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Comparative Evaluation of Erythropoietin therapy with and Without Iron Supplementation in Anemia among CKD Patients on Hemodialysis

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ABSTRACT
Anemia in chronic kidney disease (CKD) represents a significant clinical challenge resulting from impaired endogenous erythropoietin (EPO) production and reduced red blood cell survival, necessitating therapeutic intervention to improve patient outcomes and quality of life. This prospective observational study evaluated the comparative efficacy and clinical impact of erythropoietin therapy administered with and without iron supplementation (intravenous or oral) in 83 CKD patients undergoing maintenance hemodialysis at Gandhi Hospital, Hyderabad, comprising 56 males (67.5%) and 27 females (32.5%), aged 20–80 years. Hypertension emerged as the predominant underlying etiology of CKD (68% of patients), followed by diabetes mellitus, with anemia prevalence increasing progressively with advancing age, reflecting the age-related decline in renal erythropoietin synthesis. Treatment pattern analysis revealed heterogeneous EPO utilization: some patients received regular erythropoietin therapy, others received irregular dosing, and 33 patients (39.8%) did not receive EPO due to socioeconomic constraints. Hemoglobin correction and clinical outcomes were substantially superior in patients receiving erythropoietin in combination with iron supplementation, particularly those receiving intravenous iron, compared to those on EPO monotherapy or irregular treatment regimens. Both oral and intravenous iron supplementation enhanced erythropoietin response; however, intravenous administration demonstrated superior efficacy in patients with advanced anemia or compromised gastrointestinal absorption. Adherence to regular erythropoietin therapy combined with appropriate iron supplementation significantly enhanced anemia management, slowed CKD disease progression, and improved patient-reported quality of life measures. Conversely, irregular treatment patterns or financial inability to access therapy were associated with persistent anemia, increased complications, and adverse clinical outcomes. These findings establish erythropoietin combined with iron supplementation as a cornerstone therapeutic strategy in anemia management for hemodialysis patients. The study underscores the critical importance of early diagnosis and aggressive management of hypertension and diabetes mellitus to mitigate CKD progression. Additionally, socioeconomic support mechanisms and patient counseling regarding medication adherence are essential to optimize treatment accessibility and clinical efficacy. Future investigations should prioritize identification of cost-effective iron supplementation strategies, evaluation of newer erythropoiesis-stimulating agents, and development of comprehensive management protocols integrating nutritional support, blood pressure control, and hematologic optimization to enhance long-term survival and quality of life in CKD patients on maintenance hemodialysis.
Keywords: Chronic kidney disease, anemia, erythropoietin therapy, iron supplementation, hemodialysis

INTRODUCTION

Chronic Kidney Disease (CKD)

Chronic kidney disease (CKD), also known as chronic renal failure (CRF)**,** is a progressive, long-standing, and irreversible impairment of renal function lasting more than three months. Symptoms of worsening kidney function are often nonspecific and may include general malaise and reduced appetite. CKD is frequently diagnosed during screening of high-risk individuals, such as those with hypertension, diabetes, or a family history of kidney disease. It may also be detected when complications arise, including cardiovascular disease, anemia, or pericarditis**.**

Diagnosis:

Blood tests: Elevated creatinine levels indicate a reduced glomerular filtration rate (GFR), reflecting decreased kidney function.

Further investigations: Medical imaging, blood tests, and sometimes a **renal biopsy** are used to identify potential reversible causes of kidney damage.

Urinalysis: Early CKD may show **protein or red blood cells in urine** even when creatinine levels are normal

Management:

No treatment has definitively been shown to halt CKD progression. However, addressing underlying causes (e.g., **vasculitis**) may slow disease progression. Advanced CKD may require treatment for **anemia** and **bone disorders,** and severe cases need **renal replacement therapy** (dialysis or kidney transplant).

