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PHENOTYPES AND RISK FACTORS OF ANEMIA IN PRE END STAGE RENAL DISEASE CONCOMITANT WITH ULTRASONOGRAPHIC EVALUATION OF THE KIDNEY.

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Abstract

Background: Non-glomerular kidney disease is classified as progressive or end-stage renal disease (ESRD), with chronic anemia frequently arising from the progression of chronic renal insufficiency, often addressed by insufficient erythropoiesis stimulation.

Aim: This study aimed to investigate the phenotypes and risk factors of anemia in patients with pre-end-stage renal disease as well as to conduct ultrasonographic assessments of the kidneys to identify underlying etiologies and to assess disease chronicity.

Method: This research investigated the prevalence of anemia in 50 patients with chronic kidney disease (CKD) at Al-Azhar University Hospitals. The patients were categorized into two groups: individuals with chronic kidney disease (CKD) and those not undergoing therapy or dialysis. The control group comprised 20 healthy participants. All patients and controls participated in a comprehensive evaluation, encompassing medical history, physical examination, laboratory tests and abdominal ultrasonography.

Results: The results indicated no significant disparities in demographic and anthropometric variables between the CKD patient cohort and the healthy control cohort. Diabetes Mellitus and Hypertension

were the predominant co-morbidities among CKD patients, impacting 52% of the group. All CKD patients exhibited anemia, with the predominant anemia phenotype being Normocytic-Normochromic Anemia (NNA) at 72%. Prevalent risk factors for anemia in chronic kidney disease patients encompassed elevated CRP, ESR, blood urea, serum creatinine, diminished GFR, heightened serum ferritin, anorexia, positive occult blood in stool, and erythropoietin insufficiency.
Conclusion: A study of 70 Egyptian volunteers found anemia prevalent in pre-ESRD patients, with diabetes and hypertension being the main causes. The study highlights the need for further research.

Keywords: chronic kidney disease (CKD), pre-end-stage renal disease, Anemia, erythropoiesis,

Introduction

Kidney disease of non-glomerular origin is categorized as progressive or end-stage renal disease (ESRD), with chronic anemia being a common consequence of advancing chronic renal insufficiency, often inadequately resolved by erythropoiesis stimulation (Portolés et al., 2021). Risk factors of anemia in chronic kidney disease (CKD) remain unclear. A Pe-ECKD subject progressed from CKD stage 2 to 5D, with GFR <60 ml/min/1.73m2 as a recognized anemia risk factor. Interestingly, individuals with GFR 60-89 ml/min/1.73m2 show higher anemia odds compared to those with normal GFR (Kalyesubula, 2021). Non-invasive tests including ultrasonography for kidney size and structure and echogenicity, paired with Hb estimation, are valid for screening kidney disease and anemia (Klinkhammer et al., 2021).

Anemia, a prevalent metabolic disorder in CKD, is generally caused by reduced erythropoietin production resulting in low reticulocyte counts with normal iron levels, leading to complications such as heart failure and systemic hypoxia (Hanna et al., 2021). Evidence indicates anemia increases healthcare costs and elevates mortality risks significantly. Treating anemia has shown improved patient outcomes. Knowledge of CKD-related anemia is essential due to the lack of identification of specific risk factors in Asian populations (Hao et al., 2021).

Anemia, marked by lower RBC counts or hemoglobin levels, is clinically significant and can lead to systemic complications yet lacks a conclusive definition of risk regarding morbidity and mortality across different populations (Ianni et al., 2021). High hemoglobin levels are associated with better outcomes, prompting the necessity to understand developing anemia. Previous studies link factors like hemoglobin levels and comorbidities to adverse outcomes, yet the relationship remains unclear (Yoshimura et al., 2021).

Early recognition of kidney disease and associated inflammation can prevent uremic anemia development. Standardized questionnaires and ultrasonography were utilized to collect data on risk factors for anemia in pre-end stage renal disease (Scavello et al., 2021). Conditions affecting anemia included aging, gender, and other comorbidities, with the prevalence of kidney disease influencing anemia development (Michalak et al., 2021).

Anemia also has crucial implications in CKD management, often preceding the need for renal replacement therapies (Portolés et al., 2021). The interplay between anemia, renal function, and associated cardiovascular risks emphasizes the importance of timely diagnosis and treatment to improve patient outcomes and healthcare resource utilization (Portolés et al., 2021). Regular monitoring and proactive interventions for CKD and anemia are essential, especially given the high prevalence of both conditions among various demographics. The identification of predictors for anemia in CKD ensures better management strategies, potentially aiding in the disability and healthcare burden associated with both conditions (Islam et al., 2021).

This study aimed to investigate the phenotypes and risk factors of anemia in patients with pre-end-stage renal disease (CKD stages III and IV), as well as to conduct ultrasonographic assessments of the kidneys to identify underlying etiologies and to assess disease chronicity.

Method

Study Design

This study sought to examine the prevalence of anemia among 50 patients with chronic kidney disease (CKD) at Al-Azhar University Hospitals. The patients were categorized into two groups: individuals with chronic kidney disease (CKD) and those not receiving therapy or dialysis. The inclusion criteria comprised patients with confirmed chronic renal disease, serum creatinine levels of ≥ 2 mg/dl, GFR < 60, and GFR > 15 mL/minute/1.73 m².

Participants:

The control group comprised 20 healthy volunteers matched for age and sex with the sick group. **Patients group** had a comprehensive history assessment, encompassing their name, age, sex, domicile, occupation, nutritional status, anorexia, chronic disease history, medication usage, and renal disease history.

All patients and controls underwent a series of assessments following informed consent, which included a comprehensive medical history, evaluation of weight, height, body mass index, thorough physical examination, abdominal ultrasound for diagnostic purposes, laboratory investigations, serum potassium level analysis, serum iron quantification, and erythropoietin assay.

