DOI: https://doi.org/10.54393/pjhs.v7i6.3282

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 06 (June 2026)

Original Article

OPEN ACCESS

Role of Epoetin-α in the Management of Anemia in Chronic Kidney Disease (CKD) Patients

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ARTICLE INFO

Keywords:
Anemia, Epoetin-alpha, Efficacy, Chronic Kidney Disease

How to Cite:
Afzal, H., Ahmed, A., Hussain, M., Malik, M. K., & Hussain, A. (2026). Role of Epoetin-α in the Management of Anemia in Chronic Kidney Disease (CKD) Patients: Epoetin-α in the Management of Anemia in Chronic. Pakistan Journal of Health Sciences, 7(6), 03-07. https://doi.org/10.54393/pjhs.v7i6.3282

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Received Date: 30th June, 2025
1st Revision Received: 6th November, 2025
2nd Revision Received: 18th December, 2025
3rd Revision Received: 28th February, 2026
Acceptance Date: 10th March, 2026
Published Date: 30th June, 2026

ABSTRACT

Anemia in chronic kidney disease (CKD) contributes to morbidity, increased transfusion requirements, and cardiovascular risk, and is mainly caused by insufficient erythropoietin (EPO) synthesis. Erythropoietin-stimulating agents (ESAs) are a crucial therapy for managing anemia associated with CKD. Before the introduction of ESAs, blood transfusions were primarily used to manage anemia in these patients. Epoetin-α was the first erythropoietin analog to be used clinically. **Objective:** To find the efficacy of epoetin-α in increasing hemoglobin in chronic kidney disease patients. **Methods:** A cross-sectional study was conducted at Pakistan Air Force Hospital Mushaf, Sargodha, including 189 CKD patients. All patients received Epoetin-α at a dose of 4000 IU subcutaneously once weekly. Baseline complete blood count (CBC) was recorded before treatment, and a follow-up CBC was performed after one month. Data were collected through a questionnaire and analyzed using SPSS version 24.0. **Results:** The study included 189 patients, of whom 121 were male and 68 were female. The mean age was 58.7 ± 14.39 years. The mean hemoglobin before Epoetin-α therapy was 7.5 ± 0.76 g/dL, which increased to 8.9 ± 1.28 g/dL after one month. Erythropoietin was found effective in 82% of patients, while 18% showed an insufficient response. Post-treatment chi-square analysis revealed statistically significant associations for age, baseline hemoglobin, and duration of dialysis ($p<0.001$), whereas gender was not significantly associated ($p=0.202$). **Conclusions:** Epoetin-α stands as a cornerstone in managing CKD-related anemia. Despite the efficacy, optimal dosing strategies, long-term safety profiles, and personalized treatment algorithms necessitate further research.

INTRODUCTION

Chronic kidney disease (CKD) is the most common and prevailing health issue with an overall prevalence of 21.2% in all age groups in Pakistan and 24.2% in the high-risk population [1]. Anemia in CKD leads to further morbidity, transfusion requirement, and cardiovascular risks. It has a high incidence and prevalence, with a recent study in Japan suggesting a prevalence of 40.1% in stage 4 and 60.3% in stage 5 CKD [2]. The higher prevalence among CKD stage 3 to 5 was also revealed in an Ethiopian study [3]. Human Erythropoietin (EPO), a hormone secreted by kidney, which is called a glycoprotein, under the influence of Hypoxia Inducible Transcription Factor (HIF), regulates the production of erythrocytes. Normochromic normocytic anemia in CKD is mainly due to insufficient Erythropoietin (EPO) synthesis by the kidney as Glomerular Filtration Rate (GFR) falls and worsens with disease progression [4]. Iron and erythropoiesis-stimulating agents (ESAs) are a major form of treating anemia of chronic kidney disease and have been used for decades [4]. Treatment with erythropoietin analog was started in 1989, before which patients with symptomatic anemia were managed with blood transfusions [5, 6]. Epoetin-α was the 1st used erythropoietin analog, then darbepoetin was approved, and now other agents are being studied like Methoxy

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Polyethylene Glycol-Epoetin beta, Constant Erythropoiesis Receptor Activator, Prolyl Hydroxylase Inhibitors (HIF stabilizers), and others [4, 5]. Use of Erythropoietin analogs has a clear benefit in patients with Hb< 10.0g/dL with a possible increase of hemoglobin around 1 g/dL after 1st month of therapy [5]. A Thai study indicated the efficacy of epoetin-alpha, with mean Hb increased from 7.39 g/dL to 11.15g/dL [7]. Being under-responsive and over-responsive to EPO were defined as less than 1g/dL increase in hemoglobin level within 2 to 4 weeks and more than 1.0 g/dL during a 1- to 2-week period of treatment in an Iranian study [8]. Studies have been conducted worldwide on the management of anemia in CKD and have compared different agents.

