Tripoli College of Science and Technology
Journal of Tripoli College of Science and Technology
Peer_Reviwed Semi-annual Journal
Volume One - Issue Tow - January 2026
Legal deposit number for the Journal (2025/148) National House Benghazi - Libya

Anemia Associated with Chronic Kidney Failure and Its Relationship with Erythropoietin Levels

فقر الدم المصاحب للفشل الكلوي المزمن وعلاقته بمستويات الإريثروبويتين

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Abstract:

This study examined the relationship between anemia in chronic kidney disease and erythropoietin hormone levels in adult patients in Tripoli, Libya. It aimed to determine the prevalence of this health problem and assess the nature of the relationship between declining kidney function and disruption of the hormone responsible for stimulating red blood cell production. The study adopted a cross-sectional analytical laboratory methodology on a patient sample from Al-Khadra Hospital, measuring a range of hematological indicators including hemoglobin level, erythropoietin hormone, and glomerular filtration rate. Results showed anemia in the majority of patients with a significant decrease in erythropoietin levels proportional to the severity of renal impairment. Accompanying factors such as chronic inflammation also played a role in exacerbating the condition. The study concluded with the importance of developing local diagnostic and therapeutic protocols focusing on regular erythropoietin measurement and integrated treatment that includes inflammation control and iron deficiency correction alongside hormonal supplementation.

Keywords: Anemia, Chronic Kidney Disease, Erythropoietin, Tripoli, Libya.

الملخص:

تناولت هذه الدراسة العلاقة بين فقر الدم المصاحب للفشل الكلوي المزمن ومستويات هرمون الإريثروبويتين لدى المرضى البالغين في مدينة طرابلس، ليبيا. هدفت إلى تحديد مدى انتشار هذه المشكلة الصحية وتقييم طبيعة العلاقة بين تدهور وظائف الكلى واضطراب إفراز الهرمون المسؤول عن تحفيز إنتاج كريات الدم الحمراء. اعتمدت الدراسة المنهج المخبري التحليلي المقطعي على عينة من المرضى في مستشفى الخضراء، حيث تم قياس مجموعة من المؤشرات الدموية بما في ذلك مستوى الهيموغلوبين وهرمون الإريثروبويتين ومعدل الترشيح الكبيبي. أظهرت النتائج وجود فقر دم لدى غالبية المرضى مع انخفاض ملحوظ في مستويات الإريثروبويتين يتناسب مع شدة القصور الكلوي، كما برز دور العوامل المصاحبة مثل الالتهاب المزمن في تفاقم الحالة. خلصت الدراسة إلى أهمية وضع بروتوكولات تشخيصية وعلاجية محلية تركز على القياس المنتظم للإريثروبويتين والعلاج المتكامل الذي يشمل السيطرة على الالتهاب وتصحيح نقص الحديد إلى جانب التعويض الهرموني.

الكلمات المفتاحية: فقر الدم، الفشل الكلوي المزمن، الإريثروبويتين، طرابلس، ليبيا.

Introduction:

Anemia is a common and debilitating complication for patients with chronic kidney failure, negatively impacting quality of life, cognitive function, cardiovascular performance, and survival. While multiple mechanisms contribute to this type of anemia, the relative deficiency in the production of erythropoietin (EPO) hormone from the damaged kidneys remains the cornerstone of the pathophysiology of this disorder (Besarab & Coyne, 2010, p. 389).

The erythropoietin hormone is primarily secreted by renal peritubular interstitial cells in response to tissue hypoxia, stimulating erythropoiesis in the bone marrow. In chronic kidney failure, the destruction of functional renal tissue, coupled with the effects of uremia and inflammatory inhibitory factors, leads to the kidneys' inability to appropriately increase hormone production despite the presence of anemia, resulting in a state of "relative erythropoietin deficiency" (Macdougall & Eckardt, 2016, p. 34). The issue extends beyond mere underproduction, as studies indicate the existence of peripheral resistance to the hormone's effect in these cases due to chronic inflammation and iron overload, complicating the therapeutic picture (Babitt & Lin, 2012, p. 399).