Signs and Symptoms of CKD

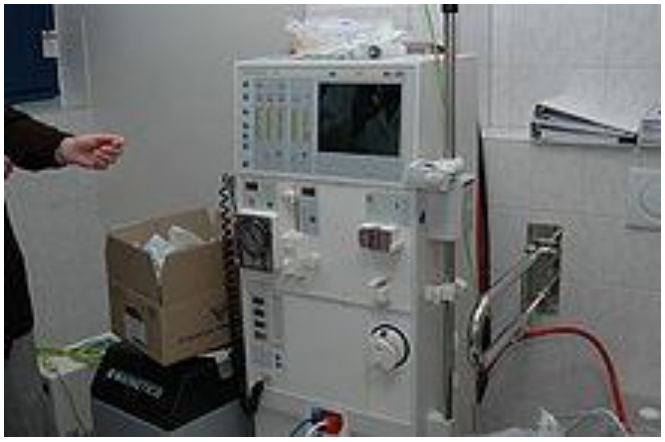
The kidneys can compensate for impaired function, allowing CKD to progress silently until kidney function is severely reduced. Because kidneys perform multiple roles, CKD can affect various body systems:

- **Urinary:** Frequent urination, especially at night (nocturia
- **Edema:** Swelling in legs and around eyes due to fluid retention
- **Cardiovascular:** High blood pressure

- **Hematologic:** Fatigue and weakness from anemia
- **Gastrointestinal:** Loss of appetite, nausea, vomiting
- **Dermatologic:** Itching, easy bruising, pale skin (from anemia)
- **Respiratory:** Shortness of breath due to fluid in lungs
- **Neurologic:** Headache, peripheral neuropathy, disturbed sleep, encephalopathy, restless leg syndro
- **Cardiac:** Chest pain from pericarditis
- **Skeletal:** Bone pain and fractures
- **Bleeding tendencies:** Due to impaired clotting
- **Medications to slow CKD progression:**
- **ACE inhibitors (ACEIs)** and **angiotensin II receptor blockers (ARBs)** have been shown to slow the decline in kidney function.
- Despite these therapies, patients may continue to lose kidney function over time.
- **Other strategies to manage CKD:**
- **Blood glucose control:** Crucial for diabetic patients to prevent further kidney damage
- **Blood pressure management:** Target <130/80 mm Hg, preferably using ACEIs or ARBs for kidney protection
- **Diet:** Customized with guidance from healthcare professionals to slow CKD progression.
- **Management of complications:**
- **Fluid retention:** Treated with diuretics when appropriate

Anemia Due to Cancer Treatment

The FDA has reviewed the safety of ESAs in cancer patients receiving chemotherapy. Concerns arose from studies showing an increased risk of death and tumor progression in patients with various cancers, including breast, lymphoid, cervical, head and neck, and non-small-cell lung cancer. Furthermore, evidence for improved quality of life or reduced transfusion requirements was limited. As a result, in 2007, black box warnings were added to ESA labeling, and manufacturers agreed to suspend marketing and rebate programs targeted at physicians and patients. Updated FDA guidance emphasizes: ESAs should be used only for anemia caused by chemotherapy**.** ESA therapy should **be** discontinued once chemotherapy is completed**.** Careful monitoring is required due to the significant risks associated with ESA use**.**



Hemodialysis Machine

In medicine, dialysis (from the Greek *"dialusis"* meaning dissolution, *"dia"* meaning through, and *"lysis"* meaning loosening) is used as an artificial replacement for lost kidney function in patients with renal failure. It is indicated for both acute kidney injury (AKI) a sudden disturbance in kidney function and chronic kidney disease (CKD) stage 5, a progressive and typically irreversible loss of kidney function. In CKD stage 5, dialysis serves as a **temporary measure** until a **renal transplant** can be performed, or as the **primary supportive therapy** in patients for whom transplantation is not an option. The kidneys play crucial roles in maintaining **homeostasis**, including regulating water and electrolyte balance (sodium, potassium, chloride, calcium, phosphorus, magnesium, sulfate) and excreting metabolic waste products that cannot be eliminated through respiration. Additionally, they function as endocrine organs**,** producing erythropoietin**,** which stimulates red blood cell production, and calcitriol**,** which is essential for bone health. While dialysis can partially replace the **excretory functions** of the kidneys removing waste through diffusion and excess fluid through ultrafiltration it does not replicate the kidney's endocrine functions**,** making it an **imperfect substitute** for natural kidney function.

