EJPMR, 2026, 13(5), 339-344 **Research Article** **Impact Factor: 8.158**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211
ISSN (P): 3051-2573
Coden USA: EJPMAG

ERYTHROPOIETIN WITH AND WITHOUT IRON: A PROSPECTIVE STUDY ON HEMATOLOGICAL OUTCOMES, QUALITY OF LIFE, AND ECONOMIC BURDEN IN DIALYSIS PATIENTS

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DOI: https://doi.org/10.5281/zenodo.19885986

How to cite this Article: Anushka Kalash*, Shubranshu Panda, Pooja Brahambhatt, Asmita Roy[5], Aman Saini[6], Navneet Saxena. (2026). Erythropoietin with and Without Iron: A Prospective Study on Hematological Outcomes, Quality of life, and Economic Burden In Dialysis Patients. European Journal of Biomedical and Pharmaceutical Sciences, 13(5), 339–344.

Article Received on 02/04/2026 **Article Revised on 23/04/2026** **Article Published on 01/05/2026**

ABSTRACT

Background: Anemia is a common complication in chronic kidney disease (CKD) patients undergoing hemodialysis due to reduced erythropoietin production and impaired iron utilization. **Methods:** This prospective observational study included 51 patients, of whom 50 completed 6-month follow- up. Patients received either erythropoietin (EPO) alone or EPO with intravenous (IV) iron. Outcomes included haematological parameters, quality of life (QoL) and economic burden. **Results:** Combination therapy was associated with higher haemoglobin levels at 6 month (11.23 ± 1.34 vs 10.45 ± 1.21 g/dl; mean difference: 0.78, 95 %CL: 0.05- 1.51; p= 0.042). Serum ferritin, serum iron, and transferrin saturation were also higher in the combination group ($p < 0.05$). Mean haemoglobin increase from baseline was greater in the combination group (+ 3.66 vs +3.07 g/dl). Quality of life scores improved across all domain, though the magnitude was modest. Total treatment cost was higher in the combination group (Rs 7,460 ±910 vs Rs 6,230 ± 850; mean difference: Rs 1,230, 95%CL: Rs 210 – RS 2,250; p = 0.029), no major safety concerns were observed. **Conclusion:** Combination therapy was associated with improved hematological outcomes but higher cost and modest QoL benefits, suggesting the need for individualized treatment strategies.

KEYWORDS: Iron therapy, Erythropoietin, Chronic Kidney Disease, Haemodialysis, Anaemia.

INTRODUCTION

Chronic kidney disease (CKD) is a progressive disorder defined by abnormalities in kidney structure or function persisting for at least three months, with implications for health, as established by the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines.[1] Anaemia is a frequent and clinically significant complication of CKD, primarily driven by inadequate erythropoietin production, iron deficiency, and chronic inflammation, and is associated with increased cardiovascular risk, hospitalization, and reduced quality of life.[31]

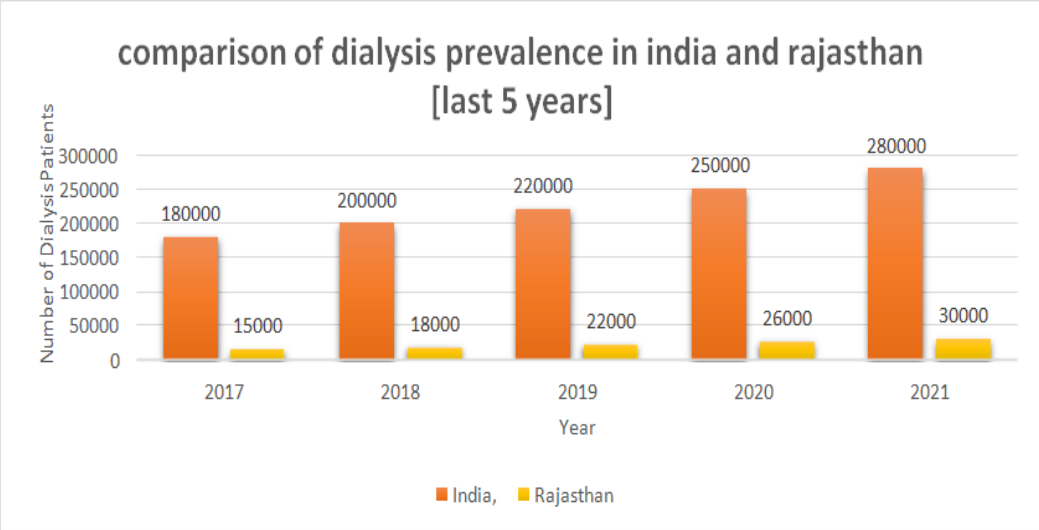
[15-32]The introduction of erythropoiesis-stimulating agents (ESAs), particularly recombinant erythropoietin, has significantly improved anaemia management in CKD patients. However, iron deficiency—both absolute and functional—remains a key contributor to suboptimal ESA response.