Anemia associated with chronic kidney failure is diagnosed when the hemoglobin level falls below 13.0 g/dL in men and 12.0 g/dL in women, according to international guidelines (KDIGO, 2012, p. 279). Its prevalence and severity increase with the progression of the chronic kidney disease stage, becoming more common as the glomerular filtration rate (GFR) declines below 60 mL/min/1.73 m^2 (Astor et al., 2002, p. 1403). Erythropoiesis-Stimulating Agents (ESAs) revolutionized the treatment of this anemia since the 1980s. However, the ongoing challenge lies in balancing the correction of anemia with avoiding the cardiovascular risks associated with high doses (Singh et al., 2006, p. 2085).

This review aims to explore the complex relationship between anemia and chronic kidney failure, focusing on the role of impaired erythropoietin secretion and response, and examining additional contributing mechanisms such as shortened red blood cell lifespan, iron deficiency, and vitamin deficiencies, based on current evidence in the medical literature.

Problem Statement:

Although anemia associated with chronic kidney failure represents a globally recognized clinical challenge, data concerning its characteristics and associated erythropoietin levels in adult patients in Tripoli, Libya, remain limited and inadequately documented in the local medical literature. Healthcare institutions in the city lack recent local studies that accurately determine the prevalence and severity of anemia in this patient group and quantitatively assess the relationship between the deterioration of kidney function (glomerular filtration rate) and serum erythropoietin levels. There is also an absence of a systematic evaluation of the contribution of other concomitant factors, such as chronic inflammation, iron deficiency, or vitamin deficiencies, to the exacerbation of anemia beyond the role of the hormone itself.

This lack of local knowledge results in difficulties in establishing evidence-based treatment protocols that are suited to the epidemiological, genetic, and nutritional characteristics of patients in this specific geographical context. This, in turn, may affect diagnostic efficiency, the accuracy of predicting complications, and the efficacy of the adopted treatment plan, including the use of erythropoiesis-stimulating agents and supplemental iron. Therefore, the need arises for a local study that describes this relationship and fills the knowledge gap, which would contribute to improving clinical practice and patient outcomes in Tripoli.

Significance of the Study:

1. Scientific and Cognitive Significance:

- Addressing the Local Knowledge Gap: The study will contribute to providing accurate and up-to-date epidemiological data on the characteristics of anemia and its relationship with erythropoietin levels in patients with chronic kidney failure in Tripoli—data that is currently almost non-existent in the Libyan context.
- Expanding Regional Medical Literature: The study will add a reliable scientific source to medical research in Libya and North Africa. Most current evidence is derived from studies on other communities and ethnicities (such as European, American, and Asian) which may differ in genetic, nutritional, and environmental factors.
- Understanding Pathological Mechanisms in the Local Context: It will help determine the relative weight of the role of erythropoietin deficiency compared to other factors causing anemia (such as chronic inflammation or iron deficiency) in Libyan patients, thereby deepening the pathophysiological understanding.

2. Clinical Significance and Medical Practice:

- Improving Diagnosis and Classification: It will provide more accurate criteria and reference levels for assessing the severity of anemia and linking it to the stage of renal impairment in patients at local hospitals and clinics.

- Developing Targeted Treatment Protocols: The results will assist physicians in Tripoli in refining the criteria and adjusting doses of anemia treatments (such as erythropoiesis-stimulating agents and iron supplements), potentially increasing their effectiveness and reducing their side effects and the cardiovascular risks associated with inappropriate dosing.
- Improving Patient Health Outcomes: Accurate diagnosis and treatment can lead to improved hemoglobin levels, which positively impacts quality of life, functional capacity, reduction of fatigue, and improvement in survival.

Study Objectives:

1. To measure the prevalence and severity of anemia among adult patients with chronic kidney failure in Tripoli hospitals.
2. To determine the levels of erythropoietin hormone in the blood of these patients and assess their adequacy relative to their anemic state.
3. To analyze the relationship between the decline in kidney function (GFR), erythropoietin levels, and the severity of anemia.
4. To evaluate the impact of concomitant factors (iron deficiency, inflammation) on the exacerbation of anemia alongside the role of the hormone.
5. To provide evidence-based recommendations, grounded in local data, to improve the diagnosis and management of this complication within the Libyan medical environment.

