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ORIGINAL ARTICLE

Prevalence of Anemia: a study on inpatients' records with chronic kidney disease at Prince Mutaib Hospital, Al-Jouf Province, Saudi Arabia

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ABSTRACT

Background: Anemia is one of the many complications of chronic kidney disease (CKD). However, studies on the prevalence of anemia among CKD patients in Saudi Arabia are very limited. Thus, the present study is aimed to estimate the prevalence and severity of anemia among patients with chronic kidney disease in Prince Mutaib Hospital, Al-Jouf, Saudi Arabia.

Methodology: A retrospective study was conducted employing patients' records of individuals with chronic kidney disease following up at Prince Mutaib Hospital during the period from 1st January 2014 to 31st December 2016.

Results: The mean age of the total sample (182 patients) incorporated in the study was 52.9 ± 17.03 years with 53.3% of patients being male and 46.7% female. About 92.9 % of the study group was in stage V of the severity of the glomerular filtration rate. All study samples underwent hemodialysis. The primary etiology of chronic renal failure was found to be hypertensive disease who had moderate anemia and severe anemia (28.7% and 6.1%), respectively.

Conclusion: There is a strong relationship between anemia and hemodialysis, especially among patients with moderate anemia in the studied population, and the majority of patients received iron with folic acid.

Keywords: Anemia, CKD, GFR, Saudi Arabia.

Introduction

Renal disease is the fifth most common disease-causing death in Saudi Arabia, the rate is 32.09% according to Saudi Arabia's top 50 causes of death. Anemia has been defined by the World Health Organization (WHO) as a hemoglobin (Hb) concentration <13.0 g/dl for adult males and postmenopausal women and Hb<12.0 g/dl for premenopausal women [1]. Based upon these criteria, nearly 90% of patients with a glomerular filtration rate (GFR) <25 to 30 ml/minute have anemia, of which many are with Hb levels <10 g/dl [2]. Chronic kidney disease (CKD) is a common condition that is more prevalent in the elderly population. Usually, CKD in younger patients is associated with loss of kidney function. Among the patients aged 65 years and above with CKD, 30% do not have a progressive disease with loss of kidney function over time [3]. One of the common complications of CKD is the anemia which is associated with increased risk for cardiovascular disease (CVD), increased morbidity and mortality, especially in the high-risk group [4]. Anemia usually is grouped into three etiologic categories: decreased RBC production, increased RBC destruction, and blood loss. Anemia of chronic illness and anemia of CKD both fall under the category of decreased RBC production [5]. The anemia of CKD is, in most patients, normocytic and normochromic. It is principally due to reduced renal erythropoietin (EPO) production and,

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to a lesser degree, to shortened red cell survival and decreased responsiveness to the hormone. When kidneys are diseased or damaged, they do not make enough EPO [6–10]. In patients with end-stage renal disease, anemia develops as a result of erythropoietin deficiency recombinant human erythropoietin is prescribed to correct the anemia partially [11–13]. As a result, the bone marrow makes fewer red blood cells, causing anemia. When blood has fewer red blood cells, it deprives the body of the oxygen, it needs this will lead to anemia in chronic kidney disease patients. It was also found that other common causes of anemia in people with kidney disease include blood loss from hemodialysis and low levels of the following nutrients found in food (iron, vitamin B12, and folic acid) [6–10]. It is well established that anemia develops in the course of chronic kidney disease and is nearly universal in patients with kidney failure [11]. The erythropoietin deficiency is the common cause of anemia in chronic kidney disease as: (1) anemia is responsive to treatment with erythropoietin in all stages of chronic kidney disease and (2) in patients with chronic kidney disease, circulating levels of erythropoietin are not sufficient to maintain hemoglobin within the normal range [11–14].

