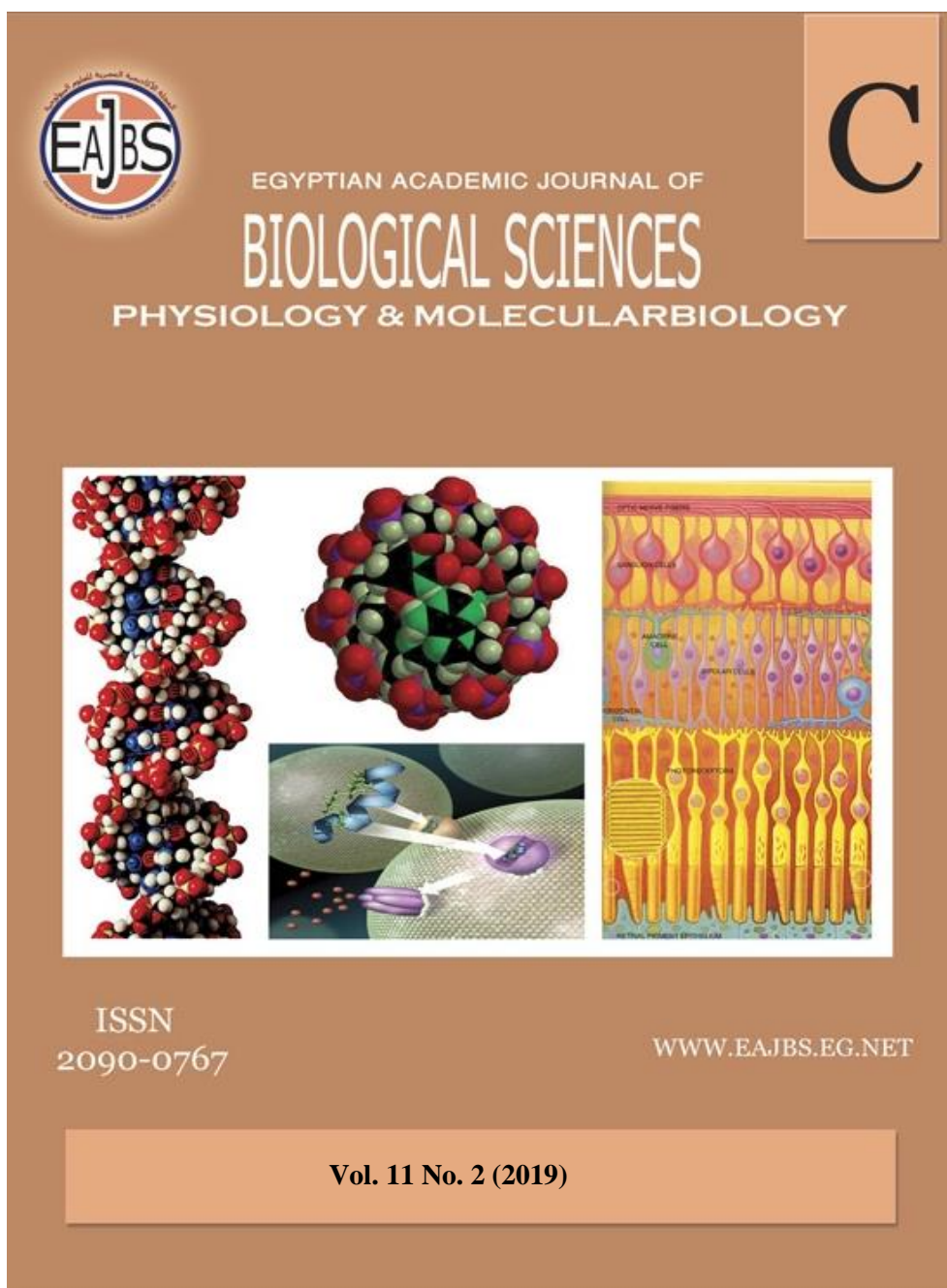


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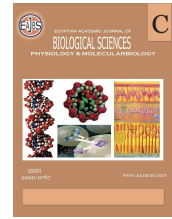
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## Prevalence and Severity of Anemia in CKD patients

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### ABSTRACT

**Background:**Anemia is one of the well-recognized and significant complications of chronic kidney disease (CKD) which manifests noteworthy association with the progression of CKD, the inevitable necessity for blood transfusion, prolonged hospitalization. This study aimed to conduct a comprehensive study as regards the prevalence of anemia and its association with laboratory parameters in CKD patients.

**Methods:**The Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation was applied to calculate the estimated glomerular filtration rate (eGFR) and the patients with hemoglobin (Hb) level < 13.0 g/dL in case of males and that < 12.0 g/dL in females was defined as anemic. The patients were stratified according to their Hb level into four different categories: Hb <10 g/dL, Hb = 10-11 g/dL, Hb =11-12 g/dL and Hb >12 g/dL.

**Results:**Demographic status of CKD patients: Male/Female = 106/123 (M/F% = 46.28/53.71) with mean age  $54.94 \pm 17.98$  and  $55.13 \pm 14.27$ , respectively. Out of 229 CKD patients, 157 (69%) were anemic, and 72 (31%) patients were non-anemic. The mean eGFR of anemic and non-anemic CKD patients was  $10.14 \pm 13.57$  and  $35.74 \pm 30.36$  with a significance level ( $P < 0.001$ ). Anemia was more prevalent in females' (36%) than males' patients (32%). The Prevalence for Hb < 12 g/dL for male and female patients was 55.29% and 79.25%, respectively, while that < 11 g/dL for male and female was found to be 39.03% and 63.21%.