No previous studies have been conducted in this setting as Pakistan has no local efficacy data on epoetin- 2 in CKD anemia. The safety profiles in the long-term, the most effective dosing regimen, and individualized treatment algorithms have not studied. Single-center at PAF Hospital Mushaf restricts the generalizability levels in Pakistan. Non-probability consecutive sampling brings about selection bias. One month follow-up will not be sufficient time to evaluate long-term response or adverse responses. This study aimed to find the efficacy of epoetin-α in the management of anemia in CKD patients, as this is the only ESA currently being used in this setting, and no such study has been conducted here previously.

METHODS

It was a cross-sectional study, carried out over a period of 6 months, from 1st June 2023 to 1st Dec, 2023, after getting approval from the hospital IRB (MSF(H)/308/3/1/Trg) Dated February, 2022, at Pakistan Air Force Hospital Mushaf, Sargodha. It included patients who were already on HD or not on dialysis. The method of non-probability consecutive sampling was used to select patients. A sample size of 189 patients was estimated using an efficacy of 60% from a recent Thai study [7]. The sample size was taken by using WHO's sample size calculator, with 95% confidence interval and total precision of 7. Inclusion criteria included age (20-80 years of any gender), patients with estimated GFR of less than 30 (CKD stage IV and V), CKD patients on hemodialysis or renal support medications, and patients with serum ferritin above 100µg/L. Exclusion criteria were CKD patients not receiving epoetin, patients who fail to follow up, Patients who deny informed consent, and patients with uncontrolled diabetes and hypertension. Permission was taken from patients. Patients were asked about their hemodialysis status and duration, as well as any comorbid conditions. All participants underwent a newly collected CBC to determine their hemoglobin concentration. CBC was performed using a Kx-21 analyzer. Epoetin was started at 4000IU once a week, subcutaneously. Epoetin injection (Eritrogen 4000 IU) was received from the hospital medical store, where its temperature was maintained at 4°C. Before each administration, blood pressure was checked, and patients were observed for any anaphylactic reaction. Red flag signs of thromboembolic events were explained to patients. Patients were asked for weekly follow-ups to confirm proper dosage and administration of epoetin on an outpatient basis. All of the patients received the same dose of iron and vitamin C supplements. After 1 month, CBC was repeated, and efficacy was labeled if Hb improved by ≥1g/dL at the end of 1st month, as was indicated in other studies, including a recent study from Iran [8].

The data were collected by using a questionnaire and was analyzed by using SPSS version 24.0. Analysis included means and SD about quantitative data like age and hemoglobin, and frequencies for qualitative data like gender and efficacy. Data collected were stratified for age, gender, pre-treatment Hb, and duration of dialysis. Post-stratification chi-square was applied, and a p-value of < 0.05 was considered significant.

RESULTS

Out of 189 patients, 121 patients were males i.e 64% and 68 were females i.e 36%. Mean age of patients was 58.7 years (SD = 14.39; 95% CI: 56.6–60.8 years). Mean Hb before starting epoetin was 7.5g/dL with (SD = 0.76; 95% CI: 7.39–7.61 g/dL). The mean hemoglobin level after 1 month of therapy was 8.9 g/dL (SD = 1.28; 95% CI: 8.72–9.08 g/dL). The mean change in Hb was 1.4g/dL (95% CI: 1.2–1.6, p<0.001). 140 patients (74.1%) were on dialysis at the time of study, while the remaining 49 (25.9%) were not on hemodialysis. Out of 140 patients, who were on hemodialysis, 26 (17.8%) were having dialysis for less than a month, 77 patients (52.7%) for a duration between 1-6 months, 16 (11%) between 6months to a year, and 27 (18.5%) patients were on dialysis for more than a year. The X-axis represents HD duration, and the y-axis the proportion of patients. It shows the %age of patients in each HD category (Figure 1).

