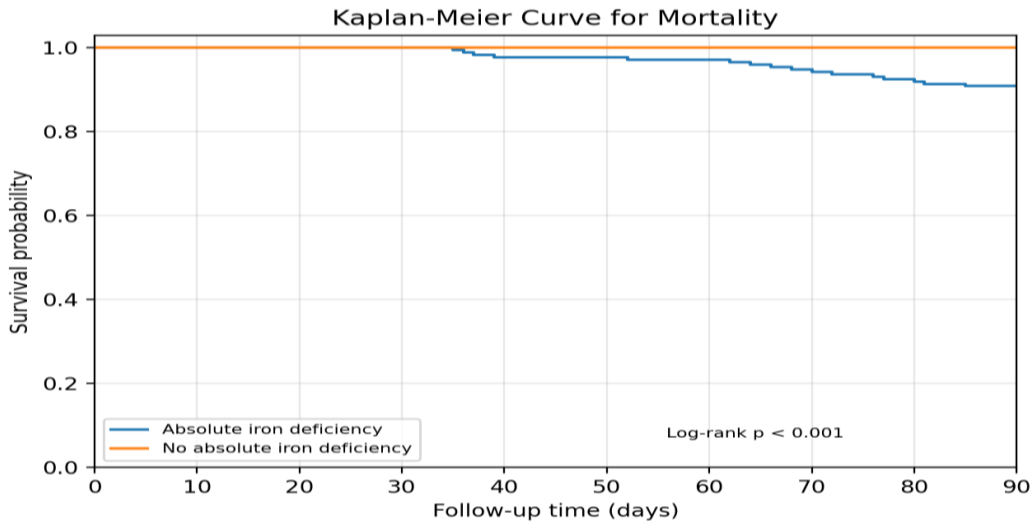


Figure 4.4: Kaplan–Meier Survival Curve for 90-Day Mortality by Absolute Iron Deficiency Status Among Patients with Acute Heart Failure

4.1.11 Predictors of Mortality

Because all 16 deaths occurred among participants with absolute iron deficiency, the hazard ratio for this variable could not be estimated using standard Cox regression, either in univariable or multivariable analysis, owing to complete separation. Firth's penalized partial likelihood regression was therefore applied to both models to obtain finite, bias-corrected estimates. This method was not part of the original pre-specified analysis plan but was adopted after the standard maximum partial likelihood estimator failed to converge for this variable. On Firth-penalized univariable analysis, absolute

iron deficiency was associated with a markedly increased hazard of mortality (CHR 30.56, 95% CI 1.68–555.55; p=0.021), and this association persisted after multivariable adjustment (AHR 25.98, 95% CI 1.44–467.76; p=0.027). NYHA class IV was significantly associated with mortality on univariable analysis (CHR 3.11, 95% CI 1.17–8.29; p=0.023) but showed only a non-significant trend after adjustment for absolute iron deficiency status and other covariates (AHR 2.55, 95% CI 0.95–6.83; p=0.064). Anaemia was not independently associated with mortality (AHR 1.27, 95% CI 0.31–5.17; p=0.734). Age ≥65 years, male sex, diabetes mellitus, chronic kidney disease, HIV infection, HFrEF, and irregular medication adherence were also not independently associated with mortality (p>0.05). Therefore, AID was significantly associated with increased mortality hazard, but the magnitude of this association was imprecisely estimated because only 16 deaths occurred and all were observed in the AID group.

Table 4.9: Univariable and Multivariable Cox Regression Analysis for Mortality

Variable	CHR (95% CI)[a]	p-value	AHR (95% CI)[a]	p-value
Absolute iron deficiency[a]	30.56 (1.68–555.55)[c]	0.021	25.98 (1.44–467.76)[c]	0.027
Age ≥65 years	0.78 (0.28–2.14)	0.624	0.78 (0.28–2.14)	0.626
Male sex	0.38 (0.12–1.18)	0.093	0.40 (0.13–1.25)	0.114
Diabetes mellitus	0.70 (0.16–3.08)	0.638	0.83 (0.21–3.39)	0.799
CKD	1.09 (0.31–3.81)	0.897	1.02 (0.29–3.53)	0.977
HIV infection	1.07 (0.14–8.09)	0.949	—	—
NYHA class IV	3.11 (1.17–8.29)	0.023	2.55 (0.95–6.83)	0.064
HFrEF	1.69 (0.59–4.87)	0.330	1.52 (0.53–4.35)	0.435
Anaemia	3.00 (0.68–13.20)	0.146	1.27 (0.31–5.17)	0.734
Irregular adherence	2.16 (0.75–6.21)	0.154	—	—

[a] *Hazard ratios for absolute iron deficiency in both the univariable and multivariable models were estimated using Firth's penalized partial likelihood Cox regression, not standard maximum partial likelihood, because all 16 deaths occurred among participants with absolute iron deficiency (complete separation). All other variables in this table were estimated using standard Cox regression.*

[c] *The wide confidence interval reflects the limited number of mortality events and the resulting imprecision of the effect estimate; therefore, the magnitude of the hazard ratio should be interpreted cautiously.*

4.1.12 Readmission within 90 Days

Participants with absolute iron deficiency had lower readmission-free survival compared with participants without absolute iron deficiency. The 90-day readmission-free probability was 81.7% among participants with absolute iron deficiency compared with 90.3% among participants without absolute iron deficiency. The log-rank test showed a statistically significant difference between the curves ($\chi^2 = 5.04$, $p = 0.025$).

Table 4.10: Kaplan-Meier Summary for Readmission

Group	N	Readmissions	90-day readmission-free probability	Median readmission-free time
Absolute iron deficiency	175	32	81.70%	Not reached
No absolute iron deficiency	155	15	90.30%	Not reached

Figure 4.5 presents the Kaplan–Meier curves comparing readmission-free survival among patients with and without absolute iron deficiency during the 90-day follow-up period. Participants with absolute iron deficiency demonstrated lower readmission-free survival probabilities compared with those without absolute iron deficiency throughout follow-up. The decline in readmission-free survival occurred earlier and was more pronounced among participants with absolute iron deficiency.

At 90 days, the estimated readmission-free survival probability was 81.7% among participants with absolute iron deficiency compared with 90.3% among participants without absolute iron deficiency. The difference between the two groups was statistically significant according to the log-rank test ($p = 0.025$), indicating that absolute iron deficiency was associated with an increased risk of hospital readmission among patients admitted with acute heart failure.

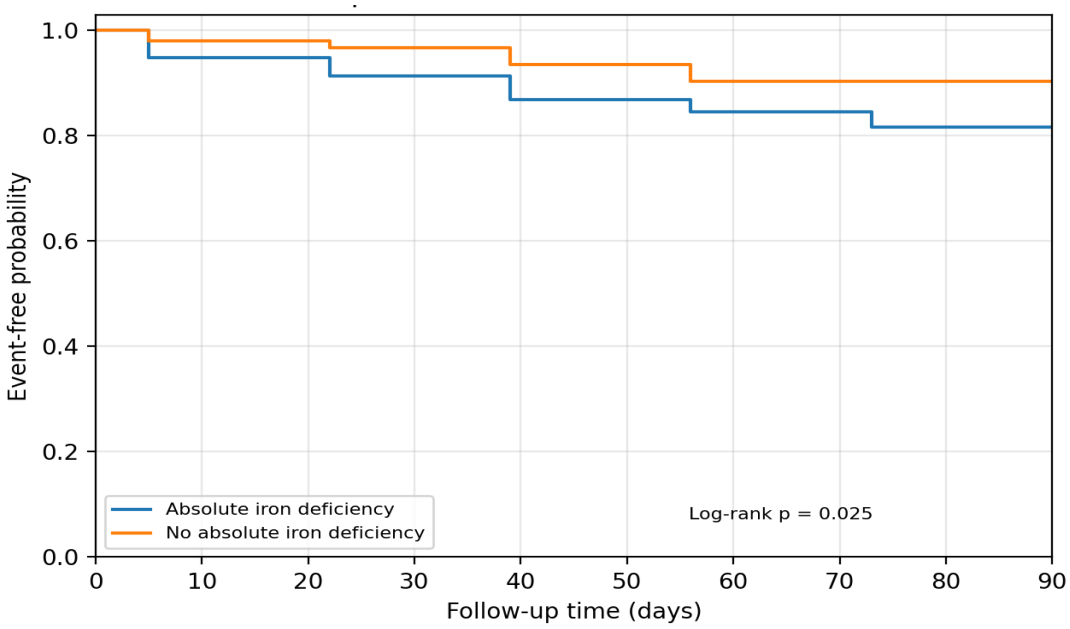


Figure 4.5: Kaplan–Meier curve showing readmission-free survival by absolute iron Deficiency status among aatients with acute heart failure

4.1.13 Predictors of Readmission

Table 4.11 presents the univariable and multivariable Cox proportional hazards regression analysis for hospital readmission within 90 days. On univariable analysis, absolute iron deficiency was significantly associated with an increased hazard of readmission (CHR 1.99, 95% CI 1.08–3.67; p=0.028). However, after adjusting for age, sex, diabetes mellitus, chronic kidney disease, NYHA functional class, ejection fraction category, and anaemia, this association was no longer statistically significant (AHR 1.66, 95% CI 0.87–3.16; p=0.123). Anaemia showed a similar pattern, with a significant univariable association (CHR 2.14, 95% CI 1.00–4.58; p=0.050) that did not persist after multivariable adjustment (AHR 1.62, 95% CI 0.73–3.61; p=0.238). None of the remaining covariates were independently associated with hospital readmission after adjustment (p>0.05).

