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## REVIEW ON IRON DEFICIENCY ANAEMIA IN CHRONIC KIDNEY DISEASE PATIENTS; PREVALENCE AND CONSEQUENCES RELATED TO OTHER COMORBIDITY CONDITIONS

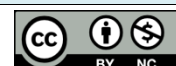
**Menta Venkata Sarayu<sup>1</sup>, M. Sowjanya<sup>2</sup>, Y Prapurna Chandra<sup>3</sup>, Venugopalaiah Penabaka<sup>4</sup>, Afroz Patan<sup>5</sup>**<sup>1</sup>B. Pharmacy, IV Year, Ratnam Institute of Pharmacy, Pidathapolur (V & P), Muthukur (M), SPSR Nellore District-524 346, Andhra Pradesh.<sup>2</sup>Assistant professor, Department of Pharmacy practice, Ratnam Institute of Pharmacy, Pidathapolur (V & P), Muthukur (M), SPSR Nellore District-524 346, Andhra Pradesh.<sup>3</sup>Principal and Professor, Department of Pharmacology, Ratnam Institute of Pharmacy, Pidathapolur (V & P), Muthukur (M), SPSR Nellore District-524 346, Andhra Pradesh.<sup>4</sup>Professor, Department of Pharmaceutics, Ratnam Institute of Pharmacy, Pidathapolur (V & P), Muthukur (M), SPSR Nellore District-524 346, Andhra Pradesh.<sup>5</sup>Professor & HOD, Department of Pharmacy practice, Ratnam Institute of Pharmacy, Pidathapolur (V & P), Muthukur (M), SPSR Nellore District-524 346, Andhra Pradesh.*Received: 15 Aug 2025 Revised: 02 Sept 2025 Accepted: 04 Oct 2025*

### Abstract

Iron Deficiency Anaemia (IDA) is a common and significant complication in patients with Chronic Kidney Disease (CKD), affecting up to 50–60% of individuals, especially in advanced stages. The presence of co morbidities such as Cardiac heart failure (CHF), Rheumatological diseases, Chronic obstructive pulmonary disease(COPD), Diabetes mellitus(DM) and cardiovascular disease(CVD) further compounds the burden of Iron deficiency Anaemia, both in terms of prevalence and clinical outcomes. Patients with CKD and diabetes are more prone to Anaemia due to heightened systemic inflammation, oxidative stress, and autonomic neuropathy affecting gastrointestinal iron absorption. Similarly, cardiovascular disease is both a consequence and a driver of Anaemia, as Iron deficiency Anaemia contributes to increased cardiac workload, left ventricular hypertrophy, and heart failure, while chronic heart conditions can suppress erythropoietin. The coexistence of Iron deficiency Anaemia with these co morbidities is associated with worsened quality of life, increased hospitalizations, accelerated CKD progression, and higher mortality rates.

**Keywords:** Iron Deficiency Anaemia, Chronic Kidney Disease, Cardiac heart failure, Diabetes Mellitus, Cardiovascular Disease, Co morbidities, Prevalence, Outcomes

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### \*Corresponding Author

M. Sowjanya

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### Introduction

Anaemia is a condition in which the body does not have enough healthy red blood cells. Red blood cells provide oxygen to body tissues.

Anaemia is defined as hemoglobin below two standard deviations of the mean for the age and gender of the patient. Iron is an essential component of the hemoglobin molecule. The most common cause of Anaemia worldwide is iron deficiency, which results in microcytic and

hypochromic red cells on the peripheral smear. Several causes of iron deficiency vary based on age, gender, and socioeconomic status. The patient often will have nonspecific complaints such as fatigue and dyspnea on exertion. Patients with iron-deficient Anaemia have been found to have a longer hospital stay, along with a higher number of adverse events [1].