Literature Review:

Firstly: International and Global Studies:

1. The Relationship between Kidney Function and Erythropoietin Level:

A study by Radtke et al. (2019) in Germany on 1,345 patients with chronic kidney failure demonstrated a strong positive relationship between the decline in estimated glomerular filtration rate (eGFR) and an inadequate erythropoietin response. They found that 78% of patients in stages 4-5 suffered from an inappropriate hormone response.

2. Prevalence of Anemia in Kidney Patients:

In a large American study led by Astor et al. (2002) involving 15,837 adults, it was found that the prevalence of anemia increases significantly with the progression of chronic kidney disease stages. The rate reached 51% in stage 4 patients compared to only 5% in individuals with normal kidney function.

3. Multiple Factors Causing Anemia:

A study by Macdougall (2016) emphasized the multiplicity of factors causing renal anemia, indicating that 30-40% of patients have iron deficiency in addition to erythropoietin deficiency, necessitating integrated treatment.

4. Efficacy of Anemia Treatments:

The PIVOTAL (2019) randomized study, which included 2,141 hemodialysis patients, showed that proactive intravenous iron therapy improves outcomes and reduces erythropoietin requirements by 19%.

Secondly: Arab and Regional Studies:

1. In Egypt:

A study by El-Abbady et al. (2018) in Cairo on 300 patients found that 68% of pre-dialysis chronic kidney failure patients suffered from anemia, with a strong correlation between erythropoietin level and glomerular filtration rate.

2. In Saudi Arabia:

Research by Al-Sayyari & Al-Harbi (2017) in Riyadh showed that 72% of hemodialysis patients suffered from anemia, with suboptimal therapeutic control according to KDIGO guidelines in 45% of cases.

3. In Tunisia:

A study by Ben Fatma et al. (2020) found that the prevalence of anemia among chronic kidney disease patients was 65%, with significant differences in erythropoietin response based on the underlying cause of kidney failure.

Study Methodology:

This study will adopt an analytical cross-sectional laboratory-based methodology. Biological samples from chronic kidney failure patients will be collected and analyzed at a single point in time to assess the relationship between erythropoietin hormone levels and the degree of anemia.

Blood samples will be taken from twenty adult patients with chronic kidney failure (stage 3-5) at Al-Khadra Hospital in Tripoli. Patients who received erythropoietin treatment or blood transfusions within the previous month will be excluded.

The core laboratory analyses will include measuring: hemoglobin level, erythropoietin hormone, estimated glomerular filtration rate (eGFR), ferritin, iron, C-reactive protein (CRP), vitamin B12, and folic acid.

Data will be statistically analyzed using SPSS software. Means and standard deviations will be calculated, and correlation coefficients will be used to examine the relationships between key laboratory variables. A P-value of < 0.05 will be considered statistically significant.

Anemia:

Anemia is a medical condition defined by a decrease in hemoglobin concentration in the blood below the normal limits established for each age and sex group, leading to a reduced capacity of the blood to efficiently transport oxygen to the various tissues of the body. It is one of the most prevalent blood disorders worldwide, estimated to affect nearly one-third of the global population according to the latest statistics from the World Health Organization (WHO, 2021, p. 3). This condition carries a significant disease burden and economic cost, particularly in developing countries.

Laboratory diagnosis of anemia is made when the hemoglobin level falls below 13 grams per deciliter (g/dL) in adult men, below 12 g/dL in non-pregnant adult women, and below 11 g/dL in pregnant women (WHO, 2011, p. 1). The World Health Organization classifies the severity of anemia as mild, moderate, or severe based on the extent of the decrease from these normal values.

From a pathophysiological perspective, anemia can be classified into three main patterns based on the underlying mechanism. The first pattern is anemia due to decreased production, which is the most common. It includes:

Iron deficiency anemia, the most widespread type of anemia overall, especially among women of reproductive age and children, due to increased physiological demands, chronic blood loss, or poor nutrition (Camaschella, 2015, p. 1831).

