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Original Research Article

PREVALENCE OF ANEMIA IN CHRONIC KIDNEY DISEASE PATIENTS

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Abstract

Background: Chronic kidney disease (CKD), defined as renal damage with persistent and usually progressive deterioration of ultrafiltration, is a worldwide public health problem. Is considered as a significant risk factor for end-stage renal disease, anemia, cardiovascular disease, and premature death. The aging of the population and the generally increasing rates of obesity, hypertension, and diabetes worldwide suggest that the incidence and prevalence of CKD will rise over the next decades.

Materials and Method: The data will consider all patients visiting outpatient's department at the primary health center attached to King Faisal University in Al-Ahsa
between 1st January 2010 and 31st December 2011. From the patients` files, we was record the age, gender, GFR, stages of CKD and state of anemia.

Results: In this study, 49.3% of participants were male, and 50.7% was female—only 2.6% of participants on hemodialysis. The prevalence of anemia among the participants in our study was 55.5%. According to the results of the participants in this research, the mean age was 57.82, with a standard deviation of 17.067. The mean Hemoglobin of the participants was 11.775, with a standard deviation of 2.5334. The mean results of the participants by using CKD-EPI formula, to calculate GFR was 74.496 with a standard a deviation of 36.6787, which was the lowest mean of GFR. In Quadratic EGFR formula that was used to calculate GFR, the mean was 84.47 with a standard deviation of 35.677, which was the highest mean of GFR. DMRD formula was also used in this research to calculate the GFR, with a mean of 78.84 with a standard deviation of 50.371.

Conclusions: In our data analysis, 100% of patients in the end stage of CKD had anemia although we used three different formulas to calculate GFR; however, the result was the same regarding patients in the end-stage. A surprising fact was found looking to other stages of CKD, and it is a correlation with anemia, the analysis of the data in this study did not show an increasing number of anemic patients to the stage of CKD in a stepwise manner.

Keyword: Anemia, CKD, Al-Ahsa

Introduction

Chronic kidney disease (CKD), defined as renal damage with persistent and usually progressive deterioration of ultrafiltration, is a worldwide public health problem. Is considered as a significant risk factor for end-stage renal disease, anemia, cardiovascular disease, and premature death. The aging of the population and the generally increasing rates of obesity, hypertension, and diabetes worldwide suggest that the incidence and prevalence of CKD will rise over the next decades. There has been a marked rise in the prevalence and incidence of end-stage chronic kidney disease (CKD) in Saudi Arabia over the last three decades (1). The incidence of dialysis in the Kingdome of Saudi Arabia was 136 new cases per million populations (2). This rise exceeds those reported from many countries. The enormous and rapid changes in lifestyle, high population growth, and rapid increase in life expectancy, and massive urbanization that has occurred over the last three decades combined to make the current CKD status different to what it was. The two major factors that influence the CKD status are the very high rate of diabetic nephropathy and shift in age demographics (1). A cross-sectional study was conducted in nephrology clinics in 11 different medical centers distributed all over the regions of the KSA found a large prevalence of anemia among the CKD population in Saudi Arabia, and the burden of patients who require treatment with erythropoietin is considerably enormous (3). Another study was conducted employing patients' records of individuals with chronic kidney disease following up at Prince Mutaib Hospital, AL-Jouf Province found a strong relationship between anemia and hemodialysis patients, especially among patients with moderate anemia. The prevalence of anemia increases at later stages of CKD (4) Erythropoietin is a signaling molecule that is produced primarily by the kidneys and stimulates red blood cell production. Erythropoietin production stimulated by low oxygen levels in the blood. Chronic kidney disease disrupts the production of erythropoietin and potentiates anemia. (5) Other possible etiologies of anemia in chronic kidney disease including, iron deficiency, inflammation, and the accumulation of

hyper uremia. (6) The impact of anemia on chronic kidney disease is worsening of kidney function, cardiovascular comorbidities, cognitive impairment and sleep disturbances. (7)(8).

