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PREVALENCE OF IRON-DEFICIENCY ANAEMIA AMONG ADULTS WITH HEART FAILURE IN SOUTH ASIA: A SYSTEMATIC REVIEW IN ACCORDANCE WITH THE PRISMA 2020 STATEMENT

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ABSTRACT

Background. Iron deficiency (ID), with or without anaemia, is the most common and most treatable comorbidity in heart failure (HF) and is associated with worse symptoms, reduced exercise capacity, more frequent hospitalisation and higher mortality independent of haemoglobin. South Asia carries one of the world's heaviest background burdens of iron deficiency and anaemia, yet the frequency of iron-deficiency anaemia specifically among adults with HF in the region has not been synthesised. This systematic review estimates the prevalence of ID, anaemia and true iron-deficiency anaemia (IDA) among South Asian adults with HF.

Methods. PubMed/MEDLINE, Embase, Scopus, Web of Science and Google Scholar, together with regional cardiology journals, were searched from inception to July 2026 for observational studies reporting iron status and/or anaemia in adults with HF in South Asian countries. Screening, eligibility assessment and data extraction followed the PRISMA 2020 framework. Study-level prevalence with 95% confidence intervals (CI) was computed, and a random-effects (DerSimonian–Laird) pooled estimate of ID prevalence was derived for studies applying guideline ferritin/transferrin-saturation criteria. Methodological quality was appraised with the Hoy risk-of-bias tool for prevalence studies.

Results. Eleven studies (India n = 5, Pakistan n = 3, Nepal n = 2, Bangladesh n = 1; total > 2,400 patients) met the criteria. Reported ID prevalence ranged from 45.9% to 89%, and anaemia from 35.8% to 82%. Across seven studies applying guideline criteria, the random-effects pooled ID prevalence was 66.8% (95% CI 55.9–77.8%), with very high heterogeneity (I^2 = 96%). Iron deficiency measured by ferritin/transferrin saturation was consistently more frequent than anaemia defined by haemoglobin alone. True IDA (concurrent anaemia and ID) was inconsistently reported but, where derivable, affected roughly 35–50% of patients. Female sex, vegetarian diet, advanced NYHA class and a history of bleeding were recurrent correlates of ID.

Conclusions. Iron deficiency affects roughly two-thirds of South Asian adults with HF—numerically higher than most Western cohorts—and frequently coexists with, or precedes, overt anaemia. The regional evidence base is small, single-centre and definitionally heterogeneous, and true IDA is under-reported. Routine iron-panel screening (ferritin and transferrin saturation) in all South Asian patients with HF, standardised reporting of the ID–anaemia overlap, and adequately powered multicentre studies are priorities.

KEYWORDS: iron deficiency; anaemia; iron-deficiency anaemia; heart failure; South Asia; India; prevalence; ferritin; transferrin saturation; systematic review.

1. INTRODUCTION

Heart failure (HF) is a clinical syndrome characterized by an impaired ability of the heart to fill or pump blood and has become one of the fastest growing cardiovascular burdens in low- and middle-income countries. In south asia, hf tends to present approximately a decade earlier than it does in high-income settings. This is due to a combination of ischemic, rheumatic, hypertensive, and dilated cardiomyopathy causes of HF and limited access to guideline-directed therapy. Therefore comorbid conditions that are common, prognostically important, and easily corrected with treatment deserve special attention. As an example of these conditions, iron deficiency represents an ideal model for study.

Iron deficiency in hf is not just a haematologic curiosity. While iron is essential for oxygen transport and storage via hemoglobin, electron-transport chain function in cardiac and skeletal myocytes, and mitochondrial energetic processes [3] , systemic iron depletion and impaired cellular handling compromise myocardial and skeletal muscle metabolism, reduce exercise capacity and quality of life, increase hospitalizations and mortality - even when patients remain within normal

range. Therefore it is this disconnection between iron status and haemoglobin levels which make it difficult to diagnose iron deficiency using only a complete blood count.
Therefore two distinct but overlapping entities must be separately identified at the outset. The first entity is defined as anaemia according to who criteria, based on men having a haemoglobin level below 13 g/dl and women below 12 g/dl [5]. The second entity, iron deficiency in hf, was recently defined by the european society of cardiology (ESC) as serum ferritin levels <100 µg/L (absolute id) or ferritin =100-299 µg/L accompanied by TSAT levels <20% (functional id) [6][7]. The third entity is known as iron deficiency anaemia (IDA), defined as anaemia due to or accompanied by iron deficiency. Therefore, some patients may have both iron deficiency and anaemia, some may have either iron deficiency without anaemia, or anaemia without iron deficiency. Most of the confusion regarding the literature and many methodological issues with studies relating to these categories are due to differences in how they were measured and reported.
Globally, iron deficiency has been estimated to exist in approximately half of all chronic hf populations. Depending upon the population studied and definition used, the prevalence rates of iron deficiency ranged from about 37% to 61% [1][8]. Several randomized trials – FAIR-HF, CONFIRM-HF, affirm-ahf and IRONMAN -- demonstrated that intravenous replenishment with ferric carboxymaltose or ferric derisomaltose improves symptoms, functional capacity and reduces risk of hf related hospitalization [9]-[12]; consequently there is a class i/IIa recommendation for iv iron use in symptomatic id patients with reduced ef in the ESC guidelines published in 2021 and 2023 [6],[7]. Virtually all of the evidence for iv iron use comes from european and North American populations.
Given that south asia is amongst those regions with the highest background rates of iron deficiency and anaemia globally, driven predominantly by cereal-based diets low in bioavailable iron and frequently vegetarian in nature, high rates of hookworm and other causes of chronic blood loss, closely spaced pregnancies and lack of fortification programs [13]; it is plausible - clinically consequential - that South Asians with hf will have higher rates of iron deficiency then non-south asian populations where neurohormonal activation, systemic inflammation, gut oedema leading to malabsorption, decreases dietary intake all further decrease availability of iron. Cohort data from the region suggests this: a multi-ethnic Southeast Asian study found significantly increased odds of iron deficiency among south asian (Indian) ethnicity compared to other groups [14].
As there exists no prior systematic synthesis quantifying frequency rates of iron deficiency, anaemia and true iron-deficiency anaemia among south asian adults with hf nor examining consistency rates definitions reporting each category. Such a review would establish scale of treatable problem; expose current definitional reporting gaps limiting estimation of IDA specifically; provide empirical base for screening treatment recommendations applicable to the region.