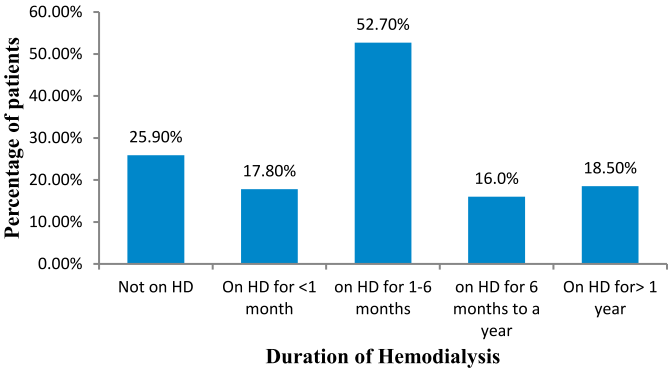

Figure 1: Distribution of Patients by Hemodialysis Status

Out of a total of 189 patients, epoetin was found efficacious (Hb improved greater than 1g/dL in 1 month) in 155 patients

DOI: https://doi.org/10.54393/pjhs.v7i6.3282

i.e 82% and was not efficacious in 34 patients i.e 18%. It demonstrates the distribution of 189 patients on the y-axis across two x-axis categories, i.e., Hb increased and not increased(Figure 2).

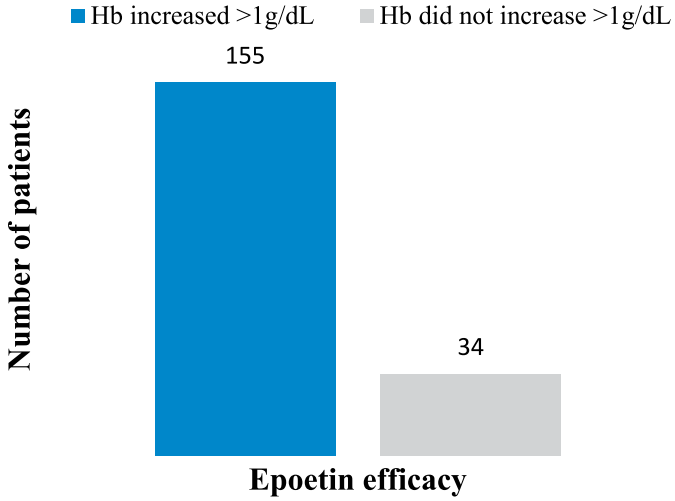

Figure 2: Epoetin Efficacy

The data were stratified for age, gender, pre-treatment Hb, and time period of dialysis, and post stratification Chi square was used to compare efficacy in different parameters. It revealed that in age groups, chi-square was statistically significant for age with a p-value of <0.001. It reveals that at both extremes of ages epoetin has higher efficacy. Epoetin-α was most effective in patients aged 20–40 years (94.7%) and 61–80 years (92.0%), but lower efficacy in the 41–60 years group (68.7%), p<0.001. For gender, chi square test was not significant, and the p-value was 0.202. For hemoglobin before epoetin, chi square was significant with a p-value of <0.001. Higher Hb was associated with better outcomes. There was no significant association between dialysis and efficacy, with a p-value of 0.008. However, for the duration of dialysis, the p-value was <0.001, and the increased duration of dialysis had better results(Table 1).

Table 1: Efficacy Analysis by Various Factors(Chi-Square Test)

Factors	Category	Hb Increased >1g/dL	Hb Didn't Increase >1g/dL	Total	p-value	X^2	df
Age (Years)	20-40	18	1	19	<0.001	17.91	2
	41-60	57	26	83			
	61-80	80	7	87			
Gender	Male	96	25	121	0.202	1.71	1
	Female	59	9	68			
Hb Before Epoetin (g/dL)	6.00	0	10	10	<0.001	>60	9
	6.40	5	0	5			
	6.50	8	0	8			
	7.00	51	14	65			
	7.80	11	0	11			
	7.90	10	0	10			
	8.00	42	10	52			
	8.30	10	0	10			
	8.40	5	0	5			
	9.00	13	0	13			
Either on Dialysis or not	Yes	121	19	140	0.008	7.14	1
	No	34	15	49			
Duration of Dialysis	Less than 30 Days	9	17	26	<0.001	80	3
	1 to 6 Months	71	6	77			
	6 Months to One Year	16	0	16			
	More than One Year	27	0	27			

