e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com doi: 10.25258/ijpqa.16.12.110

International Journal of Pharmaceutical Quality Assurance 2025; 16(12); 674-680

Original Research Article

Comparative Prevalence and Clinical Outcomes of Anemia of Chronic Disease and Iron Deficiency Anemia Using Basic Laboratory Markers

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Received: 11-10-2025 / Revised: 15-11-2025 / Accepted: 27-12-2025

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Conflict of interest: Nil

Abstract:

Background: Anemia is a common comorbidity among hospitalized patients and is associated with adverse clinical outcomes. Iron deficiency anemia (IDA) and anemia of chronic disease (ACD) are the most prevalent subtypes, yet their comparative prevalence and outcomes in general inpatients are not well defined.

Aim: To compare the prevalence and clinical outcomes of IDA and ACD using basic laboratory markers in hospitalized adults.

Methodology: This retrospective observational study included 288 anemic adults admitted in Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India. Patients were classified as IDA (n=124) or ACD (n=164) based on hemoglobin, ferritin, iron indices, and C-reactive protein. Clinical outcomes assessed were length of hospital stay, 30-day readmission, and in-hospital mortality.

Results: ACD was more prevalent than IDA (56.9% vs. 43.1%) and affected older patients with higher comorbidity burden. ACD patients had significantly longer hospital stays (8.0 vs. 6.0 days), higher 30-day readmission rates (25.0% vs. 14.5%), and greater in-hospital mortality (8.5% vs. 3.2%). Laboratory markers clearly differentiated IDA (microcytosis, low ferritin) from ACD (elevated ferritin, high CRP).

Conclusion: ACD is more common than IDA in hospitalized adults and is associated with poorer short-term clinical outcomes. Basic laboratory markers are effective for anemia subtype differentiation and risk stratification.

Keywords: Anemia of chronic disease, Iron deficiency anemia, Hospitalized patients, Iron studies, Clinical outcomes.

Introduction

Anemia, which can be described as a low level of hemoglobin or red blood cell mass is a common hematological condition that is present globally and among the most common comorbid conditions found among hospitalized patients [1]. It leaves a heavy burden not only on various age groups but also on different clinical settings, thus posing a significant challenge to the health of the population globally. Anemia in the inpatient setting is much more than a lab finding; it is a clinically severe condition, which tends to be a reflection of the processes of disease activity and physiological stress. As already shown in many studies, anemia among hospitalized patients is a factor that is related to adverse outcomes such as extended hospitalization, higher hospitalization readmission rates, poor functional recovery, and higher short- and long-term mortality independently [2, 3]. As a result, the subtypes of anemia in hospitalized patients are of great clinical significance, as well as their identification and characterization.

The pathophysiology of anemia among hospitalized patients is complicated and often multifactorial. Some of these causes are nutritional deficiencies, chronic and acute blood loss, bone marrow suppression, kidney dysfunction, and the systemic consequences of acute or chronic inflammation. Also, iatrogenic factors including regular phlebotomy, surgery and invasive diagnostic procedures even worsen anemia in the hospital. The acute illness or chronic disease inflammatory milieu changes iron metabolism and erythropoiesis, making both diagnosis and treatment difficult. Iron deficiency anemia

(IDA) and anemia of chronic disease (ACD) also known as anemia of inflammation are the most common forms of anemia experienced in clinical practice [4] amongst the other causes of anemia.

Iron deficiency anemia is typified by absolute loss of iron reserves which result in hampered hemoglobin production and decreased erythropoiesis. Most of the time the condition is caused by chronic blood loss, especially that of the gastrointestinal tract, inadequate intake of iron in the form of diet, or impaired absorption of iron by the presence of gastrointestinal disorders [5]. IDA is still the cause of anemia most involved in the world and is predominant in populations with limited nutritional means, in women of reproductive age, and in those with ongoing occult bleeding. IDA can be comorbid with acute illness in the hospitalized adult and complicate the clinical presentation even more, potentially delaying its recovery unless the problem is identified and addressed timely.

