

Research Article

Comparison of Serum Iron Ferritin and Total Iron Binding Capacity in Patients with Iron Deficiency Anaemia and Anaemia of Chronic Disease

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ABSTRACT

Background: Iron deficiency anaemia (IDA) and anaemia of chronic disease (ACD) involve impaired iron availability through different mechanisms. Serum iron, ferritin and total iron-binding capacity (TIBC) provide complementary information for evaluating these conditions, although inflammation can complicate interpretation.

Aim: To compare serum iron, ferritin and TIBC between patients with IDA and those with ACD.

Materials and Methods: The draft hospital-based analytical cross-sectional study comprised 220 participants, including 110 patients with IDA and 110 with ACD. Serum iron, ferritin and TIBC were assessed and summarised as mean and standard deviation. Between-group comparisons were performed using Welch's independent-samples t-test. Mean differences were reported with 95% confidence intervals, and a two-sided p value below 0.05 was considered statistically significant.

Results: Mean serum iron was lower in the IDA group than in the ACD group: 28.7 (9.6) versus 43.2 (13.8) µg/dL, with a mean difference of -14.50 µg/dL (95% CI: -17.66 to -11.34; p<0.001). Mean serum ferritin was also lower in IDA: 13.8 (5.7) versus 184.6 (61.3) ng/mL, with a mean difference of -170.80 ng/mL (95% CI: -182.43 to -159.17; p<0.001). Conversely, mean TIBC was higher in IDA: 426.8 (57.4) versus 238.6 (46.2) µg/dL, with a mean difference of 188.20 µg/dL (95% CI: 174.35-202.05; p<0.001).

Conclusion: The supplied comparison demonstrated lower serum iron and ferritin and higher TIBC in IDA than in ACD. Combined interpretation of these parameters supported biochemical characterisation of the two groups, but independent diagnostic performance was not established.

Keywords: Iron Deficiency Anaemia, Anaemia Of Chronic Disease, Iron Metabolism.

INTRODUCTION

Anaemia is a common clinical condition with diverse nutritional, inflammatory and systemic causes. Iron deficiency anaemia (IDA) and anaemia of chronic disease (ACD) are particularly important because both involve inadequate iron availability for erythropoiesis, although their underlying mechanisms differ.

Camaschella (2015)[1] described IDA as a consequence of depleted body iron stores arising from inadequate intake, impaired absorption, increased requirements or chronic blood loss. Accurate identification of iron deficiency is essential because management requires both correction of the deficiency and investigation of its underlying cause.

Lopez et al. (2016)[2] distinguished absolute iron deficiency, in which total body iron stores are reduced, from functional iron deficiency, in which stored iron is insufficiently available for erythropoiesis. Clinical manifestations and conventional red cell indices alone may not reliably differentiate these conditions. Assessment of biochemical indicators of iron metabolism therefore provides additional information when evaluating patients with anaemia, particularly those with coexisting chronic illnesses.

Weiss et al. (2019)[3] explained that ACD, also termed anaemia of inflammation, occurs in conditions associated with sustained immune activation, including chronic infections, autoimmune disorders and malignancies. Inflammatory cytokines increase hepcidin activity, thereby reducing intestinal iron absorption and restricting iron release from storage cells. Consequently, circulating iron becomes insufficient for haemoglobin synthesis despite preserved or increased iron stores. Impaired erythropoietic responses further contribute to the development of anaemia.

Nairz et al. (2016)[4] highlighted the diagnostic challenges arising from overlapping and combined forms of iron deficiency and inflammation. Serum iron may be reduced in both IDA and ACD, limiting its usefulness as an isolated discriminator. Ferritin generally reflects iron stores but also increases during inflammation, while total iron-binding capacity (TIBC) reflects circulating transferrin availability. Interpretation of these parameters together, alongside clinical findings and inflammatory markers, is therefore more informative than reliance on a single measurement.

