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Role of erythropoietin in anemic children with chronic renal failure in Diyala Governorate, Iraq

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Abstract

Background: Chronic conditions, such as anemia are often attributed to insufficient production of erythropoietin. This study focuses on evaluating the effectiveness and safety of recombinant erythropoietin therapy in managing anemia associated with chronic kidney disease.

Methods: A prospective cross-sectional study was conducted on 40 patients diagnosed with anemia due to chronic kidney disease. The study took place from August 1, 2022, to February 30, 2023, at Al-Batool Teaching Hospital in Diyala Province, Iraq. The participants were divided into two groups: the first group comprised 30 patients aged between 80 days and 15 years receiving conservative treatment, while the second group included 10 patients aged 6 to 13 years undergoing hemodialysis. Data analysis, including descriptive and bivariate methods, was performed using SPSS Version 20, with a p-value of less than 0.05 considered statistically significant.

Results: In this study, group I patients had a mean age of 7.1 years, with two-thirds (66.6%) falling within the 1–10 age range and a male-to-female ratio of 1.7:1. In group II, the mean age was 9.5 years, with 60% in the 5–10 age group and a balanced gender ratio (1:1). The primary causes of chronic renal failure (CRF) in Group I were cystinosis and reflux nephropathy (26.7% each), while laboratory findings revealed a mean glomerular filtration rate (GFR) of 72.19 mL/min and severe anemia with hemoglobin (Hb) levels of 4.7 g/dL before treatment. Treatment significantly improved Hb levels in Group I (7.47 to 10.17 g/dL, $P < 0.001$) but showed limited efficacy in Group II (6.9 to 8.2 g/dL, $P = 0.002$).

Conclusion: The findings underscore variable treatment responses between groups, emphasizing the need for tailored anemia management strategies.

Keywords: Erythropoietin, Anemia, Children, Chronic Renal Failure, Glomerular Filtration Rate, Iraq

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Background

Anemia is a prevalent complication among children suffering from chronic renal failure (CRF), particularly in those with stage five chronic kidney disease (CKD). It primarily results from relative deficiency of erythropoietin production [1]. In CKD, plasma erythropoietin levels remain within the typical range of 6–30 mU/mL, failing to rise to the levels observed in other severe anemias (approximately 100 mU/mL), due to the kidneys' inability to adequately respond to hypoxia-induced anemia [2]. Anemia is characterized by a reduction in red blood cell count or hemoglobin concentration below the standard range for healthy individuals [3]. Although the introduction of recombinant human erythropoietin (rHuEPO) has revolutionized the treatment of anemia in CRF, its management continues to pose significant challenges [4]. Anemia commonly occurs when the glomerular filtration rate (GFR) declines below 35 mL/min and becomes more severe as the GFR continues to decrease [5]. The underlying causes of anemia in chronic kidney disease (CKD) are diverse and include erythropoietin deficiency, blood loss, hemolysis, bone marrow suppression, iron deficiency, inadequate dialysis, malnutrition, and both acute and chronic inflammation. Additional contributing factors are infections, deficiencies in vitamin B12 or folate, hyperparathyroidism, reduced red blood cell lifespan, aluminum toxicity, carnitine deficiency, certain medications (e.g., angiotensin-converting enzyme inhibitors), and systemic conditions such as hemoglobinopathies, hypothyroidism, systemic lupus erythematosus, or malignancies [6,7]. The primary cause of anemia in children with chronic renal failure (CRF) is the kidneys' reduced capacity to produce erythropoietin. Despite the availability of recombinant human erythropoietin (rHuEPO),