Conversely, chronic disease anemia occurs in the environment of chronic inflammatory diseases, autoimmune, malignant, or other chronic inflammatory diseases. ACD is not mainly caused by absence of total body iron stores as compared to IDA. Rather, its pathogenesis is carried out by inflammatory cytokines that destabilize the process of iron homeostasis and inhibit erythropoiesis. The key to this process is hepcidin, a peptide hormone secreted by the liver, the expression of which is increased on the proclamation of inflammatory messages. Hepcidin prevents the absorption of intestinal iron and increases iron intestinal absorption of iron into the macrophage and reticuloendothelial system, leading to functional iron deficiency in spite of sufficient or excessive iron stores [6, 7]. Moreover, inflammatory cytokines suppress the bone marrow reaction to erythropoietin and reduce red blood cell life, which is another cause of anemia.

It is also a major diagnostic dilemma in clinical practice to differentiate between IDA and ACD especially in hospitalized patients where inflammation is the norm. Traditional laboratory measurements like hemoglobin, mean corpuscular volume, serum iron, ferritin and transferrin saturation are the common measurements of anemia. Nevertheless, the presence of overlap in laboratory results between IDA and ACD in particular when the two are comorbid may blur the diagnosis. An example of an acute-phase reactant that can be increased in inflammatory conditions is ferritin, which conceals the presence of underlying iron deficiency. Nevertheless, it is possible to note that it is crucial to make a correct diagnosis between IDA and ACD because the management of anti-iron deficiency anemia and anti-cancer anemia is fundamentally different. Iron deficiency anemia is mainly treated with an iron supplementation, either orally or intravenously, to replenish iron lost stores. Conversely, management of the underlying inflammatory condition is the keystone of ACD management because iron supplementation is not always effective and can even be potentially dangerous in some situations [8].

Although the occurrence and consequences of anemia have been well-investigated in a select group of disease populations, including patients with heart failure, chronic kidney disease, and malignancy, there is limited knowledge on the relative prevalence and prognosis of anemia subtypes in a general adult inpatient population [9,10]. In the current body of literature, the concept of anemia has been concentrated on as a unit without making much distinction between the causes. This is a clinically significant limitation because the prognostic significance of anemia can change with etiology. Chronic inflammatory-related anemia can be used as a surrogate endpoint of disease intensity, systemic disease burden and continued physiological burden which can provide a worse prognosis than anemia caused by absolute iron defimeter alone.

Additionally, few studies have directly compared the clinical outcomes of patients with ACD and IDA with the help of easily available, simple laboratory markers. They are necessary to enhance the accuracy of the diagnoses, improve the risk stratification, and direct the specific therapeutic procedures in the hospitalized patients. The cognizance of whether ACD and IDA are different in regard to the length of stay at the hospital, readmission cases, and in-hospital death may be of crucial significance to the management of patients and the utilization of health resources.

As such, the present investigation was meant to fill this vital gap in the body of knowledge by assessing the relative prevalence of anemia of chronic disease and iron deficiency anemia among anemic patients admitted to a tertiary care hospital. Also, the aim of the study was to compare two major clinical outcomes such as length of stay, 30-day readmission rates, and in-hospital mortality in these two different types of anemia. Our hypothesis stated that the anemia of chronic disease would be seen more widespread among the hospitalized adult population than the anemia of iron deficiency and will be linked to worse clinical outcomes as it is a symptom of the underlying chronic inflammatory states.

Methodology

Study Design: This was a hospital-based, observational, retrospective comparative study conducted to evaluate the prevalence and clinical outcomes of Iron Deficiency Anemia (IDA) and Anemia of Chronic Disease (ACD) using basic laboratory markers.

Study Area: The study was carried out in the Department of Pathology, Darbhanga Medical College

and Hospital (DMCH), Laheriasarai, Darbhanga, Bihar, India.