GFR, which represent Glomerular filtration rate, is essential in the setting of clinical practice for patients in assessing signs, symptoms or any abnormality that affects the kidney function, or in assessing the effects of medications. Indeed, the ultrafiltration of blood that occurs in the body as a natural process by the Glomerulus of the kidney. Nevertheless, as the study with the title" GFR Estimation: from physiology to public health", mentioned the reduction of the GFR to less than 60ml/min/1.73 m2 for three months or more is a diagnostic feature for chronic kidney disease (9). For the importance of estimating of GFR, many equations are developed, the commonly used are, (CKD-EPI) equation that stands for the chronic kidney disease Epidemiology Collaboration, and (MDRD) equation that stands for Modification of Diet in Renal Disease (MDRD) (10), and Mayo Clinic Quadratic equation (11). The MDRD equation initially was using six variables, which are serum creatinine, serum albumin, urea, gender, age, and ethnicity. The new version of the equation used only four variables, by excluding serum albumin and urea (10).

Modification of Diet in Renal Disease study equation: MDRD= 175 x (SCr)-1.154 X [age(years)]-0.203 X (0.742 if female) X (1.210 if African–American) (12). The CKD-EPI equation was already using the same four variables of DMRD (10). The CKD-EPI creatinine equation is: GFR=141 × min (SCr/k, 1) a × max (SCr/k,1)-1.209 × 0.993Age × 1.018 [If female] x 1.159 [If black] (12). The Mayo clinic group had developed a method to estimate GFR, named "The Mayo Clinic Quadratic' (MCQ) equation. This equation was based on the results of two subjects, subjects with healthy kidney, and subject with chronic kidney disease. Mayo Clinic Quadratic (MCQ) equation: MCQ=exponent [1.911+5.249/SCr−2.114/SCr2−0.00686×age (years)−0.205 if female] (11).

According to the study that was done in the United States with the title of" Prevalence of Anemia in Chronic Kidney Disease", it was found that 15.4 % of patients with CKD had anemia. Indeed, as there was an advancement in the stages of the disease, the percentage of developing anemia was more likely. Furthermore, in stage 1 of CKD, 8.4% of these patients developed anemia. In stage 2 of CKD, 12.2% of these patients developed anemia. In stage 3 of CKD, 17.4% of these patients developed anemia. In stage 4 of CKD, 50.3% of these patients developed anemia. In stage 5 of CKD, 53.4% of these patients developed anemia (13).

Materials and Method:

The data will consider all patients visiting outpatient's department at the primary health center attached to King Faisal University in Al-Ahsa between 1st January 2010 and 31st December 2011. From the patients` files, we was record the age, gender, GFR, stages of CKD and state of anemia.

The sample size was analyzed using SPSS (Statistical Package for the Social Sciences), version22. It expressed as a mean ± standard deviation (SD). Statistical significance differences between groups will be determined with a Student's t-test and *P* values of 0.05; a confidence interval (CI) of 95% was considered.

Study design:

This is a retrospective study analyzes Saudi patients diagnosed with CKD at the primary health center attached to King Faisal University, Al-Ahsa at Saudi Arabia.

Study area:

The study will be conducted at the primary health center attached to King Faisal University in Al-Ahsa, Saudi Arabia. The data will consider all patients with CKD visiting Outpatient Department in primary health center attached to King Faisal University in Al-Ahsa between 1st January 2010 and 31st December 2011, were included in the study evaluation.

The rationale of the study:

Chronic kidney disease is defined as the deterioration of kidney functions, mainly, affecting Erythropoietin production. As a result, anemia is positively predicted in patients with CKD. Indeed, many equations were there to estimate GFR, and for classifying CKD into stages. Hence, for these facts, classifying CKD into stages, provide an estimation in percentage, for the likely developing anemia in patients with CKD. For that, precise measurements with GFR equations are used to predict the likelihood of developing anemia in CKD patients, in their different stages.

The aim:

To determine the prevalence of anemia among CKD patients in Al-Ahsa.