Table 4.11: Univariable and Multivariable Cox Regression Analysis for Readmission.

Variable	CHR (95% CI)	p-value	AHR (95% CI)	p-value
Absolute iron deficiency	1.99 (1.08–3.67)	0.028	1.66 (0.87–3.16)	0.123
Age ≥65 years	0.98 (0.55–1.76)	0.958	0.99 (0.55–1.78)	0.965
Male sex	0.75 (0.42–1.35)	0.340	0.75 (0.42–1.35)	0.336
Diabetes mellitus	1.35 (0.67–2.71)	0.400	1.34 (0.66–2.73)	0.419
Chronic kidney disease	1.34 (0.67–2.70)	0.411	1.24 (0.61–2.53)	0.559
HIV infection	1.60 (0.57–4.46)	0.367	—[b]	—
NYHA class IV	1.60 (0.88–2.93)	0.125	1.45 (0.79–2.66)	0.235
HFrEF	1.22 (0.68–2.20)	0.503	1.17 (0.65–2.12)	0.593
Anaemia	2.14 (1.00–4.58)	0.050	1.62 (0.73–3.61)	0.238
Irregular adherence	1.19 (0.67–2.11)	0.563	—[b]	—

4.1.14 Quality of life, functional class and length of hospital stay

Participants with absolute iron deficiency had significantly lower baseline and follow-up KCCQ scores compared with those without iron deficiency. The mean improvement in KCCQ score was also lower among participants with absolute iron deficiency indicating poorer health-related quality of life and functional recovery during follow-up. The observed differences were statistically significant ($p < 0.05$).

Table 4.12: Comparison of Quality of Life by Iron Deficiency Status

Variable	Absolute iron deficiency Mean ± SD	No Absolute iron deficiency Mean ± SD	p-value
Baseline KCCQ-12 score	40.6 ± 15.0	51.4 ± 14.2	<0.001
3-month KCCQ-12 score	45.0 ± 18.4	60.6 ± 16.3	<0.001
Mean change in KCCQ-12 score	4.1 ± 9.8	9.2 ± 8.8	<0.001

4.1.15 Functional Status Outcome

At baseline, participants with absolute iron deficiency showed more severe functional impairment than those without it. A higher proportion of participants with AID were

classified as NYHA class IV (30.3% versus 18.7%), while fewer were classified as NYHA class II (17.1% versus 23.2%). The distribution of NYHA functional class differed significantly between the two groups ($\chi^2 = 6.40$, $p = 0.041$), indicating worse functional status among participants with absolute iron deficiency at admission.

Table 4.13: Baseline NYHA Functional Class by Iron Deficiency Status

NYHA class	Iron deficient n (%)	Non-iron deficient n (%)
II	30 (17.1)	36 (23.2)
III	92 (52.6)	90 (58.1)
IV	53 (30.3)	29 (18.7)

Differences in NYHA functional class distribution at 90-day follow-up between participants with and without absolute iron deficiency were assessed using the Pearson Chi-square test. A statistically significant difference was observed between the two groups ($\chi^2 = 21.20$, $df = 4$, $p < 0.001$).

Participants with absolute iron deficiency demonstrated poorer functional outcomes at 90-day follow-up compared with participants without iron deficiency. A higher proportion of participants with AID remained in NYHA class IV (20.0% vs. 11.6%), while a lower proportion achieved NYHA class II status (28.0% vs. 37.4%). In addition, all deaths observed during follow-up occurred among participants with absolute iron deficiency, accounting for 16 (9.1%) participants, whereas no deaths were recorded among participants without iron deficiency.

Overall, participants without absolute iron deficiency demonstrated more favorable functional recovery following admission for acute heart failure, while participants without AID were more likely to have persistent functional limitation or experience death during follow-up.

Table 4.14: NYHA Functional Class at 90-Day Follow-up by Iron Deficiency Status (n = 330)

NYHA Class at 90 Days	Iron Deficient n (%) (n=175)	Non-Iron Deficient n (%) (n=155)
I	14 (8.0)	14 (9.0)
II	49 (28.0)	58 (37.4)
III	61 (34.9)	65 (41.9)
IV	35 (20.0)	18 (11.6)
Died	16 (9.1)	0 (0.0)
Total	**175 (100.0)**	**155 (100.0)**

4.1.16 Change in NYHA Functional Class During Follow-up

Comparison of NYHA functional class at admission and 90-day follow-up was performed using the Wilcoxon signed-rank test. A statistically significant improvement in NYHA functional class was observed during follow-up (**$p < 0.001$**).

Table 4.17 presents the distribution of New York Heart Association (NYHA) functional class at admission and at 90-day follow-up among patients admitted with acute heart failure. At admission, the majority of participants were classified as NYHA class III (55.2%), followed by class IV (24.8%) and class II (20.0%). At the 90-day follow-up, there was a notable improvement in functional status, with 8.5% of participants achieving NYHA class I and 32.4% classified as NYHA class II. The proportion of participants in NYHA class III and class IV decreased from 55.2% to 38.2% and from 24.8% to 16.1%, respectively. In addition, 16 (4.8%) participants died during the follow-up period.

Overall, the findings demonstrate significant improvement in functional capacity following treatment and follow-up of acute heart failure patients.

Table 4.15: Change in NYHA Functional Class from Admission to 90-Day Follow-up Among Patients with Acute Heart Failure (n = 330)

NYHA Functional Class	Admission n (%)	Follow-up n (%)
I	0 (0.0)	28 (8.5)
II	66 (20.0)	107 (32.4)
III	182 (55.2)	126 (38.2)
IV	82 (24.8)	53 (16.1)
Died	0 (0.0)	16 (4.8)

4.1.17 Length of Hospital Stay

Table 4.18 compares the mean length of hospital stay between participants with and without absolute iron deficiency. Participants with absolute iron deficiency had a significantly longer mean hospital stay than those without absolute iron deficiency (**7.93 ± 2.53 days** versus **6.79 ± 2.22 days,** respectively). This difference was statistically significant (**t = 4.35, p < 0.001**), indicating that patients with absolute iron deficiency remained hospitalised for approximately **1.1** days longer on average than those without absolute iron deficiency. These findings suggest that absolute iron deficiency is associated with prolonged hospitalisation among patients admitted with acute heart failure, reflecting a greater burden of illness and potentially slower clinical recovery during the index admission.

Table 4.16: Comparison of the mean length of hospital stay between participants with and without absolute iron deficiency

Variable	Absolute Iron Deficiency (n = 175) Mean ± SD	No Absolute Iron Deficiency (n = 155) Mean ± SD	t-value	p-value
Length of hospital stay (days)	**7.93 ± 2.53**	**6.79 ± 2.22**	**4.35**	**<0.001**

4.2 Discussion

This study assessed the impact of absolute iron deficiency on short-term clinical outcomes among patients admitted with acute heart failure at Benjamin Mkapa Hospital. Specifically, the study compared the composite endpoint of all-cause mortality or hospital readmission between patients with and without absolute iron deficiency during a three-month follow-up period. It also assessed quality of life, functional status, and length of hospital stay among patients admitted with acute heart failure. The findings are broadly consistent with previous evidence linking iron deficiency with adverse outcomes in heart failure. However, the present study extends this evidence by focusing on patients admitted with AHF in Tanzania and by examining several dimensions of short-term recovery within the same cohort.

The following sections interpret these findings in relation to previous studies, possible explanations for the observed associations, and their implications for heart failure care in Tanzania.

4.2.1 Prevalence of Absolute Iron Deficiency Among Patients with Acute Heart Failure

In this study, the prevalence of absolute iron deficiency among patients admitted with acute heart failure was 53.0%. This indicates that more than half of the patients had depleted iron stores at admission.