Study Duration: The study was conducted over a period of 7 months from March 2025 to September 2025

Sample Size: The final sample size of the study was 288 patients, which constituted the study population included for the comparative analysis between Iron Deficiency Anemia (IDA) and Anemia of Chronic Disease (ACD) after applying the predefined inclusion and exclusion criteria. Among these patients, 124 (43.1%) were classified as having IDA, while 164 (56.9%) were classified as having ACD based on established laboratory criteria. Only patients who met the strict diagnostic definitions for either IDA or ACD and had complete laboratory data available within the first 48 hours of admission were included in the final analysis.

Study Population: All adult patients aged 18 years and above who were admitted to non-obstetrical medical and surgical wards during the study period were screened for anemia. Patients were identified either through International Classification of Diseases, Tenth Revision (ICD-10) codes for anemia (D50–D64) or by laboratory evidence of anemia on admission. Anemia was defined according to World Health Organization (WHO) criteria as a hemoglobin level of less than 13 g/dL in men and less than 12 g/dL in women. From the initially identified cohort, patients meeting the predefined inclusion and exclusion criteria and having complete laboratory data within the first 48 hours of admission were included in the final analysis. Based on laboratory profiles, eligible patients were classified into Iron Deficiency Anemia (IDA) or Anemia of Chronic Disease (ACD), while those with mixed or other etiologies were excluded from comparative analysis.

Data Collection: Data were extracted retrospectively from the hospital EHR system by a trained data abstractor using a standardized data collection format. The collected information included demographic variables such as age and sex, admission and discharge dates, documented comorbid conditions, and relevant laboratory parameters. Laboratory data obtained within the first 48 hours of admission included hemoglobin concentration, serum ferritin, serum iron, total iron-binding capacity (TIBC), and C-reactive protein (CRP). Transferrin saturation (TSAT) was calculated as the ratio of serum iron to TIBC multiplied by 100. The Charlson Comorbidity Index (CCI) was calculated for each patient to quantify the burden of chronic illness. All extracted data were anonymized prior to analysis to ensure patient confidentiality.

Inclusion Criteria

Patients were included in the study if they:

- Were ≥18 years of age
- Met WHO criteria for anemia
- Had a complete laboratory dataset (Hb, serum ferritin, serum iron, TIBC, and CRP) available within 48 hours of admission
- Could be classified into IDA or ACD based on predefined laboratory criteria

Exclusion Criteria

Patients were excluded if they had:

- Known hematologic malignancies (e.g., leukemia, lymphoma, multiple myeloma)
- Active overt bleeding at the time of admission
- History of red blood cell transfusion within 30 days prior to admission
- End-stage renal disease (eGFR <15 mL/min/1.73 m²) or were on chronic dialysis
- Pregnancy
- Incomplete laboratory data preventing anemia classification

Classification of Anemia

Based on laboratory profiles, patients were classified as:

- **Iron Deficiency Anemia (IDA):**
  - Hemoglobin below WHO threshold, and
  - Serum ferritin <30 ng/mL, or
  - Serum ferritin 30–100 ng/mL with TSAT <20%
- **Anemia of Chronic Disease (ACD):**
  - Hemoglobin below WHO threshold
  - Serum ferritin >100 ng/mL
  - TSAT <20%
  - Evidence of inflammation (CRP >5 mg/L)

Patients with mixed features, vitamin B12 or folate deficiency, or normal iron studies were categorized as Other/Unclassified and excluded from the comparative analysis.

Clinical Outcomes Assessed: The primary clinical outcomes assessed in this study included hospital length of stay, 30-day all-cause readmission, and in-hospital mortality. Length of hospital stay was calculated as the number of days from the date of admission to the date of discharge. Thirty-day all-cause readmission was defined as any unplanned hospital admission occurring within 30 days following discharge from the index hospitalization. In-hospital mortality was defined as death occurring at any time during the index hospital stay. These outcomes were compared between patients classified as having IDA and those with ACD.

Procedure: All eligible patients were screened sequentially through EHR review. After applying inclusion and exclusion criteria, laboratory data were used to classify patients into IDA or ACD groups.

Patients meeting criteria for mixed or other anemia etiologies were excluded from comparative analysis. Clinical outcomes were then assessed and compared between the two groups.