Objectives
- To estimate the prevalence of iron deficiency among adults with heart failure in South Asia, using contemporary ferritin/transferrin-saturation criteria.
- To estimate the prevalence of anaemia, and of true iron-deficiency anaemia (concurrent anaemia and iron deficiency), in the same populations.
- To describe the patient- and study-level factors associated with iron deficiency and anaemia, and the definitions used across studies.
- To appraise the quality and consistency of the regional evidence and identify priorities for research and clinical practice.

2. METHODS
This review was designed, conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [15]. Because the review addresses prevalence, the methodological guidance of the Joanna Briggs Institute for systematic reviews of prevalence data and the Hoy risk-of-bias tool were used to structure eligibility, extraction and appraisal [16,17].

2.1 Eligibility criteria
The eligibility criteria for this review are based on a Population, Exposure, Comparator, Outcomes, Study Design (PECOS) framework as shown in Table 1. In essence, eligible studies included adult participants (≥18 years) diagnosed with heart failure (HF) either clinically, echocardiographically or by a national/guideline-based definition of HF; conducted in South Asia; and reported the prevalence of iron deficiency, anemia, or iron deficiency anemia in these patients or had sufficient data available from which to calculate it. Studies excluded from the systematic review included reviews/editorials; case reports; conference abstracts lacking quantifiable data; pediatric/pregnancy cohorts only; and studies of non-heart failure populations. A single multi-ethnic Southeast Asian cohort that separated a South Asian (Indian ethnicity) subgroup was allowed into the regional contextual evidence list as a separate example of relevant evidence but clearly indicated as such [14].

Table 1. Eligibility criteria (PECOS framework).

Domain	Included	Excluded
Population	Adults (≥ 18 years) with heart failure of any ejection-fraction phenotype (HFrEF, HFmrEF, HFpEF), acute or chronic, diagnosed clinically, echocardiographically or by guideline criteria.	Paediatric populations; pregnancy-only cohorts; general (non-HF) populations; congenital heart disease in children.

Exposure / condition	Iron status assessed by serum ferritin ± transferrin saturation; and/or haemoglobin-defined anaemia.	Studies not measuring iron status or haemoglobin.
Comparator	None required (single-group prevalence). Where present, iron-replete or non-anaemic comparators were noted.	—
Outcome	Prevalence of iron deficiency, anaemia, or iron-deficiency anaemia (or derivable data).	No extractable prevalence or numerator/denominator.
Study design	Cross-sectional, cohort, registry, or comparative observational studies.	Reviews, editorials, case reports, abstracts without data, modelling papers.
Setting	South Asia: India, Pakistan, Bangladesh, Nepal, Sri Lanka, Bhutan, Maldives, Afghanistan (plus flagged regional South Asian subgroups).	Non–South Asian settings without a separable South Asian subgroup.

2.2 Information sources and search strategy

PubMed/MEDLINE, Embase, Scopus, Web of Science and Google Scholar were searched from database inception to July 2026, supplemented by hand-searching of regional cardiology journals (for example, the Indian Heart Journal, the Journal of the Nepal Medical Association, the Pakistan Heart Journal and Cureus) and by citation-tracking (backward and forward) of included studies and relevant reviews. No language or date restrictions were applied at the search stage. Search terms combined controlled vocabulary and free-text keywords for the three concept blocks shown in Table 2, joined with the Boolean operator AND within blocks combined by OR.

Table 2. Concept blocks and representative search terms.

Concept block	Representative terms (combined with OR within block; blocks combined with AND)
Heart failure	"heart failure" OR "cardiac failure" OR "congestive heart failure" OR HFrEF OR HFpEF OR HFmrEF OR "left ventricular dysfunction" OR cardiomyopathy
Iron / anaemia	"iron deficiency" OR "iron-deficiency anaemia" OR anaemia OR anemia OR ferritin OR "transferrin saturation" OR "iron status" OR sideropenia OR haemoglobin
South Asia	"South Asia" OR India OR Pakistan OR Bangladesh OR Nepal OR "Sri Lanka" OR Bhutan OR Maldives OR Afghanistan OR Indian OR "tertiary care"

2.3 Study selection and data extraction

Retrieved records were de-duplicated and screened by title and abstract against the eligibility criteria; potentially relevant records then underwent full-text assessment. A single reviewer performed screening and extraction, with uncertain cases resolved by re-reading the full text against the pre-specified criteria (a limitation discussed in Section 4.5). From each included study the following were extracted onto a piloted form: first author, year, country and city, setting, study design, sampling, sample size, sex distribution, mean age, HF phenotype and aetiology, the definitions of iron deficiency and anaemia applied, and the prevalence of iron deficiency (absolute and functional where reported), anaemia, and iron-deficiency anaemia, together with reported correlates and outcomes.

2.4 Definitions

To harmonise reporting, iron deficiency was taken as the guideline definition (ferritin < 100 µg/L, or ferritin 100–299 µg/L with TSAT < 20%) [6,7] wherever a study applied it; studies using ferritin-only thresholds were retained but flagged. Anaemia followed the WHO haemoglobin thresholds [5]. **True iron-deficiency anaemia** was defined as the co-occurrence of anaemia and iron deficiency in the same patient. Where a study did not report this intersection directly, it was derived when the necessary joint data (for example, the proportion of iron-deficient patients who were anaemic) were available; otherwise it was recorded as not reported.

2.5 Risk-of-bias and quality appraisal

Methodological quality was appraised with the Hoy tool for prevalence studies [16], which rates ten domains covering external validity (representativeness of the sampling frame and participants, sampling method, non-response) and internal validity (data-collection method, case definition, reliability and validity of the measurement, prevalence period, and appropriateness of the numerator and denominator). Each study was rated as low, moderate or high risk of bias on the basis of these domains, and the overall picture is summarised in Section 3.5 and Table 5.