many children remain anemic, highlighting the multifactorial nature of anemia in CRF [6]. Serum ferritin, often elevated in CRF patients with inflammation, is not always a reliable indicator of anemia [8,9]. Iron deficiency commonly develops after initiating rHuEPO therapy due to increased utilization of iron stores by the bone marrow [10]. Furthermore, children on dialysis frequently experience carnitine deficiency, attributed to low blood levels of carnitine, which may result from reduced dietary intake, impaired endogenous synthesis, or significant renal losses, such as those observed in Fanconi syndrome [11,12]. Certain medications, particularly those prescribed to children with kidney transplants, can suppress erythropoiesis [13]. For instance, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), commonly used in children with chronic renal disease (CRD), are associated with reduced responsiveness to recombinant human erythropoietin (rHuEPO) therapy [14]. In chronic renal failure (CRF) patients, aluminum toxicity may lead to microcytic anemia, although this is now a rare cause due to the declining use of aluminum-containing phosphate binders [15]. Recent research, including meta-analyses, has demonstrated that intravenous iron is effective in treating iron deficiency, raising hemoglobin levels, and decreasing the required doses of rHuEPO in pediatric patients [16]. However, complications from intravenous iron therapy do exist. For instance, iron dextran has been linked to acute anaphylactic reactions, which can be life-threatening [17]. Safer alternatives, such as iron gluconate and iron sucrose, are associated with fewer adverse effects [18]. Nonetheless, there are growing concerns about iron overload in children undergoing acute or long-term intravenous iron therapy, highlighting the need for careful monitoring and updated protocols [17]. This study aims to build on the current understanding of anemia management in children with chronic kidney disease. It provides insights into the benefits and risks of contemporary intravenous iron therapies, contributing valuable data to optimize treatment protocols and improve patient outcomes.

Methods

Study design

A prospective cross-sectional study was conducted between August 1, 2022, and February 30, 2023, at Al-Batool Teaching Hospital in Diyala Governorate.

Sample size

The estimated sample size was 40 participants, using a margin of error of ± 8.0%, a confidence level of 80.0%, and 80.0% response distribution. $n= Z^2 X P(P-1)/E^2$.

Inclusion and exclusion criteria

All children under 18 years old diagnosed with chronic kidney disease (CKD) accompanied with anemia (hematocrit (Hct) levels ranging from 30.0% to 36.0%), whether managed conservatively or through hemodialysis, who were willing to participate (with parental consent obtained) were included in the study. Exclusion criteria encompassed severely ill or complicated cases, acute renal failure, hematological disorders other than anemia, recent blood transfusion, incomplete medical data, refusal to participate, or parental refusal to provide consent.

Procedure

The study participants were randomly selected, and the eligible patients were divided into two groups. Patient file numbers were arranged sequentially, and files were electronically chosen at random. The first group consisted of 30 patients receiving conservative treatment, while the second group included 10 patients undergoing hemodialysis. CKD is defined as either renal injury (proteinuria) and/or a glomerular filtration rate <60 mL/min/1.73 m2 for >3 months. Patients started on erythropoietin therapy once the GFR fall below 35 mg/min/1.73m2. In the group receiving conservative treatment, 6 patients (20%) were in stage III chronic renal failure (CRF), while 24 patients (80%) were in stage IV CRF. All the patients in the second group, which consisted of those undergoing hemodialysis, had progressed to stage V CRF.

Intervention

The first group received conservative treatment for chronic kidney insufficiency, including oral iron supplements and subcutaneous rHuEPO injections administered at a dose of 100 IU/kg twice a week. The second group was treated with subcutaneous rHuEPO injections at a higher dose of 400 IU/kg twice weekly, combined with intravenous iron supplementation. All patients in the second group had been undergoing hemodialysis for a duration exceeding six months.

Follow up

The response to rHuEPO therapy was defined as an increase in hemoglobin levels by 1–2 g/dl per month or achieving the target level within three months after starting treatment for both groups. The hemoglobin correction goal was to reach a level that ensures a good quality of life without adverse effects, typically 10–11 g/dl in children. Patients were monitored monthly or bimonthly, and at each visit, parameters such as hemoglobin, hematocrit, GFR, serum iron, and iron-binding capacity were measured. Patients who required blood transfusions during the erythropoietin treatment period were excluded from the study.