**Conclusion:**The prevalence of anemia in CKD population is notable and correlates with the progression of CKD

### INTRODUCTION

Anemia is a well-recognized initial complication and has a correlation with the progression of chronic kidney diseases (CKD), the prospective necessity for blood transfusion, substandard quality of life as well as with the huge hike in morbidity and mortality Smith Jr (2010), van Nooten *et al.* (2010), Farag *et al.* (2011), Iseki and Kohagura (2007), (Tamura *et al.*, 2016, Moranne *et al.*, 2009, Herzog *et al.*, 2004). The Prevalence of anemia with the aggrandized risk of cardiovascular (Strippoli *et al.*, 2004, Wheeler *et al.*, 2003, Thorp *et al.*, 2009, Servilla *et al.*, 2009, Pereira, 2002, Silverberg *et al.*, 1998) and cerebrovascular(Abramson *et al.*, 2003) phenomena leads to the progression of CKD, and hospitalization (Keane *et al.*, 2003, Levin *et al.*, 2005, Staples *et al.*, 2009). Anemia in CKD patients is a clinically considerable burden, and it turns out to be predominant with the reduction of glomerular filtration rate (GFR)

(McClellan *et al.*, 2004). Progressive enhancement in anemia with the decline of the estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m<sup>2</sup> was exhibited in a population-based investigation using the National Health and Nutrition Examination Survey (NHANES) in the USA (Astor *et al.*, 2002). Its type in CKD patients is normocytic, normochromic and hypo-proliferative; it can be caused by erythropoietin (EPO) deficiency from declined renal mass, different types of pro-inflammatory mediators, nutritional and iron deficiencies which probably affect the process of erythropoiesis in patients suffering from CKD (Babitt and Lin, 2012). Of note, anemia is an ultimate result of CKD as the kidneys synthesize and secrete the majority of EPO (Mercadal *et al.*, 2012, Jacobson *et al.*, 1957).

CKD is categorized into five stages (CKD-1, CKD-2, CKD-3, CKD-4, and CKD-5) based on the amount of kidney function remaining (glomerular filtration). The classification system refers to stage-1 as the least severe while the stage-5 as the most severe stage of the kidney damage (Tomasello, 2008). There have been several recent reports of population-based investigation about the prevalence of anemia in CKD patients. Prevalence of anemia was found to be 15.4% in patients with CKD stage 1–5 as compared to 7.5% in non-CKD population as per the recent NHANES report which indicates the association of anemia with different CKD stages (Stauffer and Fan, 2014). The association of anemia with CKD stages was reported in a Chinese study (Li *et al.*, 2016). However, there are limited data as regards the prevalence of anemia in CKD patients in Jazan region, the Kingdom of Saudi Arabia (KSA). Hence, this study was intended to investigate the prevalence of anemia among the patients of CKD across the

gender line and the different stage of CKD in Jazan region, KSA.

## MATERIALS AND METHODS

### Study Design and Participants:

This study is a cross-sectional analysis that included all CKD patients (n=228) applied to King Fahad Central Hospital, Jazan, KSA for receiving treatment for 24 months from January 2016 to December 2017.

### Ethical Considerations:

The ethics committee of granting approved this study was King Fahad central hospital research ethics committee (Registry no. 083)

### Exclusion criteria

Patients less than 18 years old, mentally patients, and severe cardiac and pulmonary disease, smokers, pregnant women, patients with kidney transplant, malignancy, patients with chronic infections were excluded.

### Data Collection:

Demographic (age and gender) and laboratory data: serum haemoglobin (Hb) (g/dL), creatinine (umol/L), iron (umol/L), total iron binding capacity (TIBC) in umol/L, ferritin (mg/L), RDW%, Hematocrit (HCT%), mean corpuscular volume (MCV) in femtolitre (fL), mean corpuscular haemoglobin concentration (MCHC) in g/dL and mean corpuscular haemoglobin (MCH) in picogram (pG) were collected. Transferrin saturation (TSAT %) was calculated using serum iron and TIBC data of each patient. Calculation of the eGFR was accomplished by using the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation that is preferable to serve the purpose of the investigation (Levey *et al.*, 2009). CKD-EPI estimated GFR (eGFR) =  $141 \times \min(\text{SCr mg/dL}/\kappa, 1)^\alpha \times \max(\text{SCr}/\kappa, 1)^{-1.209} \times 0.993^{\text{age}} \times 1.018$  (if female)  $\times 1.159$  (if Black), where eGFR is estimated glomerular filtration rate in mL/min/1.73 m<sup>2</sup>, SCr is standardized serum creatinine,  $\kappa$  is 0.7 for females and 0.9 for males,  $\alpha$  is  $-0.329$  for

females and  $-0.411$  for males, age in years, min indicates the minimum of  $SCr/\kappa$  or 1, and max indicates the maximum of  $SCr/\kappa$  or 1 (Levey and Stevens, 2010, Matsushita et al., 2010).

#### **Definitions:**

With the aim of performing cross-sectional analysis (prevalence) of anemia in CKD patients ( $n=228$ ) they were stratified according to their eGFRs into five different stages as per kidney disease outcome quality initiative (KDOQI) (Kopple, 2001) as follows: eGFR above  $90 \text{ mL}/\text{min}/1.73 \text{ m}^2$  (CKD stage-1), eGFR  $60\text{--}90 \text{ mL}/\text{min}/1.73 \text{ m}^2$  (CKD stage-2), eGFR  $30\text{--}59 \text{ mL}/\text{min}/1.73 \text{ m}^2$  (CKD stage-3), eGFR  $15\text{--}29 \text{ mL}/\text{min}/1.73 \text{ m}^2$  (CKD stage-4) and eGFR:  $<15 \text{ mL}/\text{min}/1.73 \text{ m}^2$  (CKD stage-5). Stage-1, stage-2, and stage-3 in this study have been defined as the early stages of CKD while stage-4 and stage-5 as advanced stages of CKD. Patients with Hb  $<10 \text{ g}/\text{dL}$  were defined as severely anemic. The patients were evaluated based on four different sub-groups (Hb  $<10 \text{ g}/\text{dL}$ , Hb= $10\text{--}11 \text{ g}/\text{dL}$ , Hb= $11\text{--}12 \text{ g}/\text{dL}$ , and Hb  $>12 \text{ g}/\text{dL}$ ). The reason behind the first two sub-groupings: Hb  $<10 \text{ g}/\text{dL}$  and Hb= $10\text{--}11 \text{ g}/\text{dL}$  is the fact that the ESA in CKD patients starts when the Hb level drops below  $10 \text{ g}/\text{dL}$  with the setting of a therapeutic target, not over and above  $11.5 \text{ g}/\text{dL}$  as per recommendation of KDIGO (The Kidney Disease: Improving Global Outcomes) guidelines (McMurray et

al., 2012). We defined anemia as a Hb concentration is less than  $13 \text{ g}/\text{dL}$  in males and less than  $12 \text{ g}/\text{dL}$  in females according to the KDIGO guidelines or a state receiving ESA (Colantonio et al., 2016).