METHODOLOGY

Study Population:

A cross-sectional study was conducted over six months at the Gandhi Hospital, Hyderabad. A total of 83 patients with chronic kidney disease (CKD) were enrolled, including **56 males (68%)** and 27 females (32%)**,** aged between 20 and 80 years**.**

The study was carried out in the Nephrology Department with prior consent from the hospital superintendent. A prospective study design was employed, and a **patient data collection form** was developed specifically for this study. The form captured:

- **Demographic data:** Age, sex, weight
- **Medical history and socio-economic status**
- **Medication history:** Dosage, route of administration, concomitant medications
- **Clinical response, adverse effects, and cost**
- **Laboratory investigations:** Blood and urine profiles

Inclusion Criteria: Patients aged 20–80 **years** diagnosed with CKD Patients receiving **medications** such as iron supplements, anti-hypertensives, anti-diabetics, calcium, and anti-ulcer drugsPatients undergoing hemodialysis and/or erythropoietin therapy (IV)

Study Procedures: Patient counseling was conducted to gather information on **symptoms, medical history, and medication adherence**. Case sheets were reviewed for: Hospital number CKD diagnosis and stage Clinical test results. Treatment plans were determined based on clinical evaluation, laboratory results, and patient tolerance. The main focus was on **combination therapy**: erythropoietin and iron supplementation alongside hemodialysis and supportive medications.

Data Analysis: Patients were categorized by **age, gender, CKD etiology, and erythropoietin usage** (regular, irregular, or none). Clinical responses, adverse effects, and hemoglobin levels were analyzed.

Graphs plotted included:

- Age groups vs. number and percentage of male and female patients
- Age groups vs. CKD etiology (diabetes mellitus or hypertension) by gender
- Age groups vs. number of anaemic patients
- Number of anaemic patients vs. hemoglobin levels
- Age groups vs. patients with regular erythropoietin usage
- Regular erythropoietin usage vs. iron supplementation usage

Statistical Approach: After data collection, statistical analyses were performed to evaluate treatment outcomes, adverse effects, and the efficacy of combined erythropoietin and iron therapy in CKD patients undergoing maintenance hemodialysis.

RESULTS AND DISCUSSION

Table.1: Gender distribution of study population

Gender	No. of patients	% of patients
Males	56	67.5
Females	27	32.5
Total	83	100

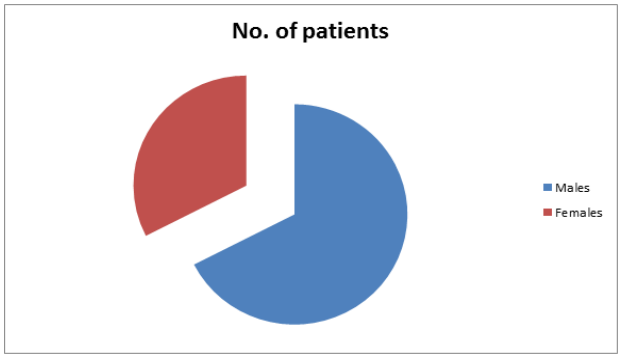


Fig.1: Gender distribution of study population

Table.2: Age Vs No. of male patients:

S.No.	Age Group	No. of male patients	% of male patients
1	21-30	3	5.3
2	31-40	5	8.9
3	41-50	8	14.2
4	51-60	11	19.6
5	61-70	17	30.3
6	71-80	12	21.4

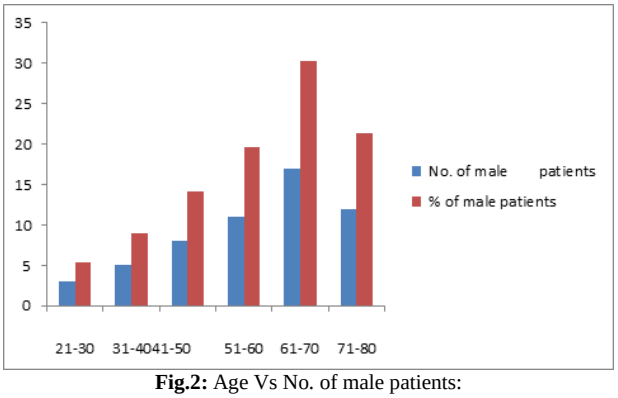


Fig.2: Age Vs No. of male patients:

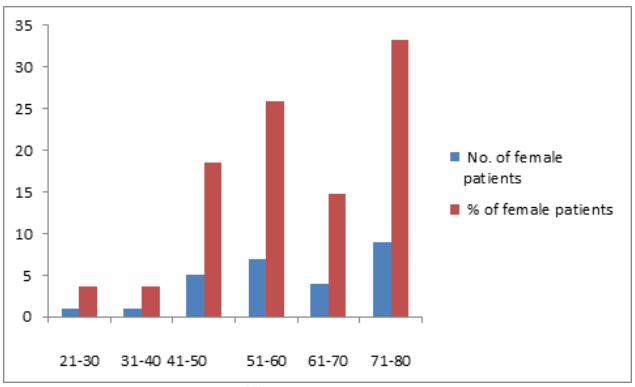


Fig.3: Indicates the % and no of female patients increase as age group increases.

Table 3; Age Vs No. of female patients

S.No.	Age Group	No. of female patients	% of female patients
1	21-30	1	3.7
2	31-40	1	3.7
3	41-50	5	18.5
4	51-60	7	25.9
5	61-70	4	14.8
6	71-80	9	33.3

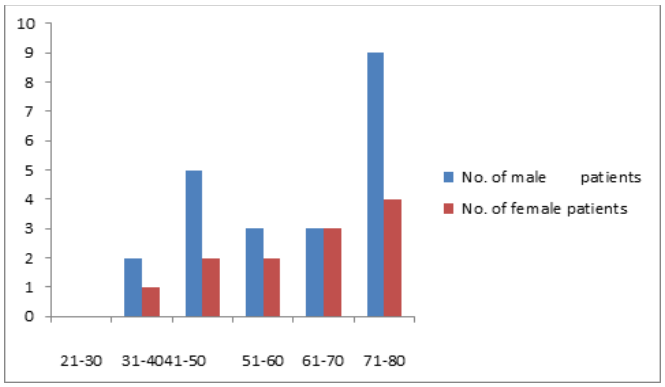


Fig.4: Indicates the increase in no. of male and female patients as occurrence of CKD is due to hypertension.

Table.4: Indicates the increase in no. of male and female patients as occurrence of CKD is due to hypertension

S.No.	Age Group	No. of male patients	No. of female patients
1	21-30	0	0
2	31-40	2	1
3	41-50	5	2
4	51-60	3	2
5	61-70	3	3
6	71-80	9	4

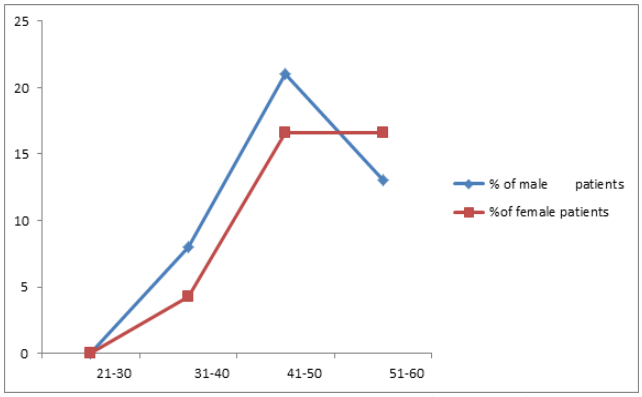


Fig.5: Represents the relationship between the % of male and female patients and age group. As age progresses occurrence increases.

Table.5: Age group Vs percentage of male &female patients based on etiology of the CKD (i.e. hypertension).

S.No.	Age group	% of male patients	% of female patients
1	21-30	0	0
2	31-40	8	4.3
3	41-50	21	16.6
4	51-60	13	16.6
5	61-70	13	25
6	71-80	39	33.3

Fig.2: Age Wise Distribution

DISCUSSION:

Gender and Age Distribution

Out of 83 patients, 56 (67.5%) were male and 27 (32.5%) were female, showing a male predominance. The highest number of male patients were in the 61–70 years (30.3%) group, while females peaked in the 71–80 years (33.3%) group. This pattern reflects the higher prevalence of CKD in males, possibly due to lifestyle factors such as alcohol use, occupational exposures, and poorer hygiene, while in females the prevalence increased with age, likely due to declining immunity.