Subjects and Methods

A retrospective study covering all patients' records of CKD from Prince Mutaib Hospital in Al-Jouf province, Saudi Arabia was conducted during the period from 1st January 2014 to 31st December 2016. Data of anemia in patients with CKD were collected from records files using the data collection sheet which also included demographics and lab findings. CKD was divided into five distinct stages according to The National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative that defines CKD based on GFR. In Stage 1 CKD, the GFR is ≥90 ml/minute/1.73 m^2. Stages 2, 3, and 4 CKD are defined by a GFR of 60–89 ml/minute/1.73 m^2, 30–59 ml/minute/1.73 m^2, and 15–29 ml/minute/1.73 m^2, respectively. The final stage, Stage 5, occurs when the GFR is < 15 ml/minute/1.73 m^2 or when patients require dialysis. Anemia, as defined by the NKF, is a hemoglobin (Hb) concentration <12 g/dl for women and <13 g/dl for men. The study was carried out in compliance with the ethical guidelines of the research ethics committee of Al-Jouf University and the Ministry of Health (MOH). Percentages of cases with anemia as a complication of CKD were calculated. The prevalence of anemia was determined in all subjects with CKD. Treatment for anemia was assessed in subjects with anemia and CKD. All data were expressed as mean ± standard deviation (SD). The data were analyzed using a one-way analysis of variance to determine the significance between different groups. The criterion for statistical significance was set at $p < 0.05$. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 17 software package (SPSS® Inc, USA).

Results

Table 1 shows the mean age of the total sample (182 patients) in the study: 52.9 ± 17.03 years with no significant difference among the different age groups ($p > 0.05$), with 53.3% of patients being male and 46.7% female which depicts significant difference among the anemic state groups ($p < 0.05$). It was also shown that there is no significant difference among the anemic state group concerning their creatinine and BUN serum levels ($p > 0.05$). The prevalence of anemia increases with age.

Table 2 and Figure 1 shows that 92.9 % of the study group was in stage V of the severity of GFR and about 51.6% of stage V individuals have moderate anemia. There was a significant difference among the anemic state groups according to GFR stage V ($p < 0.05$).

Table 3 depicts that all study samples underwent hemodialysis. There was a significant difference among the anemic state according to the occurrence of hemodialysis ($p< 0.05$). The prevalence of moderate anemia is more with hemodialysis patients than other groups of the anemic state which explore the strong relationship between anemia and hemodialysis. It was also shown that about 14.8% of CKD patients have a blood transfusion.

Table 1. *The distribution of the age, gender, serum creatinine and BUN of the study group according to their anemic state (n = 182).*

		Anemic state				*p*-value
		Non-anemia	Mild anemia	Moderate anemia	Severe anemia	
Age	<=30	1.6%	3.3%	5.5%	2.2%	0.065
	<=45	0.0%	7.1%	11.0%	5.5%	
	<=85	2.2%	13.2%	39.6%	8.8%	
Gender	Male	0.5%	17.6%	26.9%	8.2%	0.004
	Female	3.3%	6.0%	29.1%	8.2%	
Creatinine mg/dl (mean ± SD)		10 ± 4.7	9.1 ± 3.9	7.7 ± 3.4	8.8 ± 4.4	0.092
BUN mg/dl (mean ± SD)		58.1 ± 31	59.5 ± 26.9	51.1 ± 24.04	60.7 ± 40.5	0.226

Percentage (%) within the total sample, BUN: Blood urea nitrogen, SD: standard deviation. Statistically significant at the level of *p*-value < 0.05.

Table 2. *The distribution of the GFR stage of the study group according to their anemic state (n = 182).*

			Anemic state				*p*-value
			Non-anemia	Mild anemia	Moderate anemia	Severe anemia	
GFR stage	Stage I (>90)	*n*	0	0	2	0	$p < 0.05$
		%	0.0%	0.0%	1.1%	0.0%	
	Stage III (30-59)	*n*	0	1	2	0	
		%	0.0%	0.5%	1.1%	0.0%	
	Stage IV (15-29)	*n*	0	2	4	2	
		%	0.0%	1.1%	2.2%	1.1%	
	Stage V (<15)	*n*	7	40	94	28	
		%	3.8%	22.0%	51.6%	15.4%	
Total		*n*	7	43	102	30	
		%	3.8%	23.6%	56.0%	16.5%	

Percentage (%) within the total sample, GFR: glomerular filtration rate. Statistically significant at the level of *p*-value <0.05.