Statistical analysis

Patient data were entered and analyzed using IBM's Statistical Package for the Social Sciences (SPSS) software, version 20. Descriptive statistics were expressed as mean, standard deviation (SD), frequencies (number of patients), and percentages (%) based on the type of variables. A paired t-test was conducted to compare the mean hemoglobin levels before and after treatment, while the Chi-square test was utilized to evaluate the significance of treatment response. Variations in hemoglobin levels pre- and post-treatment were illustrated using a box plot (Simple Bar type). A p-value of ≤ 0.05 was deemed statistically significant, with values of 0.001 considered highly significant.

Results

The mean age of the thirty patients in Group I (on conservative treatment) was (7.1 ± 4.45) years ranged between 80 days and 15 years. Two third of them (20, 66.6%) located in the age group 1-10 years. Male to female ratio; 1.7:1. The mean age of the ten patients in Group II (on hemodialysis treatment) was (9.5±5.63) years ranged between 6 and 13 years. Sixty percent of them located in the age group 5-10 years. Male to female ratio; 1:1 (Table 1).

Table 1: Sociodemographic characteristics of patients in both groups (n=40)

		*Group I (n=30)	*Group II (n=10)
Variable	Categories	N (%)	N (%)
Age (years)	< 1	3 (10.0)	-
	1 - <5	10 (33.3)	-
	>5 – 10	10 (33.3)	6 (60.0)
	> 10	7(23.4)	4 (40.0)
Gender	Male	19 (63.3)	5 (50.0)
	Female	11 (36.7)	5 (50.0)

Group I: Patients on conservative treatment; Group II: Patients of Hemodialysis

Table 2 reported the average glomerular filtration rate (GFR) of 72.19 ± 10.4, mean hemoglobin level 4.7 ± 1.6, mean serum iron level of 40.9 ± 12.2, and mean iron-binding capacity (IBC) 153.7 ± 38.3 among patients on conservative treatment.

Table 2: Baseline laboratory findings of group of patients on conservative treatment (n=30)

Parameter	Mean ± SD
GFR	72.19 ± 10.4
Hemoglobin	4.7 ± 1.6
Serum Iron	40.9 ± 12.2
iron-binding capacity (IBC)	153.7 ± 38.3

The main causes of chronic renal failure (CRF) in patients on conservative treatment were cystinosis and reflux nephropathy in about 26.7% for each respectively. Neurogenic bladder and Meningomyelocele constitute 13.3% and 6.7%, respectively. Several other causes including conditions such as ectopic ureter, obstructive uropathy, polycystic kidney disease, post-urethral valve, renal atrophy, renal tubular acidosis, dehydration (poisoning), and single kidney anomalies compromised of 26.7% (Table 3).

Table 3: Distribution of causes of chronic renal failure (CRF) in patients on conservative treatment (n=30)

Cause	N	%
Cystinosis	8	26.7
Reflux nephropathy	8	26.7
Neurogenic bladder	4	13.3
Meningomyelocele	2	6.7
Other causes*	8	26.7

*Other causes; ectopic ureter, obstructive uropathy, polycystic kidney, post urethral valve, renal atrophy, RTA, dehydration (poisoning) and single kidney.

Table 4 outlines the mean ages for diagnosis of chronic renal failure (CRF) and the initiation of recombinant human erythropoietin (rHuEPO) treatment across various causes. The findings indicate variability in the timing of diagnosis and the initiation of treatment based on the underlying cause of CRF. (Table 4).

Table 4: Age of diagnosis of CRF and age of starting rHuEPO treatment (n=30)

Cause	Age of diagnosis Mean ± SD	Age of starting rHuEPO Mean ± SD
Cystinosis	6.6 ± 2.2	9.6 ± 3.5
Reflux nephropathy	7.1 ± 4.2	9.2 ± 5.7
Neurogenic bladder	5.7 ± 3.6	6.7 ±4.9
Meningomyelocele	4.6 ± 1.2	6.5 ± 1.8

The findings in table 5 reveal a significant improvement in hemoglobin (Hb) levels among patients on conservative treatment for chronic kidney disease. The mean Hb concentration before treatment was 7.47 ± 1.7 g/dL, which increased to 10.17 ± 1.9 g/dL after treatment (P < 0.001). Additionally, 24 patients (80%) responded positively to the treatment, while 6 patients (20%) did not show a significant response (P < 0.001). These results demonstrate the effectiveness of the administered treatment in improving anemia in most patients.