DISCUSSION

Chronic Kidney Disease(CKD)shows a very important world health burden, influencing millions of people globally. A meta- analysis from South Asia revealed that in South Asia, 1 in 7 adults had CKD. It further elaborated that the pooled prevalence of chronic kidney disease (CKD) in the general population was estimated at 14% (95% CI: 11–18%), with prevalence rates of 15% (95% CI: 11–20%) among adult males and 13% (95% CI: 10–17%) among adult females. Among high-risk groups, the prevalence of CKD was 27% (95% CI: 20–35%) in adults with hypertension, 31% (95% CI: 22–41%) in those with diabetes, and 14% (95% CI: 10–19%) in individuals who were overweight or obese. The prevalence of CKD of unknown origin in endemic regions was reported as 8% (95% CI: 3–16%)[9]. CKD might be associated with a lot of functional disabilities [10]. Among the myriads of complications associated with CKD, anemia is one of the major prevalent and clinically established impacts. Determinants of anemia in CKD are multifaceted [11]. A study in Ethiopia revealed overall prevalence of anemia was 85.33%. Among these patients, 28.67% had mild anemia, 40.67% had moderate anemia, and 16% had severe anemia. Stage 4 CKD, stage 5 CKD, and CKD duration of less than one year were significantly associated with anemia. Study indicated that the prevalence of anemia among patients with stage 3 to 5 CKD was notably high, and that anemia was significantly associated with both the severity and duration of CKD [3]. A systematic analysis of patients in Sub-Saharan countries revealed that more than half of the CKD patients had anemia [12]. The anemia found in CKD stems primarily from the impaired formation of erythropoietin by dysfunctional kidneys, leading to decreased red blood cell production and subsequent tissue hypoxia. ESAs like epoetin alpha and darbepoetin are used in the management of anemia in CKD[13]. A study in Thai patients revealed that Hb level increased in all enrolled patients, and 60% of patients achieved target or more than target Hb after completion of the drug [7]. The study's findings underscore the remarkable efficacy of epoetin alpha in ameliorating anemia among CKD patients. Mean levels of hemoglobin significantly increased from 7.39g/dL before

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therapy to 11.5 g/dL after one month of treatment, highlighting the robust erythropoietic response elicited by epoetin alpha. A recent study in patients with myelodysplastic syndrome revealed an increase in Hb in 41.1% of patients using epoetin alpha [14]. For this study, epoetin was administered via the subcutaneous route; the study employed the SC route of administration due to the multiple advantages of the SC route over the IV route, notably a lower overall dose to get a similar target Hb level as well as the levels of hematocrit and a less frequent dosing frequency [15]. All ESAs need parenteral administration [16]. However, parenteral administration might be inconvenient for patients, which has led to novel oral therapies [17]. Other than this, a lot of anemic patients are refractory to erythropoietin effects due to inflammation, deranged iron utilization, and generation of EPO antibodies [18]. Beyond the overall efficacy of epoetin alpha therapy, our study elucidated several key factors influencing treatment outcomes in CKD-related anemia. Age emerged as a significant determinant of treatment response, with both younger and older patients demonstrating higher rates of efficacy compared to middle-aged individuals, while gender was not found as determinant of treatment response. Further exploration into age-specific treatment algorithms and considerations is warranted to optimize therapeutic outcomes and tailor interventions to individual patient needs. Contrary to age, gender did not emerge as an important predictor of treatment efficacy in the study population. Both male and female patients exhibited comparable response rates to epoetin alpha therapy, suggesting that gender may not exert a substantial influence on the erythropoietic response to treatment in CKD-related anemia. The underlying mechanisms driving the differences in age and gender-based response remain incompletely understood and warrant further investigation. Baseline hemoglobin levels emerged as a strong predictor of treatment response, with patients presenting higher baseline hemoglobin levels demonstrating more robust responses to epoetin alpha therapy. This finding underscores the significance of pre-detection and treatment in managing CKD-related anemia to prevent disease progression and optimize treatment outcomes. Moreover, the time period of dialysis emerged as a critical determinant of treatment efficacy, with longer durations of dialysis correlating with improved response rates to epoetin alpha therapy. This highlights the dynamic nature of CKD-related anemia and the need for tailored treatment strategies that account for disease progression and evolving clinical needs over time. Epoetin alpha represents a cornerstone in the management of CKD-related anemia, offering a safe and effective therapeutic option for restoring hemoglobin levels and improving clinical outcomes in affected individuals. However, optimizing treatment outcomes requires a comprehensive understanding of the complex interplay between patient demographics, disease characteristics, and treatment modalities. Treatment with ESAs with a near-normal hemoglobin range can lead to increased risk of certain cardiovascular events, stroke, vascular access thrombosis, and death [19, 20]. Further research is warranted on the side effects of ESAs.