Statistical analysis

The statistical analysis was conducted utilizing the SPSS_16 software package on the Windows 7 operating system. Categorical data parameters were given as frequency and percentage, whilst quantitative data were expressed as mean and standard deviation. The ANOVA test was employed to assess the significance between the patient and control groups for quantitative data. Differences between means were assessed using Duncan's Multiple Range Test, while the Spearman correlation coefficient was employed to determine the correlation among parameters.

Ethical consideration:

The study was approved by the board of ethical committee of Al-Azhar University under IRB: ……..and was conducted according to the ethics declared by Helsinki declaration.

Results

The study comprised 50 patients with chronic kidney disease (CKD) and 20 age- and sex-matched controls. The subjects were individuals with chronic kidney disease (CKD) stages III and IV, with serum creatinine levels of ≥ 2 mg/dl and a glomerular filtration rate (GFR) ranging from > 15 ml/min to < 60 ml/min. Blood pressure and body mass index were evaluated. All patients and controls had testing for occult blood in stool, proteinuria, complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), random blood sugar (RBS), iron profile, serum albumin, total protein, blood urea nitrogen, serum creatinine, serum potassium, erythropoietin assay, abdominal ultrasonography, and glomerular filtration rate (GFR) calculation.

Table (1): Demographic data among the study groups.

Parameter	Patients (n= 50)	Control (n= 20)	P-value
Age (year):			
Mean ± SD	50.52 ± 10.77	48.45 ± 11.69	0.607
Range	22 – 72	29 – 66	
Sex: No. (%)			
Male	29 (58.0%)	10 (50.0%)	0.543
Female	21 (42.0%)	10 (50.0%)	

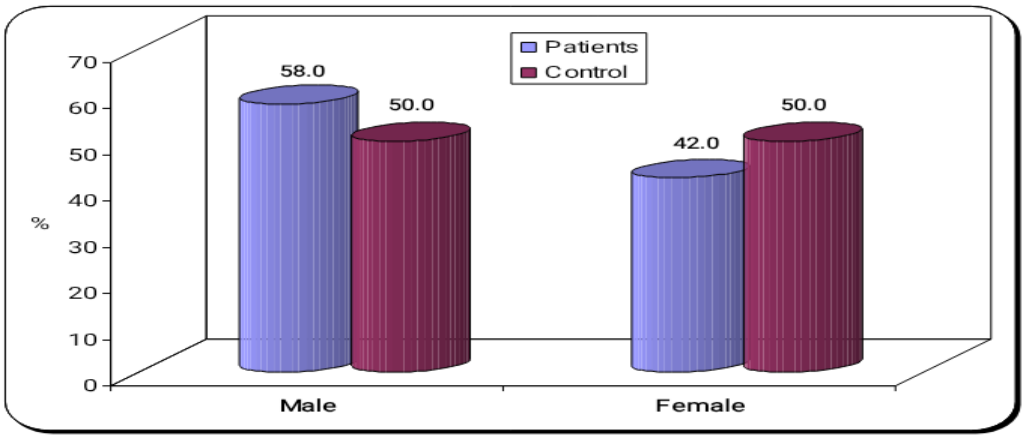


Figure (1): Gender percentages of the study groups.

Table 1 and Figure 1 indicate that there are no significant differences in age and sex between patients and controls.

Table (2): Past and nutritional history in the studied patients

Parameter	No. (n= 50)	%
DM	26	52.0
HTN	26	52.0
IHD	11	22.0
RA	2	4.0
RHD	1	2.0
SLE	8	16.0
Anorexia	22	44.0

DM: Diabetes mellitus, HTN: hypertension, IHD: ischemic heart diseases, RA: Rheumatoid arthritis, RHD: Rheumatic heart disease, SLE: systemic lupus erythematosus.

Table 2 illustrates the prevalence of other chronic diseases and anorexia among the studied patients. Diabetes Mellitus (DM) was identified in 26 patients (52%), which is equivalent to the number of patients with Hypertension (HTN), also 26 (52%). Ischemic Heart Disease (IHD) was present in 11 patients (22%), Rheumatoid Arthritis (RA) in 2 patients (4%), Rheumatic Heart Disease (RHD) in 1 patient (2%), Systemic Lupus Erythematosus (SLE) in 8 patients (16%), and anorexia was observed in 22 patients (44%).

Table (3): Anthropometric measurements of the study groups

Anthropometric measurements	Patients (n= 50)	Control (n= 20)	P-value
Weight(Kg): Mean ± SD Range	 81.10 ± 11.65 56 - 115	 79.50 ± 10.04 61 - 98	0.861
Height(cm): Mean ± SD Range	 171.06 ± 6.67 155 - 186	 171.25 ± 6.77 160 - 186	0.984
BMI: Mean ± SD Range	 27.71 ± 3.78 20.5 - 40.7	 27.09 ± 2.91 22.2 - 32.6	0.775

Table 3 indicates that there are no significant differences in weight, height, and body mass index between patients and controls.

Table (4): Systolic and diastolic blood pressure of the study groups

Parameter	Patients (n= 50)	Control (n= 20)	P-value
Systolic BP: Mean ± SD Range	 142.40 ± 18.63 110 - 180	 122.25 ± 8.19 110 - 135	0.001*
Diastolic BP: Mean ± SD Range	 91.70 ± 14.20 70 - 130	 79.50 ± 6.05 70 – 90	0.001*

Table 4 illustrates highly substantial disparities in both systolic and diastolic blood pressure between patients and controls. Mean arterial blood pressure (systolic and diastolic) is elevated in patients compared to controls.