This prevalence is closely comparable to the Tanzania Heart Failure (TAHEF) Study by Makubi et al. (13), the only other Tanzanian cohort to report iron status in heart failure, which reported iron deficiency-anaemia in approximately 49% of patients with heart failure in Tanzania. Although the exposure definition differs from that used in the present study, the similar magnitude of association provides regional evidence linking impaired iron status with adverse outcomes. However, the TAHEF study mainly assessed patients with heart failure in general, while the present study specifically focused on patients admitted with acute heart failure and followed them prospectively for short-term clinical outcomes. Therefore, the current study extends the Tanzanian evidence by showing not only the burden of iron deficiency but also its prognostic importance.

In Kenya, Omondi (12) reported a prevalence of 56.7% among patients with heart failure. The similarity between these estimates suggests that iron deficiency is a common comorbidity among patients with heart failure in East Africa. This regional consistency may reflect shared nutritional, inflammatory, and disease-related factors, although these factors were not comprehensively measured in the present study.

In Europe, Beale et al. (33) reported a prevalence of iron deficiency of 54% among hospitalised patients. Similarly, Núñez et al. (20) found iron deficiency in 48.2% of their study population, with absolute iron deficiency being more common than functional iron deficiency. More recently, Dirk et al. (5)reported a comparable prevalence of 44.1% at admission. Collectively, these findings indicate that iron deficiency is common among patients hospitalised with acute heart failure, with reported prevalence ranging from 44.1% to 54%. The prevalence observed in the present study therefore falls within the range reported internationally, despite differences in healthcare systems, study populations, and patient characteristics.

The high prevalence observed in this cohort has particular relevance in the Tanzanian setting. The study population was predominantly composed of patients presenting with advanced heart failure, with NYHA class III or IV accounting for a substantial proportion of participants, and anaemia was also common. Iron deficiency in this context may reflect a combination of chronic disease burden, nutritional factors, inflammation, recurrent illness and delayed presentation. These factors were not all measured comprehensively in the present study and therefore should be regarded as possible explanations rather than established causes of the observed prevalence.

An important distinction is that the present study focused on absolute iron deficiency, defined by ferritin <100 ng/mL. Absolute iron deficiency represents depleted iron stores and may be more persistent than functional iron deficiency, which can fluctuate with inflammation and acute illness. This distinction supports the clinical relevance of examining absolute deficiency in a cohort of patients admitted with AHF, although serial assessment of iron parameters would have provided a more complete understanding of changes during recovery.

Overall, the prevalence observed in this study supports the view that AID is not an uncommon laboratory finding in Tanzanian patients admitted with AHF. Rather, it

represents a frequent comorbidity that warrants consideration when assessing the clinical profile and prognosis of these patients.

4.2.2 Objective One: composite endpoint of all-cause mortality or hospital readmission

The principal finding of this study was that participants with AID experienced substantially poorer event-free survival than those without AID. At 90 days, the probability of remaining free from death or hospital readmission was 72.5% among participants with AID compared with 90.3% among those without AID. Moreover, after adjustment for potential clinical confounding variables, AID remained independently associated with the composite endpoint, with an adjusted hazard ratio of 2.25(95% CI 1.21–4.17; p=0.010).

This effect size is closely comparable with regional data from Tanzania. In the TAHEF study previously demonstrated a substantial burden of iron deficiency among Tanzanian HF patients, reporting a comparable 26% event rate, a similar adjusted hazard ratio (HR = 2.67), and a 70% 1-year survival rate. The convergence between two independently conducted Tanzanian cohorts strengthens confidence that this association reflects a genuine feature of iron deficiency in Tanzania heart failure patients, rather than a chance finding specific to BMH. The present study also extends this earlier registry evidence by demonstrating that the association holds specifically among acutely admitted patients followed prospectively over a defined 90-day window.

Elsewhere, absolute iron deficiency and related iron markers have been linked to adverse short-term outcomes using varied designs, lending broader external support to this finding.

These results are keeping with recent European evidence from the FERIC-RO registry, which reported that iron deficiency was independently associated with 3-month rehospitalisation after adjustment for confounders (adjusted HR 2.165, 95% CI 1.029–4.555, p = 0.042), and with markedly higher 90-day mortality among iron-deficient patients (30.9% vs 9.6%, p = 0.005) (22). Taken together with the present findings, this supports absolute iron deficiency as a consistent short-term prognostic marker

across differing healthcare settings, despite differences in the timing of iron status assessment and study population.

In Japan, Ueda et al. (21)reported that low serum iron independently predicted death or readmission (HR 1.5) in a cohort with a considerably higher overall event rate (54%); because serum iron is a more acute-phase-sensitive marker than ferritin, this finding is not directly equivalent to the present study's exposure definition, but it supports the same underlying principle, that impaired iron status, however measured, carries prognostic weight beyond anaemia. Similarly, a large Spanish registry found that lower transferrin saturation independently predicted short-term adverse events (48). Together, these findings raise a fair methodological question of whether TSAT or serum iron might have offered additional prognostic information beyond ferritin alone in the present cohort, a question this study was not designed to answer, since only ferritin-defined absolute iron deficiency was assessed.

A plausible biological basis for this association exists. Iron is a required cofactor for mitochondrial oxidative phosphorylation and myocardial energy production; its depletion has been proposed to impair myocardial energy metabolism, promote left ventricular hypertrophy, and worsen diastolic dysfunction. These mechanisms offer a biologically coherent explanation for the elevated risk observed here, although, as an observational, adjusted-association study, the present design cannot establish that iron deficiency directly causes these downstream effects; residual confounding by unmeasured markers of disease severity cannot be excluded.

These findings, together with interventional evidence from the AFFIRM-AHF trial, suggest that iron deficiency may have important clinical implications in this population. In AFFIRM-AHF, intravenous ferric carboxymaltose reduced the risk of recurrent heart failure hospitalisation following an acute admission (15,59).However, the primary analysis did not demonstrate a statistically significant reduction in the composite outcome of cardiovascular death or heart failure hospitalisation. Taken together, these findings support absolute iron deficiency as a clinically meaningful and potentially modifiable prognostic marker. They also provide a rationale for further interventional research to determine whether targeted correction of iron deficiency can improve outcomes among patients with acute heart failure in the Tanzanian setting.

4.2.3 Objective Two: quality of life among patients with absolute iron deficiency

Participants with AID had poorer health-related quality of life at baseline reflecting greater symptom burden and severe physical limitation. This gap persisted over follow-up and at 90 days demonstrated a smaller improvement in KCCQ-12 score. The mean increase in KCCQ-12 score was 4.1 ± 9.8 points among participants with AID compared with 9.2 ± 8.8 points among those without AID ($p<0.001$). By 3 months post-discharge, patients with AID maintained a significantly lower mean KCCQ-12 score compared to those without AID (45.0 ± 18.4 vs. 60.6 ±16.3, $p < 0.001$), indicating a persistent impairment in health-related quality of life.

A broadly similar pattern was recently reported in Nigeria by Akintunde & Orugun (36), who found that iron deficiency, present in 60% of patients with heart failure, was associated with significantly greater physical limitation (KCCQ-12 Overall Summary Score: 59.3 ± 22.7 vs. 70.2 ± 17.7, $p=0.003$). While the study provided cross-sectional evidence from patients with chronic heart failure in the outpatient setting, this present study extends these findings by demonstrating that absolute iron deficiency among patients hospitalised with acute heart failure was associated with greater baseline symptom severity and poorer functional recovery following discharge.

A more directly comparable design is found in a Swedish cohort of newly diagnosed heart failure patients followed prospectively, which similarly found iron deficiency associated with worse baseline quality of life (60). Notably, in that study cohort the gap between iron-deficient and iron-replete patients narrowed over a full year of outpatient follow-up, whereas the present study found a persistent gap at only 3 months. This difference may simply reflect the shorter follow-up window used here relative to the Swedish study's one-year horizon, rather than a genuinely more severe or more persistent deficit; it is equally plausible that the gap observed in this study cohort would narrow with longer follow-up, and the present 90-day design cannot distinguish between these possibilities.

These findings are consistent with the SICA-HF study by Bekfani et al. (61)which evaluated 190 symptomatic outpatients with HFpEF across Germany, England, and Slovenia. Iron deficiency was present in 58.4% of participants and quality of life, assessed using the EQ-5D questionnaire, was also significantly lower among

participants with low-ferritin iron deficiency (p=0.03). Although the SICA-HF study involved chronic outpatient HFpEF rather than patients hospitalised with acute heart failure, these findings provide supportive evidence for the association between iron deficiency and impaired functional status observed in this study cohort.