Snook et al. (2021)[5] identified serum ferritin as the most useful marker of iron deficiency in the absence of inflammation and recommended additional iron studies when a falsely normal ferritin concentration was suspected. Typically, IDA is characterised by reduced serum iron and ferritin with increased TIBC, whereas ACD commonly presents with reduced serum iron, preserved or increased ferritin, and reduced or normal TIBC. However, overlapping conditions require careful interpretation. Comparing these biochemical parameters in well-characterised patient groups may clarify their patterns in a tertiary care setting. The present study was therefore undertaken to compare serum iron, ferritin and TIBC between patients with IDA and those with ACD.

Aim

To compare serum iron, ferritin and total iron-binding capacity between patients with iron deficiency anaemia and those with anaemia of chronic disease.

Objectives

1. To compare serum iron concentrations between patients with iron deficiency anaemia and anaemia of chronic disease.
2. To compare serum ferritin concentrations between the two study groups.
3. To compare total iron-binding capacity between the two study groups.

MATERIAL AND METHODOLOGY

Source of Data

Data were obtained from adult patients with anaemia attending the outpatient departments or admitted to the inpatient wards of Seth GS Medical College and KEM Hospital, Parel, Mumbai. Clinical information was collected through patient interviews, clinical examination and review of medical records. Laboratory data were obtained from haematological and biochemical investigations performed during the study assessment.

Study Design

The study was conducted as a hospital-based, analytical cross-sectional study involving two comparison groups: patients with iron deficiency anaemia and patients with anaemia of chronic disease. Clinical and laboratory assessments were performed at a single study visit, preferably before initiation of treatment that could alter iron parameters. No therapeutic intervention was assigned as part of the study.

Study Location

The study was conducted at Seth GS Medical College and KEM Hospital, Parel, Mumbai, Maharashtra, India, with clinical recruitment from the participating departments and laboratory assessment in the Departments of Pathology and Biochemistry.

Study Duration

The study was conducted over one year. This period included participant recruitment, clinical assessment, laboratory investigations, data verification and statistical analysis.

Sample Size

The total sample size was 220 participants, comprising:

- **Group I:** 110 patients with iron deficiency anaemia.

- **Group II:** 110 patients with anaemia of chronic disease.

Sampling Technique

Consecutive eligible patients were screened during the study period. Participants were assigned to the IDA or ACD group after clinical and laboratory assessment. Recruitment continued until the required number of participants was obtained in each group. A screening record documented eligibility, group allocation and reasons for exclusion.

Inclusion Criteria

1. Adults aged 18 years or older, of either sex.
2. Patients with anaemia, defined for this draft as haemoglobin below 13 g/dL in men and below 12 g/dL in non-pregnant women.
3. Patients who fulfilled the specified diagnostic criteria for either IDA or ACD.
4. Patients who provided written informed consent and had sufficient clinical and laboratory information for classification.

Exclusion Criteria

1. Patients with suspected or confirmed combined IDA and ACD, or an uncertain cause of anaemia.
2. Pregnant women.
3. Patients with haemolytic anaemia, haemoglobinopathies, aplastic anaemia, myelodysplastic syndromes or other primary bone marrow disorders.
4. Patients with documented vitamin B12 or folate deficiency contributing to anaemia.
5. Patients with recent blood transfusion or treatment with iron preparations or erythropoiesis-stimulating agents.
6. Patients with active major bleeding or haemodynamic instability.
7. Patients with advanced kidney failure or significant hepatic dysfunction where these conditions independently altered erythropoiesis or iron-marker interpretation.
8. Patients with inadequate specimens or incomplete information preventing reliable group classification.

Procedure and Methodology

Eligible patients underwent a detailed clinical assessment. Information was obtained regarding age, sex, presenting symptoms, duration of anaemia, dietary intake, menstrual history where applicable, gastrointestinal symptoms, previous blood loss, chronic

illnesses and medication use. Previous iron supplementation, blood transfusion and anaemia treatment were specifically documented. Clinical examination included assessment of pallor, vital signs and findings suggestive of nutritional deficiency or chronic disease.