Table 5: Comparison of Hb concentration before and after treatment and the response to treatment in group of patients on conservative treatment (n=30)

Variable	Value	P. value
Hb before treatment (Mean ± SD)	7.47± 1.7	< 0.001
Hb after treatment (Mean ± SD)	10.17 ± 1.9	
Response to treatment		
Respond to treatment (no. %)	24 (80%	< 0.001
Not respond to treatment (no. (%)	6 (20 %)	

The findings in table 6 indicate that patients on hemodialysis experienced a modest improvement in hemoglobin (Hb) levels following treatment. The mean Hb concentration increased from 6.9 ± 1.2 g/dL before treatment to 8.2 ± 1.4 g/dL after treatment (P = 0.002). However, only 3 patients (30%) showed a positive response to the treatment, while the majority, 7 patients (70%), did not respond effectively (P = 0.18). This suggests limited effectiveness of the treatment in addressing anemia for most patients on hemodialysis.

Table 6: Comparison of Hb concentration before and after treatment and the response to treatment in patients on hemodialysis (n=30)

Variable	Value	P. value
Hb before treatment (Mean ± SD)	6.9 ±1.2	0.002
Hb after treatment (Mean ± SD)	8.2 ± 1.4	
Response to treatment		
Respond to treatment (no. %)	3(30%)	0.18
Not respond to treatment (no.%)	7 (70%)	

Discussion

The sociodemographic characteristics of the study population reveal differences in age distribution and gender ratios between the two groups. Group I (on conservative treatment) had a younger mean age of 7.1 ± 4.45 years, with the majority (66.6%) aged between 1 and 10 years. The male-to-female ratio in this group was 1.7:1, indicating a predominance of males. In contrast, Group II (on hemodialysis) had a higher mean age of 9.5 ± 5.63 years, with 60% of the patients aged between 5 and 10 years. The gender distribution in this group was equal, with a male-to-female ratio of 1:1.

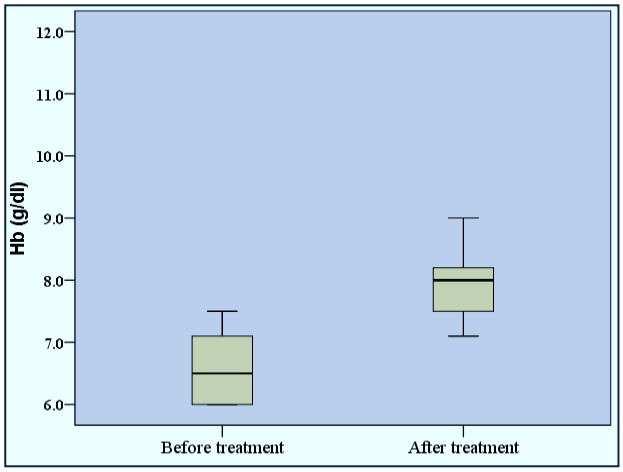

Figure 1: Comparison of the mean Hb concentration before and after treatment in patients on conservative treatment (No.=30)