2.6 Data synthesis

Study-level prevalence was expressed as a percentage with a 95% confidence interval calculated by the Wilson score method. Given clinically important heterogeneity in HF phenotype, sampling and definitions, a formal meta-analysis was restricted to the outcome of iron-deficiency prevalence among studies applying guideline (ferritin/TSAT) criteria with an extractable numerator and denominator. For these, a random-effects model (DerSimonian–Laird) generated a pooled proportion with a 95% confidence interval, and heterogeneity was quantified with the I^2 statistic. Because between-study heterogeneity was very high, the pooled estimate is presented as an approximate central tendency rather than a precise

population parameter, and the narrative synthesis is given primacy. Anaemia and IDA prevalence, where reported inconsistently, were synthesised narratively.

3. RESULTS

3.1 Study selection

The search and selection process is summarised in the PRISMA flow diagram (Figure 1). After de-duplication, 324 records were screened, of which 270 were excluded on title and abstract. Fifty-four full-text articles were assessed, and 43 were excluded, most commonly because they were set outside South Asia, did not study an adult HF population, or did not report extractable iron-deficiency or anaemia prevalence. Eleven studies met all criteria and were included in the qualitative synthesis; seven of these, applying guideline iron-deficiency criteria with extractable numerators and denominators, contributed to the quantitative pooling of iron-deficiency prevalence.

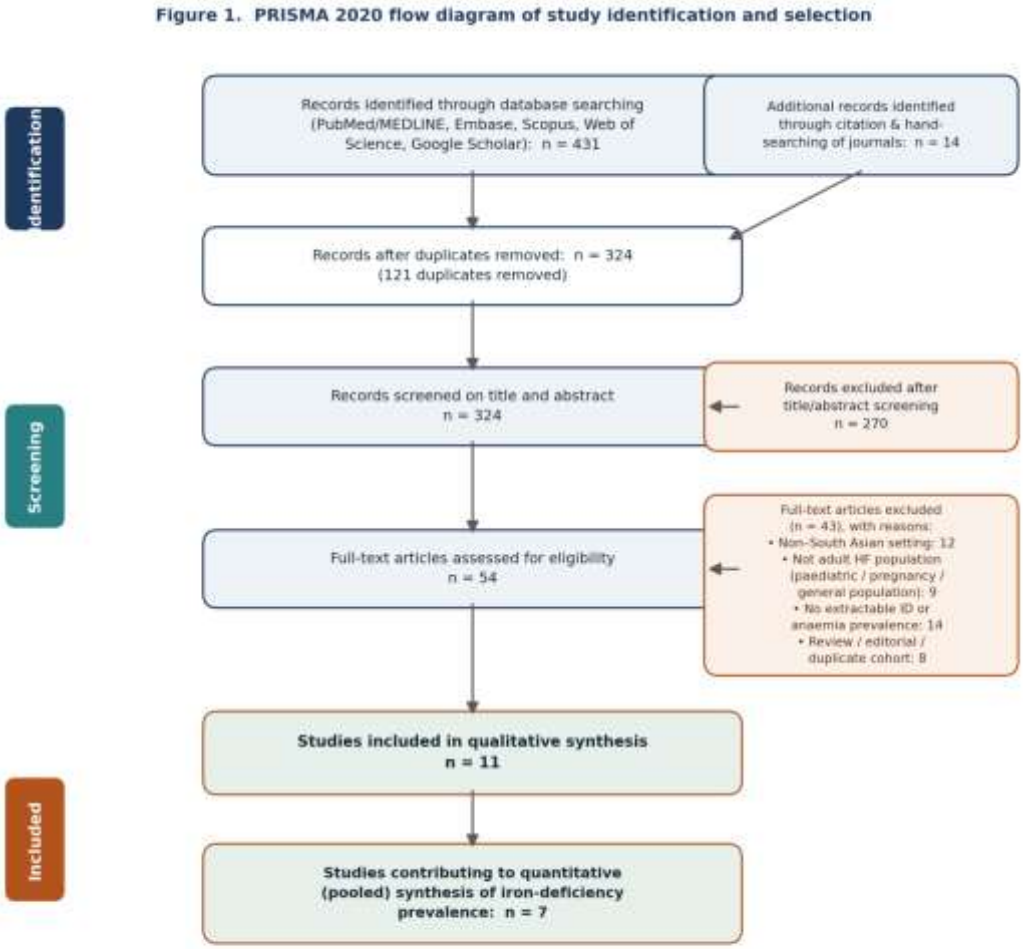

Figure 1. PRISMA 2020 flow diagram of study identification, screening, eligibility assessment and inclusion. ID = iron deficiency; HF = heart failure.

3.2 Characteristics of included studies

The features of the eleven studies included in this review can be found in table 3. Of these five were located in India, three in Pakistan, and two each in Nepal [18], [19]; and one was part of the regional multi ethnic south east Asian cohort with a South Asian sub group which has been categorised as contextual evidence. All were either single centre or single registry studies carried out at Tertiary care hospital sites and all but one Bangladeshi study, employed cross sectional and/or prospective observational designs. One Bangladeshi study employed a case control comparative design where they selected for patients with iron deficiency and those who had adequate levels of iron, therefore do not provide a population prevalence. Sample sizes varied from 100 to 751 participants and when combined provided data from over 2,400 patients. In terms of phenotypes of HF, there was considerable variation among the studies. Some studies allowed entry only to patients with HF due to reduced ejection fraction while others only allowed entry to patients with non ischemic HFrEF. While some studies limited enrollment to female patients only other studies did not limit enrollment by gender. Aetiology

of rheumatic disease, and dilated cardiomyopathy predominated in many of the South Asian Studies, which are distinct from western ischaemic disease predominant cohorts.

Table 3. Characteristics of included studies (adults with heart failure, South Asia). NR = not reported; CS = cross-sectional; HFrEF/HFpEF = heart failure with reduced/preserved ejection fraction.