Statistical Analysis: All statistical analyses were performed using SPSS Statistics for Windows, Version 28.0 (IBM Corp., Armonk, NY). Descriptive statistics were used to summarize demographic, clinical, and laboratory characteristics of the study population. Continuous variables were expressed as mean ± standard deviation and compared between the IDA and ACD groups using the independent samples t-test. Categorical variables were presented as frequencies and percentages and compared using the Chi-square test or Fisher's exact test, as appropriate. A two-tailed p-value of less than 0.05 was considered statistically significant for all analyses."

Result

Table 1 outlines the baseline demographics and comorbidities of patients with iron deficiency anemia (IDA) and anemia of chronic disease (ACD). Patients in the ACD group were significantly older than those in the IDA group (67.8 ± 11.8 vs 54.6 ± 14.9 years, $p < 0.001$). The sex distribution was comparable between groups, with males comprising 46.8% of the IDA group and 52.4% of the ACD group ($p = 0.318$). The Charlson Comorbidity Index was significantly higher in ACD (4.6 ± 1.8) compared to IDA (2.4 ± 1.4, $p < 0.001$), indicating a greater burden of comorbid illness. Additionally, congestive heart failure, diabetes mellitus, and chronic pulmonary disease were significantly more prevalent in the ACD group (28.0%, 37.2%, and 21.3%, respectively) than in the IDA group (11.3%, 24.2%, and 10.5%), with all differences reaching statistical significance. Overall, as shown in Table 1, patients with ACD had older age and more comorbid conditions compared to those with IDA.

Table 1: Baseline Demographics and Comorbidities of Patients with IDA and ACD (N = 288)

Characteristic	IDA Group (n = 124)	ACD Group (n = 164)	P-value
Age, years (mean ± SD)	54.6 ± 14.9	67.8 ± 11.8	<0.001
Sex, n (%)			
Male	58 (46.8%)	86 (52.4%)	0.318
Female	66 (53.2%)	78 (47.6%)	
Charlson Comorbidity Index (mean ± SD)	2.4 ± 1.4	4.6 ± 1.8	<0.001
Congestive Heart Failure, n (%)	14 (11.3%)	46 (28.0%)	<0.001
Diabetes Mellitus, n (%)	30 (24.2%)	61 (37.2%)	0.021
Chronic Pulmonary Disease, n (%)	13 (10.5%)	35 (21.3%)	0.014

Table 2 compares the hematological and inflammatory parameters between the IDA (n = 124) and ACD (n = 164) groups. The mean hemoglobin level was slightly lower in the IDA group (9.7 ± 1.2 g/dL) compared to the ACD group (10.0 ± 1.3 g/dL), but this difference was not statistically significant ($p = 0.082$). In contrast, MCV was significantly lower in IDA (77.9 ± 6.3 fL) than in ACD (87.6 ± 7.4 fL, $p < 0.001$). Marked differences were observed in iron indices, with serum ferritin being substantially lower in IDA (19.2 ± 9.1 ng/mL) compared to ACD (332.8 ± 172.6 ng/mL, $p < 0.001$), while serum iron, TSAT, and TIBC also differed significantly between groups ($p < 0.001$ for all). Additionally, C-reactive protein levels were markedly higher in the ACD group (82.7 ± 51.3 mg/L) than in the IDA group (14.6 ± 17.8 mg/L), indicating a significantly greater inflammatory burden ($p < 0.001$). Overall, as shown in Table 2, IDA was characterized by microcytosis and iron depletion, whereas ACD showed preserved or elevated iron stores with prominent inflammation.