Complete blood count, peripheral blood smear, serum iron, serum ferritin, TIBC and an inflammatory marker such as C-reactive protein (CRP) were assessed. Renal function, liver function and investigations for alternative causes of anaemia were reviewed where clinically indicated.

For the proposed operational classification, the IDA group comprised patients with anaemia and evidence of depleted iron stores, supported by serum ferritin below 30 ng/mL and a compatible clinical assessment, without evidence of a significant inflammatory condition. Ferritin below this threshold generally indicates reduced iron stores in the absence of inflammation.

The ACD group comprised patients with anaemia, a documented chronic inflammatory, infective or malignant condition, and evidence supporting inflammation-associated iron restriction. Classification considered the underlying disease, inflammatory markers, haematological findings and the complete iron profile rather than an elevated ferritin concentration alone. Patients with possible coexisting absolute iron deficiency were investigated further where feasible or excluded if classification remained uncertain.

The final diagnosis was reviewed by the treating clinician. The underlying condition and its duration were recorded in patients classified as having ACD.

Because iron measurements contributed to group classification, between-group differences were interpreted as biochemical descriptions of clinically classified groups. They were not treated as independent proof of diagnostic accuracy. Sensitivity, specificity and diagnostic cut-offs would require an appropriately independent reference standard.

Sample Processing

Venous blood was collected using aseptic precautions under standardised collection conditions. Sampling time and fasting status were recorded to account for variation in serum iron concentrations. Blood for complete blood count was collected into an EDTA-containing tube, while blood for biochemical investigations was collected into an appropriate serum tube.

Serum samples were allowed to clot and were centrifuged according to the laboratory's validated standard operating procedure. Separated serum was analysed promptly or stored within the temperature and stability limits specified for the relevant assay. Haemolysed, inadequately labelled or otherwise unsuitable samples were rejected and recollected when possible.

Serum iron was estimated by a validated colorimetric method, and serum ferritin was measured using the laboratory's immunoassay platform. Haematological parameters were measured using an automated haematology analyser. The analyser models, reagent manufacturers and assay reference intervals were documented.

Calibration and internal quality-control procedures were performed according to laboratory policy. Serum iron and TIBC were reported in µg/dL, ferritin in ng/mL and haemoglobin in g/dL.

Statistical Methods

Data were entered into a password-protected database, checked for completeness and consistency, and analysed using SPSS 28.0. version. Continuous variables were assessed for distribution using graphical methods and the Shapiro-Wilk test. Approximately normally distributed variables were summarised as mean and standard deviation, while skewed variables were summarised as median and interquartile range. Categorical variables were presented as frequencies and percentages.

Serum iron and TIBC were compared between groups using Welch's independent-samples t-test when appropriate. Mean differences were reported with 95% confidence intervals. Ferritin

distributions were examined carefully because of their tendency toward right skewness. When log-transformation produced a suitable distribution, ferritin was compared on the logarithmic scale and the between-group geometric mean ratio was reported with its 95% confidence interval. Otherwise, a Mann-Whitney U test was used with appropriate non-parametric summaries.

Categorical characteristics were compared using the chi-square test or Fisher's exact test, as appropriate. Age, sex and inflammatory status were considered as potential confounding variables; any adjusted regression analyses were specified according to the study analysis plan.

All tests were two-sided. A p value below 0.05 was considered statistically significant. If serum iron, ferritin and TIBC were designated as three co-primary outcomes, Holm adjustment was applied to the three principal comparisons. Missing observations and the number included in each analysis were reported; missing values were not replaced by simple mean substitution.

Data Collection

A structured case-record form was used to document participant identification codes, demographic details, clinical history, examination findings, underlying chronic diseases, treatment history and laboratory results. Records were reviewed for completeness, and discrepant entries were checked against the source documents.

Participants were identified in the analytical dataset by unique study codes. Personally identifiable information was stored separately, and access was restricted to authorised study personnel.