Table (5): Physical examination of the studied patients

Parameter	No. (n= 50)	%
Pallor: No +	 5 45	 10.0 90.0
Facial puffiness: No +	 29 21	 58.0 42.0
LL edema: No +	 31 19	 62.0 38.0
Others: Basal lung crepitation Cushionied face Malar flush Mitral regurge None	 8 3 1 1 37	 16.0 6.0 2.0 2.0 74.0

No: absent, +:present, LL edema: lower limbs edema, None: no other clinical signs.
Table (5) presents the clinical manifestations observed in the investigated patients, including pallor, facial puffiness, lower limb edema, and additional clinical symptoms.

Table (6): Proteinuria and occult blood in stool among studied patients

Parameter	No. (n= 50)	%
Proteinuria: No 1+ 2+ 3+	 15 21 10 4	 30.0 42.0 20.0 8.0
Occult blood in stool: Yes No	 3 47	 6.0 94.0

No: negative, 1+: 30 mg per dL, 2+: 100 mg per dL, 3+: 300 mg per dL,yes: positive.

Table 6 depict the prevalence of proteinuria and occult blood in stool among the examined patients as follows: Concerning proteinuria: 15 patients (30%) tested negative, 21 patients (42%) exhibited 1+,

10 patients (20%) showed 2+, and 4 patients (8%) presented 3+ for proteinuria based on dipstick urine analysis. Of the patients tested for occult blood in stool, 3 (6%) were positive, while 47 (94%) were negative.

Table (7): Random blood sugar (RBS) of the study groups

RBS	Patients (n= 50)	Control (n= 20)	P-value
Mean ± SD	163.68 ± 61.30	109.75 ± 16.01	0.001*
Range	87 - 315	85 - 140	

Table 7 and Figure 2 illustrate markedly significant disparities in random blood sugar levels between patients and the control group.

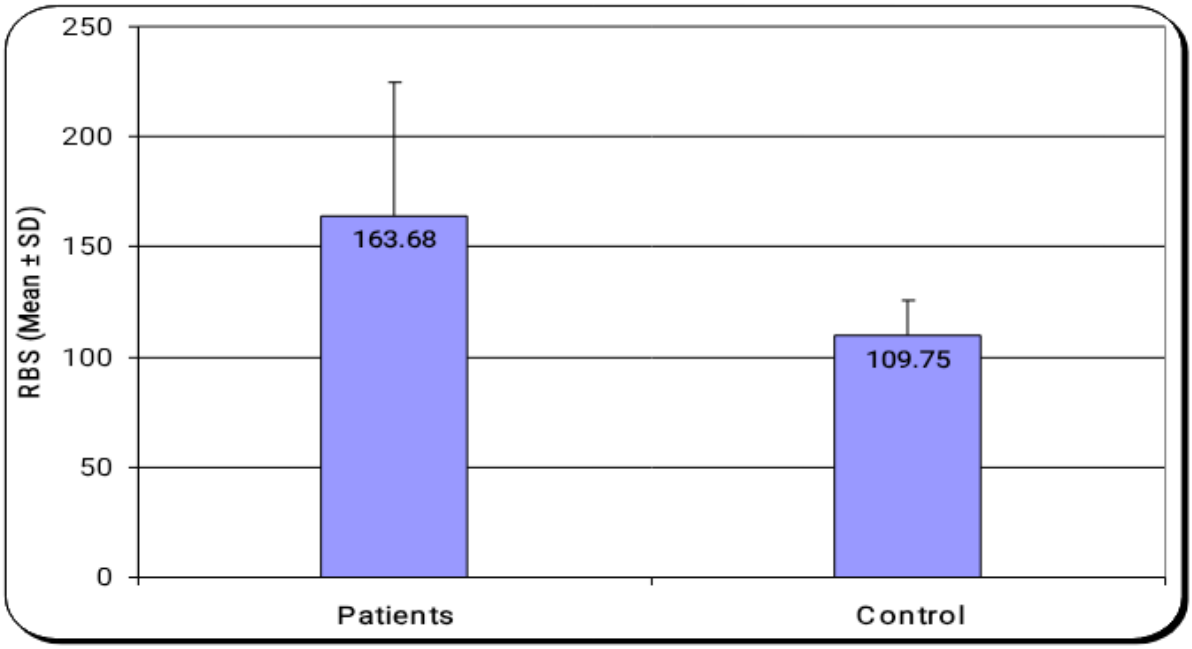


Figure (2): Random blood sugar (RBS)of the study groups.

Table (8): C-reactive protein and erythrocyte sedimentation rate of the study groups

Parameter	**Patients (n= 50)**	**Control (n= 20)**	**P-value**
CRP:			
Mean ± SD	20.90 ± 4.45	13.00 ± 3.46	0.001*
Range	12 – 35	8 - 21	
ESR 1st H:			
Mean ± SD	28.98 ± 7.56	15.45 ± 4.45	0.001*
Range	15 – 45	8 - 22	
ESR 2nd H:			
Mean ± SD	61.84 ± 16.47	32.05 ± 10.51	0.001*
Range	32 – 95	15 - 47	

CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, 1stH: first hour, 2ndH: hour

Table (8) demonstrates statistically significant differences in C-reactive protein and ESR at both the first and second hours, with the mean values elevated in the patient group.