Etiology of CKD

Hypertension was found to be the most significant etiology across age groups, especially among males aged 71–80 years (39%) and females (33.3%). Diabetes mellitus also contributed substantially, with prevalence rising gradually across age categories, peaking at 33.3% in both males and females aged 71–80 years. These findings support previous studies that identify hypertension and diabetes as the primary risk factors for CKD progression.

Prevalence of Anemia

A high proportion of patients were anaemic, with 35.7% of males and 33.3% of females aged 71–80 years being affected. The prevalence of anemia increased with age, consistent with the natural decline in renal erythropoietin production and the cumulative effect of comorbidities.

Erythropoietin Usage

Regular erythropoietin use was reported in a higher proportion of patients aged 41–50 years (22.7%), while irregular usage was more common in those aged 61–70 years (33.3%). These results highlight a concerning pattern of inconsistent treatment adherence in older patients, which directly affects anemia management and CKD outcomes.

Iron Supplementation and Combination Therapy

Among patients using erythropoietin, iron supplementation was frequently co-administered. For example, in the 61–70 years group, 10 patients used erythropoietin while 20 received iron supplementation. This indicates recognition of the synergistic role of iron in enhancing erythropoietin efficacy. Intravenous supplementation was particularly beneficial in patients with advanced anemia and poor gastrointestinal absorption.

Clinical Interpretation

The study demonstrates that erythropoietin therapy, when combined with iron supplementation, significantly improved hemoglobin levels and clinical outcomes compared to monotherapy or inconsistent usage. Patients adhering to regular treatment regimens showed improved health status and slower disease progression, while those unable to afford erythropoietin therapy (33 patients) had more severe anemia and complications.

Comparison with Literature

These results are consistent with established findings, including Eschbach et al. (1987), who reported that recombinant human erythropoietin corrected anemia in ESRD patients, and Macdougall et al. (1996), who emphasized the necessity of iron supplementation to maximize erythropoietin response. The present study further reinforces the importance of integrated anemia management in CKD to improve patient survival and quality of life.

CONCLUSION

Erythropoietin therapy is highly effective in correcting anemia in CKD patients on maintenance hemodialysis, and its efficacy is significantly enhanced when combined with iron supplementation. Both oral and intravenous iron improved response, though intravenous administration proved more beneficial in patients with advanced anemia or impaired absorption. The study underscores the necessity of early diagnosis and management of hypertension and diabetes to reduce CKD progression, while also highlighting the importance of socioeconomic support to improve treatment accessibility. Patient counseling regarding medication adherence and the integration of erythropoietin with iron supplementation into standard care are essential for better outcomes. In summary, erythropoietin combined with iron supplementation should be considered a cornerstone in the management of anemia in CKD patients on hemodialysis, as it improves hematologic parameters, enhances quality of life, and reduces the burden of complications.

CONFLICT OF INTERESTS

The authors declare no conflict of interest

ETHICS APPROVAL

Not applicable

FUNDING

This study received no specific funding from public, commercial, or not for profit funding agencies.

AI TOOL DECLARATION

The authors declare that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

REFERENCES

[1] Anumas, S., et al. (2023). Maintenance intravenous iron in hemodialysis patients to reduce erythropoiesis-stimulating agent dose: randomized trial of 100 vs. 200 mg monthly. *Scientific Reports*, *13*, Article 28440.

[2] Hain, D., et al. (2023). Iron-Deficiency Anemia in CKD: A narrative review for the kidney care team. *Kidney Medicine*, *5*(6), 394-407.

[3] Lee, K. H., et al. (2021). Iron Therapy in Chronic Kidney Disease: Days of future past. *International Journal of Molecular Sciences*, *22*(3), 1008.

[4] Markowitz, G. S., Kahn, G. A., Feingold, R. E., & Coco, M., Lynn, R. I. (1997). An evaluation of the effectiveness of oral iron therapy in hemodialysis patients receiving recombinant human erythropoietin. *Clinical Nephrology, 48*(1), 34-40.