OBSERVATION AND RESULTS

Table 1. Comparison of serum iron, ferritin and total iron-binding capacity between patients with iron deficiency anaemia and anaemia of chronic disease (N=220)

Parameter	IDA (n=110), mean (SD)	ACD (n=110), mean (SD)	Mean difference (95% CI)	Welch's t statistic	P value
Serum iron (µg/dL)	28.7 (9.6)	43.2 (13.8)	-14.50 (-17.66 to -11.34)	-9.05	<0.001
Serum ferritin (ng/mL)	13.8 (5.7)	184.6 (61.3)	-170.80 (-182.43 to -159.17)	-29.10	<0.001
Total iron-binding capacity (µg/dL)	426.8 (57.4)	238.6 (46.2)	188.20 (174.35 to 202.05)	26.79	<0.001

The table compared serum iron, ferritin and total iron-binding capacity (TIBC) between the IDA and ACD groups, comprising 110

participants each. Mean serum iron was significantly lower in the IDA group than in the ACD group, at 28.7 (SD 9.6) versus 43.2 (SD

13.8) $\mu\text{g/dL}$, with a mean difference of -14.50 $\mu\text{g/dL}$ (95% CI: -17.66 to -11.34; Welch's $t=-9.05$; $p<0.001$). Similarly, mean serum ferritin was lower in the IDA group, at 13.8 (SD 5.7) versus 184.6 (SD 61.3) ng/mL , with a mean difference of -170.80 ng/mL (95% CI: -182.43

to -159.17; $t=-29.10$; $p<0.001$). Conversely, mean TIBC was significantly higher in the IDA group, at 426.8 (SD 57.4) versus 238.6 (SD 46.2) $\mu\text{g/dL}$, with a mean difference of 188.20 $\mu\text{g/dL}$ (95% CI: 174.35-202.05; $t=26.79$; $p<0.001$).

Table 2. Comparison of serum iron concentrations between the study groups (N=220)

Study group	Number of patients	Serum iron ($\mu\text{g/dL}$), mean (SD)	95% CI for the group mean
Iron deficiency anaemia	110	28.7 (9.6)	26.89-30.51
Anaemia of chronic disease	110	43.2 (13.8)	40.59-45.81
Statistical comparison			Value
Mean difference, IDA - ACD ($\mu\text{g/dL}$)			-14.50
95% CI for the mean difference			-17.66 to -11.34
Welch's t statistic (degrees of freedom)			-9.05 (194.48)
Two-sided p value			<0.001

Mean serum iron concentration was 28.7 (SD 9.6) $\mu\text{g/dL}$ in the IDA group, with a 95% confidence interval of 26.89-30.51 $\mu\text{g/dL}$, compared with 43.2 (SD 13.8) $\mu\text{g/dL}$ in the ACD group, with a 95% confidence interval of 40.59-45.81 $\mu\text{g/dL}$. The mean difference, calculated as IDA minus ACD, was -14.50 $\mu\text{g/dL}$ (95% CI:

-17.66 to -11.34). Welch's independent-samples t-test demonstrated a statistically significant difference between the groups ($t=-9.05$; degrees of freedom=194.48; $p<0.001$), indicating a lower mean serum iron concentration in the IDA group.

Table 3. Comparison of Serum Ferritin Concentrations between the Study Groups (N=220)

Study group	Number of patients	Serum ferritin (ng/mL), mean (SD)	95% CI for the group mean
Iron deficiency anaemia	110	13.8 (5.7)	12.72-14.88
Anaemia of chronic disease	110	184.6 (61.3)	173.02-196.18
Statistical comparison			Value
Mean difference, IDA - ACD (ng/mL)			-170.80
95% CI for the mean difference			-182.43 to -159.17
Welch's t statistic (degrees of freedom)			-29.10 (110.88)
Two-sided p value			<0.001

Mean serum ferritin concentration was 13.8 (SD 5.7) ng/mL in the IDA group, with a 95% confidence interval of 12.72-14.88 ng/mL , compared with 184.6 (SD 61.3) ng/mL in the ACD group, with a 95% confidence interval of 173.02-196.18 ng/mL . The mean difference between the groups was -170.80 ng/mL (95%

CI: -182.43 to -159.17). This difference was statistically significant on Welch's independent-samples t-test ($t=-29.10$; degrees of freedom=110.88; $p<0.001$), demonstrating a substantially lower mean serum ferritin concentration in the IDA group.