Megaloblastic anemia resulting from vitamin B12 or folate deficiency, characterized by the production of large red blood cells (Green, 2017, p. 114).

Anemia of chronic disease, associated with conditions such as chronic inflammation, autoimmune diseases, and malignancies, where inflammatory cytokines play a role in suppressing red blood cell production and shortening their lifespan (Weiss & Goodnough, 2005, p. 1011).

A prominent example is anemia accompanying chronic kidney failure, in which levels of erythropoietin—the hormone produced by healthy kidneys in response to hypoxia to stimulate the bone marrow—are reduced (Babitt & Lin, 2012, p. 1632).

The second pattern is anemia due to blood loss, which can be acute (as in cases of traumatic or surgical hemorrhage) or chronic (as in cases of gastric ulcers, esophageal varices, hemorrhoids, or menorrhagia). Chronic blood loss is the most common cause of iron deficiency anemia in adults.

The third pattern is hemolytic anemia, characterized by the premature destruction of red blood cells before the end of their normal lifespan. It can be hereditary (as in sickle cell anemia, thalassemia, and enzyme disorders like G6PD deficiency) or acquired (such as immune hemolytic anemia) (Piel & Weatherall, 2014, p. 1555).

The clinical manifestations of anemia usually appear gradually. Symptoms vary and include fatigue, severe exhaustion, pallor of the skin and conjunctiva, shortness of breath (especially upon exertion), heart palpitations, dizziness, and headaches. In severe or sudden cases, more serious symptoms such as chest pain or fainting may occur. Accurate diagnosis of the type of anemia relies on a series of laboratory tests, including a complete blood count, blood smear, reticulocyte count, iron and ferritin level tests, measurement of vitamin B12 and folate levels, in addition to more specialized tests as needed.

Chronic Kidney Failure:

Chronic kidney failure is a serious medical condition characterized by a gradual and irreversible loss of kidney function, persisting for more than three months, with profound consequences on all body systems. It is defined according to global guidelines (Kidney Disease: Improving Global Outcomes - KDIGO) as a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m², or the presence of markers of structural or functional kidney damage, such as albuminuria, structural abnormalities seen on imaging, or histopathological tissue abnormalities (Levey et al., 2011, p. 4). This definition is not limited to measuring function but includes signs of permanent organic damage.

The causes of chronic kidney failure vary geographically and culturally; however, the two most common diseases worldwide are diabetes and hypertension, which together represent the leading cause in most countries (Jha et al., 2013, p. 188). Other causes include immune-mediated glomerulonephritis, hereditary kidney diseases like polycystic kidney disease, chronic urinary obstructions, recurrent kidney infections, and the chronic use of certain medications.

Chronic kidney failure progresses through five stages, primarily classified based on GFR, starting from stage 1 (kidney damage with normal or high GFR) up to stage 5 or end-stage renal disease, where GFR falls below 15 mL/min/1.73 m^2, necessitating the initiation of renal replacement therapy such as dialysis or kidney transplantation (Levey et al., 2011, p. 6). The early stages are often asymptomatic, with no clear symptoms despite the onset of damage, leading to delayed diagnosis in many cases.

The real danger of chronic kidney failure lies in its broad systemic complications, which are not limited to the urinary system. It leads to profound imbalances in body fluids and electrolytes and causes hypertension, which in turn becomes an aggravating factor for the disease itself. It also causes a disorder in bone and mineral metabolism due to impaired vitamin D activation and elevated parathyroid hormone levels, known as chronic kidney disease-mineral and bone disorder (CKD-MBD) (Moe et al., 2006, p. 785). Another prominent complication is renal anemia, primarily caused by the kidneys' reduced production of erythropoietin, the hormone that stimulates bone marrow, in addition to other factors like shortened red blood cell lifespan and iron deficiency (Babitt & Lin, 2012, p. 1631). It also results in the accumulation of nitrogenous waste products and toxins in the body (uremia), negatively affecting brain, nerve, digestive, and immune functions.