Study subjects:

Saudi males and females age 18 – 60 years old. The sample size was statistically calculated based on population size with a confidence interval of 95% and a margin of error 5% using n = z2 p(1-p)/d2 formula. Subjects recruited from primary health center attached to King Faisal University in Al-Ahsa based on stratified random sampling.

The inclusion criteria for subjects' recruitment into the study:

- Saudi citizen
- The subjects aged 18-60
- Subjects visiting primary health center attached to King Faisal University in Al-Ahsa

Excluding criteria:

- Non-Saudi citizen

- Subjects younger than 18 years or older than 60 years
- Patients do not have CKD.

Ethical consideration:

An authorization letter will be taken from the research center in KFU.

Results:

Table 1: Demographic data

		Frequency	Percent
Sex	Male	112	49.3
	Female	115	50.7
Hemodialysis	Yes	6	2.6
	No	221	97.4
Does the patient have anemia?	yes	126	55.5
	no	101	44.5
Formula 1	End	16	7.0
	sever	19	8.4
	moderate 3B	16	7.0
	moderate 3A	20	8.8
	Mild	57	25.1
	normal	91	40.1
Formula 2	End	9	4.0
	sever	10	4.4
	moderate 3B	7	3.1
	moderate 3A	7	3.1
	Mild	37	16.3
	normal	82	36.1
Formula 3	End	16	7.0
	sever	20	8.8
	moderate 3B	19	8.4
	moderate 3A	24	10.6
	Mild	60	26.4
	normal	88	38.8
		Mean	Std. Deviation
Age		57.82	17.067
Hb		11.775	2.5334
GFR (CKD-EPI formula)		74.496	36.6787
GFR (Quadratic EGFR formula)		84.47	35.677
GFR (DMRD FORMULA)		78.84	50.371

Table 2: distribution of anemia among formulas and stages

			Patient has anemia.		Total	Chi-square	P-value
			yes	no			
formula1	**End**	**Count**	**16**	**0**	**16**	**35.509**	**0.000**
		% within formula1	**100.0%**	**0.0%**	**100.0%**		
	sever	**Count**	**18**	**1**	**19**		
		% within formula1	**94.7%**	**5.3%**	**100.0%**		
	moderate 3B	**Count**	**12**	**4**	**16**		
		% within formula1	**75.0%**	**25.0%**	**100.0%**		
	moderate 3A	**Count**	**9**	**11**	**20**		
		% within formula1	**45.0%**	**55.0%**	**100.0%**		
	Mild	**Count**	**29**	**28**	**57**		
		% within formula1	**50.9%**	**49.1%**	**100.0%**		
	normal	**Count**	**38**	**53**	**91**		
		% within formula1	**41.8%**	**58.2%**	**100.0%**		
formula2	**End**	**Count**	**9**	**0**	**9**	**23.888**	**0.000**
		% within formula2	**100.0%**	**0.0%**	**100.0%**		
	sever	**Count**	**9**	**1**	**10**		
		% within formula2	**90.0%**	**10.0%**	**100.0%**		
	moderate 3B	**Count**	**5**	**2**	**7**		
		% within formula2	**71.4%**	**28.6%**	**100.0%**		
	moderate 3A	**Count**	**7**	**0**	**7**		
		% within formula2	**100.0%**	**0.0%**	**100.0%**		
	Mild	**Count**	**20**	**17**	**37**		
		% within formula2	**54.1%**	**45.9%**	**100.0%**		
	normal	**Count**	**35**	**47**	**82**		
		% within formula2	**42.7%**	**57.3%**	**100.0%**		

formula3	End	Count	16	0	16	38.687	0.000
		% within formula3	100.0%	0.0%	100.0%		
	sever	Count	19	1	20		
		% within formula3	95.0%	5.0%	100.0%		
	moderate 3B	Count	15	4	19		
		% within formula3	78.9%	21.1%	100.0%		
	moderate 3A	Count	10	14	24		
		% within formula3	41.7%	58.3%	100.0%		
	Mild	Count	27	33	60		
		% within formula3	45.0%	55.0%	100.0%		
	normal	Count	39	49	88		
		% within formula3	44.3%	55.7%	100.0%		