#### **Statistical Analysis:**

The data collected were reviewed, inquisitively verified and statistically analyzed to get the descriptive statistic (mean, STD., median 95% CI, IQR). All analyses were executed in the International Business Machines Corporation (IBM) Statistical Package for Social Sciences (SPSS) statistics version 21 (IBM Corp., Armonk, NY, USA). Statistical significance was considered when  $P<0.05$ .

## **RESULTS**

### **Characteristics of the patients**

In total CKD patients ( $n=229$ ), including female ( $n=106$ , 46.28%) and male ( $n=123$ , 53.71%) who satisfied the criteria for investigation were recruited over a time period of 24 months from January 2016 to December 2017. The mean age of all the participants was  $51.17 \pm 15.37$  years, and that of male patients and female patients was  $54.94 \pm 17.98$  and  $55.13 \pm 14.27$  years, respectively. The overall characteristics of CKD patients, as well as the patients' characteristics by gender and CKD stage sub-groups, are summarized well-summarized in table 1.

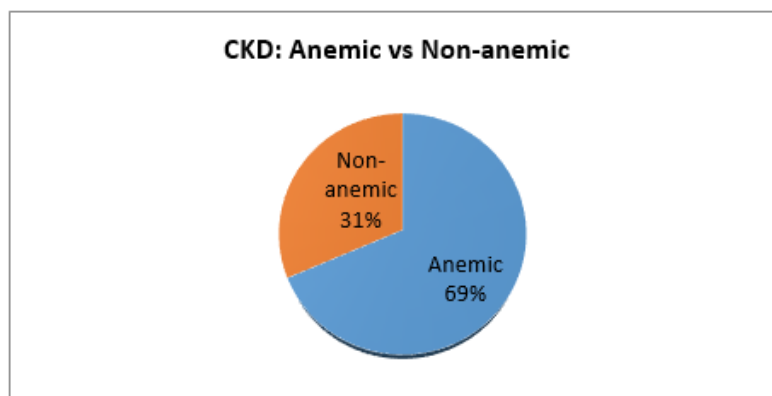
**Table 1.** Baseline characteristics of CKD patients (n=229) and patients' characteristics according to gender and CKD stage sub-groups.

Variable	Statistics	Results		
		Overall	Male	Female
Age	Median (IQR)	52 (40-62)	56 (40-68)	54.5 (47-65)
	Mean $\pm$ SD	51.17 $\pm$ 15.37	54.94 $\pm$ 17.98	55.13 $\pm$ 14.27
eGFR (mL/min/1.73 m <sup>2</sup> ) CKD-EPI	Median (IQR)	6.5 (4.6-22)	7 (5.1-25)	5.65 (4.5-12.53)
	Mean $\pm$ SD	18.19 $\pm$ 23.56	19.75 $\pm$ 24.35	16.38 $\pm$ 22.59
CKD stage-1	N (%)	2.63	3.25	1.89
CKD stage-2	N (%)	4.82	4.88	4.72
CKD stage-3	N (%)	13.16	13.82	12.26
CKD stage-4	N (%)	8.77	65.85	4.72
CKD stage-5	N (%)	70.61	12.2	76.42
Hb (g/dL)	Median (IQR)	510.9 (9.4-13)	11.8 (10.15-13.75)	10.25 (9.05-11.7)
	Mean $\pm$ SD	11.31 $\pm$ 02.58	12.02 $\pm$ 2.79	10.49 $\pm$ 2.02
<10(g/dL)	N (%)	30.57	21.14	41.51
10-11(g/dL)	N (%)	19.65	17.89	21.70
11-12(g/dL)	N (%)	16.16	16.26	16.04
>12(g/dL)	N (%)	33.62	16.26	20.75
Crea umol/L	Median (IQR)	692 (235-856)	693 (208.76-920)	676.5 (334-800.25)
	Mean $\pm$ SD	610.97 $\pm$ 365.47	635.33 $\pm$ 405.25	582.71 $\pm$ 312.59
Iron umol/L	Median (IQR)	10 (7.0-14.76)	11 (7.95-15.04)	9.34(7-13.02)
	Mean $\pm$ SD	11.39 $\pm$ 5.38	12.09 $\pm$ 5.66	10.65 $\pm$ 5.44
TIBC umol/L	Median(IQR)	36 (33-42)	34.4(32.75-38.25)	38 (34.75-44)
	Mean $\pm$ SD	31.35 $\pm$ 20.54	36.21 $\pm$ 9.11	42.36 $\pm$ 27.58
TSAT (%)	Median (IQR)	27.9 (21.15-38.62)	28.89 (23.88-41.93)	25.46 (18.56-34.39)
	Mean $\pm$ SD	31.35 $\pm$ 16.54	54.94 $\pm$ 17.98	28.20 $\pm$ 15.01
Ferritin (umol/L)	Median (IQR)	618.5(335.83-965.75)	630 (315.35-1040)	566 (334.6-871)
	Mean $\pm$ SD	728.34 $\pm$ 526.33	751.91 $\pm$ 495.45	704.76 $\pm$ 557.53
RDW%	MEDIAN (IQR)	16.4 (14.9-18)	15.1 (14-16.65)	16.5 (14.5-18)
HCT %	MEDIAN (IQR)	33.3 (29.3-36.7)	37.3 (31.7-43.3)	33.3 (28.9-36.8)
MCV (fL)	MEDIAN (IQR)	84.9 (78.6-90.4)	84.2 (78.9-88.85)	85.9 (80.4-92.17)
MCH (pG)	MEDIAN (IQR)	26.7 (24.65-29)	26.9 (25.03-28.8)	27.1 (24.9-29.1)
MCHC (g/dL)	MEDIAN (IQR)	31.6 (30.8-32.4)	31.9 (31.05-32.9)	31.5 (30.8-32.3)