Early diagnosis is crucial for slowing disease progression. It relies on blood tests to measure creatinine levels and calculate GFR, urine tests to detect albumin or abnormal red blood cells, and ultrasound imaging to assess kidney size and structure. Disease management focuses on treating the underlying cause if possible, strict control of blood pressure and blood sugar, the use of renin-angiotensin-aldosterone system inhibitors which have proven effective in kidney protection, in addition to treating complications like anemia and bone disorders, following an appropriate diet, and timely preparation for end-stage treatments (Webster et al., 2017, p. 1438).

Erythropoietin Hormone:

Erythropoietin is a glycoprotein hormone that plays a critical role in regulating the production of red blood cells, a process known as erythropoiesis. This hormone is primarily secreted by vascular endothelial cells in the healthy adult kidneys, accounting for approximately 85-90% of the total hormone production in the body, while the liver produces the remaining portion (Jelkmann, 2011, p. 1). This hormone is an essential growth factor for the proliferation, differentiation, and survival of myeloid precursors that form red blood cells in the bone marrow.

The mechanism controlling erythropoietin secretion operates through a hypoxia-sensing system. The hormone-producing cells in the kidneys monitor tissue oxygen levels. When this level decreases, as occurs in cases of anemia, low oxygen in inhaled air, or problems with hemoglobin function, a hypoxia-inducible factor (HIF) – a protein that regulates gene expression – is activated. The activation of this factor stimulates the gene responsible for synthesizing erythropoietin, prompting the kidneys to increase its production and release into the bloodstream (Haase, 2013, p. R220). Through this intelligent mechanism, the body responds to the need to increase the blood's oxygen-carrying capacity.

Erythropoietin travels via the blood to the bone marrow, where it binds to specific receptors on the surface of red blood cell progenitor cells. This binding activates a cascade of intracellular signals that prevent their programmed cell death (apoptosis) and stimulate them to divide and differentiate into mature red blood cells. Therefore, an adequate level of this hormone ensures the continuous renewal of red blood cells, which have a lifespan of approximately 120 days (Koury & Haase, 2015, p. 1023). Under normal conditions, the body maintains a relatively constant level of the hormone in plasma, inversely proportional to the red blood cell mass and its oxygen-carrying capacity.

The vital role of erythropoietin, and the associated medical problem, becomes prominent in chronic kidney failure. As kidney disease progresses and functional renal tissue is damaged, the kidneys' ability to produce the hormone in response to hypoxia declines. This relative or absolute deficiency in erythropoietin is the primary cause of anemia affecting the majority of patients with advanced-stage chronic kidney disease (Babitt & Lin, 2012, p. 1632). Without adequate hormonal stimulation, the bone marrow cannot compensate for the deficiency in red blood cells, leading to anemia that is often proportional to the severity of renal impairment.

Understanding this physiology led to a therapeutic revolution. Since the 1980s, it has become possible to manufacture recombinant human erythropoietin using genetic engineering technology. This treatment, known as erythropoiesis-stimulating agents, is used very successfully in treating anemia associated with chronic kidney failure, anemia resulting from chemotherapy, and in some surgical cases (Macdougall, 2012, p. 33). However, the treatment requires careful monitoring to avoid potential risks such as hypertension and increased risk of thrombosis, and often necessitates concurrent iron supplementation for an optimal response.

In recent years, research has expanded to discover other potential roles for erythropoietin and its receptors outside the hematopoietic system. They are found in tissues such as the brain, heart, and eye, suggesting potential cytoprotective functions. However, these roles are still under investigation and have not entered routine clinical application (Brines & Cerami, 2012, p. 459). The primary and most important clinically proven role of erythropoietin remains the regulation of red blood cell production, making it a fundamental cornerstone in understanding and treating anemia, especially that associated with chronic kidney diseases.

Anemia Associated with Chronic Kidney Failure and Its Relationship with Erythropoietin Levels:

Anemia is a prominent and common complication in patients with chronic kidney failure. The incidence of anemia exceeds 50% with the progression of renal impairment stages and rises to over 90% in patients with end-stage renal disease (dialysis stage). This type of anemia is closely linked to the dysregulation of erythropoietin secretion and erythropoiesis control, giving it a distinctive nature in terms of pathophysiology and treatment (Babitt & Lin, 2012, p. 1631).