[4]To address this, intravenous iron supplementation is commonly used alongside ESA therapy to enhance erythropoiesis and improve haematological outcomes. Existing evidence suggests improved correction of anaemia with combination therapy.[2-3] however, these findings are largely derived from controlled experimental settings.[8-9]

Despite these advances, prior studies have several notable limitations.[11] Many are conducted under controlled conditions that may not reflect real-world clinical practice.[6] Additionally, the majority focus predominantly on laboratory parameters such as haemoglobin levels, with comparatively less emphasis on patient-centred outcomes, including quality of life.[21-23] Economic burden—an essential determinant of treatment sustainability in routine care, especially in resource-limited settings—has also been insufficiently explored. Furthermore, heterogeneity in treatment protocols and

relatively short follow-up durations limit the broader applicability of existing findings.[5-9]

[14]In this context, the present study adopts a prospective observational design to evaluate and compare erythropoietin monotherapy with combination therapy using intravenous iron in patients with CKD undergoing maintenance haemodialysis[7] By integrating haematological outcomes with quality of life assessment and cost analysis, this study aims to provide clinically relevant, real-world evidence to inform individualized anaemia management strategies.[12] However, real-world data integrating clinical outcomes, economic burden, and patient-reported quality-of-life measures in Indian haemodialysis populations remain limited.[13] However, real-world data integrating clinical outcomes, economic burden, and patient-reported quality-of-life measures in Indian haemodialysis populations remain limited.[10]



METHODS

Study Design

Prospective observational comparative study conducted over 6 months.

Study Population and Selection Criteria

A total of 51 patients were screened and enrolled : 50 completed the study (EPO: n = 25, EPO+ iron : n= 25). One patient was lost to follow up.

Patients were allocated into groups based on physician treatment discussion

- Group A (EPO monotherapy): 25 patients
- Group B (EPO + IV iron): 25 patients

Inclusion Criteria

- CKD patients aged 18- 70 years
- On maintenance hemodialysis
- Haemoglobin ≤ 10 g/dl

Exclusion Criteria

- Pregnancy
- Active infection
- Malignancy
- Hypersensitivity to EPO

Intervention Details

Group A received erythropoietin alone. Group B received erythropoietin with intravenous iron (EPO = 4000 IU. iron sucrose = 100 mg/ kg in 100 ml NS)

Outcomes

Primary outcome: Change in haemoglobin from baseline to 6 months, Secondary outcomes: Iron indices, QoL, Economic burden and safety.

QoL Assessment

WHOQOL – BREF questionnaire (score range 0- 100)