Systemically, iron depletion reduces myoglobin concentration and mitochondrial density in skeletal muscle, causing early anaerobic glycolysis during exertion that manifests as reduced exercise capacity, severe physical limitation, and persistent fatigue operating independently of anaemia. Clinically, because routine examination often misses underlying metabolic exhaustion and oral iron is poorly absorbed due to inflammation-driven hepcidin elevation, combining iron studies with KCCQ-12 screening provides a practical strategy to identify high-risk patients.

Therefore, the finding that iron-deficient patients had poorer quality of life is consistent with previous evidence; these results suggest that AID may be an important and unaddressed contributor to poor patient-reported outcomes among Tanzanian patients recovering from acute heart failure.

4.2.4 Objective Three: functional status among patients with absolute iron deficiency

Participants with AID had poorer functional status at baseline and remained more likely to have advanced NYHA functional class at 90 days. At follow-up, 20.0% of participants with AID remained in NYHA class IV compared with 11.6% of those without AID, whereas 28.0% and 37.4%, respectively, achieved NYHA class II. The overall distribution of NYHA class differed significantly between groups (χ^2=21.20, df=4, p<0.001).

The observed difference in functional status is supported by interventional evidence that showed correcting iron deficiency improved symptoms and NYHA functional class(50). Similarly, the HEART-FID trial reported associations between markers of iron availability and functional capacity (62). Because the present study used ferritin-defined absolute iron deficiency rather than TSAT or serum iron, this raises the same methodological question previously discussed: whether a TSAT- or serum-iron-based definition might have shown an even stronger functional association. The findings therefore support the clinical relevance of impaired iron status, while also highlighting

that the strength of the observed association may depend on the biomarker definition used.

Not all studies have reported similar findings. For example, Beale et al. (33)assessed a hospitalised European cohort comprising patients with both preserved and reduced ejection fraction and found no significant difference in NYHA class according to iron deficiency status. This discrepancy may reflect differences in cohort acuity, the extent of medical optimization in high-resource settings, or the cross-sectional rather than longitudinal assessment used in that study. However, these explanations remain plausible rather than established in the absence of directly comparable data

The mechanistic pathway linking iron deficiency to impaired oxygen utilization and skeletal muscle energetics is discussed in 4.2.2 and 4.2.3. Overall, these findings are consistent with the broader literature associating iron deficiency with reduced functional capacity, and extend that evidence by tracking functional status prospectively over 90 days in a Tanzanian acute heart failure population not previously studied in this way.

4.2.5 Objective Four: absolute iron deficiency and length of hospital stay

Participants with AID had a longer mean hospital stay than those without AID (7.93 ± 2.53 vs. 6.79 ± 2.22 days, $p<0.001$), corresponding to a mean difference of 1.14 days. This difference is comparable to findings reported in several other cohorts. Beale et al. (2019), in 503 patients admitted with acute decompensated heart failure, found that iron-deficient patients with HFpEF had longer hospital stays than their iron-replete counterparts (11 ± 7.7 vs. 9 ± 6 days, $p=0.036$). Similarly, Alharbi et al. (2023), using data from more than 112,000 heart failure hospitalisations in the US National Inpatient Sample, reported an adjusted mean difference of 1.31 days in hospital stay among patients with concomitant iron deficiency anaemia (95% CI: 0.71–1.47, $p<0.01$). Beattie, Khatib, Phillips & Williams (63) also reported longer hospitalisation among iron-deficient patients in a registry of 78,805 acute heart failure admissions from England and the United States (15.8 vs. 12.2 days, $p<0.0001$). Although the absolute duration of hospitalisation varied considerably between these studies, the direction of the association was similar to that observed in this study cohort at BMH.

This pattern, however, has not been universal. Van Dalen et al. (5)found no significant difference in hospital stay across iron status categories, with a median duration of 7 days (p=0.639). Such differences may reflect variation in patient characteristics, illness severity, healthcare resources, and discharge practices across study settings.

Importantly, our finding of a 1.14-day longer stay among participants with AID should therefore be interpreted as an association rather than evidence that AID itself prolongs hospitalisation. Greater disease severity, anaemia, renal dysfunction, persistent congestion, and reduced functional reserve may contribute to both iron deficiency and delayed clinical recovery, potentially explaining part of the observed association.

The relevance of this finding is particularly important in the Tanzanian setting. Even an additional day of hospitalisation can increase costs for patients and families while occupying already limited inpatient capacity and adding pressure to healthcare resources. The observed association with AID may help identify patients at greater risk of prolonged hospitalisation. Whether treatment of iron deficiency can reduce length of stay or accelerate recovery in this setting remains an important question for future interventional research.

4.2.6 General interpretation of findings

Across all four objectives, absolute iron deficiency was consistently associated with worse outcomes: higher risk of death or readmission, poorer quality of life, worse functional status, and longer hospital stay, a pattern broadly consistent with international and regional evidence. This study adds to that evidence in several specific ways: it is among the first to examine this relationship prospectively in a Tanzanian acute heart failure population, it assessed multiple clinically meaningful outcomes within a single cohort, and its prospective design allowed exposure status to be established before outcomes occurred.

These findings are consistent with absolute iron deficiency functioning as a prognostic marker of poor outcomes in this population and biologically plausible as a contributor as discussed in 4.2.2 and 4.2.3, although this cannot be established from the present observational design. Distinguishing between these possibilities would require interventional data, which lies beyond the scope of this observational study.

4.2.7 Clinical and public health implications

The findings have important clinical implications. First, these findings support consideration of routine assessment of iron status in patients admitted with acute heart failure, consistent with contemporary heart failure guideline recommendations. Second, patients with absolute iron deficiency should be regarded as a high-risk group requiring closer monitoring during admission and after discharge. Third, iron deficiency assessment may improve risk stratification and discharge planning.

The findings also have policy implications. In Tanzania, routine screening and management of iron deficiency in heart failure is not yet standardized. The evidence from this study may support local evidence in integration of iron studies into acute heart failure care protocols. It may also support future consideration of evaluation of intravenous iron therapy, particularly ferric carboxymaltose, where feasible and clinically indicated.

4.2.8 Strengths of the Study

This study had several strengths. First, the prospective cohort design allowed exposure status to be determined before outcome occurrence, strengthening the temporal relationship between absolute iron deficiency and clinical outcomes. Second, the study assessed multiple relevant outcomes, including mortality, readmission, quality of life, functional status, and length of hospital stay. Third, the study site hospital manages a substantial number of patients with acute heart failure, providing a clinically relevant setting for studying this population. Fourth, the use of standardized tools such as NYHA classification and KCCQ improved the assessment of functional status and quality of life.

4.2.9 Summary of the Discussion

This prospective cohort study found that AID was common among patients admitted with AHF at BMH and was associated with a worse short-term clinical course. Participants with AID had lower event-free survival and a higher adjusted hazard of the composite endpoint of all-cause mortality or hospital readmission. AID was also associated with poorer quality of life recovery, less favourable functional status at 90 days and longer hospitalisation.

The findings are broadly consistent with previous international and regional evidence, while extending the available evidence to a Tanzanian population with AHF.

Importantly, the consistency of associations across several clinically relevant outcomes suggests that AID may serve as an important prognostic marker in this population.

However, the observational design means that residual confounding and other sources of bias cannot be excluded, and the study does not establish that correction of AID would improve outcomes. The findings therefore provide a strong rationale for routine assessment of iron status and for appropriately designed interventional studies to determine whether treatment of AID can modify the adverse clinical trajectory observed in patients with AHF.

4.3 Limitations of the Study

1. The study was conducted at a single tertiary referral hospital, where patients may differ systematically from patients with acute heart failure who were managed in other healthcare facilities or in the community, which may limit the generalizability of the findings to the broader population of patients with acute heart failure.

2. Single baseline assessment and limited characterization of iron status**:** Iron status was assessed at baseline using serum ferritin and TSAT, and changes in these parameters during follow-up were not evaluated. Although the ferritin/TSAT-based definition is an established clinical approach for identifying iron deficiency in heart failure, ferritin is an acute-phase reactant and may be influenced by systemic inflammation, particularly during acute illness. Additional biomarkers such as soluble transferrin receptor (sTfR), which may provide complementary information regarding tissue iron availability and iron-restricted erythropoiesis, were not assessed. Therefore, a single baseline assessment based on ferritin and TSAT may not completely characterize the dynamic or functional aspects of iron status during follow-up.

3. Although multivariable Cox regression was used to adjust for measured potential confounders, residual confounding cannot be completely excluded

because of the observational nature of the study. Some factors that may influence both iron status and clinical outcomes, including nutritional status, inflammatory burden, socioeconomic circumstances, treatment adherence, and other aspects of heart failure severity, may not have been fully measured or captured in the analysis. In addition, potential measurement error in some clinical and laboratory variables may have resulted in incomplete adjustment for their effects. The potential for inter-rater variability in NYHA classification should also be considered. Previous research has demonstrated only moderate agreement between physicians assigning NYHA class, with a weighted κ of 0.41, highlighting the subjectivity inherent in this classification (28,64) .Therefore, the observed association between absolute iron deficiency and the 90-day composite outcome should be interpreted as an adjusted association rather than evidence of a causal relationship. The relatively small number of outcome events also necessitated a parsimonious multivariable model, limiting the number of potential confounders that could be simultaneously evaluated.