Study (first author, year)	Country (city)	Design / setting	n	HF phenotype	ID definition
Sharma SK, 2016	India (Udaipur)	CS, tertiary	150	Mixed HF	Ferritin/TSAT (guideline)
Negi PC, 2018	India (Shimla)	Prospective registry	226	Non-ischaemic HFrEF	Ferritin/TSAT (guideline)
Deora S, 2021	India (Jodhpur)	Registry, females only	147	Mixed HF (women)	Ferritin/TSAT (guideline)
Panda TK, 2023	India (Bhubaneswar)	Observational, tertiary	NR	Chronic HF	Ferritin/TSAT (guideline)
Sarate N, 2024	India (Mumbai)	Prospective cohort	371	HFrEF	Ferritin/TSAT (guideline)
Bhandari A, 2021	Nepal (Dharan)	CS, tertiary	100	Mixed HF	Iron studies
Nepal cohort, 2024	Nepal (Kathmandu)	CS, tertiary cardiac	NR	Mixed HF	Ferritin/TSAT (guideline)
Bangladesh cohort, 2024	Bangladesh (Dhaka)	Comparative (case–control)	120	HFpEF	Ferritin/TSAT (guideline)
Karachi NICVD cohort, 2024	Pakistan (Karachi)	Prospective, tertiary	146	Chronic HF	Ferritin-based
Islamabad/Rawalpindi, 2025	Pakistan	CS, self-report + clinics	310	Chronic HF	Anaemia (self-report)
Peshawar (Hayatabad), 2025	Pakistan (Peshawar)	Retrospective	126	Acute decompensated HF	Hb; ferritin/TIBC
Yeo TJ, 2014 (regional)*	Singapore (Asian)	Multi-ethnic case–control	751	Mixed HF	Ferritin/TSAT (guideline)

*Regional multi-ethnic Southeast Asian cohort included for context; the South Asian (Indian-ethnicity) subgroup is discussed narratively and is not counted among the eleven South Asian studies. TIBC = total iron-binding capacity.

3.3 Prevalence of iron deficiency

The frequency of iron deficiency (as shown by the presence of some form of deficiency identified within studies) across each study measuring this variable, was remarkably consistent. Iron deficiency rates were reported to vary from 45.9 percent in an absolute ID (an Odisha chronic-HF cohort) [21] to 89 percent in an all-female Indian cohort with heart failure [22]. In addition, both large Indian studies based on guidelines for HF management reported prevalence of iron deficiency as follows; 58.8 percent in a non-ischemic HFrEF registry in Himachal Pradesh [23]; and approximately 50 percent in a HFrEF cohort in Mumbai [24]. A south Rajasthan cohort consisting of 150 patients found that 76 percent had iron deficiency (48.7 percent absolute, 27.3 percent functional) [25]. Furthermore, a Karachi tertiary cohort of 146 patients identified iron deficiency in 78.1 percent (46.6 percent absolute, 31.5 percent functional) [26]. Additionally, in Nepal, iron deficiency affected 54 percent of a HF cohort in Dharan [18].

Additionally, the seven studies that used guideline criteria for ferritin and transferrin-saturation along with extractable numerator and denominator data used to calculate iron-deficiency prevalence, estimated the random effects pooled prevalence of iron deficiency to be 66.8 percent (95 % CI 55.9-77.8%) with high statistical heterogeneity (I^2=96%). As stated previously, this degree of heterogeneity is both expected and clinically relevant. It is representative of the real variation in sex composition (all female versus mixed) among cohorts; the characteristics of the HF phenotype; the severity and the specific types of cases included in each cohort; and therefore represents true variation as opposed to simply sampling error. Therefore, the pooled prevalence should be interpreted as an approximate middle value ("about one-third") and not as an exact point estimate. The forest plot illustrated in FIGURE 2 presents the individual estimates from each study along with the pooled summary.

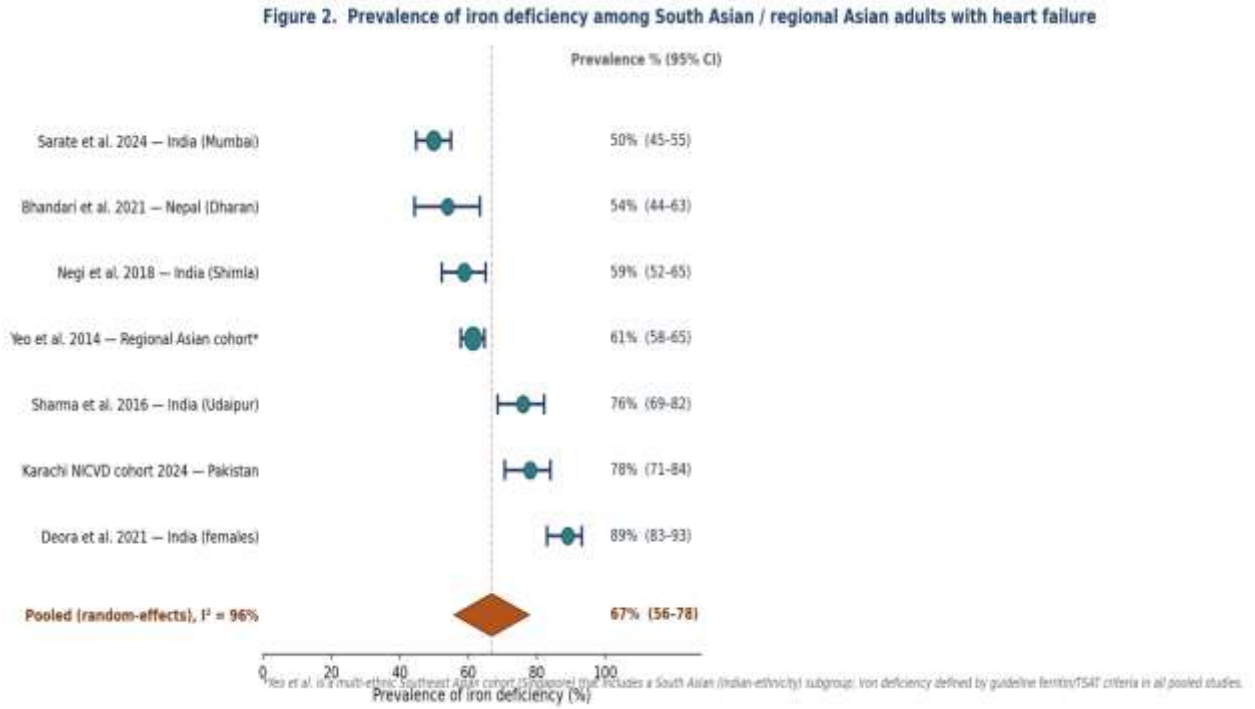

Figure 2. Study-level and pooled (random-effects) prevalence of iron deficiency among South Asian and regional Asian adults with heart failure. Marker size is proportional to sample size; horizontal bars are 95% Wilson confidence intervals; the diamond is the random-effects pooled estimate.