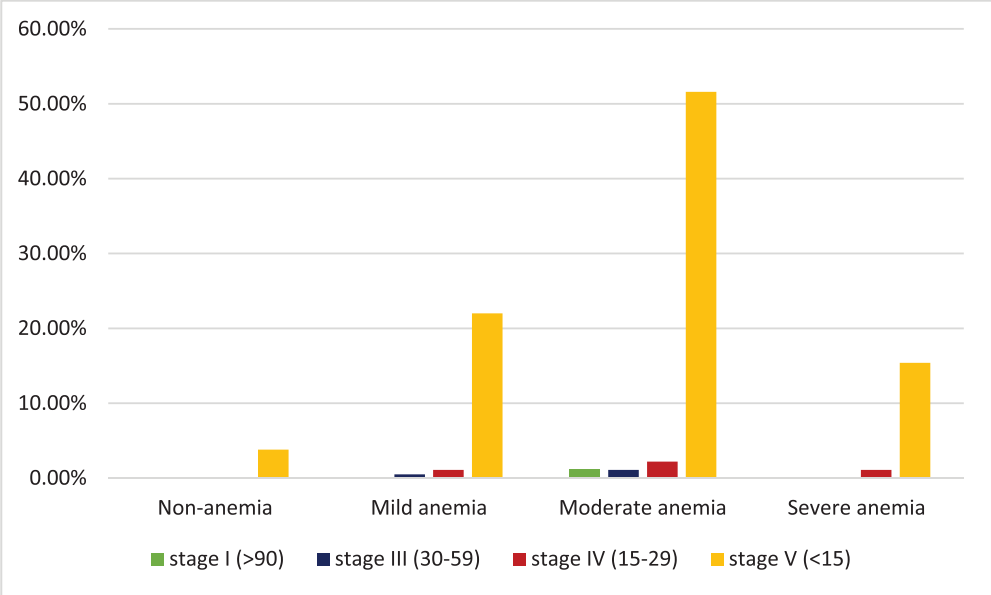

Figure 1. *The distribution of the GFR stage of the study group according to their anemic state (n = 182).*

Table 3. *The distribution of Hemodialysis patient and the blood transfusion state of the study group according to their anemic state (n = 182).*

		Anemic state				*p*-value
		Non-anemia	Mild anemia	Moderate anemia	Severe anemia	
Hemodialysis	Yes	7(3.8%)	43(23.6%)	102(56.0%)	30(16.5%)	$p < 0.05$
	No	0	0	0	0	
Blood transfusion	Yes	1(0.5%)	2(1.1%)	14(7.7%)	10(5.5%)	
	No	6(3.3%)	41(22.5%)	88(48.4%)	20(11.0%)	

Table 4 shows that the main primary etiology of chronic renal failure was hypertensive disease who had their patients have moderate anemia and severe anemia (28.7% and 6.1%, respectively). Diabetes is considered the second most common cause with moderate anemia (17.2%). It was also shown that 7.1% of the moderate anemic group had ischemic heart disease (IHD). However, there is no significant difference among the anemic state groups according to the primary etiologies of CKD ($p>0.05$).

Table 5 and Figure 2 shows that most of the patients with CKD were treated with iron and folic acid, and

Table 4. *The distribution of the causes of primary etiologies and other chronic diseases among the study subjects according to their anemic state (n = 182).*

		Anemic state				*p*-value
		Non-anemia	Mild anemia	Moderate anemia	Severe anemia	
Primary etiologies	Diabetes	0.6%	2.8%	3.9%	1.7%	*p* > 0.05
	Hypertension	1.1%	9.9%	28.7%	6.1%	
	Diabetes andhypertension	1.7%	3.9%	13.3%	6.1%	
	Down syndrome	0.0%	0.6%	0.0%	0.0%	
	Unknown	0.6%	6.6%	10.5%	2.2%	
Other diseases	IHD	2.2%	2.7%	7.1%	2.2%	*p* > 0.05
	Bronchial asthma	0.0%	0.5%	0.5%	0.5%	
	SLE	0.0%	0.0%	0.5%	0.0%	
	Non	1.6%	20.3%	47.8%	13.7%	

Percentage (%) within the total sample, IHD: ischemic heart disease, SLE: systemic lupus erythematosus. statistically significant at the level of *p*-value <0.05.