4. Loss to follow-up and attrition bias: Nine participants (2.7%) were lost to follow-up, resulting in missing information regarding their 90-day outcomes. Baseline characteristics of participants lost to follow-up were broadly comparable with those retained in the study; however, meaningful statistical comparisons were limited by the small number of participants lost to follow-up. Although the proportion lost to follow-up was small, attrition bias cannot be completely excluded because participants lost to follow-up may have differed systematically from those retained, particularly with respect to iron status or risk of mortality or readmission. Nevertheless, the high follow-up rate of 97.3% is likely to have limited the potential impact of attrition bias.

5. Limited number of outcome events: The relatively small number of outcome events, particularly the limited number of deaths and the absence of deaths among participants without absolute iron deficiency, may have reduced the precision and stability of the estimated associations. The number of observed events also limited the number of potential covariates that could be simultaneously evaluated in the multivariable model, necessitating a parsimonious modelling approach

6. Short duration of follow-up: The study followed participants for 90 days and therefore primarily assessed short-term clinical outcomes. The findings may not reflect the longer-term effects of absolute iron deficiency on mortality, recurrent hospitalisation, functional status, or quality of life.

4.4 Contribution of the Study to Knowledge

This study contributes important evidence regarding the burden and prognostic significance of absolute iron deficiency among patients admitted with acute heart failure in Tanzania. It demonstrates that absolute iron deficiency is not only highly prevalent but also independently associated with mortality, hospital readmission, poorer quality of life, impaired functional status, and prolonged hospitalisation. The findings provide a strong foundation for future clinical practice improvements, policy development, and research aimed at optimizing heart failure care in Tanzania and similar resource-limited settings.

CHAPTER FIVE

CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

This prospective cohort study assessed the impact of absolute iron deficiency (AID) on short-term clinical outcomes among patients admitted with acute heart failure at Benjamin Mkapa Hospital. AID was highly prevalent, affecting more than half of participants, and was significantly associated with adverse outcomes: patients with AID had a higher risk of the composite endpoint of 90-day mortality or hospital readmission, with mortality and readmission both occurring more frequently in this group. AID was also associated with poorer quality of life, worse functional status, and prolonged hospital stay, with implications for healthcare resource use in resource-constrained settings.

These findings should be interpreted in light of the study's single-centre, observational design, which does not permit causal inference. Overall, AID emerges as an important prognostic marker in acute heart failure, providing local evidence to support incorporating iron status assessment into routine care in Tanzania.

5.2 Recommendations

5.2.1 Recommendations for Clinical Practice

1. Routine screening for iron deficiency should be incorporated into the standard evaluation of all patients admitted with acute heart failure. Assessment of serum ferritin and transferrin saturation should be considered during initial admission workup to facilitate early identification of high-risk patients.

2. Patients identified with AID may warrant consideration for closer clinical assessment and follow-up, particularly where resources permit due to their increased adverse outcomes.

3. Healthcare providers managing patients with acute heart failure should recognize absolute iron deficiency as an important prognostic factor and

incorporate iron status assessment into risk stratification and discharge planning processes.

4. Quality of life and functional status assessments should be routinely performed during follow-up visits to identify patients requiring additional clinical support and rehabilitation interventions.

5.2.2 Recommendations for Hospital Management and Policymakers

1. Benjamin Mkapa Hospital and other tertiary healthcare facilities should strengthen laboratory capacity to ensure routine availability of iron profile investigations, including serum ferritin and transferrin saturation testing, while accounting for the additional resource and cost implications of expanding this testing in a constrained public-hospital setting.

2. The Ministry of Health and relevant professional bodies should consider incorporating routine iron deficiency screening into national heart failure management guidelines and clinical protocols.

3. Policymakers should monitor emerging international trial evidence on intravenous iron replacement therapy in heart failure and consider future evaluation of access strategies for eligible patients, pending confirmatory local or regional trial data.

4. Resource allocation for cardiovascular care should include support for diagnostic services and management of common comorbidities such as iron deficiency that significantly influence patient outcomes.

5.2.3 Recommendations for Future Research

1. Multicentre studies involving larger and more diverse patient populations should be conducted to validate the findings and improve generalizability across Tanzania and Sub-Saharan Africa.

2. Randomized controlled trials should be undertaken to evaluate the effectiveness of iron replacement therapy, particularly intravenous iron

formulations, in improving clinical outcomes among Tanzanian patients with acute heart failure and absolute iron deficiency.

3. Future studies should assess the long-term impact of absolute iron deficiency on mortality, recurrent hospitalisation, healthcare costs, and quality of life beyond the 90-day follow-up period.

4. Further research should explore the relative prognostic value of different iron status markers, including serum ferritin, transferrin saturation, soluble transferrin receptor (sTfR), serum iron, and hepcidin, among patients with acute heart failure.

5. Qualitative and mixed-method studies should be conducted to explore barriers and facilitators to routine iron deficiency screening and management among healthcare providers caring for patients with heart failure.

5.2.4 Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to restrictions related to the privacy and confidentiality of individual patient data but are available from the corresponding author on reasonable request and subject to approval by the relevant institutional authorities.

5.2.5 Competing interests

The authors declare that they have no competing interests.

5.2.6 Funding

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5.2.7 Author contribution

DM conceived the study, developed the study protocol and methodology, collected and analysed the data, interpreted the findings, and drafted the manuscript. AM

provided overall academic supervision throughout the study, contributed to study design and methodological refinement, reviewed and critically revised the manuscript, and provided guidance on interpretation of the findings. JM contributed to academic supervision, reviewed the study methodology and manuscript, and provided critical intellectual input during the research process. KM contributed to academic supervision, reviewed the manuscript, and provided critical input on the study and its interpretation. All authors reviewed and approved the final manuscript and agreed to be accountable for all aspects of the work.

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APPENDICES

Appendix I: Research Workflow Plan and Timeline

Phase	Activities	Timeline	Duration
1. Preparation & Ethics	Finalize proposal, obtain ethical clearance, refine tools, train assistants	Sep – Oct 2025	2 months

2. Pilot Testing	Pretest data collection tools, validate questionnaires, adjust methodology	Early Nov 2025	2 weeks
3. Data Collection	Recruit participants, collect baseline and follow-up data	January 2026 – June 2026	6 months
4. Data Cleaning	Code, enter, and clean data (check for missing or inconsistent values)	July 2026	1 weeks
5. Data Analysis	Statistical analysis using IBM SPSS Statistics version 25.0.	July 2026	1 weeks
6. Drafting of Dissertation	Write chapters: Introduction, Methods, Results, Discussion	July 2026	2 weeks
7. Review & Corrections	Supervisor feedback, internal review, address comments	Early-Mid August 2026	3 weeks
8. Final Submission	Print, bind, and submit dissertation	Late August 2026	1 week
9. Viva / Defense Preparation	Prepare presentation, anticipate questions, rehearse defense	September-October	1-2 months

Appendix II: Informed Consent Form (English Version)

Study Title: Impact of Iron Deficiency on Short-Term Clinical Outcomes in Patients Admitted with Acute Heart Failure at Benjamin Mkapa Hospital: A Prospective Cohort Study

Principal Investigator: Daniel Mukky, Resident, Master of Internal Medicine, University of Dodoma
Institution: University of Dodoma (UDOM), School of Medicine and Dentistry, Department of Internal Medicine, in collaboration with Benjamin Mkapa Hospital (BMH)
Ethical Clearance: UDOM-IRREC MA.84/261/98/4 (5th January 2026); BMH AB.150/293/01/'B'/283 (6th January 2026)

Introduction

My name is Daniel Mukky, and I am a resident pursuing a Master's degree in Internal Medicine at the University of Dodoma. I am the Principal Investigator of this study, being conducted at Benjamin Mkapa Hospital. I would like to invite you to take part in this research. Before you decide, please take time to read the information below carefully, and feel free to ask me any questions you may have.

Purpose of the Study

Iron deficiency is common among people admitted to hospital with acute heart failure, but it often goes unrecognized, and its effect on recovery has not been well studied in Tanzania. This study aims to find out whether iron deficiency affects how patients with acute heart failure recover over the following three months including their risk of death, hospital readmission, symptoms, and quality of life.

Why You Have Been Chosen

You have been chosen because you have been admitted to this hospital with acute heart failure and meet the criteria set for this study.