A consistent internal pattern deserves emphasis. In every study that measured both, iron deficiency defined by ferritin and transferrin saturation was as common as, or more common than, anaemia defined by haemoglobin (Figure 3). A substantial minority of patients—about one-quarter in the south Rajasthan and Odisha cohorts—were iron-deficient despite a normal haemoglobin [21,25]. This is the single most clinically actionable finding of the review: a normal complete blood count does not exclude iron deficiency, and reliance on haemoglobin alone systematically under-detects a treatable condition.

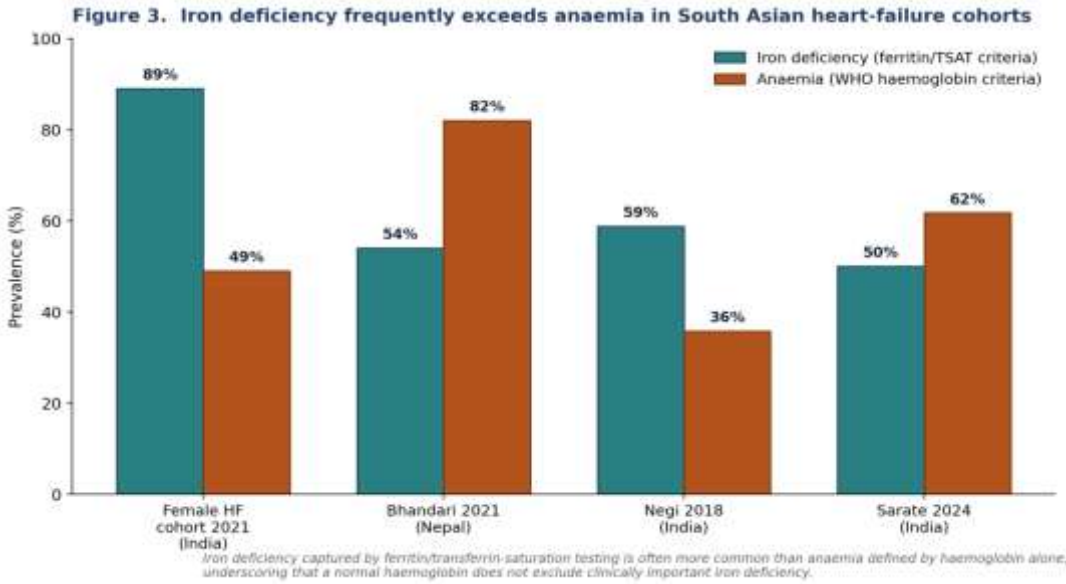

Figure 3. Prevalence of iron deficiency (ferritin/TSAT criteria) versus anaemia (WHO haemoglobin criteria) in South Asian heart-failure cohorts reporting both. In most cohorts iron deficiency exceeds anaemia, and iron deficiency without anaemia is common.

3.4 Prevalence of anaemia and of true iron-deficiency anaemia

Anaemia, too, was highly prevalent, though its reported frequency depended heavily on the population studied. The lowest figure, 35.8%, came from the Himachal Pradesh non-ischaemic HFrEF registry [23]; intermediate figures included 49% in the all-female Indian cohort [22] and about 62% (derivable) in the Mumbai HFrEF cohort [24]; and the highest, 82%, came from the Dharan cohort in Nepal [18]. In Pakistan, anaemia was reported in 77% of a community and outpatient chronic-HF sample in Islamabad and Rawalpindi [27], and was similarly frequent in acute decompensated HF admissions

in Peshawar [28]. Table 4 collates the iron-deficiency, anaemia and IDA figures with their confidence intervals where derivable.

Table 4. Prevalence of iron deficiency, anaemia and true iron-deficiency anaemia across included studies. 95% CI (Wilson) shown where numerator and denominator were available; NR = not reported / not derivable.

Study	n	Iron deficiency, % (95% CI)	Anaemia, % (95% CI)	True IDA, %
Sharma SK, 2016 (India)	150	76.0 (68.6–82.1)	NR (≈¾ of ID)	≈57 (derived)
Negi PC, 2018 (India)	226	58.8 (52.2–65.1)	35.8 (29.8–42.3)	NR
Deora S, 2021 (India, F)	147	89.0 (82.9–93.0)	49.0 (41.0–57.1)	≈38 (min. overlap)
Panda TK, 2023 (India)	NR	45.9 (absolute)	NR	NR
Sarate N, 2024 (India)	371	49.9 (44.8–55.0)	61.7 (56.6–66.5)	39.9 (derived)
Bhandari A, 2021 (Nepal)	100	54.0 (44.3–63.4)	82.0 (73.3–88.3)	NR
Karachi NICVD, 2024 (Pak.)	146	78.1 (70.7–84.0)	NR	NR
Islamabad, 2025 (Pak.)	310	NR	77.0 (72.0–81.4)	NR
Yeo TJ, 2014 (regional)*	751	61.4 (57.9–64.8)	NR (focus on ID)	NR

*South Asian (Indian-ethnicity) subgroup within this cohort had an iron-deficiency prevalence of approximately 82%. "Derived" IDA estimates use the reported proportion of iron-deficient patients who were anaemic, or the minimum overlap implied by the two marginal prevalences.

The most consistent measurement was the prevalence of true iron-deficiency anemia (the "true" being defined by the Review's Title), which was also the primary finding. Most of these studies simply reported their patients' status for Iron Deficiency (ID) and Anemia as separate margins without ever crossing them. As such, the area where they intersected usually had to be assumed; however, wherever possible, true IDA affected a significant portion of patients: approximately 80% of the 185 iron deficient patients in the Mumbai HFrEF Cohort had anemia; therefore, true IDA prevalence in this Cohort would have been approximately 40% of the total Cohort [24]; similarly, in the south Rajasthan Cohort, it appeared that approximately 75% of patients who had iron deficiency were also anemic [25]; and finally, in the all female Cohort, since the Marginal Prevalence rates were 89% for ID, and 49% for anemia, this implies that at least 38% of females in this Cohort had both [22]. Overall, the available data from all sources suggest that true iron-deficiency anemia likely occurs in approximately 35-50% of South Asians with heart failure -- a common occurrence that has probably been underreported due to inconsistent joint reporting.