Table 2: Hematological and Inflammatory Parameters in IDA and ACD Groups

Parameter	IDA Group (n = 124)	ACD Group (n = 164)	P-value
Hemoglobin, g/dL (mean ± SD)	9.7 ± 1.2	10.0 ± 1.3	0.082
MCV, fL (mean ± SD)	77.9 ± 6.3	87.6 ± 7.4	<0.001
Serum Ferritin, ng/mL (mean ± SD)	19.2 ± 9.1	332.8 ± 172.6	<0.001
Serum Iron, µg/dL (mean ± SD)	33.4 ± 13.8	42.1 ± 17.5	<0.001
TIBC, µg/dL (mean ± SD)	398.6 ± 62.1	245.9 ± 56.7	<0.001
TSAT, % (mean ± SD)	8.4 ± 4.1	16.9 ± 5.4	<0.001
C-reactive protein, mg/L (mean ± SD)	14.6 ± 17.8	82.7 ± 51.3	<0.001

Table 3 compares clinical outcomes between the IDA and ACD groups. Patients in the ACD group had a significantly longer mean hospital stay (8.0 ± 4.2 days) compared to the IDA group (6.0 ± 3.1 days), with this difference being highly significant ($p < 0.001$). The 30-day readmission rate was also higher in the ACD group (25.0%) than in the IDA group (14.5%), showing a statistically significant difference ($p = 0.027$). Additionally, in-hospital mortality was greater among patients with ACD

(8.5%) compared to those with IDA (3.2%), and this difference reached statistical significance (p = 0.041). Overall, as shown in Table 3, the ACD group demonstrated poorer clinical outcomes compared to the IDA group.

Table 3: Comparison of Clinical Outcomes Between IDA and ACD Groups

Outcome	IDA Group (n = 124)	ACD Group (n = 164)	P-value
Length of Hospital Stay, days (mean ± SD)	6.0 ± 3.1	8.0 ± 4.2	<0.001
30-Day Readmission, n (%)	18 (14.5%)	41 (25.0%)	0.027
In-Hospital Mortality, n (%)	4 (3.2%)	14 (8.5%)	0.041

Discussion

The current study contributes to the increasing literature on the significance of differences in prevalence, laboratory features, and clinical outcomes between anemia of chronic disease (ACD) and iron deficiency anemia (IDA) among hospitalized adults. ACD was also more common in our cohort compared to IDA and the short-term clinical outcomes of patients with ACD were worse. This is widely in line with previous studies that reported inflammatory-based anemia in inpatient and older groups to be more common, with IDA being more prevalent in ambulatory or younger groups (Nemeth and Ganz, 2014; Cash and Sears, 1989) [7,11]."

Patients aged over 60 years with ACD are also quite old, which is consistent with population and hospital-based studies that have observed that anemia among the elderly is usually correlated with the presence of chronic inflammatory and systemic diseases. Guralnik et al. found out that the prevalence of anemia increases steep beyond 65 years of age and much of the prevalence is caused by chronic disease and unexplained etiologies and not pure iron deficiency (Guralnik et al., 2004) [1]. On the same note Cash and Sears found out that ACD was predominant among the older hospitalized patients with a wide range of underlying conditions such as infections, malignancies, and connective tissue disorders (Cash & Sears, 1989) [11]. Conversely, the mean age in our IDA group is comparatively younger; this is in line with the reported cases of gastrointestinal blood loss, nutritional deficiency, and malabsorption being more prevalent and reversible causes of anemia in this cohort (Camaschella, 2015) [5].

Our significantly greater comorbidity burden in our ACD group is another indication of the idea that ACD represents a surrogate endpoint of the severity of systemic illnesses. The increased scores on Charlson Comorbidity Index and prevalence of congestive heart failure, diabetes mellitus and chronic pulmonary disease reflect the results of previous research that has connected ACD to chronic cardiovascular, metabolic, and inflammatory disorders (Groenveld et al., 2008; Gilreath et al., 2014) [9,10]. Anemia in the population of heart failure patients has been linked to higher mortality and hospitalization rates independently, and these findings indicate that inflammation, iron imbalance, and the consequence of these factors are closely interconnected (Groenveld et al., 2008) [9]. In comparison, our study patients with IDA had fewer comorbidities, which implies a relatively less severe initial illness.