### Different Types of Anaemia Include

- Anaemia due to vitamin B12 deficiency
- Anaemia due to iron deficiency
- Hemolytic Anaemia
- Idiopathic aplastic Anaemia
- Megaloblastic Anaemia

- Pernicious Anaemia
- Sickle cell Anaemia
- Thalassemia

#### Iron Deficiency Anaemia

- Iron deficiency Anaemia is the most common type of Anaemia. Iron deficiency Anaemia occurs when your body does not have enough iron. Iron helps make red blood cells [2].

#### Causes of Iron Deficiency Anaemia

Red blood cells bring oxygen to your body's tissues. Red blood cells are made in your bone marrow. Red blood cells circulate through your body for 3 to 4 months. Parts of your body, such as your spleen, remove old blood cells. Iron is a key part of red blood cells. Without iron to make haemoglobin, your blood cannot carry oxygen effectively. Your body normally gets iron through your diet. It also reuses iron from old red blood cells. Iron deficiency Anaemia develops when your body's iron stores run low. This can occur because:

- You lose more blood cells and iron than your body can replace
- Your body does not absorb iron well
- Your body is able to absorb iron, but you are not eating enough foods that contain iron
- Your body needs more iron than normal (such as if you are pregnant or breastfeeding) [3].

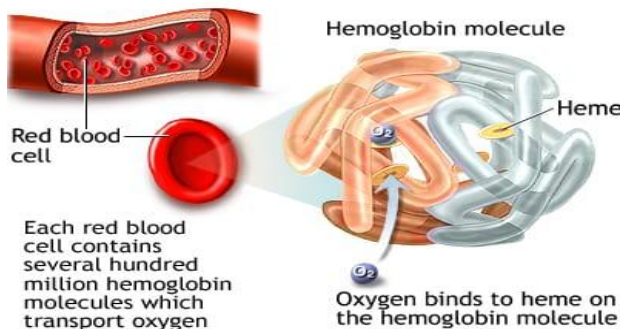


Figure 01: Iron Deficiency Anemia

#### Chronic Kidney Disease

Chronic kidney disease (CKD) is characterized by the presence of kidney damage or an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 m<sup>2</sup>, persisting for 3 months or more, irrespective of the cause[4]. CKD is a state of progressive loss of kidney function, ultimately resulting in the need for renal replacement therapy, such as dialysis or transplantation. Kidney damage refers to pathologic abnormalities suggested by imaging studies or renal biopsy, abnormalities in urinary sediment, or increased urinary albumin excretion rates.

The 2012 Kidney Disease Improving Global Outcomes (KDIGO) CKD classification recommends specifying the cause of CKD and classifies the condition into 6 categories based on GFR (G1 to G5, with G3 split into 3a and 3b). In addition, it also includes staging based on 3 levels of albuminuria (A1, A2, and A3), with each stage of CKD

subcategorized according to the urinary albumin-creatinine ratio (ACR; mg/g or mg/mmol) in an early morning "spot" urine sample [5].

#### Types

The 6 CKD categories, known as stages 1 through 5, are described below (stage 3 is separated into 3a and 3b)

- G1: GFR 90 mL/min/1.73 m<sup>2</sup> and above with evidence of kidney disease, such as hematuria or proteinuria
- G2: GFR 60 to 89 mL/min/1.73 m<sup>2</sup>
- G3a: GFR 45 to 59 mL/min/1.73 m<sup>2</sup>
- G3b: GFR 30 to 44 mL/min/1.73 m<sup>2</sup>
- G4: GFR 15 to 29 mL/min/1.73 m<sup>2</sup>
- G5: GFR less than 15 mL/min/1.73 m<sup>2</sup> or treatment by dialysis

#### The 3 levels of albuminuria include an ACR:

- A1: ACR less than 30 mg/g (<3.4 mg/mmol)
- A2: ACR 30 to 299 mg/g (3.4-34 mg/mmol)
- A3: ACR greater than 300 mg/g (>34 mg/mmol)

#### Symptoms of Anaemia in CKD Patients

Anaemia related to CKD typically develops slowly and may cause few or no symptoms in early kidney disease. Symptoms of Anaemia in CKD may include [6-9]

- Fatigue or tiredness
- Shortness of breath
- Unusually pale skin
- Weakness
- Body aches
- Chest pain
- Dizziness
- Fainting

#### How Anaemia Related to CKD Patients

Anaemia is a common complication of chronic kidney disease [CKD]. CKD means your kidneys are damaged and can't filter blood the way they should. This damage can cause wastes and fluid to build up in your body. CKD can also cause other health problems.