Table 5. *The distribution of the treatment of anemia and the outcome in the patients of the study group according to their anemic state (n = 182).*

		Anemic state				*p*-value
		Non-anemia	Mild anemia	Moderate anemia	Severe anemia	
Treatment of anemia	Iron	1.1%	3.8%	14.8%	4.4%	*p* > 0.05
	Erythropoietin	0.0%	0.0%	0.5%	0.0%	
	Folic acid	0.5%	1.1%	1.1%	0.5%	
	Iron and folic Acid	1.1%	15.4%	29.1%	7.7%	
	Iron, folic acid and Vit. D	1.1%	3.3%	10.4%	3.8%	
Outcome of patient	Follow up	3.8%	23.6%	53.3%	15.4%	*p* > 0.05
	Died	0.0%	0.0%	2.7%	1.1%	

Statistically significant at the level of *p*-value <0.05.

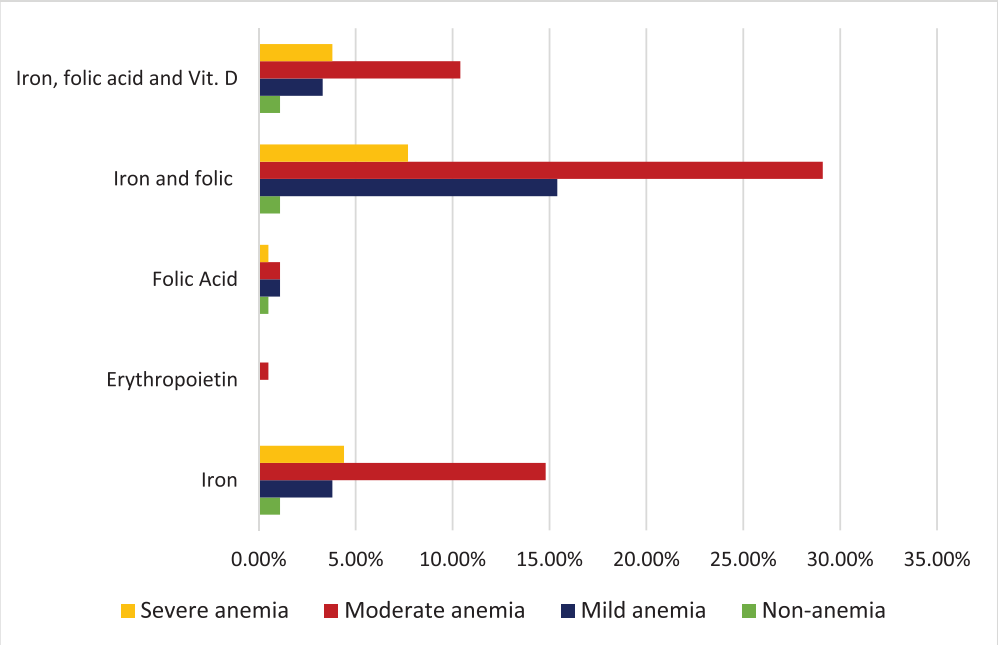

Figure 2. *The distribution of the treatment of anemia in the patients of the study group according to their anemic state (n = 182).*

only a few patients were with moderate anemia who received Erythropoietin. It was also shown that 96.2% out of all study patients presented with follow up had no complete recovery. Only 3.8% of all patients died. However, there was no significant difference among the anemic state groups according to their treatment and outcomes ($p > 0.05$).