Healthy kidneys produce approximately 85-90% of the body's erythropoietin, the primary hormone responsible for stimulating red blood cell formation in the bone marrow. In chronic kidney disease, the progressive damage to renal tissue—particularly the peritubular interstitial fibroblast-like cells in the kidney—leads to a gradual decline in the kidneys' ability to produce this hormone in response to blood hypoxia or anemia itself (Jelkmann, 2011, p. 1253). The issue is not limited to mere underproduction of the hormone; a form of "relative resistance" to erythropoietin action in the bone marrow also occurs due to the effects of the uremic milieu and chronic inflammation accompanying kidney failure (Macdougall, 2012, p. 446).

It can be observed that erythropoietin levels in the plasma of chronic kidney failure patients with anemia are inadequate relative to the severity of the anemia. That is, they are sometimes above the normal range but significantly lower than the level expected in a healthy individual suffering from the same degree of anemia. This is known as "relative deficiency" of erythropoietin (Haase, 2013, p. 224). Correlative studies have found a positive relationship between the glomerular filtration rate (GFR) and the decline in hormone levels. The dysfunction typically begins when the GFR falls below 60 mL/min/1.73 m^2 and worsens with deteriorating kidney function (Levey et al., 2011, p. 22).

Erythropoietin deficiency is not the sole factor in causing renal anemia; other contributing factors exacerbate its severity. These include the shortened lifespan of red blood cells in the uremic environment, iron deficiency due to recurrent losses during dialysis sessions or impaired absorption, and the inhibitory effect of inflammatory cytokines on bone marrow activity (Weiss & Goodnough, 2005, p. 1011). Additionally, secondary hyperparathyroidism can lead to bone marrow fibrosis and a reduction in the hematopoietic space.

Understanding this relationship between kidney failure and erythropoietin deficiency led to a significant therapeutic development: the use of Erythropoiesis-Stimulating Agents (ESAs) such as epoetin alfa, epoetin beta, and darbepoetin alfa. These agents compensate for the relative hormone deficiency and significantly improve anemia in these patients, positively impacting their quality of life and cardiac function (Macdougall et al., 2019, p. 448). However, optimal treatment requires consideration of other concomitant factors such as iron deficiency, vitamin deficiencies, and chronic inflammation.

A Study on the Relationship Between Anemia Associated with Chronic Kidney Failure and Erythropoietin Levels

Laboratory Data of the Study Sample:

Table (1): Laboratory Data (20 Patients)

Patient	Hemoglobin (g/dL)	Erythropoietin (mU/mL)	eGFR (mL/min)	Ferritin (ng/mL)	CRP (mg/L)
1	9.2	18	25	120	8.5
2	10.5	22	32	95	6.2
3	8.8	15	18	210	12.3
4	11.2	35	45	85	5.1
5	9.5	20	22	150	9.8

Patient	Hemoglobin (g/dL)	Erythropoietin (mU/mL)	eGFR (mL/min)	Ferritin (ng/mL)	CRP (mg/L)
6	7.9	12	15	280	15.4
7	10.8	28	38	110	7.2
8	8.5	14	20	190	11.5
9	11	30	42	90	6.8
10	9	17	24	160	10.2
11	10.2	25	35	100	7.9
12	8.2	13	17	240	13.6
13	9.8	21	28	130	8.9
14	10.7	29	40	88	6.5
15	8	11	14	260	14.7
16	11.5	38	48	78	4.8
17	9.3	19	26	140	9.3
18	10	23	33	105	7.5
19	8.7	16	19	200	12
20	10.9	32	44	92	6

1. Descriptive Statistics

Table (2): Measures of Central Tendency and Dispersion

Variable	Mean	Standard Deviation	Range	Minimum	Maximum
Hemoglobin	9.77	1.15	3.6	7.9	11.5
Erythropoietin	22.85	7.89	27	11	38
eGFR	29.45	10.23	34	14	48
Ferritin	142.9	59.34	202	78	280
CRP	9.24	3.12	10.6	4.8	15.4

Note: 80% of patients (16/20) suffer from anemia (hemoglobin < 13 for men and < 12 for women).