Anaemia is less common in early kidney disease, and it often gets worse as kidney disease progresses and more kidney function is lost [10].

#### Complications of Anaemia in CKD Patients

Anaemia of CKD is highly associated with adverse outcomes such as cardiovascular events and increased mortality. Additionally, the severity of Anaemia correlates with decreased quality of life and increased hospitalizations. Understanding the diverse mechanisms involved, recommended treatment guidelines, and new therapeutic developments are crucial for managing this condition effectively [11].

#### Epidemiology of Anaemia in CKD Patients

Anaemia is a common complication in chronic kidney disease (CKD), and is associated with a reduced quality of

life [12-13], a worse renal survival [14], an increase in morbidity and mortality [15-16], and higher costs [17]. Several studies focused on prevalence of anaemia on CKD non-dialysis dependent (NDD) report variable anaemia rates up to 60%.

Anaemia is more prevalent and severe as the estimated glomerular filtration rate (eGFR) declines. An analysis of the cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) in 2007–2008 and 2009–2010[18] revealed that anaemia was twice as prevalent in patients with CKD as in the general population (15.4% vs. 7.6). The prevalence of anaemia raised with the progression of CKD: 8.4% at stage 1 to 53.4% at stage 5. Similar data was observed in a more recent paper by the CKD Prognosis Consortium [19]. In addition, they observed an increased prevalence of anaemia among diabetic patients, independent of eGFR and albuminuria.

### Prevalence of Anaemia in CKD Patients

The prevalence of Anaemia in CKD depends on several factors, including stage, aetiology, food, healthcare accessibility, and genetic predispositions. Studies show that severe CKD increases Anaemia [20].

- Globally, studies have shown that Anaemia affects approximately 30–60% of patients with CKD, with higher rates observed as kidney function declines. In early stages (CKD stage 1–2), the prevalence is relatively low, around 10–20%, whereas in advanced stages (CKD stage 4–5) or end-stage renal disease (ESRD), the prevalence can rise to 70–90%.
- Among these, iron deficiency Anaemia (IDA) contributes to nearly 50–70% of total Anaemia cases in CKD. This occurs due to factors such as reduced dietary iron intake, chronic inflammation, impaired intestinal absorption, and blood loss during dialysis or laboratory testing.
- In non-dialysis CKD (ND-CKD) patients, studies report iron deficiency Anaemia prevalence rates ranging from 35–45%, whereas in hemodialysis patients, the prevalence can exceed 60%. Regional data suggest that in India, approximately 40–50% of CKD patients are iron deficient, often associated with poor nutritional status and late diagnosis [Table 1].
- The coexistence of iron deficiency Anaemia with other co morbidities such as diabetes mellitus, hypertension, and cardiovascular diseases further worsens patient outcomes, leading to increased hospitalization rates, progression of renal dysfunction, and higher mortality.

Table 01: Stages of chronic kidney diseases.

CKD Stages	Estimated Anaemia prevalence	Iron deficiency contribution
Stage 1-2	10-20%	~30%
Stage 3	30=40%	~50%
Stage 4-5	60-90%	~70%
Dialysis patients	70-90%	>60%
Indian(regional data)	40-50%	-

The overall prevalence of Anaemia across all stages of CKD is 53.5%. From the stage of CKD, stage 5 CKD has a higher (90.9%) Anaemia prevalence compared to others, and females showed a higher frequency of Anaemia when compared with males. Therefore, situation-based interventions and country context-specific preventive strategies should be developed to reduce the prevalence of Anaemia in this patient group

Studies have shown a wide variation in the prevalence of Anaemia in CKD across regions. For instance, the reported prevalence of Anaemia in CKD is 14% in the USA,[21] 39.36% in India,[22] 51.5% in China,[23] 43.18% in South Africa,[24] and 79% in Cameroon.[25] [Table 2]. Moreover, the prevalence increases with the CKD stage, with an overall prevalence of 22.4%, 41.3%, and 53.9% in CKD stages 3, 4, and 5, respectively [26].