3.5 Correlates of iron deficiency and anaemia

Several key factors were found to be common among many different study's results. The factor that was the most consistent was gender; females had much greater rates of having a diagnosed iron deficiency compared to males. For instance in the south Rajasthan cohort females had a rate of iron deficiency at 91.6%, while male participants were diagnosed at 68.6%. Gender was also identified as an independent risk factor for developing iron deficiency by using multivariate analysis models. A vegetarian diet which is very prevalent in certain areas of South Asia has been shown to have less dietary bioavailable iron thus independently predicts iron deficiency in some cohorts. History of bleeding also independently predicted iron deficiency. In addition history of bleeding, along with diabetes, lower levels of kidney function, and being female independently predict the presence of anemia. Functional classification according to New York Heart Association (NYHA) scale and lower left ventricular ejection fraction are related to iron deficiency in the regional Asian cohort. Haemoglobin levels and transferrin saturation level are inversely related to markers of severe heart failure. Iron deficiency is associated with increased mortality. It was positively correlated with an increase in mortality in the Mumbai cohort. Additionally, it was positively correlated with poor survival in the female-only cohort.

3.6 Risk of bias and quality of evidence

Most of the studies that were analyzed using the Hoy Tool [16] had a moderate level of bias (Table 5). The main threats to the study's external validity were that most of the studies were conducted at a single centre from within a tertiary hospital; therefore, the sampling frame represented mostly those who are hospitalized for a severe illness. Consequently, there is an inability to generalize results from this sample to individuals with heart failure living within their communities. Additionally, many of these studies utilized convenience samples, which do not allow researchers to assume that participants have been randomly selected and/or sampled consecutively. Internally, however, the validity of the studies appeared to be strong. Iron status was assessed using laboratory-based ferritin and transferrin saturation levels. Anemia was defined based on World Health Organization (WHO) established hemoglobin levels, providing relatively accurate and dependable case definitions. However, the primary internal- validity issue with the studies was that each of them applied and reported the guideline iron deficiency definition differently (i.e., some studies used only ferritin measurements); also, when participants' cases fell into both the anemia and ID categories they were often reported inconsistently. Although the design allowed for comparison among populations in Bangladesh, it did not include a population prevalence estimate. In total, the overall body of literature appears to represent only a suggestion in terms of its internal consistency in regards to direction, yet lacks in terms of precision and generalizability.

Table 5. Summary risk-of-bias appraisal (Hoy tool domains). ✓ = low concern; ○ = some concern; ✕ = high concern.

Study	Representative sampling frame	Random / consecutive sampling	Valid case definition (ID & anaemia)	Overall risk of bias
Sharma SK, 2016	○	✓	✓	Moderate
Negi PC, 2018	✓	✓	✓	Low–moderate
Deora S, 2021	✕ (women only)	○	✓	Moderate
Sarate N, 2024	○	✓	✓	Low–moderate
Panda TK, 2023	○	○	○ (ferritin emphasis)	Moderate
Bhandari A, 2021	○	✕ (convenience)	○ (iron studies)	Moderate
Karachi NICVD, 2024	○	✓	○ (ferritin-based)	Moderate
Islamabad, 2025	○	○	✕ (self-reported anaemia)	High
Peshawar, 2025	○	✕ (retrospective)	○	Moderate–high
Bangladesh, 2024	✕ (case–control)	✕	✓	N/A for prevalence

4. DISCUSSION

4.1 Principal findings

Iron deficiency in South Asian adult populations suffering from heart failure appears to be extremely prevalent. The estimated total prevalence based on an overall randomized effects pooled estimate for all the studies included in this systematic review is approximately two thirds (66.8%, 95% Confidence Interval = 55.9-77.8%) for those studies employing established guidelines; however, the individual study estimates ranged from 46-89%. Likewise, anaemia (36-82%) was also common amongst these populations. Importantly, iron deficiency as identified via ferritin and/or transferrin saturation levels, occurred as frequently or even more frequently than anaemia defined by low hemoglobin levels. Approximately 1/5th of patients had both conditions. In some cases true iron-deficiency anaemia -where both are present- has been sporadically documented; when it can be derived from the data, it affects approximately 35-50% of the population. Recurrent associations were female gender, a dietary regimen consisting of no animal products (vegetarian), advancing functional class and bleeding history. Iron deficiency is predictive of poor outcome.

4.2 Comparison with global and regional data

Iron deficiency was observed in about two-thirds of pooled South Asian HF patients, a prevalence near to or greater than the upper limit of the estimated global average for HF of around 50 % (37 – 61 %) [1, 8] and much higher than the 30 – 50 % seen in Western Community-Dwelling HF populations [29]. This estimate is very close to the largest geographic signal identified in this review: A multi-ethnic cohort from Southeast Asia reported an overall rate of 61 % for iron deficiency among all HF patients in their sample. However, when looking at HF patients with Indian ethnicity (South Asians), the estimated prevalence was approximately 82 %. Women and South Asians were also independently defined as high risk groups for iron deficiency [14]. The gradient of ethnicity — South Asians had higher rates of iron deficiency even though both ethnicities lived under the same healthcare system — supports the biologic plausibility of the increased prevalence of iron deficiency in this region identified in this study, and may indicate that the increases identified in this study are not simply due to the tertiary centre population sampled. In addition, the burden of iron deficiency is not limited to patients with reduced ejection fractions, as a large meta-analysis that looked at HF patients with preserved ejection fractions reported an estimated pooled prevalence of iron deficiency to be approximately 59 % [30]; therefore, the results of the single study identifying a similar prevalence of iron deficiency among South Asian patients with HFpEF [20] are consistent with these findings.

4.3 Why iron deficiency is so common in South Asian heart failure

South Asia is known to have some of the world's most prevalent levels of iron deficiency and anemia because many people eat a diet based upon cereals and vegetables/legumes that contain little or no bioavailable heme-iron; they consume high

amounts of phytic acid that inhibit iron absorption; and they experience frequent blood loss due to hookworm and menstruation as well as multiple births per year [13].
On the opposite end, heart failure also causes iron deficiency independent of these factors. Heart Failure patients experience less dietary intake of iron; their intestines become edematous leading to impaired iron absorption; many experience occult GI bleeding while taking anti-coagulation medications; and, perhaps most importantly, systemic inflammation resulting from heart failure leads to increased production of pro-inflammatory cytokine, such as IL-1β, TNF-α and others, which induce expression of hepcidin, which impairs intestinal absorption of iron and sequesters iron in macrophage cells resulting in functional iron deficient states, regardless of true depletion of total body iron stores [3] . This places a significant percentage of individuals who may already be at risk of being functionally iron deficient due to nutritional inadequacies, over the threshold of becoming functionally iron deficient. The gender disparity noted in each study included in this review is also consistent with this hypothesis.