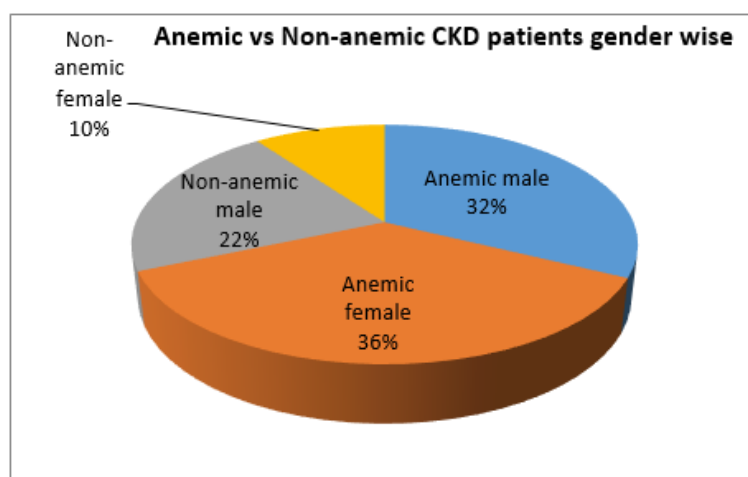
CKD= chronic kidney disease, eGFR=estimated glomerular filtration rate, TSAT=transferrin saturation, TIBC=total iron binding capacity, RDW= Red blood cell distribution width, HCT% = Hematocrit, MCV= mean corpuscular volume, MCHC= mean corpuscular haemoglobin concentration, MCH =mean corpuscular haemoglobin, fL = femtolitre and pG = pictogram.

### The Prevalence of Anemia in Overall CKD Patients:

In totality among 229 CKD patients ranging from stage-1 to stage-5, 157 (69%) and 72 (31%) patients were anemic and non-anemic, respectively (Fig. 1). The mean age of anemic and non-anemic CKD patients were  $52.73 \pm 15.82$  and  $60.04 \pm 16.42$ , respectively ( $P < 0.0019$ ). The mean eGFR of anemic and non-anemic CKD patients was  $10.14 \pm 13.57$  and  $35.74 \pm 30.36$  ( $P < 0.001$ ). Comparison of anthropometric data and the laboratory parameters of anemic and non-anemic CKD patients with the level of their significance ( $P < 0.001$ ) were summarized in (Table 2). Female CKD patients (36%) were found to be more anemic than male patients (32%) (Fig. 2).



**Fig. 1** Percentage distribution of anemic and non-anemic CKD patients recruited for the study



**Fig. 2** Percentage distribution of anemic and non-anemic CKD patients by gender recruited for the study

**Table 2.** Comparisons of Anthropometric data and laboratory parameters between anemic and non-anemic CKD patients

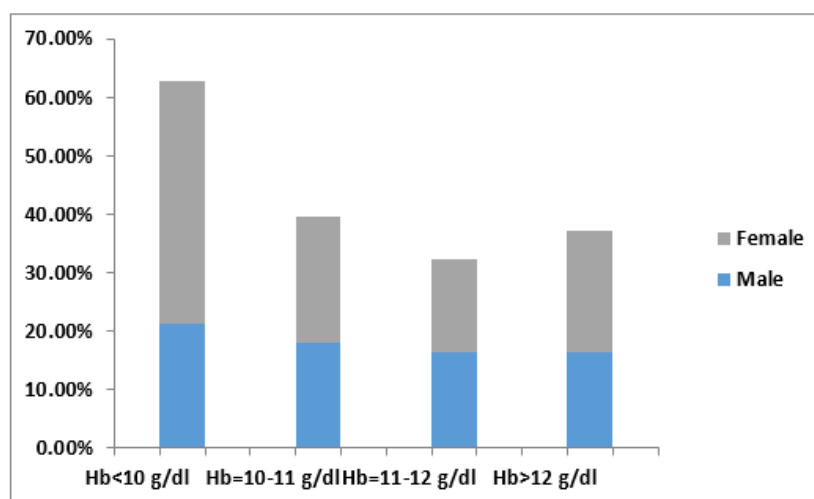
Variables	Anemic (n=157)	Non-anemic (n=72)	P value
<b>Anthropometric data</b>			
Age, yr	52.73 ± 15.82	60.04 ± 16.42	0.0019
<b>Laboratory parameters</b>			
Hb (g/dL)	9.9 ± 1.491	14.38 ± 1.58	<0.001
Crea umol/L	711.62 ± 311.90	391.52 ± 379.39	<0.001
eGFR (mL/min/1.73 m <sup>2</sup> )	10.14 ± 13.57	35.74 ± 30.36	<0.001
CKD-EPI			
Iron umol/L	10.82 ± 5.73	13.5 ± 4.45	0.002
TIBC umol/L	38.13 ± 22.4	43.23 ± 10.45	0.041
TSAT (%)	31.06 ± 17.6	32.4 ± 11.93	0.5
Ferritin umol/L	738.39 ± 538.85	674.22 ± 458.6	0.5
RDW%	16.64 ± 2.61	14.79 ± 2.19	<0.001
HCT %	31.5 ± 4.75	44.71 ± 4.65	<0.001
MCV fL	83.89 ± 9.18	85.5 ± 5.97	0.11
MCH pG	26.46 ± 3.20	27.57 ± 2.23	0.003
MCHC g/dL	31.29 ± 2.69	34 ± 15.81	0.15

eGFR=estimated glomerular filtration rate, TSAT=transferrin saturation, TIBC=total iron binding capacity, RDW= Red blood cell distribution width, HCT%= Hematocrit, MCV= mean corpuscular volume, MCHC=mean corpuscular haemoglobin concentration, MCH=mean corpuscular haemoglobin, fL= femtolitre and pG = pictogram.

### Anemic Characteristics of CKD Patients by Gender and eGFR:

All the study patients were stratified based on their GFR into five CKD stages (from stage-1 to stage-5). 70.61% of total patients belonged to stage-5 category while stage-3: 13.16%, stage-4: 8.77%, stage-2: 4.82% and stage-1: 2.63%. Stage-4 (N%=65.81) was the most common CKD condition in the male category while stage-5 (N%=76.42%) in female patients (**Table 1**). The distribution of the differences in the prevalence level of Hb between male and female CKD patients are shown in (Fig. 3). The patients were stratified according to

their Hb level into four different categories: Hb <10 g/dL, Hb = 10-11 g/dL, Hb =11-12 g/dL and Hb >12 g/d. A total of 41.51% female patients and 21.14% of male CKD patients had Hb level <10 g/dL (male to female ratio of Hb <10g/dL = 1:2). The Hb level prevalence < 12 g/dL (the level of Hb at which the anemia workup ought to be begun) for male and female patients was 55.29% and 79.25%, respectively, while that < 11 g/dL (the level of Hb at which the EPO therapy for treating anemia ought to be started) for male and female was found to be 39.03% and 63.21%, respectively.