Table (9): Hematology Panel

	Patients (n= 50)	**Control (n= 20)**	**P-value**
HB (g/dl):			
Mean ± SD	10.20 ± 1.22	14.02 ± 1.40	0.001*
Range	7.6 - 12.7	11.5 - 16	
HCT (%):			
Mean ± SD	32.26 ± 3.63	41.21 ± 4.05	0.001*
Range	23.9 ± 40.2	33.2 - 47	
WBCs (x 10^3):			
Mean ± SD	6.06 ± 1.49	6.63 ± 1.36	0.120
Range	3.8 - 10.5	4.5 - 9.2	
Platelets (x 10^3):			
Mean ± SD	222.86 ± 42.33	248.40 ± 36.43	0.021*
Range	110 – 320	170 - 315	
RBCs (x 10^6):			
Mean ± SD	4.22 ± 0.28	4.79 ± 0.41	0.001*
Range	3.5 - 4.7	4.1 - 5.7	
MCV (femtoliter):			
Mean ± SD	85.74 ± 7.64	83.84 ± 5.11	0.128
Range	67.2 – 98	68.9 - 90	
MCH (picograms/cell):			
Mean ± SD	28.19 ± 2.20	29.55 ± 1.83	0.008*
Range	23 - 32.1	25 - 32	
MCHC(g/deciliter):			
Mean ± SD	32.31 ± 2.25	34.69 ± 1.81	0.001*
Range	25.2 - 35.2	31.1 – 37	
Retics (%):			
Mean ± SD	0.62 ± 0.19	0.84 ± 0.17	0.001*
Range	0.3 - 1.2	0.5 - 1.2	
Anemia type according to RBC indices (MCV, MCH &MCHC)			
MHA	7 (14.0%)	2 (10.0%)	
NHA	7 (14.0%)	1 (5.0%)	0.001*
NNA	36 (72.0%)	0 (0.0%)	
Normal CBC	0 (0.0%)	17 (85.0%)	

HB: Hemoglobin in g/dl, HCT: hematocrit value (%), WBCs: white blood cells (x 10^3), RBCs: red blood cells(x10^6), MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin,MCHC: mean corpuscular hemoglobin concentration,Retics: reticulocytic count (%),MHA: Microcytic-Hypochromic anemia,NHA: Normocytic-Hypochromic anemia,NNA: Normocytic-Normochromic anemia, CBC: complete blood count.

Table 9 reveals significant differences between patients and controls in various blood tests, including Hb, HCT, RBCs count, MCH, MCHC, and reticulocytic count. Platelets count is also higher in the control group. No significant differences were found in WBCs count and MCV. However, the patients' group had a higher prevalence of anemia, with all 50 patients having anemia (100%), compared to only 3 (15%) in the control group and 85% in the patients group. Additionally, 7 (14%)

patients had MHA, 7 (14%) had NHA, and 72% had NNA, compared to only 2 (10%) and 1 (5%) in the control group.

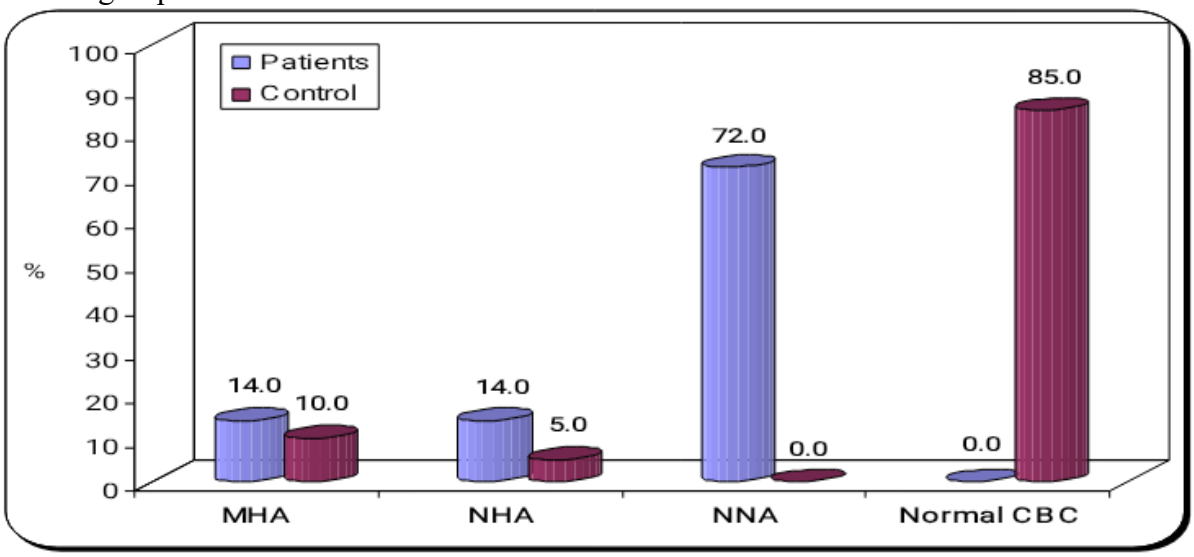


Figure 3: Classification of anemia types based on RBC indices (MCV, MCH, and MCHC) and the distribution percentages of various anemia types within the study groups.

The research indicates substantial disparities in anemia prevalence between patient and control groups. Patients exhibited elevated rates of MHA(Microcytic-Hypochromic anemia) and NHA (Normocytic-Hypochromic anemia) in comparison to the control group (5%). NNA (Normocytic-Normochromic anemia) prevalence was significantly elevated in patients at 72% compared to 0% in the control group. Notably, 85% of the control exhibited normal hemoglobin levels, suggesting that 100% of the patients were anemic in contrast to 15% of the control group.