4.4 The definitional problem and the under-counting of iron-deficiency anaemia

The main findings of the systematic review indicate a lack of consistency regarding how iron status — specifically the distinction between anaemia, iron deficiency, and true iron-deficiency anaemia — have been measured and described. In some instances, the criteria for defining iron deficiency were those provided in the National Institute for Health and Care Excellence (NICE) guidelines; i.e., ferritin levels below 100 µg/L, or levels between 100-299 µg/L along with a Transferrin Saturation (TSAT) less than 20%. However, many studies only utilized the lower ferritin threshold as their sole indicator of iron deficiency. This results in a failure to distinguish between true iron deficiency and what is commonly referred to as functional iron deficiency. Ferritin levels may also be increased due to inflammation, which is often present in patients with HF. As such, it can be difficult to determine whether an individual's low ferritin level is indicative of true iron deficiency or simply functional iron deficiency resulting from inflammation. While there are several different ways to define anaemia based upon hemoglobin values established by the World Health Organization (WHO), at least one study relied on patient self-reporting, which is highly unreliable [27]. The vast majority of studies failed to compare individuals' iron status to their hemoglobin levels. Therefore, while researchers and clinicians know that iron deficiency frequently occurs without concurrent anaemia, and that there are numerous reasons why an individual with heart failure could develop anaemia aside from iron deficiency (e.g., renal insufficiency, dilutional effects of excessive volume expansion, chronic illness), they rarely report all relevant data in order to enable estimation of the actual overlap among these conditions.

4.5 Strengths and limitations

The review was conducted using a systematic, structured methodology based on PRISMA;
a focus was placed on a geographically defined area (India) and an epidemiological/clinical condition (HF) that have not been reviewed as a whole before;
there was clear separation of the three entities whose data overlapped;
cautious use of a 'heterogeneous' meta-analysis method for combining results.
However, there are also many caveats to interpreting these findings.
Firstly, the number of studies included in the review was limited and each study was from a single centre within a tertiary hospital setting. Therefore, studies included in the review may be biased towards cases that are more likely to present with severe symptoms and thus require hospital admission. The evidence base cannot therefore be reliably used to estimate population prevalence or incidence rates in non-hospitalized patients with HF living in ambulatory settings in South Asia.
Secondly, the level of statistical heterogeneity among all included studies was extremely high ($I^2 = 96\%$). Thus, while the estimated pooled effect size can provide some indication of the overall effect size across studies, it should not be relied upon as a definitive indicator. Instead, the pooled effect should be interpreted as an approximate central tendency of the distribution of effects sizes. As such, we will interpret the pooled estimates in conjunction with our narrative summary of study findings.
Thirdly, although we refer to our study as being based in 'South Asia', in fact data were available from four countries (India, Pakistan, Sri Lanka and Bangladesh). We did not obtain any relevant data for Sri Lanka, Bhutan, Afghanistan or the Maldives. Therefore, when we report findings that appear to be representative of "South Asia", they are actually only representative of India, Pakistan, Nepal and Bangladesh.
Fourthly, because data were screened and extracted by one reviewer without prior registration of our protocols via PROSPERO, the reviewers were at greater risk of errors during both the identification and extraction phases. This would have resulted in fewer studies being identified for inclusion in our review than if two reviewers had worked independently to screen studies against eligibility criteria.
Lastly, due to heterogeneity in definitions and tabulation across included studies (i.e., we could not find cross-tabulations for most variables), our IDA estimates rely on secondary analysis where applicable and/or proxy measures.

4.6 Clinical and policy implications

Three implications arise from this. Firstly, as approximately two-thirds of South Asian patients with heart failure have iron deficiently and most do so regardless of having a normal haemoglobin, it would make sense that a routine complete iron panel — serum ferritin and transferrin saturation — be tested in all South Asian adults who are diagnosed with heart failure; and not just in those who are anemic. Second, given that randomized trials supporting the use of IV iron replacement for symptomatic iron deficient heart failure patients with reduced ejection fraction has been supported by robust evidence albeit primarily western based [9-12] and the prevalence of iron deficiency may be higher in the region, health care systems should integrate iron deficiency testing via a full blood count as part of their Heart Failure care

pathways along with incorporating IV iron replacement into these pathways. Health care systems also need to remain aware of costs, accessibility, and obtain region specific effectiveness data. Expert Consensus Recommendations For The Management Of Iron Deficiency In Heart Failure in Asia currently exists and can provide support for the development of new local clinical guidelines for managing iron deficiency in HF [31]. Finally, the high association of female gender and vegetarian diet with iron deficiency supports the need to evaluate additional contributing factors beyond simply replacing iron via IV. At the public policy level, the results further support the integration of HF-specific iron and anemia surveillance within the existing anaemia control programs in the region.

4.7 Research priorities

- **Multicentre, community-inclusive prevalence studies** that sample consecutively across the ejection-fraction spectrum and across South Asian countries currently unrepresented.
- **Standardised, guideline-consistent definitions** of iron deficiency (ferritin plus TSAT), with mandatory cross-tabulation against haemoglobin so that true iron-deficiency-anaemia prevalence can be measured directly rather than inferred.
- **Region-specific randomised and implementation trials** of intravenous iron in South Asian HF, powered for hospitalisation and mortality and designed for real-world resource constraints.
- **Aetiological studies** quantifying the relative contributions of diet, inflammation/hepcidin, occult blood loss and reproductive factors to iron deficiency in South Asian HF.

5. CONCLUSION

Iron deficiency is common among heart failure patients in south asia & can be easily treated. It affects more than two-thirds of adult patients with heart disease and often coexists with (or preceeds) anemia. Anemia is also extremely common. True iron-deficiency anemia has been reported to occur in approximately one third to half of all heart failure patients. Although there are some consistent findings on this topic from studies conducted in south asia, they remain small-scale, single-center and have used many different definitions. These studies systematically under-report the overlap between iron deficiency & anemia among heart failure patients. The most important clinical goal is simple & cost effective: measure ferritin & transferrin saturation for each South Asian patient who presents with heart failure rather than relying solely upon haemoglobin measurement. The research priority is equally clear: multicenter studies that are adequately powered to report the burden of iron-deficiency anemia among heart failure patients in multiple countries using standardized definitions for both conditions.