What Participation Involves

If you agree to take part:

1. You will be asked to answer a study questionnaire about your health and medical history.

2. A blood sample will be collected to measure your iron levels (ferritin) and related blood tests, using standard safe procedures.

3. Your heart failure symptoms and functional status will be assessed during your hospital stay.

4. You will be followed up for 90 days after enrollment to assess your recovery, including your symptoms, quality of life, any hospital readmission, and, where applicable, survival status. Follow-up may be done through clinic visits or phone contact.

5. Taking part does not require any procedure beyond what is already part of your routine care, other than the blood sample for iron studies and the study questionnaire.

Risks and Discomforts

The main risk is mild discomfort or bruising at the site where blood is drawn, similar to any routine blood test. If you experience any problem related to the blood draw, you will receive appropriate medical attention at no cost to you.

Benefits

There is no direct personal benefit to you for taking part. However, the information gathered may help doctors better understand and manage iron deficiency in future heart failure patients in Tanzania. Please note that being part of this study is separate from your medical treatment your doctors will continue to make all decisions about your care independently of this research, based on your clinical needs.

Voluntary Participation and Right to Withdraw

Taking part in this study is entirely voluntary. You are free to decline, or to withdraw at any time during the study, without giving a reason. Your decision will not affect the medical care you receive at this hospital, now or in the future, in any way.

Confidentiality

All information collected will be kept strictly confidential. You will be assigned a unique study number, and your name will not appear on any study document, report, or publication. Only the research team will have access to your identifiable information, which will be stored securely.

Compensation for Study-Related Harm

If you suffer any harm directly caused by a study procedure, you will receive free medical treatment for that harm through the hospital's standard care pathways.

Whom to Contact

If you have questions or enquiries during the course of the study, you may contact:

Daniel Mukky
Resident/Principal Investigator
The University of Dodoma (UDOM)
School of Medicine and Dentistry
Department of Internal Medicine
P.O. Box 259, Dodoma
Mobile phone: 0714884553
Email address: mukkymaliq@gmail.com

In case of any questions about your rights as a participant in this study, you may contact:

The Director
Directorate of Research, Publications and Consultancy (DRPC)
The University of Dodoma (UDOM)
P.O. Box 951, Dodoma
Tel: (+255) 262310301
Email address: research@udom.ac.tz

Participant's Statement

I have read, or had read to me, the information about this study on the impact of iron deficiency on short-term outcomes among patients admitted with acute heart failure at Benjamin Mkapa Hospital. I understand the purpose of the study and what my participation involves, including completing a study questionnaire, providing a blood

sample, and being followed up for 90 days. This has been explained to me by Daniel Mukky. I understand that my participation is voluntary and that I may withdraw at any time without affecting the medical care I receive.

I agree / do not agree *(circle one)* to take part in this study.

Signature of participant: ……
Signature of witness/relative (for participants unable to sign):
……
Date: ……

I confirm that I have explained the purpose, procedures, risks, and benefits of this study to the participant named above, in a language they understand, and that consent was given freely.

Signature of investigator: …… Date:
……

Appendix III: Informed Consent Form (Kiswahili Version)

Kichwa cha Utafiti: Athari za Upungufu wa Madini ya Chuma katika Matokeo ya Kiafya ya Muda Mfupi kwa Wagonjwa Waliolazwa sababu ya Kufeli kwa moyo katika Hospitali ya Benjamin Mkapa: Utafiti wa ufutialiaji kwa muendelezo.

Mtafiti Mkuu: Daniel Mukky, Mkazi, Shahada ya Uzamili katika Tiba za Ndani, Chuo Kikuu cha Dodoma
Taasisi: Chuo Kikuu cha Dodoma (UDOM), Shule ya Tiba na Meno, Idara ya Tiba za Ndani, kwa ushirikiano na Hospitali ya Benjamin Mkapa (BMH)
Vibali vya Kimaadili: UDOM-IRREC MA.84/261/98/4 (5 Januari 2026); BMH AB.150/293/01/'B'/283 (6 Januari 2026)

Utangulizi

Jina langu ni Daniel Mukky, na mimi ni Daktari mkazi ninayesomea Shahada ya Uzamili katika Tiba za Ndani katika Chuo Kikuu cha Dodoma. Mimi ndiye Mtafiti Mkuu wa utafiti huu, unaofanyika katika Hospitali ya Benjamin Mkapa. Ningependa kukualika ushiriki katika utafiti huu. Kabla ya kuamua, tafadhali soma taarifa zifuatazo kwa makini, na usisite kuniuliza swali lolote.

Madhumuni ya Utafiti

Upungufu wa madini ya chuma ni tatizo la kawaida miongoni mwa wagonjwa walioalazwa hospitalini kwa homa ya moyo ya ghafla, lakini mara nyingi halitambuliwi, na athari yake katika kupona kwa wagonjwa haijafanyiwa utafiti wa kutosha nchini Tanzania. Utafiti huu unalenga kujua kama upungufu wa madini ya chuma unaathiri kupona kwa wagonjwa wenye kufeli kwa moyo ghafla katika kipindi cha miezi mitatu ijayo, ikiwa ni pamoja na hatari ya kifo, kulazwa tena hospitalini, dalili, na ubora wa maisha.

Kwa Nini Umechaguliwa

Umechaguliwa kwa sababu umelazwa katika hospitali hii kwa homa ya moyo ya ghafla na unakidhi vigezo vilivyowekwa kwa ajili ya utafiti huu.

Utakachofanywa Ukikubali Kushiriki

Ukikubali kushiriki:

1. Utaulizwa kujibu maswali ya utafiti kuhusu afya yako na historia yako ya kiafya.

2. Sampuli ya damu itachukuliwa kupima kiwango cha madini ya chuma (ferritin) na vipimo vinavyohusiana, kwa kutumia taratibu salama za kawaida.

3. Dalili zako za homa ya moyo na hali yako ya utendaji zitatathminiwa wakati wa kulazwa hospitalini.

4. Utafuatiliwa kwa siku 90 baada ya kujiunga na utafiti ili kutathmini kupona kwako, ikiwa ni pamoja na dalili zako, ubora wa maisha, kulazwa tena hospitalini, na, inapohitajika, hali yako ya uhai. Ufuatiliaji unaweza kufanyika kupitia ziara za kliniki au mawasiliano ya simu.

5. Kushiriki hakuhitaji utaratibu wowote zaidi ya unaofanyika kama sehemu ya matibabu yako ya kawaida, isipokuwa sampuli ya damu kwa ajili ya vipimo vya madini ya chuma na dodoso la utafiti.

Hatari na Usumbufu

Hatari kuu ni maumivu kidogo au kuvimba mahali damu ilipochukuliwa, sawa na kipimo chochote cha kawaida cha damu. Endapo utapata tatizo lolote linalohusiana na uchukuaji wa damu, utapatiwa matibabu stahiki bila malipo.

Faida

Hakuna faida ya moja kwa moja kwako binafsi kwa kushiriki. Hata hivyo, taarifa zitakazokusanywa zinaweza kusaidia madaktari kuelewa vizuri zaidi na kudhibiti upungufu wa madini ya chuma kwa wagonjwa wa homa ya moyo watakaokuja baadaye nchini Tanzania. Tafadhali fahamu kuwa kushiriki katika utafiti huu ni tofauti na matibabu yako — madaktari wako wataendelea kufanya maamuzi yote kuhusu matibabu yako bila kuathiriwa na utafiti huu, kulingana na mahitaji yako ya kiafya.

Ushiriki wa Hiari na Haki ya Kujitoa

Kushiriki katika utafiti huu ni kwa hiari kabisa. Una uhuru wa kukataa, au kujitoa wakati wowote wa utafiti, bila kutoa sababu yoyote. Uamuzi wako hautaathiri kwa namna yoyote matibabu unayopokea katika hospitali hii, sasa au baadaye.

Usiri

Taarifa zote zitakazokusanywa zitahifadhiwa kwa usiri mkubwa. Utapewa namba maalum ya utafiti, na jina lako halitaonekana kwenye hati, ripoti, au machapisho yoyote. Ni timu ya utafiti pekee itakayokuwa na uwezo wa kufikia taarifa zako binafsi, ambazo zitahifadhiwa kwa usalama.

Fidia kwa Madhara Yatokanayo na Utafiti

Endapo utapata madhara yoyote yanayosababishwa moja kwa moja na taratibu za utafiti, utapatiwa matibabu bila malipo kupitia njia za kawaida za huduma za hospitali.