Table (10): Serum total protein and albumin of study groups

	Patients (n= 50)	Control (n= 20)	P-value
Total protein:			
Mean ± SD	6.57 ± 0.49	7.32 ± 0.39	0.001*
Range	5.6 - 7.5	6.7 - 8	
Serum albumin:			
Mean ± SD	3.50 ± 0.41	4.32 ± 0.35	0.001*
Range	2.6 - 4.2	3.7 - 4.9	
Blood urea:			
Mean ± SD	105.62 ± 31.13	33.70 ± 4.65	0.001*
Range	58 – 189	25 - 41	
Serum creatinine:			
Mean ± SD	2.56 ± 0.58	0.79 ± 0.11	0.001*
Range	2 - 4.5	0.7 - 1	
GFR			
Mean ± SD	26.46 ± 6.91	100.97 ± 9.87	0.001*
Range	15.4 - 43.4	90 - 127.5	

Table (10) indicates notable disparities in serum albumin and total protein concentrations between patients and the control group, with the latter exhibiting elevated mean levels of both parameters. Significantly substantial disparities in blood urea and serum creatinine levels between patients and the control group and show highly significant differences in GFR between patients and control

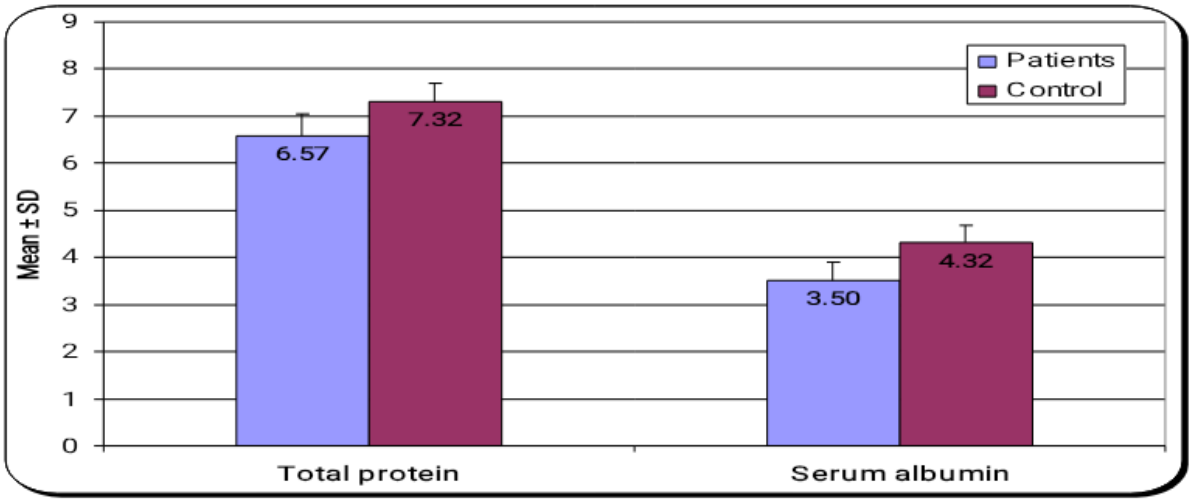


Figure (4) Serum total protein and albumin of the study groups.

Figure (4) demonstrates substantial changes in serum albumin and total protein levels between patients and controls.

Table (11): CKD stages (III & IV) in the studied patients

CKD stage	No. (n= 50)	%
Stage III	16	32.0
Stage IV	34	68.0

CKD: chronic kidney disease

Table 11 depicts the prevalence of chronic kidney disease stages III and IV among the examined patients as follows: Sixteen patients (32%) are classified as CKD stage III, whereas thirty-four patients (68%) are classified as CKD stage IV.

Table (12) indicates notable disparities in serum iron, TSAT, and serum ferritin between patients and controls, whereas no significant changes in TIBC are observed between the two groups.

Table (12): Iron profile of study groups

	Patients (n= 50)	**Control (n= 20)**	**P-value**
S. iron:			
Mean ± SD	52.38 ± 12.40	76.90 ± 22.16	0.001*
Range	33 – 80	33 - 114	
TIBC:			
Mean ± SD	244.40 ± 58.99	260.25 ± 35.33	0.187
Range	117 – 423	189 - 312	
TSAT:			
Mean ± SD	23.03 ± 8.25	30.28 ± 10.35	0.009*
Range	9.3 - 39.32	11.87 - 54.29	
S. ferritin:			
Mean ± SD	686.69 ± 336.89	387.71 ± 186.37	0.001*
Range	210 - 1687.4	57.48 - 820.7	

S. Iron: serum iron, TIBC: Total iron binding capacity, TSAT: Transferrin saturation, S. Ferritin: Serum ferritin.

Table (13): Erythropoietin of study groups

Erythropoietin	**Patients (n= 50)**	**Control (n= 20)**	**P-value**
Mean ± SD	4.00 ± 0.87	17.16 ± 8.26	0.001*
Range mIU/mL	2.5 - 5.7	9.5 - 43	

Table (14): Serum potassium

Serum potassium	Patients (n= 50)	Control (n= 20)	P-value
Mean ± SD	4.33 ± 0.66	3.72 ± 0.28	0.001*
Range mEq/L	3.2 - 5.7	3.2 - 4.2	

Table (14) demonstrates significantly substantial disparities in serum potassium levels between patients and the control group.

Table (15): Abdominal ultra-sonogram of studied patients

Abdominal ultra-sonogram	**No. (n= 50)**	**%**
G I MRD	6	12.0
G II MRD	20	40.0
G III MRD	24	48.0

G I: grade I, G II: grade II, G III: grade III, MRD: medical renal disease

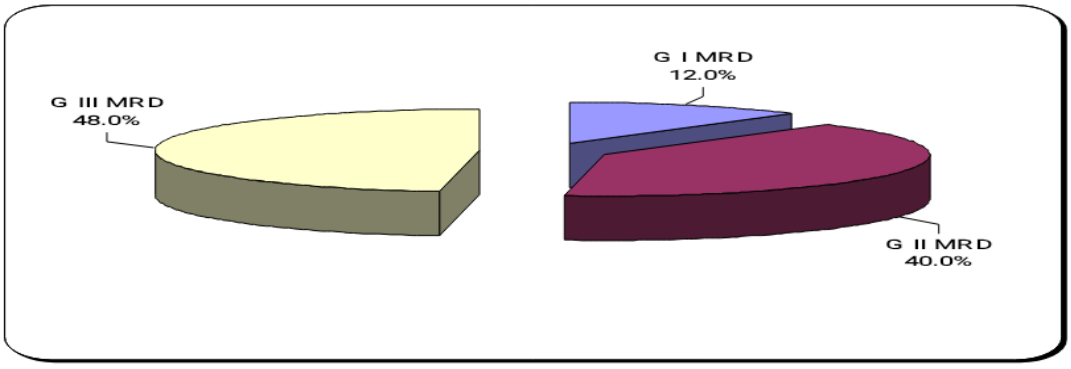


Figure (5) Percentages of different grades of MRD by Abdominal ultra-sonography in studied patients

Table 15 and Figure 5 depict the various grades of medical renal disorders in the examined patients as identified by abdominal ultrasonography: 6 patients (12%) are classified as grade I MRD, 20 patients (40%) as grade II MRD, and 24 patients (48%) as grade III MRD.