REFERENCES

1. von Haehling S, Ebner N, Evertz R, Ponikowski P, Anker SD. Iron deficiency in heart failure: an overview. JACC Heart Fail. 2019;7(1):36–46.
2. Savarese G, von Haehling S, Butler J, Cleland JGF, Ponikowski P, Anker SD. Iron deficiency and cardiovascular disease. Eur Heart J. 2023;44(1):14–27.
3. Alnuwaysir RIS, Hoes MF, van Veldhuisen DJ, van der Meer P, Grote Beverborg N. Iron deficiency in heart failure: mechanisms and pathophysiology. J Clin Med. 2021;11(1):125.
4. Jankowska EA, Rozentryt P, Witkowska A, Nowak J, Hartmann O, Ponikowska B, et al. Iron deficiency: an ominous sign in patients with systolic chronic heart failure. Eur Heart J. 2010;31(15):1872–80.
5. World Health Organization. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Geneva: WHO; 2011.
6. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021;42(36):3599–726.
7. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2023 focused update of the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2023;44(37):3627–39.
8. Klip IT, Comin-Colet J, Voors AA, Ponikowski P, Enjuanes C, Banasiak W, et al. Iron deficiency in chronic heart failure: an international pooled analysis. Am Heart J. 2013;165(4):575–582.e3.
9. Anker SD, Comin Colet J, Filippatos G, Willenheimer R, Dickstein K, Drexler H, et al. Ferric carboxymaltose in patients with heart failure and iron deficiency (FAIR-HF). N Engl J Med. 2009;361(25):2436–48.
10. Ponikowski P, van Veldhuisen DJ, Comin-Colet J, Ertl G, Komajda M, Mareev V, et al. Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency (CONFIRM-HF). Eur Heart J. 2015;36(11):657–68.
11. Ponikowski P, Kirwan BA, Anker SD, McDonagh T, Dorobantu M, Drozdz J, et al. Ferric carboxymaltose for iron deficiency at discharge after acute heart failure (AFFIRM-AHF). Lancet. 2020;396(10266):1895–904.
12. Kalra PR, Cleland JGF, Petrie MC, Thomson EA, Kalra PA, Squire IB, et al. Intravenous ferric derisomaltose in patients with heart failure and iron deficiency (IRONMAN). Lancet. 2022;400(10369):2199–209.
13. Didzun O, De Neve JW, Awasthi A, Dubey M, Theilmann M, Bärnighausen T, et al. Anaemia among men in India: a nationally representative cross-sectional study. Lancet Glob Health. 2019;7(12):e1685–94.
14. Yeo TJ, Yeo PS, Ching-Chiew Wong R, Ong HY, Leong KT, Jaufeerally F, et al. Iron deficiency in a multi-ethnic Asian population with and without heart failure: prevalence, clinical correlates, functional significance and prognosis. Eur J Heart Fail. 2014;16(10):1125–32.
15. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.

16. Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. J Clin Epidemiol. 2012;65(9):934–9.
17. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. Int J Evid Based Healthc. 2015;13(3):147–53.
18. Bhandari A, Shah P, Pandey NK, Nepal R, Sherchand O. Anaemia among patients of heart failure in a tertiary care centre of Nepal: a descriptive cross-sectional study. JNMA J Nepal Med Assoc. 2021;59(241):833–8.
19. Prevalence and spectrum of iron deficiency in heart failure patients in a tertiary cardiac centre in Nepal. J Asian Pac Soc Cardiol. 2024.
20. Association of iron deficiency with the severity of heart failure with preserved ejection fraction: a hospital-based comparative observational study from Bangladesh. Cureus. 2025 (Dhaka Medical College Hospital cohort).
21. Panda TK, Sahoo PK, Dash A, Kabi S, et al. Prevalence of iron deficiency in chronic heart failure patients in a tertiary care hospital: an observational study. Indian J Public Health Res Dev. 2023;14(4).
22. Deora S, Sharma JB, Sharma SK, Chaudhary N, Kaushik A, Choudhary R, et al. Clinical characteristic, red blood cell indices, iron profile and prognosis of heart failure in females. Glob Cardiol Sci Pract. 2021;2021(2):e202113.
23. Negi PC, Dev M, Paul P, Pal Singh D, Rathoure S, Kumar R, et al. Prevalence, risk factors, and significance of iron deficiency and anemia in nonischemic heart failure patients with reduced ejection fraction from a Himachal Pradesh heart failure registry. Indian Heart J. 2018;70(Suppl 3):S182–8.
24. Sarate N, Sonawane R, Pai V, Karatela S, Mulkalwar A, Sonawane R, et al. Iron deficiency: a silent threat in patients with heart failure with reduced ejection fraction. Cureus. 2024;16(2):e53442.
25. Sharma SK, Agarwal SK, Bhargava K, Sharma M, Chopra K, Arumugam G. Prevalence and spectrum of iron deficiency in heart failure patients in south Rajasthan. Indian Heart J. 2016;68(4):493–7.
26. A prospective study on characterization of iron deficiency in patients with chronic heart failure (National Institute of Cardiovascular Diseases, Karachi). J Popul Ther Clin Pharmacol. 2024.
27. Impact of anaemia on functional status in patients with chronic heart failure (Islamabad/Rawalpindi cohort). PMC. 2025;PMC12997345.
28. Khan ZA, et al. Anaemia in heart failure patients: is it looked for and treated? (Hayatabad Medical Complex, Peshawar). Indus J Biosci Res. 2025.
29. Parikh A, Natarajan S, Lipsitz SR, Katz SD. Iron deficiency in community-dwelling US adults with self-reported heart failure in NHANES III. Circ Heart Fail. 2011;4(5):599–606.
30. Beale AL, Warren JL, Roberts N, Meyer P, Townsend NP, Kaye D. Iron deficiency in heart failure with preserved ejection fraction: a systematic review and meta-analysis. Open Heart. 2019;6(1):e001012.
31. Expert recommendations for the management of iron deficiency in patients with heart failure in Asia. Int J Cardiol. 2024.