Table 4. Comparison of total iron-binding capacity between the study groups (N=220)

Study group	Number of patients	TIBC ($\mu\text{g/dL}$), mean (SD)	95% CI for the group mean
Iron deficiency anaemia	110	426.8 (57.4)	415.95-437.65
Anaemia of chronic disease	110	238.6 (46.2)	229.87-247.33

Statistical comparison	Value
Mean difference, IDA - ACD ($\mu\text{g/dL}$)	188.20
95% CI for the mean difference	174.35-202.05
Welch's t statistic (degrees of freedom)	26.79 (208.48)
Two-sided p value	<0.001

Mean TIBC was 426.8 (SD 57.4) $\mu\text{g/dL}$ in the IDA group, with a 95% confidence interval of 415.95-437.65 $\mu\text{g/dL}$, compared with 238.6 (SD 46.2) $\mu\text{g/dL}$ in the ACD group, with a 95% confidence interval of 229.87-247.33 $\mu\text{g/dL}$. The mean difference between the groups was 188.20 $\mu\text{g/dL}$ (95% CI: 174.35-202.05). Welch's independent-samples t-test showed that this difference was statistically significant ($t=26.79$; degrees of freedom=208.48; $p<0.001$), indicating a higher mean TIBC in the IDA group.

DISCUSSION

The overall pattern was consistent with the distinction between absolute iron depletion and inflammation-associated iron restriction. Camaschella (2015)[1] described IDA as a consequence of depleted iron stores, whereas Lopez et al. (2016)[2] distinguished absolute deficiency from functional deficiency, in which available iron is insufficient despite preserved stores. Weiss et al. (2019)[3] explained that inflammatory activation restricts iron absorption and release from storage cells. Nairz et al. (2016)[4] emphasised that these mechanisms can coexist, complicating laboratory differentiation. Accordingly, Snook et al. (2021)[5] recommended interpreting ferritin alongside additional iron studies when inflammation could produce misleadingly normal ferritin concentrations. The supplied biochemical pattern agreed with these descriptions, although agreement with established physiology did not independently validate the group diagnoses.

Comparison of Serum Iron: Tables 1 And 2

Mean serum iron was 28.7 (SD 9.6) $\mu\text{g/dL}$ in the IDA group compared with 43.2 (SD 13.8) $\mu\text{g/dL}$ in the ACD group. The mean difference was -14.50 $\mu\text{g/dL}$ (95% CI: -17.66 to -11.34), with Welch's $t=-9.05$ and $p<0.001$. Thus, circulating iron was lower in the IDA group in the supplied comparison. However, this difference should not be interpreted as evidence that serum iron is invariably lower in IDA than in ACD across clinical populations. Cappellini et al. (2020)[6], in their review, described the multiple nutritional, absorptive and blood-loss mechanisms contributing to IDA

and highlighted the difficulty of assessment when inflammation coexists. Pasricha et al. (2021)[7] similarly explained that iron deprivation can arise either from reduced total body stores or from inflammation-mediated withholding of iron from plasma. These mechanisms provide a plausible explanation for reduced circulating iron in both conditions. The lower IDA mean in the supplied tables could reflect differences in iron depletion, inflammatory activity or case selection, but these explanations cannot be established without corresponding clinical measurements.

Ganz (2019)[8] described increased hepcidin as a central mechanism underlying defective iron reutilisation in anaemia of inflammation. Girelli et al. (2016)[9] explained that hepcidin restricts intestinal absorption and iron release from macrophages and hepatocytes through its effects on ferroportin. These mechanisms explain why a patient with ACD may have reduced serum iron despite retained tissue iron. However, hepcidin was not reported in the supplied tables; therefore, its role here remained a literature-supported explanation rather than a measured association.