These findings align with literature suggesting that chronic kidney disease (CKD) can manifest at varying ages, with treatment modality often influenced by the severity of the disease. Conservative management tends to be applied to younger patients or those with less severe disease, while hemodialysis is more common in older children or those with advanced CKD [19]. Additionally, the male predominance in Group I is consistent with studies indicating higher CKD prevalence in males during childhood, potentially due to genetic and hormonal factors [20]. The equal gender distribution in Group II may reflect the progression of CKD and the need for dialysis, which may not differ significantly by gender in advanced stages. These findings align closely with data reported in other regional studies. For example, Ahmed and Hussain showed similar gender distribution patterns in Iraq [21]. Likewise, a study conducted by Akhtar et al. [22] in Pakistan found comparable results, where 58% of the patients were male and 42% were female, with a male-to-female ratio of 1.38:1. Another study by the same author reported a male-to-female ratio of 1.68:1, with 62% males and 38% females. These statistics suggest a consistent trend of male predominance among pediatric patients with chronic kidney disease across these studies. The baseline laboratory findings for patients undergoing conservative treatment indicate significant impairment of kidney function, as reflected by a mean GFR of 72.19 ± 10.4 mL/min, accompanied by severe anemia with an average hemoglobin level of 4.7 ± 1.6 g/dL. Low serum iron levels (40.9 ± 12.2 µg/dL) and an increased iron-binding capacity (IBC) of 153.7 ± 38.3 µg/dL further suggest iron deficiency anemia, which is a common complication in chronic renal failure (CRF) due to reduced erythropoiesis and nutritional deficiencies. These results are consistent with earlier studies highlighting anemia and disrupted iron metabolism as hallmark features in children with CRF [23]. In the current study, over half of the chronic renal failure (CRF) cases were attributed equally to cystinosis (26.7%) and Reflux nephropathy. This finding contrasts with the results of Loro MP et al. [24], who reported congenital abnormalities as the predominant cause of CRF. Similarly, the findings differ from those of Klaus R [25], where posterior urethral valve was identified as the leading cause of CRF. These discrepancies highlight regional and population-specific variations in the underlying causes of CRF, emphasizing the need for localized studies to tailor preventive and management strategies [26]. The data in Table 4 highlights notable differences in the mean ages of diagnosis and initiation of recombinant human erythropoietin (rHuEPO) therapy among children with chronic renal failure (CRF), depending on the underlying etiology. Cystinosis patients were diagnosed on average at 6.6 years and started rHuEPO at 9.6 years, reflecting a delay between diagnosis and treatment initiation. Similarly, those with reflux nephropathy were diagnosed at 7.1 years and began rHuEPO at 9.2 years. In contrast, patients with neurogenic bladder and meningomyelocele had younger ages of diagnosis (5.7 and 4.6 years, respectively) and began treatment earlier at 6.7 and 6.5 years, respectively. These findings underscore the variability in CRF progression and treatment timing, which may be influenced by the nature of the disease, its progression rate, and healthcare access. Early diagnosis and timely initiation of rHuEPO therapy are critical in managing anemia associated with CRF, as suggested by other studies that emphasize the importance of proactive interventions to improve clinical outcomes in pediatric patients [27]. This variability also highlights the need for individualized treatment plans tailored to the specific underlying causes and patient needs. The findings from Figure 3 and Table 5 highlight the significant improvement in hemoglobin (Hb) levels among patients undergoing conservative treatment for chronic kidney disease (CKD). The mean Hb concentration increased substantially from 7.47 ± 1.7 g/dL before treatment to 10.17 ± 1.9 g/dL after treatment ($P < 0.001$). Additionally, 80% of patients (24 out of 30) showed a positive response to treatment, achieving a meaningful rise in Hb levels, while 20% (6 patients) did not respond as effectively ($P < 0.001$). This improvement underscores the effectiveness of conservative management, which often includes erythropoiesis-stimulating agents (ESAs) like recombinant human erythropoietin (rHuEPO), iron supplementation, and other supportive therapies in addressing anemia. The rise in Hb levels is critical for reducing the symptoms of anemia and improving the quality of life in patients with CKD. These findings align with previous study, such as those by Tartarone et al. [28], which reported significant benefits of ESA therapy combined with iron supplementation in managing anemia in CKD patients. The variability in response to treatment, where 20% of patients did not show a significant improvement, might be attributed to factors like iron deficiency, inflammation, or resistance to ESA therapy, which have been reported in other study conducted by Chung et al. [29]. This suggests the need for individualized treatment approaches, including the correction of underlying causes like iron deficiency or addressing inflammation, to optimize patient outcomes. The findings in Table 6 reveal a modest improvement in hemoglobin (Hb) levels among patients on hemodialysis following treatment. The mean Hb increased from 6.9 ± 1.2 g/dL to 8.2 ± 1.4 g/dL ($P = 0.002$), indicating some effect of the treatment in alleviating anemia. However, the response to treatment was limited, with only 30% of patients (3 out of 10) showing significant improvement, while the majority, 70% (7 patients), did not respond effectively ($P = 0.18$). These results highlight the challenges of managing anemia in hemodialysis patients. Hemodialysis often contributes to persistent anemia due to blood loss during dialysis sessions, reduced erythropoietin production, and inflammation, which can inhibit the efficacy of erythropoiesis-stimulating agents (ESAs). Similar findings have been reported in study conducted by Chen