Wa Kuwasiliana Naye

Endapo una maswali au maulizo wakati wowote wa utafiti, unaweza kuwasiliana na:

Daniel Mukky
Mkazi/Mtafiti Mkuu
Chuo Kikuu cha Dodoma (UDOM)
Shule ya Tiba na Meno
Idara ya Tiba za Ndani
S.L.P. 259, Dodoma
Simu: 0714884553
Barua pepe: mukkymaliq@gmail.com

Endapo una maswali kuhusu haki zako kama mshiriki wa utafiti, unaweza kuwasiliana na:

Mkurugenzi
Idara ya Utafiti, Machapisho na Ushauri (DRPC)
Chuo Kikuu cha Dodoma (UDOM)
S.L.P. 951, Dodoma
Simu: (+255) 262310301
Barua pepe: research@udom.ac.tz

Tamko la Mshiriki

Nimesoma, au nimesomewa, taarifa kuhusu utafiti huu wa athari za upungufu wa madini ya chuma katika matokeo ya kiafya ya muda mfupi kwa wagonjwa waliolazwa na homa ya moyo ya ghafla katika Hospitali ya Benjamin Mkapa. Naelewa madhumuni ya utafiti na kile kinachohusika katika ushiriki wangu, ikiwa ni pamoja na kujaza dodoso la utafiti, kutoa sampuli ya damu, na kufuatiliwa kwa siku 90. Hili limeelezwa kwangu na Daniel Mukky. Naelewa kuwa ushiriki wangu ni wa hiari na naweza kujitoa wakati wowote bila kuathiri matibabu ninayopokea.

Nakubali / Sikubali *(zunguka moja)* kushiriki katika utafiti huu.

Sahihi ya mshiriki: ……
Sahihi ya shahidi/ndugu (kwa asiyeweza kusaini): ……
Tarehe: ……

Nathibitisha kuwa nimemweleza mshiriki aliyetajwa hapo juu madhumuni, taratibu, hatari, na faida za utafiti huu, kwa lugha anayoielewa, na kwamba ridhaa yake imetolewa kwa hiari.

Sahihi ya mtafiti: …… Tarehe:
……

Appendix IV: Questionnaire (English version)

Part I: Sociodemographic characteristics

1. Age (years)…….

2. Sex 1. Male 2. Female
3. Residence……1. Rural 2. Urban
4. Marital status……..1. Single 2. Married/cohabiting
5. Level of education…….1. Informal 2. Primary 3. Secondary 4. Tertiary
6. Body weight (kg)……..
7. Height (m)……..
8. BMI (kg/m^2)…….
9. Hip circumference …….
10. Waist circumference …….
11. Waist to hip ratio …….
12. Comorbidities……1. Yes 2. No
13. If yes in question number 12, list it/them……
14. Hypertension……1. Yes 2. No
15. Diabetes mellitus ……1. Yes 2. No
16. Dyslipidemia ……1. Yes 2. No
17. Alcoholism……..1. Yes 2. No
18. Smoking……..1. Yes 2. No
19. Medical adherence …….1. Regular 2. Irregular (assessment tool)
20. Heart failure medications

ARB/ACEi/ANRi	Diuretics	Beta Blockers	MRA	SGLT2i	Digitalis	Nitrates/vasodilators	

Part II: Clinical characteristics

21. Systolic BP (mmHg)……..
22. Diastolic BP (mmHg)…….
23. Pulse pressure ……
24. BP status…….1. Normal 2. Hypotension 3. Hypertension
25. Heart rate (beats/minute)…….
26. Pulse deficit (≥10beats/min) 1. Yes 2. No
27. Duration of symptoms/signs (days)……....

28. Assessment of drug adherence

MARS-5 (Medication Adherence Report Scale-5).

Item	Always	Often	Sometimes	Rarely	Never
"I forget to take them"	1	2	3	4	5
"I alter the dose"	1	2	3	4	5
"I stop taking them for a while"	1	2	3	4	5
"I decide to skip a dose"	1	2	3	4	5
"I take less than instructed"	1	2	3	4	5
Total score					

29. **Assessment of heart failure**

Major Criteria	**Minor Criteria**
Paroxysmal nocturnal dyspnea	Bilateral leg edema
Orthopnea	Nocturnal cough
Elevated jugular venous pressure	Dyspnea on ordinary exertion
Pulmonary rales	Hepatomegaly
Third heart sound	Pleural effusion
Cardiomegaly on chest radiograph	Tachycardia (heart rate ≥120 beats/min)
Pulmonary edema on chest radiograph	Weight loss ≥4.5 kg in 5 days If the cause for weight loss is unclear and not response to treatment
Weight loss ≥4.5 kg in 5 days in response to treatment of presumed heart failure*	
Diagnosis:	

30. Baseline KCCQ score

31. Baseline New York Heart Association (NYHA) class

    1. Class I
    2. Class II
    3. Class III

4. Class IV

Part III: ECG findings

32. QRS findings
    1. 120 – 150 ms
    2. ≥150 ms
33. Ischemic heart disease……1. Yes 2. No
34. If yes in question 32, name it……..
35. Atrial fibrillation 1. Yes 2. No

Part IV: ECHO findings

36. Mechanical dyssynchrony type…1. Atrioventricular 2. Interventricular
    3. Intraventricular. 4. No
37. Ejection Fraction
    1. ≤40% ( )
    2. 41-49% ( )
    3. ≥50% ( )
38. TAPSE (cm) ……
39. IVC diameter (cm) ……..
40. IVC collapsibility (%) ……..

Part V: Laboratory parameters

41. Serum Creatinine	42. **HDL**
43. BUN	44. LDL
45. Full blood picture Hb	46. Triglyceride
47. Serum Na+	48. Total Cholesterol
49. Serum K+	50. Serum ferritin
51. HbA1C	52. TSAT
53. Troponin I or T	
54. HDL	

Part VI: Follow-up information at 90 days

55. Duration of stay in-hospital admission (days)…….
56. Lost to follow-up 1. Yes..... 2. No……
57. NYHA class at 90 days……
58. KCCQ score at 90 days…….

59. Clinical outcome

1. All-cause Mortality……Rehospitalisation…….Censored…....

6. Over the past 2 weeks, how much has your **heart failure** limited your enjoyment of life?

It has **extremely** limited my enjoyment of life	It has limited my enjoyment of life **quite a bit**	It has **moderately** limited my enjoyment of life	It has **slightly** limited my enjoyment of life	It has **not limited** my enjoyment of life at all
O	O	O	O	O
1	2	3	4	5

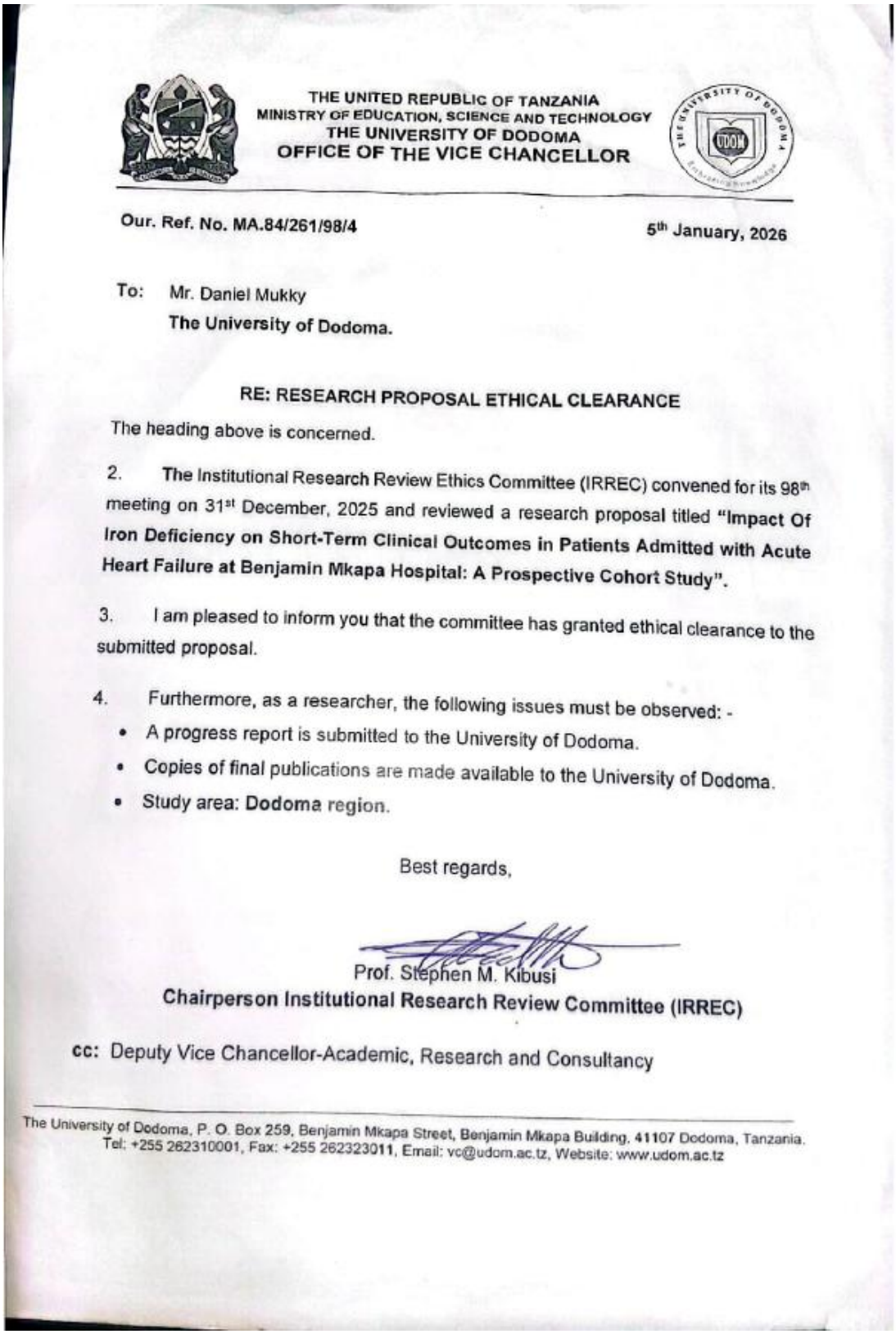
7. If you had to spend the rest of your life with your **heart failure** the way it is right now, how would you feel about this?