Table 3: formulas and stages to determine the anemia status

Stages number	stage name	Formula 1	Formula 2	Formula 3	p value
stage 1	Normal	38	35	39	0.32
stage 2	Mild	29	20	27	0.24
stage 3	Moderate 3A	9	7	10	0.46
stage 4	Moderate 3B	12	5	15	0.07
stage 5	Sever	18	9	19	0.09
stage 6	End	16	9	16	0.08

In this study, 49.3% of participants were male, and 50.7% was female—only 2.6% of participants on hemodialysis. The prevalence of anemia among the participants in our study was 55.5%. According to the results of the participants in this research, the mean age was 57.82, with a standard deviation of 17.067. The mean Hemoglobin of the participants was 11.775, with a standard deviation of 2.5334. The mean results of the participants by using CKD-EPI formula, to calculate GFR was 74.496 with a standard a deviation of 36.6787, which was the lowest mean of GFR. In Quadratic Egfr formula that was used to calculate GFR, the mean was 84.47 with a standard deviation of 35.677, which was the highest mean of GFR. DMRD formula was also used in this research to calculate the GFR, with a mean of 78.84 with a standard deviation of 50.371.

Table 3 showed the formulas and stages to determine the anemia status. In stage 1, normal stage, it was found that in formula (1), there were 41.7% of participants with anemia which was the lowest, and in formula (2), 42.7% of participants with anemia, and in formula (3),44.3% of participants with anemia, which was the highest. Since the p-value = 0.32, there was no significant difference in the normal stage regarding anemia percentage by using different formulas.

In stage 2, the mild stage, it was found that in formula (1), 50.9% of participants with anemia, and in formula (2), 54.1% of participants with anemia which was the highest percentage of anemia in this stage, and in formula (3), 45.0% of participants with anemia which was the lowest, with a p-value 0.24 indicating no significant difference in the mild stage regarding anemia percentage by using different formulas.

In stage 3, named the moderate stage 3A, according to formula (1), 45.0% of participants had anemia, and in formula (2), 100.0% of participants with anemia indicating the highest percentage of anemia in this stage, and in formula (3), 41.7% of participants had anemia which was the lowest. As p-value 0.46 in the moderate stage 3A, there was no significant difference in this stage regarding anemia percentage by using different formulas.

In stage 4, named the moderate 3B, it was found that, in formula (1), 75.0% of participants had anemia, in formula (2), 71.4% of participants had anemia indicating the lowest percentage of anemia in this stage, in formula (3), 78.9% of participants had anemia which was the highest percentage of anemia, with a p-value 0.07 indicating no significant difference in this stage regarding anemia percentage by using different formulas.

In stage 5, the severe stage, it was shown that, in formula (1), 94.7% of participants had anemia, and in formula (2), 90.0% of participants had anemia which was the lowest percentage of anemia in this stage, and in formula (3), 95.0% of participants had anemia indicating the highest level of anemia in this stage. Since the p-value 0.09, there was no significant difference regarding anemia percentage in this stage by using different formulas.

In the 6th stage, the end stage, it was found in formula (1), 100.0% of participants had anemia, and in formula (2), 100.0% of participants had anemia, and in formula (3), 100.0% of participants had anemia, it was clear that all patients have the same percentage of anemia despite using different formals in the end-stage. Since the p-value 0.08, there was no significant difference regarding anemia percentage in this stage by using different formulas.

Discussion:

In our data analysis, 100% of patients in the end stage of CKD had anemia although we used three different formulas to calculate GFR; however, the result was the same regarding patients in the end-stage. A surprising fact was found looking to other stages of CKD, and it is a correlation with anemia, the analysis of the data in this study did not show an increasing number of anemic patients to the stage of CKD in a stepwise manner. Indeed, a comparison was made with research titled" Prevalence of Anemia in Chronic Kidney Disease in the United States (13), and

another research with the title" The Prevalence and Management of Anemia in Chronic Kidney Disease Patients: Result from the Korean Cohort Study for Outcomes in Patients with Chronic Kidney Disease (KNOWCKD) (14), in which the results were contrary to our research results. As it was mentioned in the results, in the normal stage, stage (1), in formula 1, 38 patients with anemia, in formula 2, 35 patients with anemia, in formula 3, 39 patients with anemia.