et al. [30], where inflammation and resistance to ESAs were common barriers to achieving optimal Hb levels in dialysis patients. This limited response emphasizes the need for comprehensive anemia management in hemodialysis patients, including addressing underlying factors such as iron deficiency, correcting inflammation, and optimizing ESA dosing. Combining ESA therapy with intravenous iron supplementation has been shown to improve treatment outcomes in this population [31]. Additionally, strategies should focus on personalized treatment plans to enhance the effectiveness of anemia management in hemodialysis patients. Accessibility to healthcare services plays a vital role in managing chronic renal failure (CRF) in anemic children. Limited access to specialized health systems often delays diagnosis and appropriate treatment, exacerbating disease progression. Availability of essential drugs, such as erythropoiesis-stimulating agents (rHuEPO) and iron supplements, is crucial for managing anemia in CRF. However, supply chain constraints or high costs frequently hinder access to these medications, compromising treatment outcomes. Similarly, a shortage of adequately trained healthcare staff adds to the burden, limiting the provision of consistent care and monitoring for children with CRF. The lack of skilled personnel can result in suboptimal anemia management, further affecting children's growth and quality of life. Strengthening health systems through better resource allocation, improved availability of medications, and enhanced workforce training is critical for ensuring equitable access and effective management of anemic children with CRF [32].

Conclusion

This study highlights the distinct clinical and demographic characteristics of pediatric patients with chronic renal failure (CRF) receiving conservative treatment versus hemodialysis. Patients on conservative treatment demonstrated significant improvement in hemoglobin (Hb) levels, with 80% responding positively to therapy. Conversely, the response to anemia management among hemodialysis patients was limited, with only 30% showing improvement. The findings emphasize the efficacy of early intervention with erythropoiesis-stimulating agents (rHuEPO) and iron supplementation in conservative management. However, the challenges faced by hemodialysis patients, including persistent anemia due to blood loss and inflammation, highlight the need for individualized treatment strategies. The study also reveals regional differences in the causes of CRF, emphasizing the importance of tailored preventive and therapeutic approaches. Overall, the results underscore the critical need for proactive, patient-specific management to optimize clinical outcomes and improve the quality of life in children with CRF.

Abbreviation

GFR: Glomerular Filtration Rate; CRF: Chronic Renal Failure; Hb: Hemoglobin; CKD: Chronic Kidney Disease; rHuEPO: Recombinant Human Erythropoietin; ACE: Angiotensin-Converting Enzyme; ARBs: Angiotensin Receptor Blockers; SD: Standard Deviation; IBC: Iron-Binding Capacity

Declaration

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Availability of data and materials

Data will be available by emailing Haider.jawad82@yahoo.com

Authors' contributions

All authors were equally participated in designing, supervising, the study and conceiving the idea. They worked together in data analysis, interpreted the results and curated and drafted the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

We conducted the research following the declaration of Helsinki. The ethical approval was obtained from department of pediatrics, Albatool Teaching Hospital, Diyala Health directorate, Iraq (January 2023).

Consent for publication

Not applicable

Competing interest

The authors declare that they have no competing interests.