Economic Analysis

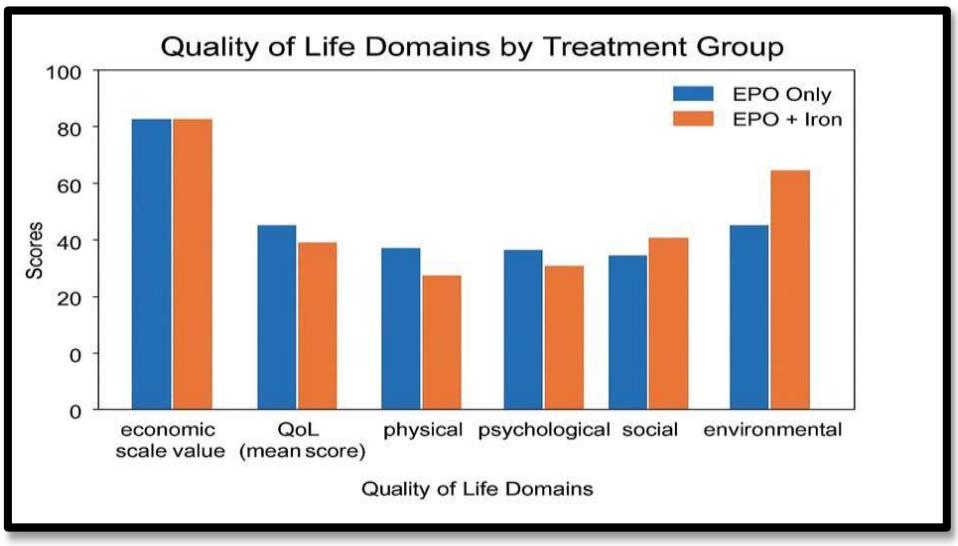
Direct cost (drugs, dialysis, investigations) and indirect costs (travel, wages loss) calculated over 6 months.

Statistical Analysis

Data expressed as mean ±SD. Independent t- test used for between group comparison and paired t – test for within – group baseline vs endpoint comparison. One – way ANOVA applied where appropriate for multiple parameter comparison and mean difference with 95% confidence intervals reported with p- value < 0.05 considered statistically significant. Normality was assessed using Shapiro – wilk test.

Sample size and Power

Based on the observed difference in haemoglobin levels between grouped (mean difference : 0.78 g/dl , pooled SD≅ 1.28) The calculated effect size (cohen's d) was approximately 0.61, indicating a moderate effect. With a total sample size of 50 patients 25 in each and a significance level (α) of 0.05, the study achieved an estimated statistical power of approximately78% to detect difference in haemoglobin between groups.



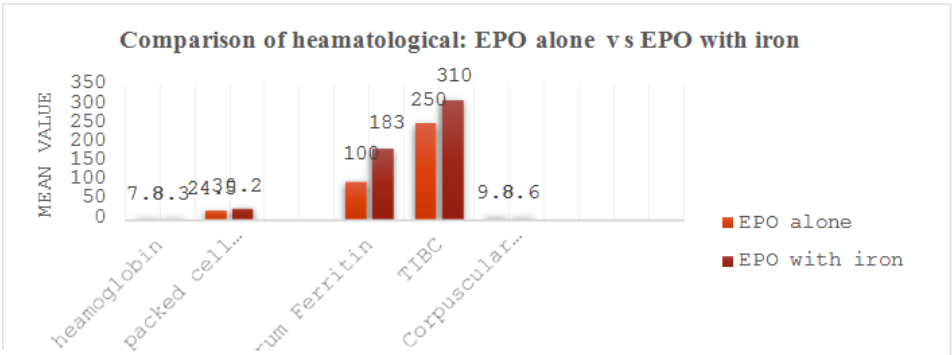


Figure 1: Mean values of haemoglobin and iron indices at 6 months in patients receiving erythropoietin (EPO) alone versus EPO with intravenous iron. Error bar represents standard deviations.