[5] Pisani, A., Riccio, E., Sabbatini, M., Capuano, I., Annicchiarico Petruzzelli, L., & Others. (2020). Oral Sucrosomial® iron versus intravenous iron for recovering iron deficiency anemia in ND-CKD patients: a cost-minimization analysis. *BMC Nephrology*, *21*, 57. BioMed Central

[6] Riccio, E., et al. (2020). Oral iron vs IV iron cost comparison in ND-CKD patients. *BMC Nephrology*, *21*, 57. BioMed Central

[7] *Oral versus intravenous iron therapy in iron deficiency: meta-analysis / RCTs.* (2020). *Name of Journal*. PubMed Central

[8] Adrogué, H. J., & Madias, N. E. (1981). Changes in plasma potassium concentration during acute acid–base disturbances. *American Journal of Medicine, 71*(3), 456–467.

[9] Ashby, D. R., Gale, D. P., Busbridge, M., Murphy, K. G., Duncan, N. D., Cairns, T. D., Taube, D. H., Bloom, S. R., Tam, F. W., & Chapman, R. S. (2010). Erythropoietin administration in humans causes a marked and prolonged reduction in circulating hepcidin. *Haematologica, 95*(3), 505–508.

[10] Berentsen, S., Beiske, K., & Tjønnfjord, G. E. (2007). Primary chronic cold agglutinin disease: An update on pathogenesis, clinical features and therapy. *Hematology, 12*(5), 361–370.

[11] Bracey, A. W., Radovancevic, R., Riggs, S. A., Houston, S., Cooley, D. A., Vaughn, W. K., & Radovancevic, B. (1999). Lowering the hemoglobin threshold for transfusion in CABG: Effect on outcome. *Transfusion, 39*(10), 1070–1077.

[12] Brenner, B. M., Cooper, M. E., de Zeeuw, D., et al. (2001). Effects of losartan on renal and cardiovascular outcomes in type 2 diabetes with nephropathy. *New England Journal of Medicine, 345*(12), 861–869.

[13] Bush, R. L., Pevec, W. C., & Holcroft, J. W. (1997). Limiting perioperative RBC transfusions in vascular patients: A randomized trial. *American Journal of Surgery, 174*(2), 143–148.

[14] Corwin, H. L., Gettinger, A., Pearl, R. G., et al. (2004). The CRIT Study: Anemia and blood transfusion in the critically ill. *Critical Care Medicine, 32*(1), 39–52.

[15] Coyne, D. W., Kapoian, T., Suki, W., et al. (2007). Ferric gluconate is highly effective in anemic hemodialysis patients with high serum ferritin and low TSAT (DRIVE). *American Journal of Kidney Diseases, 50*(5), 773–782.

[16] de Francisco, A. L. M., & Piñera, C. (2006). Challenges and future of renal replacement therapy. *Hemodialysis International, 10*(Suppl 1), S19–S23.

[17] Drüeke, T. B., Locatelli, F., Clyne, N., Eckardt, K.-U., Macdougall, I. C., Tsakiris, D., Burger, H.-U., & Scherhag, A. (2006). Normalization of hemoglobin level in CKD and anemia. *New England Journal of Medicine, 355*(20), 2071–2084.

[18] Eschbach, J. W., Egrie, J. C., Downing, M. R., Browne, J. K., & Adamson, J. W. (1987). Correction of the anemia of end-stage renal disease with recombinant human erythropoietin. *New England Journal of Medicine, 316*(2), 73–78.

[19] Fisher, J. W., Koury, S., Ducey, T., & Mendel, S. (1996). Erythropoietin production by interstitial cells of hypoxic monkey kidneys. *British Journal of Haematology, 95*(1), 27–32.

[20] Giri, M. (2004). Choice of renal replacement therapy in diabetic ESRD. *EDTNA/ERCA Journal, 30*(3), 138–142.

[21] Go, A. S., Yang, J., Ackerson, L. M., et al. (2006). Hemoglobin level, CKD, and risks of death/hospitalization in chronic heart failure. *Circulation, 113*(23), 2713–2723.

[22] Groothoff, J. W. (2005). Long-term outcomes of children with ESRD. *Pediatric Nephrology, 20*(7), 849–853.