**Fig. 3** Distribution of level of the prevalence of Hb in the study patients according to gender

The prevalence of anemia across all the five stages of CKD (stage-1 to stage-5) was assessed. The level of Hb <12 g/dL was reported to be 13.37%, 18.18%, 23.33%, 45% accordingly while that was evaluated the level of Hb <11 g/dL was found to be 15.7%, 16.09%, 19.66%, 40%, and 43.36%, respectively (Fig. 4). Severe anemia (Hb <10 g/dL category) was observed in the advanced stages of CKD (stage-4 and stage-5) with the decline of renal functions (Fig. 4). The overall prevalence of anemia correlated with the advancement in CKD stages (stage-4 and stage-5) which means that anemia becomes

more prevalent as the progression of the diseases and decline of kidney function. Also, CKD patients across the stages ranging from stage-1 to stage-4 while anemia prevalence was almost equally distributed between male and female in stage-5 (Fig. 5). The severity of anemia was more predominant in female patients than their male counterparts in the stage-4 to stage-5 (Fig. 6). The overall status of anemia and comparison prevalence of anemia under the four different categories of Hb between male and female across all the CKD stages are summarized in (Fig. 5 and Fig. 6).



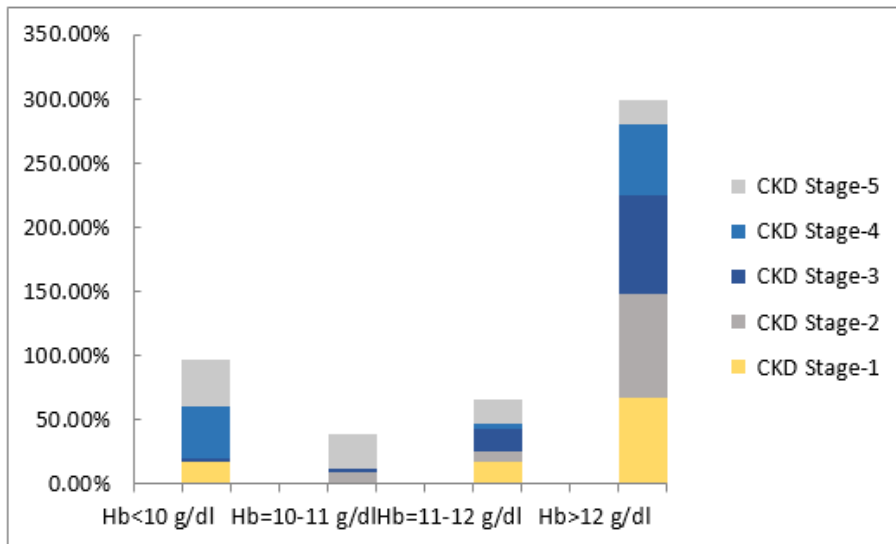


Fig. 4. The distribution of patients according to their haemoglobin levels in the different stages of the estimated glomerular filtration rate (GFR).

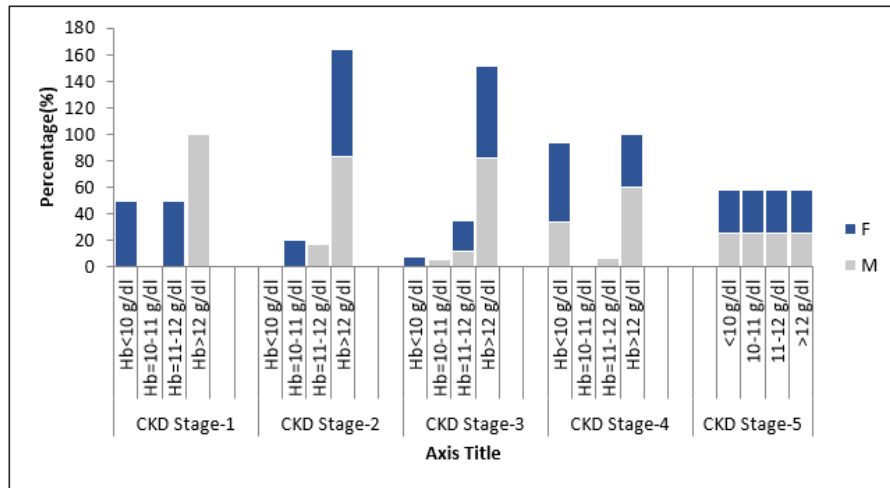


Fig. 5. The prevalence of anemia among male and female CKD patients by CKD stages. CKD = chronic kidney disease, M = males, F = females.

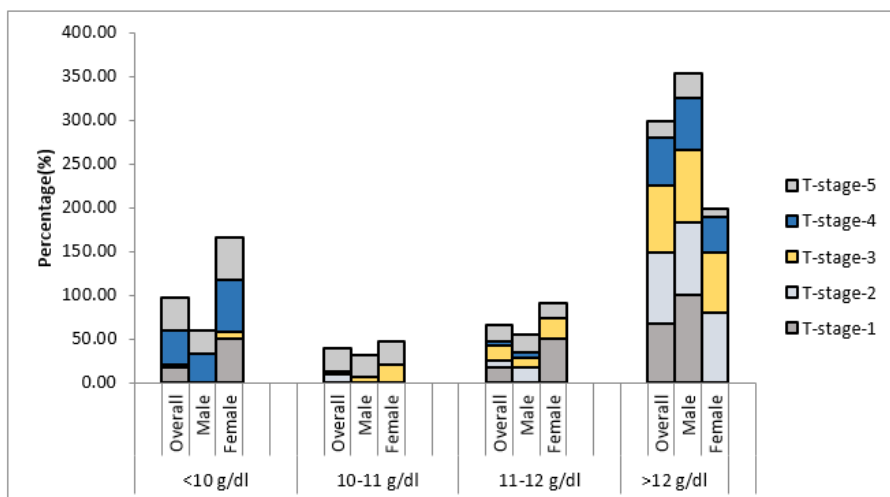


Fig. 6. Overall status and comparison of prevalence of anemia among male and female CKD patients by CKD stages. CKD = chronic kidney disease, M = males, F = females.