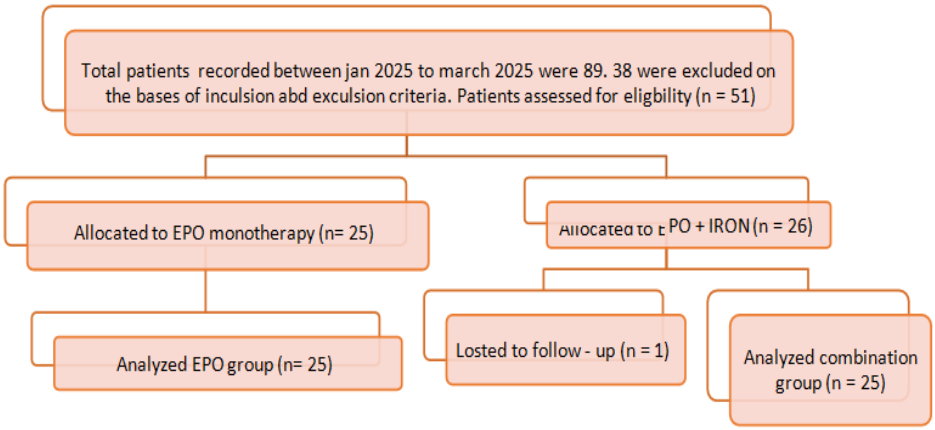


Fig. 2: A schematic STROBE diagram of patients exclusion and inclusion methodology: The flowchart outline the methodological process used to screen the study population in accordance with STROBE guidelines. It presents the applied inclusion and exclusion criteria, along with the resulting final sample size, in a stepwise schematic representation.

DISCUSSION

[21-20]The present prospective observational study conducted over a 6-month period starting from jan to june demonstrates that erythropoietin (EPO) combined with intravenous (IV) iron is associated with greater improvement in haemoglobin and iron indices compared to EPO monotherapy in patients undergoing maintenance haemodialysis.[21-24] These findings reinforce the role of iron repletion in addressing functional iron deficiency and enhancing erythropoietin responsiveness.The results are consistent with previous studies, including Zahid et al.[25], Lain et al.[27-29], and Roger et al.[28] which have reported

improved haematological response with IV iron supplementation and reduced erythropoiesis-stimulating agent requirements. The observed association between serum ferritin and post-treatment outcomes further supports the importance of adequate iron availability in erythropoiesis. The findings are also consistent with data from Indian settings, including studies by Kaur et al.[17] and Shaikh et al.[15], which highlight the dual challenge of optimizing treatment outcomes while managing economic burden in haemodialysis populations.[18-19] This alignment with real-world Indian data enhances the generalizability and clinical relevance of the present study. No significant differences in renal function or electrolyte parameters were observed between groups, suggesting a favourable short-term safety profile of combination therapy, consistent with previous reports.[26]

A key strength of this study is the integration of clinical, economic, and patient-reported outcomes. Although statistically significant improvements were observed in quality-of-life domains, the magnitude of improvement was modest, indicating that correction of anaemia alone may not translate into substantial overall improvement in patient well-being. These findings are consistent with prior studies[29] Additionally, the significantly higher cost associated with combination therapy is in agreement with previous economic evaluations[30-32], highlighting an important limitation in resource-constrained settings.[33] The magnitude of the observed between-group differences suggests a large effect size, supporting the adequacy of the sample size in detecting clinically meaningful differences. However, several limitations should be considered.[16] The single-centre design and relatively small sample size may limit generalizability. The six-month follow-up period may be insufficient to assess long-term safety outcomes, including iron overload and cardiovascular risk. Furthermore, treatment allocation based on physician discretion introduces potential selection bias, and the absence of adjustment for confounding variables may influence the observed associations. Overall, the findings highlight an important efficacy–cost trade-off. While combination therapy is associated with improved haematological outcomes, its higher economic burden and modest impact on quality of life underscore the need for individualized, context-specific treatment strategies.[34]

RESULT

A total of 51 patients undergoing maintenance hemodialysis were included in which one was lost to follow up. Patients receiving erythropoietin in combination with intravenous iron demonstrated improved hemoglobin levels compared to the monotherapy group (mean ± SD: 10.45 ± 1.21 vs 11.23± 1.34 g/dL, $p < 0.05$). Similarly, serum ferritin, serum iron, and transferrin saturation were improved in the combination group, while total iron-binding capacity was reduced, indicating improved iron availability and utilization (Table 1.1, $p < 0.05$).

The economic evaluation revealed that the total treatment cost was significantly higher in the combination therapy group compared to erythropoietin alone (mean ± SD: 6,230 ± 850 vs 7,460 ± 910 INR, $p < 0.05$), reflecting increased financial burden (Table 1.2). Over Quality-of-life assessment demonstrated statistically significant improvements in the combination therapy group across multiple domains, including physical, psychological, social, and environmental domains ($p < 0.05$). However, despite statistical significance, the overall magnitude of improvement was modest and may be of limited clinical relevance (Table 1.3). all, combination therapy resulted in improved hematological outcomes at the expense of higher treatment cost, with only limited improvement in quality-of-life measures (Table 1.4).