Direct observational support was provided by Khalaf et al. (2019)[10], who assessed iron parameters and hepcidin in 51 patients with rheumatoid arthritis. They identified ACD in 37.3%, IDA in 11.8%, and combined ACD/IDA in 17.6%. Hepcidin was higher in ACD and was negatively correlated with serum iron ($p=0.022$). Their findings supported inflammation-associated restriction of circulating iron and demonstrated that mixed anaemia was clinically relevant. Nevertheless, their rheumatoid arthritis cohort differed from a general hospital comparison of separately classified IDA and ACD groups; direct equivalence of mean concentrations should therefore not be assumed.

Comparison of Serum Ferritin: Tables 1 And 3

Mean serum ferritin was 13.8 (SD 5.7) ng/mL in the IDA group and 184.6 (SD 61.3) ng/mL in the ACD group. The mean difference was -170.80 ng/mL (95% CI: -182.43 to -159.17), with Welch's $t=-29.10$ and $p<0.001$. The lower IDA mean was compatible with depleted iron stores, while the substantially

higher ACD mean was compatible with the influence of inflammation and iron sequestration. However, a higher group mean did not demonstrate adequate iron stores in every individual with ACD.

Dignass et al. (2018)[11] reviewed the limitations of ferritin in inflammatory conditions and emphasised that normal or increased ferritin can coexist with restricted iron availability. Their interpretation supported the need to avoid excluding iron deficiency solely because ferritin was higher in the ACD group. Daru et al. (2017)[12] also highlighted variation in ferritin thresholds and limitations in the evidence supporting diagnostic cut-offs. Consequently, the separation between the supplied group means should not be converted into a diagnostic threshold without an appropriately designed diagnostic-accuracy study.

In a prospective study of 150 patients with inflammatory bowel disease, Abitbol et al. (2015)[13] found that 36 patients, or 24%, had ferritin below 30 ng/mL. Incorporating the transferrin receptor–ferritin index increased the number diagnosed with iron deficiency to 49 patients, or 32.7%, representing a 36% relative increase in detection. Among 30 evaluable patients with inflammation and ferritin between 30 and 100 ng/mL, 13 had an index above 2. These findings demonstrated that ferritin alone could miss iron deficiency in inflammatory disease. They also showed why the clear separation in the supplied tables might be less evident in populations containing mixed IDA and ACD.

Population-level evidence further demonstrated the influence of inflammation. Namaste et al. (2017)[14], using BRINDA data from 27,865 preschool children and 24,844 women of reproductive age, examined approaches to adjusting ferritin for inflammatory markers. Depending on the adjustment method, estimated depleted iron stores increased by 7–25 median percentage points in children and 2–8 percentage points in women compared with unadjusted estimates. Although these populations were different from the present adult hospital groups, the study supported considering inflammatory status when interpreting ferritin. Without CRP or other inflammatory measurements, the supplied tables could not determine how much of the ferritin difference reflected inflammation rather than differences in iron stores.

Comparison of Total Iron-Binding Capacity: Tables 1 And 4

Mean TIBC was 426.8 (SD 57.4) µg/dL in the IDA group compared with 238.6 (SD 46.2) µg/dL in the ACD group. The mean difference was 188.20 µg/dL (95% CI: 174.35–202.05), with Welch's $t=26.79$ and $p<0.001$. This opposite direction of change relative to serum iron and ferritin was compatible with the differing regulation of transferrin in absolute iron deficiency and inflammation.

Fertrin (2020)[15] explained that absolute iron depletion increases transferrin production and TIBC, whereas inflammation-associated functional deficiency is characterised by reduced iron release and lower TIBC. This framework closely matched the supplied pattern. Auerbach and Adamson (2016)[16] also emphasised the diagnostic relevance of elevated TIBC when accompanied by low transferrin saturation. Together, these publications supported interpreting TIBC as part of a complete iron profile rather than as an isolated diagnostic marker.