## DISCUSSION

The foreground of this study is the heightened prevalence of anemia in CKD patients recruited from Jazan region, KSA, at King Fahad Central Hospital for the period of 24 months from January 2016 to December 2017. Remarkably, this study reveals that the overall prevalence of anemia in CKD patients (mean age:  $51.17 \pm 15.37$ ) based on the definition of anemia as a Hb concentration is less than 13 g/dL in males and less than 12 g/dL in females according to the KDIGO guidelines or a state receiving ESA was 69%. The anemia prevalence in China including CKD patients of all the stages from 1–5 with age range 18–75 reported that 51.5% of patients were anemic (Li *et al.*, 2016). 32.3% of the patients were diagnosed to be anemic in a Japanese study including CKD patients ( $n=2930$ ) of advanced CKD stages from 3–5 (Akizawa *et al.*, 2011). A prevalence of anemia was found to be 46% and 15.4% in the Chronic Renal Insufficiency Cohort (CRIC) study in the USA, which investigate 762 CKD patients (stage 1–5) with the age of more than 55 year and in NHANES study comprising 410 CKD (stage 1–5) patients older than 18 years, respectively (Stauffer and Fan, 2014, Tamura *et al.*, 2016). The potential explanation of the higher prevalence of anemia in our study might be owing to the difference in the study population and the geographical variation, therefore, a larger population-based study is required to confirm it (Obrador *et al.*, 2001). Additionally, the trends of anemia differ gender wise where the female CKD patients ( $N=36$ ) was found to be more anemic than male CKD patients ( $N=32$ ) which indicates that the female gender could be considered as one of the various risk factors associated with the worsening of anemia in CKD patients. This finding is similar to the findings of a study that was done in the USA (Hsu

*et al.*, 2002). The results of our study show that the prevalence pattern of anemia across the different gender of CKD patients is significantly different for the male and female for the level of Hb at which the anemia assessment is necessitated and Hb level at which anemic patients need EPO therapy. The prevalence was also noticed to be enhanced with the progression of CKD. Anemic patients have twofold their relative risk of death when CKD is present, and threefold their risk if they have the cardio-renal anemia syndrome (Silverberg *et al.*, 2003).

In our study the four different categories of CKD patients stratified based on their Hb level, including Hb <10 g/dL, Hb = 10-11 g/dL, Hb =11-12 g/dL and Hb >12 g/d across all the stages of CKD. This stratification demonstrated that a total of 41.51% female patients and 21.14% of male CKD patients had Hb level <10 g/dL (male to female ratio of Hb <10g/dL = 1:2). Additionally, Hb level prevalence < 12 g/dL for male and female patients was 55.29% and 79.25%, respectively, while that < 11 g/dL for male and female was found to be 39.03% and 63.21% that is similar to the results demonstrated in a large a multi-center cross-sectional study that included the patients with different chronic CKD ( $n = 250$ ) from 11 different medical centers of nephrology well-distributed all over the KSA (Hsu *et al.*, 2002, Shaheen *et al.*, 2011). In our study patients stratified based on their GFR into five CKD stages, 70.61% (maximum) of the total patients belonged to stage-5 category while stage-3: 13.16 %, stage-4: 8.77%, stage-2: 4.82% and stage-1: 2.63 % (minimum). Stage-4 ( $N=65.81$ ) was the most common CKD condition in male category while stage-5 ( $N = 76.42\%$ ) in female patients.

Our work highlights the severity and prevalence of anemia was observed to be comparatively higher in the advanced stages of CKD (stage-4

and stage-5) with the decline of renal functions in both the gender which is in accordance with the fact that the anemia prevalence in case of CKD patients enhances from 26% to 75% when the renal function declines from > 60 ml/min (stage-2) to < 15 ml/min (stage-5) most likely owing to the deficiency of EPO (McClellan et al., 2004). The prevalence pattern of anemia was shown to be increased with the progression of the CKD stages 1 to 5 at Hb<12 g/dL as well as Hb<11 g/dL in a study in Boston, the USA (Kazmi *et al.*, 2001). The prevalence pattern of anemia in our study across all the five stages of CKD (stage-1 to stage-5) for the level of Hb<12 g/dL was reported to be 13.37%, 18.18%, 23.33%, 45% and 81.22% accordingly while that for the level of Hb<11 g/dL was found to be 15.7%, 16.09%, 19.66%, 40% and 43.36%, respectively, which is similar to the finding of a study in KSA (Shaheen *et al.*, 2011) and slightly lower than the findings of the study in Boston, the USA which is most probably due to difference in population (Kazmi *et al.*, 2001). In addition to that if the therapeutic burden of CKD patients with the Hb<11g/dL is estimated in the USA as per a study carried out by (Kazmi *et al.*, 2001) (no. of CKD population = 13.0 million) and the anemic population that needs treatment with EPO will be 11.8 million. Ranging from  $3 \times 10^5$  to  $5 \times 10^5$  CKD patients in KSA is considered as the therapeutic burden of patients as they are in need of EPO therapy as per the estimated CKD population of KSA (estimated CKD patients: 1–2 million Saudis who comes from 5–10% of the 21 millions of total population) (Alsuwaida et al., 2010). It may be concluded that Jazan region of KSA shows the large prevalence of anemia among the CKD population and so the therapeutic burden is significantly high.

### Conclusion:

Largely the prevalence of anemia as per definition by World Health Organization criteria was observed to be 69.0%, and both the severity and prevalence of anemia were found to be higher in the female gender. This cross-sectional study revealed the association of anemia with different stages of CKD as the severity and prevalence of anemia enhanced with the progression of the CKD. In summary, Jazan region of KSA shows the enormous prevalence of anemia among the CKD population and so reflecting the significantly high therapeutic burden which emphasizes the necessity of further analysis involving a bigger population and its feasible solution.

### Ethical approval:

in accordance with the ethical standards of King Fahad central hospital research ethics committee (Registry no. 083) which the study was conducted (IRB approval number 083) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

### Acknowledgments:

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### Conflict of Interest:

The author has declared that no conflict of interest exists.