Discussion

To the best of our knowledge, anemia in different stages of CKD has not been reported from Saudi Arabia. Thus, we had undertaken this study to find out the incidence of anemia in patients with different stages of CKD as well as the association of anemia and CKD in records based setting. The total population of our study is 182. We examined the association of anemia with the patient in all age groups between 16 and 85. Anemic state for each age group was divided into stages according to the anemic state into (non-anemic, mild anemic, moderate anemia, and severe anemia). The majority of the study population was found to be anemic (moderate anemia) 63.7% at age ≤85. These findings are in line with previous research [15,16] that indicate a study with sample size 162 of patients had Hb<10 g/dl and were thus classified as being anemic with CKD. The relationship between gender and the anemic state was assessed. We found that male represents about 53.3% and the female 46.7%. These findings complied with the finding of Ponte et al. [17],. All anemic patients in our study had hemodialysis sessions weekly. These findings were in agreement with Weisbord et al. [18] who reported that while hemodialysis (HD) does not cure renal disease, it least allows patients with CKD to survive. Nevertheless, HD is a lifelong treatment that significantly and sometimes adversely affects patients both physically and mentally [19]. Many patients with CKD in the present study had a blood transfusion in their treatment course. This finding was in line with Pfeffer et al. [20] who also reported that repeated transfusions or use of an erythropoiesis-stimulating agent (ESA) acted as treatment options for chronic anemia in CKD. We assessed the relationship between chronic diseases and anemic states, such as IHD, bronchial asthma, diabetes, and hypertension, and Down syndrome. Hypertension was found as the highest prevalent primary etiology among patients who developed CKD than other primary causes. These findings were in line with the previous study which reported that HTN occurred in 85% to 95% of patients with CKD. Lau et al. [15] reported in their study that hypertension is prevalent among the anemic patients with CKD (92%) and IHD is (41.4%) which was in agreement with our findings. Shulman [21] explored in his research that CVD is the leading cause of mortality in patients having CKD and accounts of 58% of patients die from CVD in CKD. Foley [22] mentioned that even mild form of renal insufficiency has been reported to be linked with an increased incidence of CVD. The incidence of mortality due to CVD in CKD patients has 10 to 20 times higher when compared with the general population. These findings came in the same line of our research results. Lau et al. [15] reported in their study that iron supplementations (42.6%), folates, (8%) and vitamins (18.5%) as primary medications for anemia which was in agreement with our findings. Optimal treatment of anemia due to CKD requires appropriate diagnosis, ESA and iron therapy, and close monitoring of response. Without adequate iron stores, ESAs will not be effective. Patients with CKD may become iron deficient for several reasons. In addition to physiological blood loss, patients with CKD often exhibit increased erythropoiesis and iron utilization from occult gastrointestinal blood loss resulting from platelet dysfunction that occurs with uremia. Patients on dialysis, especially those receiving hemodialysis, lose blood and, therefore, iron consequent to frequent phlebotomies for laboratory testing, vascular access manipulations, and surgery, bleeding from puncture sites after dialysis, or blood clotting in the dialyzer or tubing. Thus, a periodic assessment of serum iron parameters is necessary [23]. Thus, iron supplementation is necessary for optimal management of anemia and can attenuate the progression of anemia in CKD [24]. Our results may be representative of the entire country. Yet this study provides the much-needed data regarding the degree of anemia in the CKD population in Saudi Arabia which has not been done before so far. Comprehension study is required in a large population for the estimation of the prevalence of anemia in CKD in the Saudi population. Studies on the different tertiary level hospitals of different parts of Saudi involving a large population size will be more representative of the entire country.