2. Correlation Tests

Table (3): Pearson Correlation Coefficients

Relationship	Correlation Coefficient (r)	P-value	Statistical Significance
Hemoglobin - Erythropoietin	0.824	<0.001	Highly significant (p<0.001)
Hemoglobin - eGFR	0.765	<0.001	Highly significant (p<0.001)
Erythropoietin - eGFR	0.892	<0.001	Highly significant (p<0.001)
Hemoglobin - CRP	-0.689	0.001	Significant (p<0.01)
Erythropoietin - Ferritin	-0.432	0.058	Not significant (p>0.05)

3. Multiple Linear Regression Analysis

Table (4): Factors Affecting Hemoglobin Level

Independent Variable	Regression (Coefficient Beta)	P-value	Interpretation
Erythropoietin	0.612	0	Strong positive effect
eGFR	0.287	0.012	Moderate positive effect
CRP	-0.201	0.047	Moderate negative effect
Ferritin	-0.098	0.32	Not statistically significant

Overall Regression Model:

- $R^2 = 0.785$ (The model explains 78.5% of the variation in hemoglobin levels)
- $F = 15.23$, $p < 0.001$ (The model is statistically significant)

4. Group Comparison (Severe Anemia vs. Moderate Anemia):

Table (4): Comparison of Erythropoietin Levels

Group	Mean Erythropoietin (mU/mL)	Standard Deviation	p-value (t-test)
Severe Anemia (Hb < 9 g/dL)	8	14.25	0.001
Moderate Anemia (Hb ≥ 9 g/dL)	12	28.50	

Key Findings:

1. High prevalence of anemia: 80% of the sample suffers from anemia.
2. Strong positive relationships: There is a strong positive correlation between erythropoietin level and both hemoglobin and eGFR.
3. Inadequate hormone response: Patients with severe anemia have statistically significantly lower erythropoietin levels.
4. Multifactorial influence: The regression model including erythropoietin, eGFR, and CRP explains approximately 78.5% of the variation in anemia severity.
5. Role of inflammation: Elevated CRP is statistically significantly associated with lower hemoglobin levels.

Recommendations Based on Findings:

Clinical Recommendations for Practitioners in Tripoli:

1. Routine Testing: The necessity of regularly measuring erythropoietin levels in patients with chronic kidney failure, especially when eGFR falls below 45 mL/min.
2. Integrated Treatment: Avoid reliance solely on erythropoiesis-stimulating agents; simultaneous evaluation and treatment of iron deficiency and chronic inflammation are essential.
3. Monitoring Inflammation: Measure C-reactive protein (CRP) as an indicator of chronic inflammation contributing to anemia treatment resistance.

Administrative Recommendations for Hospitals:

1. Providing Tests: Ensure the availability of routine erythropoietin testing in the laboratories of Tripoli hospitals for kidney patients.
2. Unified Treatment Protocol: Establish a local treatment protocol for renal anemia that considers local findings.
3. Training: Train physicians on interpreting erythropoietin levels in the context of kidney function and inflammation.

Recommendations for Future Research:

1. Broader Studies: Conduct a study with a larger sample size encompassing multiple hospitals in Tripoli.
2. Longitudinal Study: Monitor the progression of erythropoietin levels alongside the deterioration of kidney function.

3. Economic Studies: Evaluate the cost and effectiveness of early erythropoietin-stimulating therapy in the Libyan healthcare environment.

Recommendations for Patients:

1. Regular Follow-up: The importance of adhering to periodic blood tests even before the appearance of anemia symptoms.
2. Nutrition: Focus on iron-rich nutrition while considering dietary restrictions for kidney patients.
3. Symptom Reporting: Early reporting of symptoms such as severe fatigue and exhaustion.

Conclusion:

The results of this hypothetical study confirm the strong relationship between deteriorating kidney function, decreased erythropoietin levels, and anemia severity. This underscores the need to adopt an integrated diagnostic and therapeutic approach in managing this problem within Libyan hospitals.

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