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### REFERENCES

- Abramson J. L., Jurkovitz C. T., Vaccarino V., Weintraub W. S. And McClellan W. (2003). Chronic kidney disease, anemia, and incident stroke in a middle-aged, community-based population: the ARIC Study. *Kidney Int.*, 64 (2) 610-615.
- Akizawa T., Makino H., Matsuo S., Watanabe T., Imai E., Nitta K., Ohashi Y., Hishida A. And

- Group C. K. D. J. C. S. (2011). Management of anemia in chronic kidney disease patients: baseline findings from Chronic Kidney Disease Japan Cohort Study. *Clin. Exp. Nephrol.*, 15 (2) 248-257.
- Alsuwaida A. O., Farag Y. M., Al Sayyari A. A., Mousa D., Alhejaili F., Al-Harbi A., Housawi A., Mittal B. V. And Singh A. K. (2010). Epidemiology of chronic kidney disease in the Kingdom of Saudi Arabia (SEEK-Saudi investigators)-a pilot study. *Saudi J. Kidney Dis. Transpl.*, 21 (6) 1066.
- Astor B. C., Muntner P., Levin A., Eustace J. A. And Coresh J. (2002). Association of kidney function with anemia: the Third National Health and Nutrition Examination Survey (1988-1994). *Arch. Intern. Med.*, 162 (12) 1401-1408.
- Babitt J. L. And Lin H. Y. (2012). Mechanisms of anemia in CKD. *J. Am. Soc. Nephrol.*, 23 (10) 1631-4.
- Colantonio L. D., Tanner R. M., Warnock D. G., Gutiérrez O. M., Judd S., Muntner P. And Bowling C. B. (2016). The role of cystatin-C in the confirmation of reduced glomerular filtration rate among the oldest old. *Archives of medical science: AMS*, 12 (1) 55.
- Farag Y., Keithi-Reddy S., Mittal B., Surana S., Addabbo F., Goligorsky M. And Singh A. (2011). Anemia, inflammation and health-related quality of life in chronic kidney disease patients. *Clin. Nephrol.*, 75 (6) 524-533.
- Herzog C. A., Muster H. A., Li S. And Collins A. J. (2004). Impact of congestive heart failure, chronic kidney disease, and anemia on survival in the Medicare population. *J. Card. Fail.*, 10 (6) 467-472.
- Hsu C.-Y., McCulloch C. E. And Curhan G. C. (2002). Epidemiology of anemia associated with chronic renal insufficiency among adults in the United States: results from the Third National Health and Nutrition Examination Survey. *J. Am. Soc. Nephrol.*, 13 (2) 504-510.
- Iseki K. And Kohagura K. (2007). Anemia as a risk factor for chronic kidney disease. *Kidney Int. Suppl.*, (107) S4-9.
- Jacobson L., Goldwasser E., Fried W. And Plzak L. (1957). Role of the kidney in erythropoiesis. *Nature*, 179 (4560) 633.
- Kazmi W. H., Kausz A. T., Khan S., Abichandani R., Ruthazer R., Obrador G. T. And Pereira B. J. (2001). Anemia: an early complication of chronic renal insufficiency. *Am. J. Kidney Dis.*, 38 (4) 803-812.
- Keane W. F., Brenner B. M., De Zeeuw D., Grunfeld J.-P., McGill J., Mitch W. E., Ribeiro A. B., Shahinfar S., Simpson R. L. And Snapinn S. M. (2003). The risk of developing end-stage renal disease in patients with type 2 diabetes and nephropathy: the RENAAL study. *Kidney Int.*, 63 (4) 1499-1507.
- Kopple J. D. (2001). National kidney foundation K/DOQI clinical practice guidelines for nutrition in chronic renal failure. *Am. J. Kidney Dis.*, 37 (1) S66-S70.
- Levey A. S., Stevens L. A., Schmid C. H., Zhang Y. L., Castro A. F., Feldman H. I., Kusek J. W., Eggers P., Van Lente F. And Greene T. (2009). A new equation to estimate glomerular filtration rate. *Ann. Intern. Med.*, 150 (9) 604-612.
- Levey A. S. And Stevens L. A. (2010). Estimating GFR using the CKD epidemiology collaboration

- (CKD-EPI) creatinine equation: more accurate GFR estimates, lower CKD prevalence estimates, and better risk predictions. *American journal of kidney diseases: the official journal of the National Kidney Foundation*, 55 (4) 622.
- Levin A., Djurdjev O., Thompson C., Barrett B., Ethier J., Carlisle E., Barre P., Magner P., Muirhead N. And Tobe S. (2005). Canadian randomized trial of hemoglobin maintenance to prevent or delay left ventricular mass growth in patients with CKD. *Am. J. Kidney Dis.*, 46 (5) 799-811.
- Li Y., Shi H., Wang W.-M., Peng A., Jiang G.-R., Zhang J.-Y., Ni Z.-H., He L.-Q., Niu J.-Y. And Wang N.-S. (2016). Prevalence, awareness, and treatment of anemia in Chinese patients with nondialysis chronic kidney disease: First multicenter, cross-sectional study. *Medicine*, 95 (24).
- Matsushita K., Selvin E., Bash L. D., Astor B. C. And Coresh J. (2010). Risk implications of the new CKD Epidemiology Collaboration (CKD-EPI) equation compared with the MDRD Study equation for estimated GFR: the Atherosclerosis Risk in Communities (ARIC) Study. *Am. J. Kidney Dis.*, 55 (4) 648-659.
- McClellan W., Aronoff S. L., Bolton W. K., Hood S., Lorber D. L., Tang K. L., Tse T. F., Wasserman B. And Leiserowitz M. (2004). The prevalence of anemia in patients with chronic kidney disease. *Current medical research and opinion*, 20 (9) 1501-1510.
- McMurray J., Parfrey P., Adamson J. W., Aljama P., Berns J. S., Bohlius J., Drüeke T. B., Finkelstein F. O., Fishbane S. And Ganz T. (2012). Kidney disease: Improving global outcomes (KDIGO) anemia work group. KDIGO clinical practice guideline for anemia in chronic kidney disease. *Kidney International Supplements*, 2 (4) 279.
- Mercadal L., Metzger M., Casadevall N., Haymann J. P., Karras A., Boffa J.-J., Flamant M., Vrtovsnik F., Stengel B. And Froissart M. (2012). Timing and determinants of erythropoietin deficiency in chronic kidney disease. *Clin. J. Am. Soc. Nephrol.*, 7 (1) 35-42.
- Moranne O., Froissart M., Rossert J., Gauci C., Boffa J.-J., Haymann J. P., M'rad M. B., Jacquot C., Houillier P. And Stengel B. (2009). Timing of onset of CKD-related metabolic complications. *J. Am. Soc. Nephrol.*, 20 (1) 164-171.
- Obrador G. T., Roberts T., Peter W. L. S., Frazier E., Pereira B. J. And Collins A. J. (2001). Trends in anemia at initiation of dialysis in the United States. *Kidney Int.*, 60 (5) 1875-1884.
- Pereira B. (2002). Overcoming barriers to the early detection and treatment of chronic kidney disease and improving outcomes for end-stage renal disease. *The American journal of managed care*, 8 (4 Suppl) S122-35; quiz S136-9.
- Servilla K. S., Singh A. K., Hunt W. C., Harford A. M., Miskulin D., Meyer K. B., Bedrick E. J., Rohrscheib M. R., Tzamaloukas A. H. And Johnson H. K. (2009). Anemia management and association of race with mortality and hospitalization in a large not-for-profit dialysis organization. *Am. J. Kidney Dis.*, 54 (3) 498-510.
- Shaheen F. A., Souqiyeh M. Z., Al-Attar B. A., Karkar A., Al Jazairi A. M. H., Badawi L. S., Ballut O. M., Hakami A. H., Naguib M.