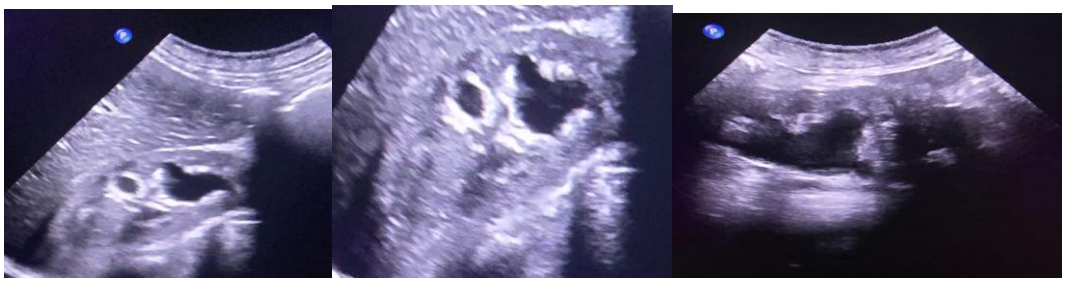


Figure (6): showing ultrasound of 54 years old female of chronic kidney disease . 2D ultrasound reveals increased echogenicity of renal parenchyma (grade II nephropathy) associated with moderate dilatation of pelvicalyceal system (moderate hydronephrosis).

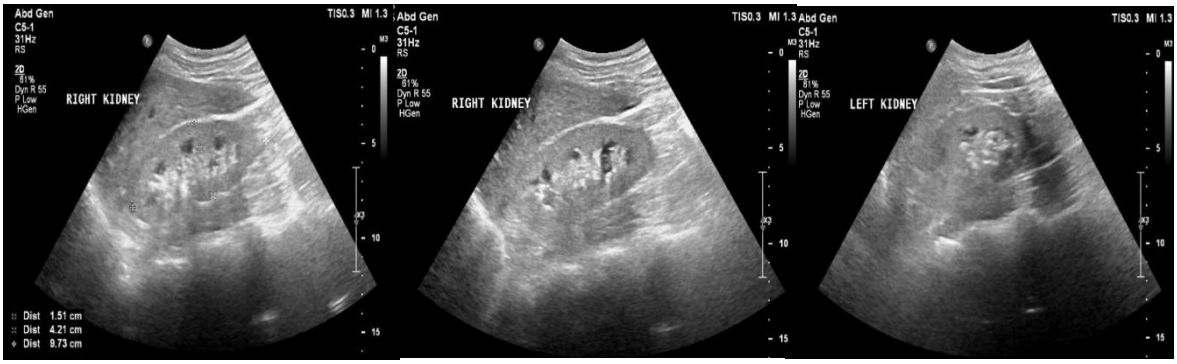
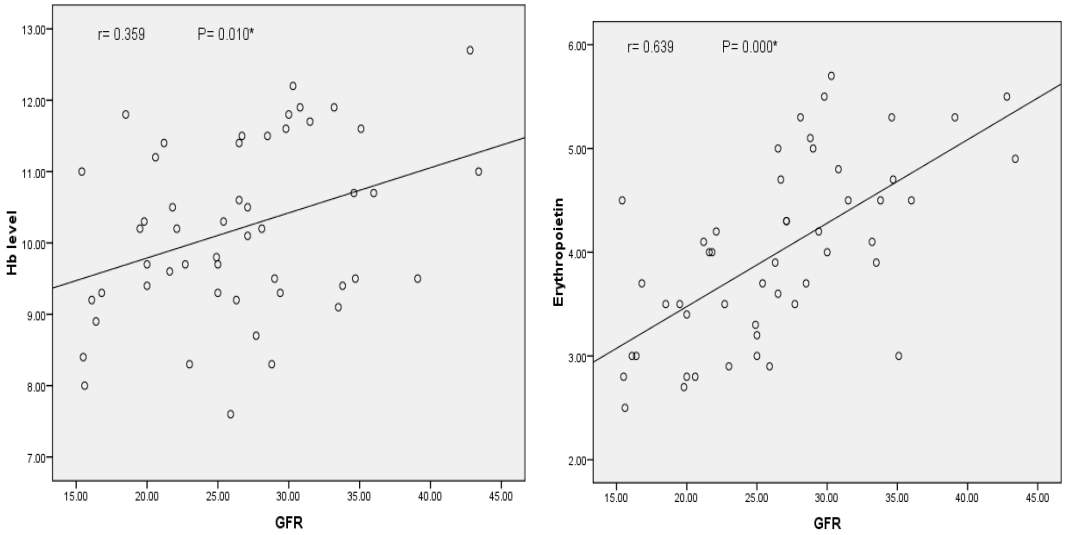


Figure (7): 40 years old female patient of high renal function tests.



2D ultrasound shows bilateral average sized kidneys with mild increased echogenicity of renal parenchyma grade (II) nephropathy,normal pelvicalyceal system

Figure (7): (a): Correlation between Hemoglobin (Hb) level and Glomerular Filtration Rate (GFR). (b): Correlation between erythropoietin level and glomerular filtration rate (GFR).