In stage (2), the mild stage, in formula (1), 29 patients with anemia, in formula 2,20 patients with anemia, in formula 3, 27 patients with anemia. In stage (3), the moderate 3A, in formula 1, 9 patients with anemia, in formula 2, 7 patients with anemia, in formula 3, 10 patients with anemia. In stage (4), the moderate 3B stage, in formula 1, 12 patients with anemia, in formula 2, 5 patients with anemia, in formula 3, 15 patients with anemia. In stage (5), the sever stage, in formula 1, 18 patients with anemia, in formula 2, 9 patients with anemia, in formula 3, 19 patients with anemia. In the end stage, the 6th stage, in formula 1, 16 patients with anemia, in formula 2, 9 patients with anemia, in formula 3, 16 patients with anemia.

In comparison to research's results of Prevalence of Anemia in Chronic Kidney Disease in the United States (13), there was a correlation between the advancement of the CKD stages and the prevalence of anemia. Indeed, in stage (1) of CKD, 8.4% of the patients had anemia. In stage (2), 12.2% of the patients had anemia. In stage (3), 17.4% of the patients had anemia. In stage (4), 50.3% of the patients had anemia. In stage (5), 53.4% of the patients had anemia. Over and above, in the research titled" The Prevalence and Management of Anemia in Chronic Kidney Disease Patients: Result from the Korean Cohort Study for Outcomes in Patients with Chronic Kidney Disease (KNOWCKD) (14), had shown results also supporting the fact, which is, the advancement of CKD stages matches with the prevalence of anemia. In stage (1), 10% of the CKD patients had anemia.

In stage (2), 15.9% of CKD patients had anemia. In stage (3A), 32.8% of CKD patients had anemia. In stage (3B), 46.6% of CKD patients had anemia. In stage (4), 78.9% of CKD patients had anemia. In stage (5), 96.5% of CKD patients had anemia. The last two pieces of research had shown results contrary to our results. It might suggest that there were other factors related to developing anemia in CKD patients, other than only considering CKD. As we can conclude based on our results, there was no matching in the severity of the CKD stages and the prevalence of anemia.

Limitations:

In this study, it was not mentioned if the participants previously had anemia or newly diagnosed, which may affect the interpretation of the result. Also, other contributing factors to anemia and other chronic diseases of participants were unknown. Also, the participants were a small population from primary health center attached to King Faisal University, which may affect the result.

Future studies:

The prevalence of anemia among patients in the end stage of CKD is high what interesting is that although we used three different formulas to calculate GFR but the result was the same regarding patients in the end stage. What may explain this result is that in this study, it was not mentioned if the participants previously had anemia or newly diagnosed also other contributing factors to anemia and other chronic diseases of participants were unknown.

It may mean that many factors are required to be assessed in these patients. This means that the future scope and focus should be on various factors that have a possible link with the overall complication of CKD, including the medical status of the participants. Likewise, this study does not reflect the overall prevalence in Al-Ahsa region because the participants were a small population from primary health center attached to King Faisal University. So, further study may be needed to assess the actual prevalence of anemia in CKD Patients in Al-Ahsa region.

Conclusion:

CKD occurs when there is a persistent and progressive worsening of renal function, ultrafiltration function. As many factors are contributing to the increasing prevalence of CKD, two significant factors are appreciated as the influence for the status of the CKD, which are, Diabetic Nephropathy and shifting in age demography. Over and above, erythropoietin production from the kidney, as a consequence of kidney damage, is disrupted, and as a result, anemia is developing.

Hence, our study focuses on the relation of developing anemia in different stages of CKD, in which three formulas are used to calculate the GFR and to classify CKD stages.

Our study results had shown that there is no correlation between the advancement of CKD stages and in increasing prevalence of anemia in these patients. This fact encourages us to explore other factors contributing to developing anemia, rather than considering CKD alone.

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