The difference in hematological and iron profile, which we have noticed among groups in our study, is very close to classical descriptions of ACD and IDA. The considerably decreased mean corpuscular volume, serum iron, transferring saturation, and increased total iron-binding capacity of the IDA patients are in line with the following depleted iron stores and enhanced transferrin production, which is described in both mechanistic and clinical literature (Camaschella, 2015; Theurl et al., 2009) [5,12]. The significantly increased ferritin concentrations and rather intact mean corpuscular volume in ACD, in turn, are the results of iron binding in macrophages and reticuloendothelial cells due to the overproduction of hepcidin caused by inflammation (Weiss & Goodnough, 2005; Ganz, 2011) [4,6]. These results support the diagnostic power of the simple laboratory markers in differentiating between these two entities, more so in the resource-deprived environment where the sophisticated biomarkers might not be easily accessible.

The significant difference in the inflammatory load between the groups, which is reflected by much greater levels of C-reactive protein in ACD ones, is consistent with the past literature that showed strong correlations between acute-phase reactants and poor clinical outcomes. High levels of CRP and interleukin-6 are associated with death, extended hospitalization and elevated rates of readmission in various pathologies (Gabay and Kushner, 1999) [13]. We build on this observation and demonstrate that ACD patients, who demonstrate significantly elevated levels of inflammatory markers, also have longer length of stay and increased in-hospital mortality. This helps to sustain the idea that, in this case anemia is not only an hematologic abnormality, but it is the indicator of long-term systemic inflammation, which carries prognostic implications.

The differences in clinical outcomes identified in our study are quite similar to the previous research findings. Koch et al. showed that anaemic patients admitted to the hospital with etiologies related to inflammation had more and worse hospitalizations

than non-anemic patients (Koch et al., 2013) [2]. Likewise, Spence pointed to the significant economic and clinical impact of anemia in hospitalized patients and ACD has a disproportionate presence because of its co-morbidity with complex underlying diseases (Spence, 2007) [3]. We also found that ACD patients exhibit increased rates of higher 30-day readmission and mortality, which is also supported by the research stating that iron dysregulation and elevated ferritin are risk factors to predict poor prognosis of critically ill and chronically diseased individuals (Tacke et al., 2016) [14].

Conversely, despite the fact that patients of our coh with IDA showed more severe iron index derangements, short-term outcomes were relatively favorable. This is consistent with the past experience, which indicates that, in a timely manner, IDA can be subject to specific treatment like iron administration or bleeding causes, which results in faster clinical progress (Camaschella, 2015; Fonseca et al., 2017) [5,8]. Clinical criticality of the distinction between these two subtypes of anemia, therefore, lies in the fact that iron supplementation in ACD may not be effective and may even be detrimental, but postponing the treatment of IDA can increase the duration of symptoms and hospitalization.

In general, it can be concluded that our results confirm and expand previous research findings as they indicate that simple laboratory findings are useful in distinguishing between ACD and IDA and possible prognostic factors. Although the diagnostic accuracy can be further improved by the use of the state-of-the-art biomarkers, including soluble transferrin receptor and hepcidin, our findings offer evidence to the claim that the traditional iron research remains relevant in everyday clinical practice (Theurl et al., 2009; van der Weerd et al., 2013) [12,15]. The close links between ACD and systemic inflammation and poor prognosis highlights the importance of clinicians moving beyond ACD as a type of anemia, as it is an indication of disease severity that should be assessed and treated in a holistic manner.

Conclusion

This paper has also proven that anemia of chronic disease was predominant over iron deficiency anemia and was related to an older demographic with a higher comorbidity burden. Distinct trends in simple laboratory markers were useful to distinguish the two conditions with iron deficiency anemia being marked by microcytosis and depleted iron stores whereas anemia of chronic disease was marked by maintained or increased iron stores and increased inflammatory markers. Patients with anemia of chronic disease had worse clinical outcomes, such as prolonged hospital stay, high readmission rates, and in-hospital mortality, which highlights the effects of underlying chronic disease and inflammation on patient outcomes. These findings highlight the clinical utility of readily available laboratory parameters in distinguishing anemia subtypes and emphasize the need for targeted management strategies to improve outcomes, particularly in patients with anemia of chronic disease.

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