Table 2: Prevalence of chronic kidney diseases.

S.no	Country	Prevalence of Anaemia in CKD
1.	USA	14%
2.	India	39.36%
3.	China	51.5%
4.	South Africa	43.18%
5.	Cameroon	79%

### Prevalence and patterns of Anaemia among stage 3 to 5 CKD patients

Overall, 1 hundred 28 (85.34%) patients were found to have Anaemia. Of this, 61 (47.65%) had iron deficiency Anaemia. Of these patients, 43 (28.67%), 61 (40.67%), and 24 (16%) had mild, moderate, and severe Anaemia, respectively (Fig. 1).

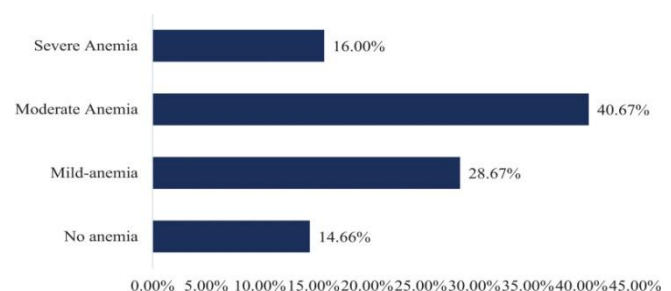


Figure 02: Prevalence and patterns of anaemia among mild, moderate, and severe anaemia

The prevalence of Anaemia was proportional to CKD stage: - 79 (52.67%), 29 (19.33%), and 20 (13.33%) had stage 5, stage 4, and stage 3 CKD, respectively. The severity of Anaemia also varied across CKD stages and a higher percentage of severe Anaemia was found in stage 5 CKD, 17 Figure 2: Image of Prevalence and patterns of Anaemia among stage 3 to 5 CKD patients

Nearly 70% of the participants were diagnosed having stage 3 and stage 4 CKD while only 2.8% of them were at an early stage (stage 1) of CKD. [Figure 2]

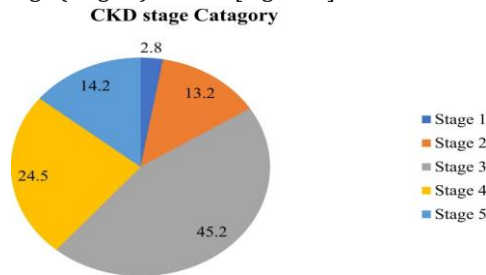


Figure 3: Catagory of chronic kidney diseases.

Figure 3 CKD stages of adult CKD patients attending outpatient department at Addis Ababa Public Hospital, Addis Ababa, Ethiopia, 2020 (n= 387).

### Co Morbidity Disease

A co morbidity is any coexisting health condition. The prefix “co” means together and the word “morbidity” is the medical term for a health condition. It can also be described as cooccurring or coexisting conditions. Comorbidities sometimes interact with each other, but they can also exist entirely separately. Some conditions may raise your risk of developing others, or may commonly occur together. For example, a heart attack often occurs with stroke or vascular disease. Chronic kidney disease may occur with hypertension and Anaemia. Comorbidities are often chronic conditions and can include physical or mental health[27].

### Common co morbidities:

Co morbidities are often long-term conditions. Some of these conditions are very common. For example, about 22.7% of adults in the United States have arthritis. Many adults have at least one chronic condition. The World Health Organization estimates that 87% of deaths in high income countries are due to chronic conditions.