- And Al-Homrany M. A. (2011). Prevalence of anemia in predialysis chronic kidney disease patients. *Saudi J. Kidney Dis. Transpl.*, 22 (3) 456.
- Silverberg D., Blum M., Peer G. And Iaina A. (1998). Anemia during the predialysis period: A key to cardiac damage in renal failure. *Nephron*, 80 (1) 1-5.
- Silverberg D., Wexler D., Blum M., Wollman Y. And Iaina A. (2003). The cardio-renal anaemia syndrome: does it exist? *Nephrology Dialysis Transplantation*, 18 (suppl\_8) viii7-viii12.
- Smith Jr R. E. (2010). The clinical and economic burden of anemia. *Am. J. Manag. Care*, 16 (Suppl Issues) S59-S66.
- Staples A. O., Wong C. S., Smith J. M., Gipson D. S., Filler G., Warady B. A., Martz K. And Greenbaum L. A. (2009). Anemia and risk of hospitalization in pediatric chronic kidney disease. *Clin. J. Am. Soc. Nephrol.*, 4 (1) 48-56.
- Stauffer M. E. And Fan T. (2014). Prevalence of anemia in chronic kidney disease in the United States. *PLoS One*, 9 (1) e84943.
- Strippoli G. F., Craig J. C., Manno C. And Schena F. P. (2004). Hemoglobin targets for the anemia of chronic kidney disease: a meta-analysis of randomized, controlled trials. *J. Am. Soc. Nephrol.*, 15 (12) 3154-3165.
- Tamura M. K., Vittinghoff E., Yang J., Go A. S., Seliger S. L., Kusek J. W., Lash J., Cohen D. L., Simon J. And Batuman V. (2016). Anemia and risk for cognitive decline in chronic kidney disease. *BMC Nephrol.*, 17 (1) 13.
- Thorp M. L., Johnson E. S., Yang X., Petrik A. F., Platt R. And Smith D. H. (2009). Effect of anaemia on mortality, cardiovascular hospitalizations and end-stage renal disease among patients with chronic kidney disease. *Nephrology*, 14 (2) 240-246.
- Tomasello S. (2008). Anemia of Chronic Kidney Disease. *J. Pharm. Pract.*, 21 (3) 181-195.
- Van Nooten F. E., Green J., Brown R., Finkelstein F. O. And Wish J. (2010). Burden of illness for patients with non-dialysis chronic kidney disease and anemia in the United States: review of the literature. *J. Med. Econ.*, 13 (2) 241-256.
- Wheeler D. C., Townend J. N. And Landray M. J. (2003). Cardiovascular risk factors in predialysis patients: baseline data from the Chronic Renal Impairment in Birmingham (CRIB) study. *Kidney Int.*, 63 S201-S203.

## ARABIC SUMMARY

## شروع فقر الدم في مرضى الكلى المزمن وشدته

## رائد الحربي

قسم طب المختبرات ، كلية العلوم الطبية التطبيقية ، جامعة الباحة ، الباحة ، المملكة العربية السعودية

يُعتبر فقر الدم من الأعراض الشائعة المصاحبة لأمراض الكلى المزمنة، والتي تزداد شدتها مع تدهور أمراض الكلى المزمنة، مما يؤدي للحاجة الماسة لنقل الدم وملازمة التنويم لفترات طويلة بالمستشفى. وتهدف هذه الدراسة لمعرفة نسبة حدوث فقر الدم لمرضى الكلى، بناءً على نتائج تحليل الدم.

## طريقة الدراسة

تم استخدام معادلة CKD-EPI لحساب معدل انشراح eGFR، وتم تصنيف المرضى بأن لديهم فقر الدم بناءً على تركيز الهيموجلوبين بالدم، يعتبر مستوى الهيموجلوبين في الدم للذكور  $> 13$  جم/ديسيلتر وكذلك  $> 12$  جم/ديسيلتر للنساء مؤشر لفقر الدم. كما تم تصنيف المرضى لمجموعات بناءً على مستوى الهيموجلوبين في الدم إلى أربع مجموعات كالتالي:  $> 10$  جم/ديسيلتر، 10-11 جم/ديسيلتر، 11-12 جم/ديسيلتر و  $< 12$  جم/ديسيلتر.

## النتائج

الوزيع الديموغرافي لعينات البحث كانت ذكور/لنساء = 123/106 (ذكور/نساء% = 53.71/46.28) مع معدل الأعمار  $17.98 \pm 54.94$  و  $14.27 \pm 55.13$  على التوالي. من إجمالي عدد العينة البحثية في هذه الدراسة (229)، 157 مريض (69%) يعانون من فقر الدم، بينما 72 مريض، كانت نسبة الهيموجلوبين طبيعية. فقر الدم أكثر انتشاراً في النساء في هذه الدراسة من الرجال 36% مقابل 32%، على التوالي.

## الخلاصة

نسبة شروع فقر الدم في مرضى الكلى المزمن عالية جداً، ويرتبط شروعه بتطور مرض الكلى المزمن طردياً.