Figure (7) illustrates an extremely strong positive association between erythropoietin levels and glomerular filtration rate (GFR).

Table (16): Prevalence of risk factors of anemia in the studied patients

Risk factors	**No.**	**%**
Anorexia	22	44.0
Positive occult blood in stool	3	6.0
Increased CRP	50	100.0
Increased ESR	50	100.0
Increased Serum Ferritin	40	80.0
Increased Blood urea	50	100.0
Increased Serum creatinine	50	100.0
Decreased GFR	50	100.0
Erythropoietin deficiency	27	54.0

The research indicated that anorexia was observed in 44% of patients, but occult blood in stool was positive in 6%. Inflammatory markers comprised elevated concentrations of CRP, ESR, and serum ferritin in 50% of individuals. Blood urea and serum creatinine levels were elevated in all patients, accompanied by a reduction in GFR in every instance. Fifty-four percent of patients exhibited erythropoietin deficiency. These findings underscore the need of comprehending the risk factors associated with anemia in patients.

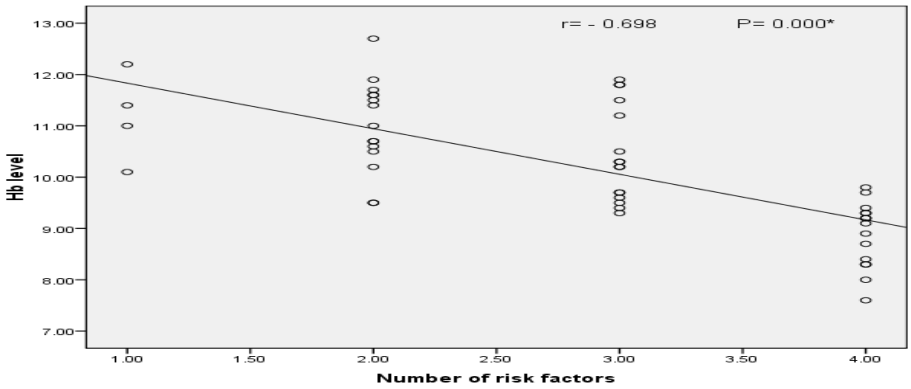


Figure (8): Correlation between number of risk factors of anemia in CKD and Hb level

Figure (8) shows highly significant inverse correlation between number of risk factors and hemoglobin level. The more increase in the number of risk factors of anemia in renal patients, the more decrease in hemoglobin level.

Table (17): Relation between type of anemia and CKD stage in studied patients

CKD stage	MHA (n= 7)		NHA (n= 7)		NNA (n= 36)		P-value
	No.	%	No.	%	No.	%	
Stage III	2	28.6	1	14.3	13	36.1	0.515
Stage IV	5	71.4	6	85.7	23	63.9	

CKD: chronic Kidney disease, HA: Microcytic-Hypochromic anemia, NHA: Normocytic-Hypochromic anumarana: Normocytic-Normochromic anemia

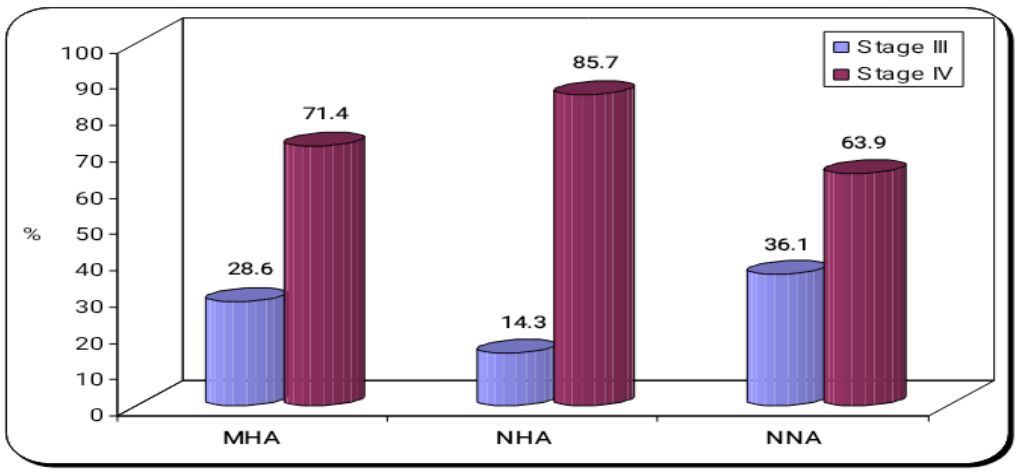


Figure (9): Relation between type of anemia and CKD stage in studied patients

The research indicates that 28.6% of patients with MHA, NHA, and NNA are classified as having stage III CKD, whereas 71.4% are categorized as having stage IV CKD. 14.3% of individuals with

NHA exhibit stage III CKD, whereas 84.7% present with stage IV CKD. Among NNA patients, 36.1% exhibit stage III CKD, whereas 63.9% present with stage IV CKD. The frequency of each category escalates throughout the shift from stage III to stage IV.

Discussion

Chronic kidney disease (CKD) is a prevalent disorder, particularly among the elderly, and is linked to an elevated risk of cardiovascular disease and chronic renal failure. Anemia frequently complicates chronic kidney disease (CKD), however the ideal hemoglobin targets for patients across different disease stages remain ambiguous. Anemia is a significant predictor of complications and mortality from cardiovascular causes in people with chronic kidney disease (CKD) (Hanna et al., 2021).