### Common Co Morbidities Include

- Diabetes
- Chronic Obstructive Pulmonary disease
- High blood pressure
- Heart disease
- Arthritis
- Asthma
- Osteoarthritis
- **Cardiovascular Diseases(CVD):** This is major comorbidity where Anaemia in CKF magnifies the risk of cardiovascular events such as:
  - Heart failure
  - Coronary Artery Disease (CAD)

- Left ventricular hypertrophy (thickening of the heart's main pumping chamber)
- Myocardial infraction

- **Diabetes millites:** A significant cause of CKF, diabetes is often seen alongside Anaemia, creating a high-risk combination.
- **Hypertension:** High blood pressure is another common cause and comorbidity of CKD.
- **Other inflammatory conditions:** Rheumatologic diseases and other inflammatory conditions are associated with higher Anaemia prevalence in CKD patients.

Our study demonstrated three important findings: increasing age was associated with increased prevalence of Anaemia; females, African-American race and Hispanic race were at higher risk for having Anaemia; and the presence of one or more comorbidities (such as essential hypertension, hypothyroidism, Chronic kidney disease (CKD), malignancy, rheumatologic disease, Cardiac heart failure (CHF), and coronary artery disease, COPD) was associated with a higher prevalence of Anaemia compared to the patients without these factors. Furthermore, our results also show that patients with a greater severity of Anaemia underwent further diagnostic tests to investigate to cause.

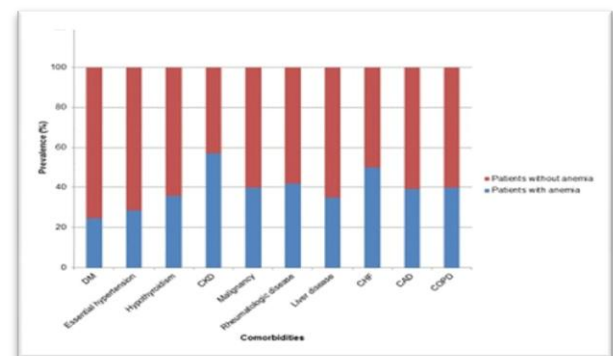


Figure 4: Anaemia on co morbidities in CKD Patients

### Consequences of anaemia on co morbidities in CKD Patients

Anaemia in chronic kidney disease (CKD) patients significantly worsens outcomes and increases risks, especially when combined with other comorbidities like CHF, COPD, diabetes, hypertension. The presence of anaemia exacerbates cardiovascular issues such as heart failure, increases the likelihood of strokes and other complications, elevates the risk of mortality and hospitalizations, and decreases a patient's quality of life [28].

### Impact of Co morbidities

#### Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) in chronic kidney disease patients of anaemia significantly worsens a patient's health outcomes due to the compounding effects of each condition. The combination increases systemic



inflammation, reduces oxygen delivery, and places greater stress on the heart and other organ systems.

#### Cardiac Heart Failure (CHF)

Iron deficiency anaemia significantly worsens outcomes for chronic heart failure (CHF) patients with chronic kidney disease (CKD), increasing mortality, hospitalizations, worsening cardiac and kidney function, and diminishing quality of life by creating a detrimental cardio-renal anaemia syndrome.

#### Rheumatological Diseases

Rheumatologic conditions in CKD patients (like rheumatoid arthritis) can exacerbate anaemia and CKD-Mineral and Bone Disorder (CKD-MBD) through inflammation and iron deficiency, increasing the risk of cardiovascular disease, worsening kidney function, and leading to more severe bone problems.

#### Diabetes

Diabetes is a leading cause of CKD and a significant comorbidity, often leading to the development of anaemia and worsening cardiovascular complications.

#### Hypertension

High blood pressure is another common comorbidity in CKD patients that contributes to both the development and management challenges of anaemia.

#### Cardiac Heart Failure (CHF) Complications

- **Reduced cardiac function**  
Anaemia leads to worse heart function and increased cardiac workload.
- **Progression of kidney disease**  
Anaemia and CHF accelerate the decline of kidney function, potentially leading to end-stage kidney disease (ESKD).
- **Increased hospitalizations**  
Patients with Anaemia and CHF are resistant to standard CHF therapies and experience more frequent hospital stays.