Conclusion

Our study showed that there is a strong relationship between anemia and hemodialysis patient, especially among patients with moderate anemia and there is a strong relationship between few chronic diseases and the anemic state of the patients. Patients in the moderate anemic state were more likely to be older, female, hypertensive and received a blood transfusion and iron with folic acid, while mild anemic patients were more likely to be male, hypertensive, and diabetics. Severe anemic patients had an equal percentage of male and female, hypertensive, and diabetics. Most of the patients with CKD presented with GFR at stage V. The prevalence of anemia increases at later stages of CKD. Anemia in CKD is the established risk factor for the development of the cardiovascular disease. Therefore, it is necessary to identify anemia in CKD as soon as possible and manage them properly before the development of the cardiovascular disease. The authors also recommend early identification of anemia in CKD leads to retarded development of end-stage renal disease and consequently improves from CVD morbidity and mortality. Proper and healthy food intake containing iron, folic acid, and vitamins is also recommended.

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List of Abbreviations

ANOVA	Analysis of variance
BUN	Blood urea nitrogen
CKD	Chronic kidney disease
CVD	Cardiovascular disease
ESA	Erythropoiesis-stimulating agent
GFR	Glomerular filtration rate
IHD	Ischemic heart disease
KDOQI	Kidney Disease Outcomes Quality Initiative
MOH	Ministry of health
NKF	National Kidney Foundation
SD	Standard deviation
SPSS	Statistical Package for the Social Sciences
WHO	World Health Organization

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent for publication

Informed consent was obtained from all the participants.

Ethical approval

The study was approved by the research ethics committee of Al-Jouf University and the Ministry of Health (MOH).

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References

1. WHO Scientific Group on Nutritional Anaemias & World Health Organization. (1968). Nutritional anaemias : report of a WHO scientific group [meeting held in Geneva from 13 to 17 March 1967]. World Health Organization. Available from: https://apps.who.int/iris/handle/10665/40707
2. Kazmi WH, Kausz AT, Khan S, Abichandani R, Ruthazer R, Obrador GT, et al. Anemia: an early complication of chronic renal insufficiency. Am J Kidney Dis. 2001;38(4):803–12. https://doi.org/10.1053/ajkd.2001.27699
3. O'Hare AM, Choi AI, Bertenthal D, Bacchetti P, Garg AX, Kaufman JS, et al. Age affects outcomes in chronic kidney disease. J Am Soc Nephrol. 2007;18(10):2758–65. https://doi.org/10.1681/ASN.2007040422
4. McCullough PA, Lepor N. The deadly triangle of anemia, renal insufficiency, and cardiovascular disease: implications for prognosis and treatment. Rev Cardiovasc Med. 2004;6(1):1–10.
5. McGonigle RJ, Wallin JD, Shadduck RK, Fisher JW. Erythropoietin deficiency and inhibition of erythropoiesis in renal insufficiency. Kidney Int. 1984;25(2):437–44. https://doi.org/10.1038/ki.1984.36
6. Hakim YA, Abbas A, Khalil A, Ibrahim TH, Mustafa A. The effect of hemodialysis on hemoglobin concentration, platelets count and white blood cells count in end stage renal failure. Int J Med Res Health Sci. 2016;5(5):22–35.
7. Inrig JK, Barnhart HX, Reddan D, Patel UD, Sapp S, Califf RM, et al. Effect of hemoglobin target on progression of kidney disease: a secondary analysis of the CHOIR (Correction of Hemoglobin and Outcomes in Renal Insufficiency) trial. Am J Kidney Dis. 2012;60(3):390–401. https://doi.org/10.1053/j.ajkd.2012.03.009
8. Parfrey PS, Foley RN, Wittreich BH, Sullivan DJ, Zagari MJ, Frei D. Double-blind comparison of full and partial anemia correction in incident hemodialysis patients without symptomatic heart disease. J Am Soc Nephrol. 2005;16(7):2180–9. https://doi.org/10.1681/ASN.2004121039
9. Ritz E, Laville M, Bilous RW, O'Donoghue D, Scherhag A, Burger U, et al. Target level for hemoglobin correction in patients with diabetes and CKD: primary results of the Anemia Correction in Diabetes (ACORD) Study. Am J Kidney Dis. 2007;49(2):194–207. https://doi.org/10.1053/j.ajkd.2006.11.032
10. Strippoli GF, Craig JC, Manno C, Schena FP. Hemoglobin targets for the anemia of chronic kidney disease: a meta-analysis of randomized, controlled trials. J Am Soc Nephrol. 2004;15(12):3154–65. https://doi.org/10.1097/01.ASN.0000145436.09176.A7
11. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med. 2003;139(2):137–47. https://doi.org/10.7326/0003-4819-139-2-200307150-00013
12. Naets J, Garcia J, Tousaaint C, Buset M, Waks D. Radioimmunoassay of erythropoietin in chronic uraemia or anephric patients. Eur J Haematol. 1986;37(5):390–4. https://doi.org/10.1111/j.1600-0609.1986.tb02626.x
13. Ross RP, McCrea JB, Besarab A. Erythropoietin response to blood loss in hemodialysis patients is blunted but preserved. ASAIO J. 1994;40(3):M880–M5. https://doi.org/10.1097/00002480-199407000-00122
14. Winearls C. Recombinant human erythropoietin: 10 years of clinical experience. Nephrol Dial Transpl. 1998;13(suppl 2):3–8. https://doi.org/10.1093/ndt/13.suppl_2.3
15. Lau BCV, Ong KY, Yap CW, Vathsala A, How P. Predictors of anemia in a multi-ethnic chronic kidney disease population: a case-control study. SpringerPlus. 2015;4(1):233. https://doi.org/10.1186/s40064-015-1001-z
16. Ponte B, Pruijm M, Marques-Vidal P, Martin P-Y, Burnier M, Paccaud F, et al. Determinants and burden of chronic kidney disease in the population-based CoLaus study: a cross-sectional analysis. Nephrol Dial Transpl. 2013:gft206. https://doi.org/10.1093/ndt/gft206
17. McFarlane SI, Chen S-C, Whaley-Connell AT, Sowers JR, Vassalotti JA, Salifu MO, et al. Prevalence and associations of anemia of CKD: Kidney early evaluation program (KEEP) and national health and nutrition examination survey (NHANES) 1999-2004. Am J Kidney Dis. 2008;51(4):S46–55. https://doi.org/10.1053/j.ajkd.2007.12.019
18. Weisbord SD, Fried LF, Mor MK, Resnick AL, Kimmel PL, Palevsky PM, et al. Associations of race and ethnicity with anemia management among patients initiating renal replacement therapy. J Natl Med Assoc. 2007;99(11):1218.