Not at all satisfied	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Completely satisfied
O	O	O	O	O
1	2	3	4	5

8. How much does your **heart failure** affect your lifestyle? Please indicate how your **heart failure** may have limited your participation in the following activities over the past 2 weeks.

Activity	**Severely** Limited	Limited **quite a bit**	**Moderately** limited	**Slightly** limited	**Did not** limit at all	Does not apply or did not do for other reasons
a. Hobbies, recreational activities	O	O	O	O	O	O
b. Working or doing household chores	O	O	O	O	O	O
c. Visiting family or friends out of your home	O	O	O	O	O	O
	1	2	3	4	5	6

Appendix V: Research Proposal Ethical Clearance



THE UNITED REPUBLIC OF TANZANIA
MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY
THE UNIVERSITY OF DODOMA
OFFICE OF THE VICE CHANCELLOR

Our. Ref. No. MA.84/261/98/4

5th January, 2026

To: Mr. Daniel Mukky
The University of Dodoma.

RE: RESEARCH PROPOSAL ETHICAL CLEARANCE

The heading above is concerned.

2. The Institutional Research Review Ethics Committee (IRREC) convened for its 98th meeting on 31st December, 2025 and reviewed a research proposal titled **"Impact Of Iron Deficiency on Short-Term Clinical Outcomes in Patients Admitted with Acute Heart Failure at Benjamin Mkapa Hospital: A Prospective Cohort Study".**

3. I am pleased to inform you that the committee has granted ethical clearance to the submitted proposal.

4. Furthermore, as a researcher, the following issues must be observed: -

- A progress report is submitted to the University of Dodoma.
- Copies of final publications are made available to the University of Dodoma.
- Study area: **Dodoma** region.

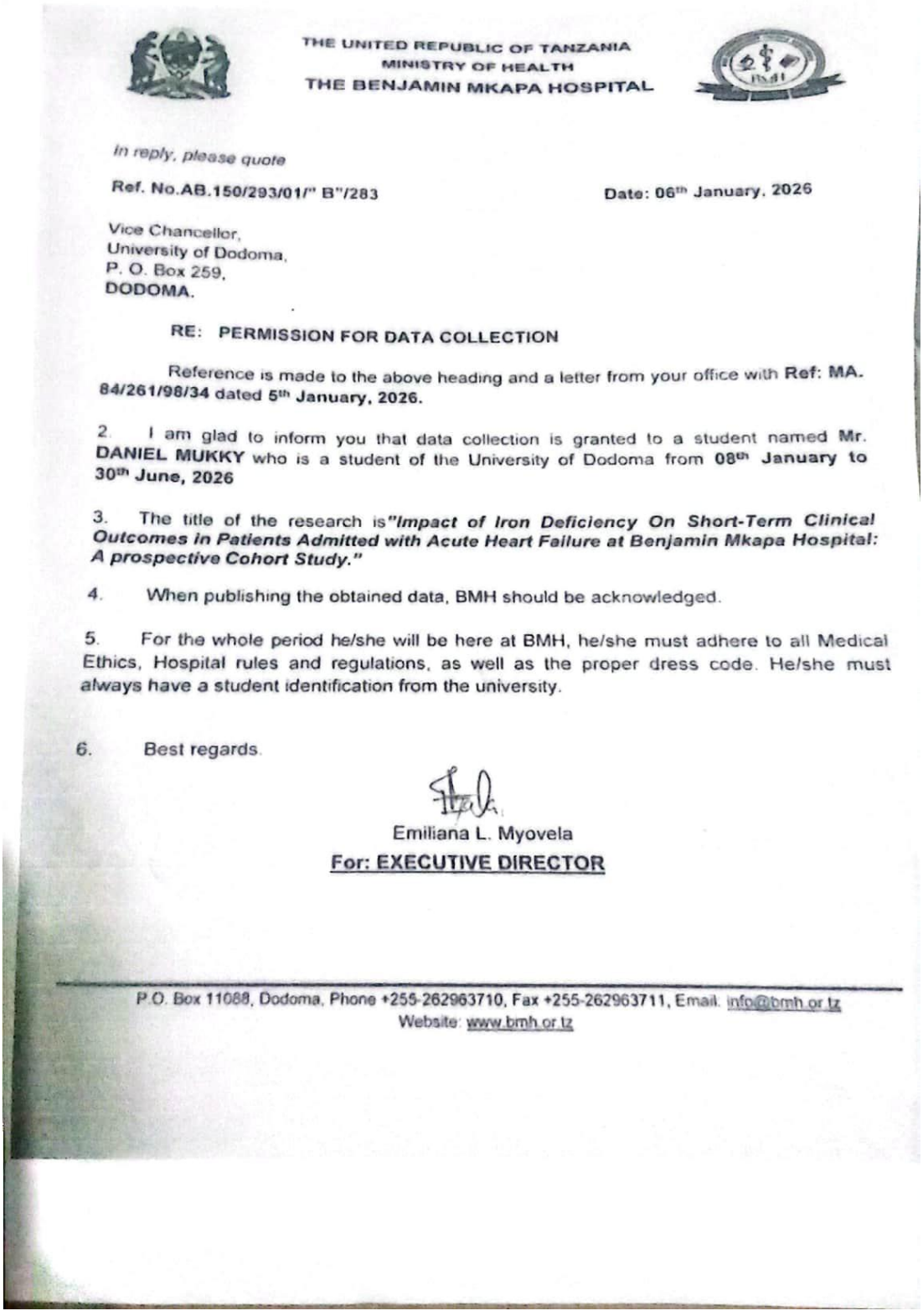
Best regards,

Prof. Stephen M. Kibusi
Chairperson Institutional Research Review Committee (IRREC)

cc: Deputy Vice Chancellor-Academic, Research and Consultancy

The University of Dodoma, P. O. Box 259, Benjamin Mkapa Street, Benjamin Mkapa Building, 41107 Dodoma, Tanzania.
Tel: +255 262310001, Fax: +255 262323011, Email: vc@udom.ac.tz, Website: www.udom.ac.tz

Appendix VI: Permission for data collection



THE UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH
THE BENJAMIN MKAPA HOSPITAL

In reply, please quote

Ref. No.AB.150/293/01/" B"/283 **Date: 06th January, 2026**

Vice Chancellor,
University of Dodoma,
P. O. Box 259,
DODOMA.

RE: PERMISSION FOR DATA COLLECTION

Reference is made to the above heading and a letter from your office with **Ref: MA. 84/261/98/34** dated **5th January, 2026.**

2. I am glad to inform you that data collection is granted to a student named **Mr. DANIEL MUKKY** who is a student of the University of Dodoma from **08th January to 30th June, 2026**

3. The title of the research is ***"Impact of Iron Deficiency On Short-Term Clinical Outcomes in Patients Admitted with Acute Heart Failure at Benjamin Mkapa Hospital: A prospective Cohort Study."***

4. When publishing the obtained data, BMH should be acknowledged.

5. For the whole period he/she will be here at BMH, he/she must adhere to all Medical Ethics, Hospital rules and regulations, as well as the proper dress code. He/she must always have a student identification from the university.

6. Best regards.

Emiliana L. Myovela
For: EXECUTIVE DIRECTOR

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