#### Cardiovascular Complications

- **Increased Cardiac Workload:** Anaemia forces the heart to work harder to deliver enough oxygen to tissues, which can lead to conditions like increased cardiac workload, heart failure, and arrhythmias [29].
- **Ischemic Heart Disease:**  
The added strain on the cardiovascular system due to Anaemia can contribute to or worsen ischemic heart disease[30].
- **Hypertension:**  
The interplay between Anaemia and comorbidities like diabetes can lead to or worsen high blood pressure [31].

#### Diabetic Complications

- **Diabetic Retinopathy**  
Anaemia can worsen damage to the blood vessels in the eyes, a condition called retinopathy.
- **Diabetic Neuropathy:**  
The nerve damage associated with diabetes can be worsened by Anaemia.
- **Hyperkalemia:**  
High levels of potassium in the blood are a risk, which can be dangerous for the heart [32, 33].

#### Diet management for Anaemia in ckd patients:

A diet for iron deficiency Anaemia in Chronic Kidney Disease (CKD) patients should focus on iron-rich foods like meat, poultry, fish, beans, and iron-fortified cereals, along with vitamin C-rich foods to boost iron absorption. However, the best approach depends on the patient's CKD stage and individual needs, so consulting a healthcare team, including a dietitian, is crucial for creating a personalized, kidney-friendly plan that addresses potential phosphorus or potassium restriction [34].

Table 3: Based on Nutrients Sources.

S.no	Nutrients	Source (Recommended)	Remarks
1.	Iron	Eggs, chicken, fish, lentils,fortied cereals	Take with vitamin C foods for special treatment.
2.	Vitamin c	Amla guava papaya bell pepper	Helps absobs iron
3.	Folic acid	Cabbage, peas,okra fortified grains	Supports RBC formation
4.	Vitamin B12	Eggs, fish, milk,chicken	Needed for RBC production.
5.	Protein	Egg whites, leon poultry,tofu	Adjust as per CKD stages
6.	Sodium	Fresh foods	Low- salt diet prevents BP rise

#### Kidney-Friendly Iron Sources: Fruit!

Support your iron stores and prevent anemia!

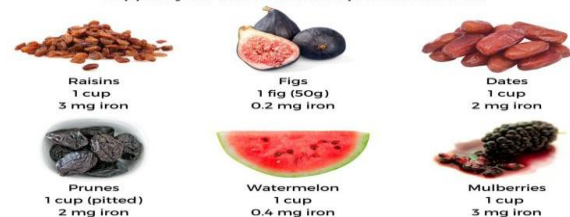


Figure 5: Image of Iron Sources.



Figure 6: Image of Iron Sources.

### Conclusion

Iron deficiency Anaemia is a common and serious complication in patients with chronic kidney disease (CKD), especially in those suffering from associated comorbidities such as diabetes mellitus, cardiovascular diseases, rheumatologic disorders, chronic obstructive pulmonary disease (COPD) and chronic heart failure. The coexistence of these conditions worsens the patient's clinical status by increasing the risk of cardiovascular events, hospitalizations, and mortality while also accelerating the progression to end-stage renal disease (ESRD). The burden of Anaemia in CKD results from multiple factors, including reduced erythropoietin production, inflammation, and poor iron absorption. Therefore, early identification, regular monitoring, and individualized management strategies focusing on correcting iron deficiency are crucial. Proper iron supplementation, dietary modification, and control of comorbid conditions can improve hemoglobin levels; enhance quality of life, and slow CKD progression. Timely and comprehensive Anaemia management can significantly reduce complications and improve overall outcomes in CKD patients.

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Not Declared

### Conflicts of Interest

The authors declare no conflicts of interest.

### Author Contribution

Both are contributed equally

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### Ethical Considerations and Inform Consent

Not Applicable

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