There were some shortcomings in the study. However, the current cross-sectional design of the observation cannot establish causality. There is no point in giving the same dose of 4000 IU of normal vitamin D weekly to everyone, rather than adjusting the dosage according to each patient's clinical condition. There was no evaluation of erythropoietin (EPO) resistance variables, such as inflammation or malnutrition. Future research should employ multicenter randomized controlled trials with extended follow-up periods (6–12 months) to compare epoetin-α with newer agents such as darbepoetin and HIF stabilizers, while incorporating assessments of iron status, inflammatory biomarkers, and malnutrition to identify predictors of erythropoietin resistance and to develop evidence-based, individualized dosing algorithms specifically for Pakistani CKD populations.

CONCLUSIONS

The findings of current study underscored the significant efficacy of epoetin-alpha in ameliorating anemia. Our study identified several key factors influencing treatment outcomes in CKD-related anemia, including age, gender, baseline hemoglobin levels, and the duration of dialysis. Age, baseline hemoglobin, and duration of dialysis had a significant impact on the increase in hemoglobin after erythropoietin in our study.

Authors' Contribution

Conceptualization: HA
Methodology: HA, AA, MH, MKM, AH
Formal analysis: HA, MKM, AH
Writing and Drafting: HA, AA, MH, AH
Review and Editing: HA, AA, MH, MKM, AH

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

DOI: https://doi.org/10.54393/pjhs.v7i6.3282

REFERENCES

[1] Khan A, Cheema MF, Fatima R, Cheema SS, Butt Z, Gillani S *et al.* Prevalence of Chronic Kidney Disease in a High-Risk Population in Urban Lahore, Pakistan: A Cross-Sectional Study. Cureus. 2024 Jun; 16(6). doi: 10.7759/cureus.63296.

[2] Sofue T, Nakagawa N, Kanda E, Nagasu H, Matsushita K, Nangaku M *et al.* Prevalence of Anemia in Patients with Chronic Kidney Disease in Japan: A Nationwide, Cross-Sectional Cohort Study Using Data from the Japan Chronic Kidney Disease Database. PLOS One. 2020 Jul; 15(7): e0236132. doi: 10.1371/journal.pone.0236132.

[3] Bishaw F, Woldemariam MB, Mekonen G, Birhanu B, Abebe A. Prevalence of Anemia and Its Predictors among Patients with Chronic Kidney Disease Admitted to a Teaching Hospital in Ethiopia: A Hospital-Based Cross-Sectional Study. Medicine. 2023 Feb; 102(6): e31797. doi: 10.1097/MD.0000000000031797.

[4] Shen Y, Wang J, Yuan J, Yang L, Yu F, Wang X *et al.* Anemia among Chinese Patients with Chronic Kidney Disease and Its Association with Quality of Life-Results from the Chinese Cohort Study of Chronic Kidney Disease (C-STRIDE). BioMed Central Nephrology. 2021 Feb; 22(1): 64. doi: 10.1186/s12882-021-02247-8.

[5] Hazin MA. Anemia in Chronic Kidney Disease. Revista da Associação Médica Brasileira. 2020 Jan; 66(Suppl 1): s55-8. doi: 10.1590/1806-9282.66.s1.55.

[6] Macdougall IC. Anaemia in CKD—Treatment Standard. Nephrology Dialysis Transplantation. 2024 May; 39(5): 770-7. doi: 10.1093/ndt/gfad250.

[7] Chuengsaman P, Narenpitak S, Sritippayawan S. Efficacy and Safety of Recombinant Human Erythropoietin (Hema-Plus®) for Management of Anemia in Thai Patients on Peritoneal Dialysis. World Journal of Nephrology. 2021 Nov; 10(6): 109. doi: 10.5527/wjn.v10.i6.109.