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References

1. Vadakedath S, Kandi V. Dialysis: A review of the mechanisms underlying complications in the management of chronic renal failure. Cureus. 2017; Available from: http://dx.doi.org/10.7759/cureus.1603
2. El-Shafei AM, El-Mashad GM, Azzam AA. Oxidative stress markers in children with end-stage kidney disease. J Clin Pediatr Nephrol. 2014;2(2):25. Available from: http://dx.doi.org/10.15401/jcpn/2014/v2i2/66344
3. Brundha MP, Pathmashri VP, Sundari S. Quantitative changes of red blood cells in cancer patients under palliative radiotherapy: A retrospective study. Res J Pharm Technol. 2019;12(2):687. Available from: http://dx.doi.org/10.5958/0974-360x.2019.00122.7
4. Hasegawa T, Bragg-Gresham JL, Pisoni RL, Robinson BM, Fukuhara S, Akiba T, et al. Changes in anemia management and hemoglobin levels following revision of a bundling policy to incorporate recombinant human erythropoietin. Kidney Int. 2011;79(3):340–6. Available from: http://dx.doi.org/10.1038/ki.2010.382

5. Sanyaolu A, Okorie C, Annan R, Turkey H, Akhtar N, Gray F, et al. Epidemiology and management of chronic renal failure: A global public health problem. Biostatistics Epidemiol Int J. 2018;1(1):11–6.
6. Guzzo I, Atkinson MA. Anemia in chronic kidney disease. In: Pediatric Nephrology. Cham: Springer International Publishing; 2022. p. 1779–94.
7. Agarwal N, Khatri N, Singh P. Pancytopenia in pregnant patients with COVID-19 infection and vitamin B12 deficiency: A case report study. J Ideas Health. 2021 Jul 21;4(Special2):415–8. doi: 10.47108/jidhealth.Vol4.IssSpecial2.138
8. Fertrin KY. Diagnosis and management of iron deficiency in chronic inflammatory conditions (CIC): Is too little iron making your patient sick? Hematology Am Soc Hematol Educ Program. 2020 ;2020(1):478–86. Available from: http://dx.doi.org/10.1182/hematology.2020000132
9. Ali Jadoo SA, Salman RE, Ali AY, Haider AI. Factors influencing hemoglobin levels in pregnant women: A cross-sectional study in Iraq. J Lifelong DentoMed Health. 2024;1(1):01–6. Available from: https://jldmhealth.com/Jldmh/article/view/1
10. Fishbane S, Spinowitz B. Update on anemia in ESRD and earlier stages of CKD: Core curriculum 2018. Am J Kidney Dis. 2018;71(3):423–35. Available from: http://dx.doi.org/10.1053/j.ajkd.2017.09.026
11. Bazargani B, Mojtahedi SY, Fahimi D, Askarian F, Moghtaderi M, Abbasi A, et al. Evaluation of the relationship between serum carnitine levels and intradialytic complications in children with kidney failure. Pediatr Nephrol. 2022 ;37(9):2179–83. Available from: http://dx.doi.org/10.1007/s00467-022-05449-w
12. Heidari R, Jafari F, Khodaei F, Shirazi Yeganeh B, Niknahad H. Mechanism of valproic acid-induced Fanconi syndrome involves mitochondrial dysfunction and oxidative stress in rat kidney. Nephrology (Carlton). 2018;23(4):351–61. Available from: http://dx.doi.org/10.1111/nep.13012
13. Faught LN, Greff MJE, Rieder MJ, Koren G. Drug-induced acute kidney injury in children. Br J Clin Pharmacol. 2015;80(4):901–9. Available from: http://dx.doi.org/10.1111/bcp.12554
14. Lullo D, Di Lullo L, Magnocavallo MD, Vetta M, Lavalle G, Barbera C, et al. Atrial fibrillation, oral anticoagulation and nephroprotection: Caution or bravery? G Ital Nefrol. 2022.
15. Gosik R, Danel K. The rising risk of chronic kidney disease (CKD) and how it is dealt with: A review of current and potential phosphate binders (PB). Mini Rev Med Chem. 202;21(19):3052–61. Available from: http://dx.doi.org/10.2174/1389557521666210616161728