1.1) COMPARATION BETWEEN EPO ALONE AND EPO WITH IRON GROUP

Table 1.1: combination therapy (epo + intravenous iron) demonstrated a statistically significant improvement in haematological parameters compared to EPO monotherapy (p< 0.05).

S.NO	PARAMETER	GROUP A (Mean ± SD)	GROUP B (Mean ± SD)	Mean difference (95% CL)	P- value
1	Haemoglobin (g/dl)	10.45 ± 1.21	11.23 ± 1.34	0.78(0.05 – 1.51)	0.042
2	Serum ferritin (ng/ml)	25.6 ± 6.8	32.4 ± 7.1	6.8(1.2 – 12.4	0.031
3	Serum Iron (µg/dl)	54.8 ± 9.3	63.2 ± 8.7	8.4(2.1 – 14.7)	0.027
4	TIBC (µg / dl)	312 ± 28.4	298 ± 25.6	-14(- 28.5 – 0.5)	0.056
5	Transferrin Saturation (%)	18.2 ± 4.1	21.7 ± 3.8	3.5(0.2 – 6.8)	0.040

1.2) ECONOMIC BURDEN

Table 1.2: the total treatment cost was significantly higher in the combination therapy group compared to EPO monotherapy ($p<0.05$)

1.3) Quality of Life (QoL)

S.NO	PARAMETER	GROUP A (Mean ± SD)	GROUP B (Mean ± SD)	Mean difference (95% CL)	P-value
1	Direct medical cost (Rs)	4,250 ± 680	5,120 ± 720	870(120- 1,620)	0.038
2	Indirect cost (Rs)	1,980 ± 410	2,340 ± 460	360(50 – 670)	0.044
3	Total Economic Burden (Rs)	6,230 ± 850	7,460 ± 910	1,230 – 2,250	0.029

Table 1.3: Combination therapy showed modest improvement in quality of life domains, with limited overall statistical signification between groups.

S.NO	DOMAIN	GROUP A(Mean ±SD)	GROUP B (Mean ± SD)	Mean difference (955 CL)	P-value
1	Physical Health	52.4 ± 8.7	61.2 ± 9.1	8.8(1.5 – 16.1)	0. 022
2	Psychological health	48.6 ± 7.9	56.8 ± 8.2	8.2(1.0 – 15.4)	0.031
3	Social Relationships	55.1 ± 9.4	62.7 ± 8.9	7.6(0.8 – 14.4)	0.041
4	Environmental well- being	50.8 ± 8.2	58.3 ± 7.6	7.5(0.9 – 14.1)	0.037

Table 1.4: Baseline demographic and clinical characteristics stating all baseline variables have p> 0.05. there is no significant difference between the two groups at baseline.

S.NO	Variable	Group A(EPO alone)	Group B (EPO +Iron)	P- value
1	Age(years)	37.0 ± 12.4	37.7 ± 9.8	0.84
2	Haemoglobin(g/dl)	7.38 ± 0.95	7.57 ± 1.18	0.54
3	Gender(M/F)	14/9	15/10	0.82

CONCLUSION

Combination therapy was associated with improved haematological parameters but higher cost and limited QoL benefits which show the modest improvement in quality of life and substantially higher cost underscore a disconnect between biological efficacy and patient-centred benefit. These findings emphasize the need for individualized, cost-conscious anaemia management**,** particularly in resource-limited settings, and highlight the importance of integrating clinical, economic, and quality-of-life outcomes in future research.

FUTURE RECOMMENDATION

Future studies should focus on including a larger and more diverse population to improve the generalizability of findings, along with conducting long – term follow up to better understand disease progression. Multi- centre studies are warranted to minimize selection bias and improve generalizability across diverse health care settings.

Ethical Approval

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee. (JNUIMSRC/IEC/2025/07).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest in this paper.

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