[8] Karimzadeh I, Rasekh H, Karimian A, Shabani-Borujeni M, Vazin A. Drug Utilization Evaluation of Erythropoietin at a Referral Teaching Hospital in Iran. Advances in Pharmacological and Pharmaceutical Sciences. 2023; 2023(1): 6685602. doi: 10.1155/2023/6685602.

[9] Shrestha N, Gautam S, Mishra SR, Virani SS, Dhungana RR. Burden of Chronic Kidney Disease in the General Population and High-Risk Groups in South Asia: A Systematic Review and Meta-Analysis. PLoS One. 2021 Oct; 16(10): e0258494. doi: 10.1371/journal.pone.0258494.

[10] Deme S, Janakiraman B, Alamer A, Wayessa DI, Yitbarek T, Sidiq M. Predictors of Functional Status and Disability Among Patients Living with Chronic Kidney Diseases at St Paul's Hospital Millennium Medical College, Ethiopia: Findings from a Cross-Sectional Study. BioMed Central Nephrology. 2024 Oct; 25(1): 343. doi: 10.1186/s12882-024-03783-9.

[11] Prapaiwong P, Ruksakulpiwat S, Jariyasakulwong P, Kasetkala P, Puwarawuttipanit W, Pongsuwun K. Determinants of Anemia Among Patients with Chronic Kidney Disease: A Systematic Review of Empirical Evidence. Journal of Multidisciplinary Healthcare. 2025 Dec: 3765-80. doi: 10.2147/JMDH.S535423.

[12] Taderegew MM, Wondie A, Terefe TF, Tarekegn TT, GebreEyesus FA, Mengist ST *et al.* Anemia and Its Predictors Among Chronic Kidney Disease Patients in Sub-Saharan African Countries: A Systematic Review and Meta-Analysis. PLoS One. 2023 Feb; 18(2): e0280817. doi: 10.1371/journal.pone.0280817.

[13] Hashmi MF and Shaikh H, Rout P. Anemia of Chronic Kidney Disease. In Stat-Pearls [Internet]. 2024 Jul. https://www.ncbi.nlm.nih.gov/books/NBK539871/.

[14] Aboulela M and Collins A. Efficacy of Epoetin Alfa in Managing Symptomatic Anemia in Low-Risk Myelodysplastic Syndromes: A Retrospective Analysis. Cureus. 2024 Oct; 16(10). doi: 10.7759/cureus.72460.

[15] Shahab MH and Khan SS. Erythropoietin Administration for Anemia Due to Chronic Kidney Disease-Subcutaneous or Intravenous, What Do We Know So Far? Cureus. 2020 Sep; 12(9). doi: 10.7759/cureus.10358.

[16] Wish JB, Eckardt KU, Kovesdy CP, Fishbane S, Spinowitz BS, Berns JS. Hypoxia-Inducible Factor Stabilization as an Emerging Therapy For CKD-Related Anemia: Report from a Scientific Workshop Sponsored by the National Kidney Foundation. American Journal of Kidney Diseases. 2021 Nov; 78(5)709-18. doi: 10.1053/j.ajkd.2021.06.019.

[17] Singh AK, Carroll K, Perkovic V, Solomon S, Jha V, Johansen KL *et al.* Daprodustat for the Treatment of Anemia in Patients Undergoing Dialysis. New England Journal of Medicine. 2021 Dec; 385(25): 2325-35. doi: 10.1056/NEJMoa2113379.

[18] Joharapurkar AA, Patel VJ, Kshirsagar SG, Patel MS, Savsani HH, Kajavadara C *et al.* Prolyl Hydroxylase Inhibitor Desidustat Improves Anemia in the Erythropoietin Hyporesponsive State. Current Research in Pharmacology and Drug Discovery. 2022 Jan; 3: 100102. doi: 10.1016/j.crphar.2022.100102.

[19] Chertow GM, Pergola PE, Farag YM, Agarwal R, Arnold S, Bako G *et al.* Vadadustat in Patients with Anemia and Non–Dialysis–Dependent CKD. New England Journal of Medicine. 2021 Apr; 384(17): 1589-600. doi: 10.1056/NEJMoa2035938.

[20] Eckardt KU, Agarwal R, Aswad A, Awad A, Block GA, Bacci MR *et al.* Safety and Efficacy of Vadadustat for Anemia in Patients Undergoing Dialysis. New England Journal of Medicine. 2021 Apr; 384(17): 1601-12. doi: 10.1056/NEJMoa2025956.