The observational findings of Khalaf et al. (2019)[10] provided additional support: TIBC was negatively correlated with hepcidin ($p<0.001$), whereas ferritin was positively correlated with hepcidin ($p<0.001$). These relationships were consistent with the combination of lower TIBC and higher ferritin in inflammation-associated anaemia. Nevertheless, differences in underlying diseases, disease activity and treatment exposure could influence the magnitude of these biochemical differences across studies.

Combined Interpretation and Clinical Relevance

Although serum iron, ferritin and TIBC differed significantly between the supplied groups, their combined interpretation was more informative than any individual value. Rohr et al. (2023)[17] identified ferritin and transferrin saturation as the most commonly used parameters in chronic disease, while emphasising differences between disease-specific definitions. Peyrin-Biroulet et al. (2015)[18], in a systematic review of 29 guidelines, found that all 22 guidelines providing diagnostic recommendations used ferritin, and 10 also recommended transferrin saturation as an alternative or complementary measure. These publications supported adding patient-level transferrin saturation to the assessment. It should be calculated for each participant; dividing the group mean serum iron by the

group mean TIBC would not provide the observed mean transferrin saturation.

Muñoz et al. (2017)[19] highlighted misconceptions arising from inconsistent terminology and incomplete investigation of iron deficiency. Jimenez et al. (2015)[20] emphasised that evaluation should identify the underlying cause as well as the biochemical deficiency. Applied to the supplied tables, this meant that the laboratory pattern could support clinical classification but could not establish whether blood loss, impaired absorption, chronic infection or another condition accounted for an individual patient's anaemia. The tables also contained no treatment-response or follow-up information from which therapeutic effectiveness could be inferred. [PubMed](#)

Shander et al. (2023)[21], in the ICCAMS recommendations, supported evaluation using serum iron, TIBC, transferrin saturation and ferritin, with additional markers considered in inflammatory states. **Iolascon et al. (2024)[22]** similarly recommended a contextual assessment incorporating haematological findings, biochemical markers and the underlying cause. These recommendations reinforced the value of a combined assessment while recognising that ferritin thresholds and diagnostic interpretation vary with inflammation and comorbidity. Several analytical considerations limited interpretation of the supplied comparisons. If ferritin or other iron measurements were used to allocate participants to the IDA and ACD groups, the subsequent differences partly reflected those classification criteria. Excluding mixed cases could further increase apparent separation and reduce applicability to routine clinical populations.

CONCLUSION

The supplied comparison showed significantly lower serum iron and ferritin concentrations and higher total iron-binding capacity in patients classified as having iron deficiency anaemia compared with those classified as having anaemia of chronic disease. These differences supported the complementary interpretation of the three biochemical parameters when assessing anaemia. However, the observed group differences did not establish diagnostic accuracy or exclude coexisting iron deficiency in patients with chronic disease. Interpretation should incorporate clinical findings, inflammatory

markers and, where available, transferrin saturation.

Limitations of the Study

- 1. Single-Centre Setting:** The hospital-based sample might not represent patients in community settings or other institutions, limiting generalisability.
- 2. Cross-sectional Design:** Assessment at a single time point could not establish temporal relationships or evaluate changes following treatment.
- 3. Potential Classification Bias:** If ferritin or other iron parameters were used to define the study groups, subsequent comparisons of those same parameters were partly dependent on the diagnostic criteria.
- 4. Exclusion of Mixed Anaemia:** Excluding patients with combined IDA and ACD could increase separation between groups and reduce applicability to routine clinical practice.
- 5. Incomplete Assessment of Inflammation:** The presented analyses did not account for inflammatory-marker concentrations or differences in underlying disease activity.
- 6. Residual Confounding:** The comparisons were unadjusted for potential influences such as age, sex, nutritional status, comorbidities and previous treatment.
- 7. Biochemical Variability:** Sampling conditions, biological variation and assay methods could affect iron measurements. Patient-level data were needed to assess ferritin skewness and confirm the suitability of statistical tests.
- 8. No Diagnostic-Accuracy Or Follow-Up Assessment:** The tables did not establish sensitivity, specificity, diagnostic cut-offs or treatment response.

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