19. Kimmel PL. Psychosocial factors in dialysis patients. Kidney Int. 2001;59(4):1599–613. https://doi.org/10.1046/j.1523-1755.2001.0590041599.x

20. Pfeffer MA, Burdmann EA, Chen C-Y, Cooper ME, de Zeeuw D, Eckardt K-U, et al. A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease. N Engl J Med. 2009;361(21):2019–32. https://doi.org/10.1056/NEJMoa0907845

21. Shulman NB, Ford CE, Hall WD, Blaufox MD, Simon D, Langford HG, et al. Prognostic value of serum creatinine and effect of treatment of hypertension on renal function. Results from the hypertension detection and follow-up program. The Hypertension Detection and Follow-up Program Cooperative Group. Hypertension. 1989;13(5 Suppl):I80. https://doi.org/10.1161/01.HYP.13.5_Suppl.I80

22. Foley RN, Parfrey PS, Sarnak MJ. Epidemiology of cardiovascular disease in chronic renal disease. Journal of the American Society of Nephrology: JASN. 1998;9(12 Suppl):S16.

23. O'Mara NB. Anemia in patients with chronic kidney disease. Diabetes Spectrum. 2008;21(1):12–9. https://doi.org/10.2337/diaspect.21.1.12

24. Kim S, Lee C, Oh Y, Joo K, Kim Y, Kim S, et al. The effects of oral iron supplementation on the progression of anemia and renal dysfunction in patients with chronic kidney disease. Clin Nephrol. 2011;75(5):472–9. https://doi.org/10.5414/CNP75472