16. Ralley FE. Erythropoietin and intravenous iron in PBM. Transfus Apher Sci. 2014;50(1):16–9. Available from: http://dx.doi.org/10.1016/j.transci.2013.12.007
17. Kalra PA, Bhandari S. Safety of intravenous iron use in chronic kidney disease. Curr Opin Nephrol Hypertens [Internet]. 2016;25(6):529–35. Available from: http://dx.doi.org/10.1097/MNH.0000000000000263
18. Behera V, Chauhan R, Sinha S, Nair V. Anaphylactic shock secondary to intravenous iron sucrose in chronic kidney disease. Indian J Hematol Blood Transfus. 2015;31(3):391–3. Available from: http://dx.doi.org/10.1007/s12288-014-0475-0
19. Chen TK, Knicely DH, Grams ME. Chronic kidney disease diagnosis and management: a review. JAMA. 2019 Oct 1;322(13):1294–304. doi: 10.1001/jama.2019.14745
20. Harris RC, Zhang MZ. The role of gender disparities in kidney injury. Ann Transl Med. 2020 Apr;8(7):514. doi: 10.21037/atm.2020.01.23
21. Ahmed NF, Hussain H. Chronic renal failure in children admitted to Children Welfare Teaching Hospital. Iraqi Postgrad Med J. 2008;7:12–7.
22. Akhtar N, Tahir M, Kiran S. Recombinant human erythropoietin therapy in predialysis patients of chronic kidney diseases. Home. 2010;2(1):180–5.
23. Hain D, Bednarski D, Cahill M, Dix A, Foote B, Haras MS, et al. Iron-deficiency anemia in CKD: a narrative review for the kidney care team. Kidney Med. 2023 May 25;5(8):100677. doi: 10.1016/j.xkme.2023.100677
24. Loro MP, Ramírez DS, Álvarez FO, Rodríguez FS. Congenital anomalies of the kidney and urinary tract. A vision for the paediatrician. An Pediatr (Engl Ed). 2015;83(6):442-e443.
25. Klaus R, Lange-Sperandio B. Chronic kidney disease in boys with posterior urethral valves-pathogenesis, prognosis, and management. Biomedicines. 2022;10(8):1894. Available from: http://dx.doi.org/10.3390/biomedicines10081894
26. Alezzi JI, Taghlub HA, Yahia A, Al-ezzi BNA, Ali Jadoo SA. Impact of maternal age on congenital heart disease among children in Diyala Province, Iraq. J Lifelong DentoMed Health. 2024;1(1):22–6. Available from: https://jldmhealth.com/Jldmh/article/view/6
27. Badura K, Janc J, Wąsik J, Gnitecki S, Skwira S, Młynarska E, et al. Anemia of chronic kidney disease—a narrative review of its pathophysiology, diagnosis, and management. Biomedicines. 2024;12(6):1191. doi: 10.3390/biomedicines12061191
28. Tartarone A, Lerose R, Tartarone M. Erythropoiesis-stimulating agents in the treatment of chemotherapy-induced anemia: what do guidelines say? AME Med J. 2023;8:32. doi: 10.21037/amj-23-79
29. Chung EY, Palmer SC, Saglimbene VM, Craig JC, Tonelli M, Strippoli GF. Erythropoiesis-stimulating agents for anemia in adults with chronic kidney disease: a network meta-analysis. Cochrane Database Syst Rev. 2023 Feb 13;2(2):CD010590. doi: 10.1002/14651858.CD010590.pub3
30. Chen N, Hao C, Peng X, Lin H, Yin A, Hao L, et al. Roxadustat for anemia in patients with kidney disease not receiving dialysis. N Engl J Med. 2019 Sep 12;381(11):1001–10. doi: 10.1056/NEJMoa1813599
31. Fishbane S, Ford M, Fukagawa M, McCafferty K, Rastogi A, Spinowitz B, et al. Randomized, double-blind, placebo-controlled study of sodium zirconium cyclosilicate for reducing the incidence of predialysis hyperkalemia. J Am Soc Nephrol. 2019 Sep;30(9):1723–33. doi: 10.1681/ASN.2019050450
32. Ali Jadoo SA, Alhusseiny AH, Yaseen SM, Al-Samarrai MAM, Mahmood AS. Evaluation of health system in Iraq from people's point of view: a comparative study of two different eras. J Ideas Health. 2021 May 20;4(2):380-8. doi: 10.47108/jidhealth.vol4.iss2.100