The morbidity and mortality are significantly influenced by the underlying etiology of the patient's anemia and the disease stage, whether early or advanced. (Portolés et al., 2021). In persons with severe chronic renal disease, the pathogenesis is typically complex. In individuals with chronic kidney illness, normochromic normocytic anemia mostly arises from diminished renal production of erythropoietin, worsening as the glomerular filtration rate (GFR) declines (Lippi et al.2021). A lack of reticulocyte response is noted, indicating that the lifespan of red blood cells is reduced. Additionally, there is an increased tendency for bleeding, which can be linked to platelet dysfunction caused by uremia. (Thiagarajan et al., 2021)

Iron deficiency frequently occurs in individuals with chronic kidney disease (CKD). Additional etiologies of anemia in chronic kidney illness encompass the presence of uremic inhibitors (e.g., parathyroid hormone, inflammatory cytokines), decreased half-life of circulating erythrocytes, and deficiencies in folate or vitamin B12. The rectification of anemia correlates with enhanced results (Agarwal, 2021).

Erythropoiesis-stimulating drugs (ESAs) have been utilized for nearly two decades and continue to be the primary approach for managing anemia in patients with chronic kidney disease (CKD). The utilization of erythropoiesis-stimulating agents in the treatment of renal anemia has demonstrated improvements in mortality, reductions in cardiovascular morbidity, and enhancements in quality of life (Weir, 2021).

This research involved 70 Egyptian participants, categorized into two groups: 50 individuals with chronic kidney disease (CKD) stages III and IV (pre-end-stage renal disease) and 20 healthy individuals serving as a control group. This study aimed to examine the various risk factors associated with anemia and the prevalence of anemia in pre-ESRD patients (stages III and IV CKD).

Ultrasonography (US) of the abdomen was employed to identify the underlying etiology and to provide proof of the chronicity of renal disease (Robba et al.2021). The results indicated the presence of varying degrees of medical renal disease (MRD) among the individuals examined, with diabetes and hypertension identified as the predominant etiologies of chronic kidney disease (CKD). Anorexia was identified in only 44% of patients, which can be attributed to the inclusion of individuals with chronic kidney disease and those undergoing hemodialysis (Mahmoud & Borgi, 2021).

No substantial differences in anthropometric data, including weight, height, and body mass index, were seen among the study groups.The study sought to examine the clinical manifestations of chronic kidney disease (CKD) patients, emphasizing pallor, face edema, and lower limb swelling. The findings contradicted earlier research, which indicated that facial puffiness accompanied by lower limb edema is the predominant clinical manifestation in CKD patients.

The study revealed that 30% of individuals exhibited no proteinuria, whereas 70% presented varying degrees of proteinuria. Proteinuria is associated with the etiology of chronic kidney disease (CKD) and escalates in its advanced phases (Yan et al., 2021). The American Diabetes Association and the National Kidney Foundation assert that dipstick positive proteinuria of 1+ or above can replace the albumin:creatinine ratio. (Mejia et al., 2021)

Occult blood in stool was detected in 3 patients (6%), but it was not detected in 47 patients (94%). This discord can be elucidated by the substantial cohort of individuals, alongside those with stage 2 and stage 5 chronic kidney disease, incorporated in the recent study.The research identified markedly

significant disparities between patients and control groups in random blood sugar (RBS), C-reactive protein, erythrocyte sedimentation rate (ESR), hemoglobin (Hb) level, hematocrit value (HCT), red blood cell (RBC) count, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and reticulocyte count. No significant difference was seen between patients and controls in the counts of white blood cells (WBCs) and mean corpuscular volume (MCV) (Shi et al., 2021)

The disparity in platelet counts between the study groups was considerable, with elevated levels observed in the control group. The mean platelet count ± SD was (248.40 ± 36.43 and 222.86 ± 42.33) $x10^3$/microliter in the control and patient groups, respectively. These findings corroborate earlier research indicating that platelets may diminish in chronic kidney disease (CKD) due to uremia and the fundamental etiology of renal dysfunction. (Baaten et al., 2021)

The study classified men and postmenopausal women with hemoglobin levels below 13 gm/dl, and other women with hemoglobin levels below 12 gm/dl, as anemic, in accordance with the World Health Organization (WHO) guidelines. Anemia is characterized by a hemoglobin concentration below 13 gm/dl in men and postmenopausal women, and below 12 gm/dl in other women. (Vigneshwaran, 2021).

The study demonstrated statistically substantial disparities in anemia prevalence between patients and controls, with all 50 patients (100%) exhibiting anemic. Of the patients, 72% exhibited normocytic-normochromic anemia (NNA), 14% presented with normocytic-hypochromic anemia (NHA), and 14% were diagnosed with microcytic-hypochromic anemia (MHA). These findings corroborate earlier research indicating that 100% of advanced CKD patients not undergoing treatment exhibited anemia. (Bissinger et al., 2021)

In conclusion, the study offers significant insights into the clinical manifestations of CKD patients and their related clinical features. Additional study is required to elucidate the fundamental causes of CKD and to formulate appropriate treatments for affected people.

The research sought to examine the prevalence of microcytic-hypochromic anemia (MHA), normocytic-hypochromic anemia (NHA) and normocytic-normochromic anemia (NNA) in individuals with chronic kidney disease (CKD). The incidence of each category escalated as the patient progressed from stage III to stage IV. The study identified notable disparities in serum albumin and total protein levels between patients and controls, with the mean values of both being elevated in the control group. This aligns with prior research indicating diminished appetite resulting from the increasing deterioration of renal function, which subsequently leads to reduced protein consumption.

The investigation revealed notable disparities in renal profiles, with mean blood urea and serum creatinine levels elevated in patients relative to the control group. This aligns with prior research indicating that anemia is prevalent in pre-dialysis CKD patients, with a significant incidence of iron shortage. The study identified significant disparities in transferrin saturation (TSAT%) and total iron binding capacity (TIBC) across individuals

Serum ferritin levels were enhanced in patients relative to the control group, corroborating other research that indicated reduced transferrin saturation and increased serum ferritin levels in chronic kidney disease patients due to impaired iron transport and stored iron reserves. Increased serum ferritin levels were noted in predialysis chronic kidney disease patients as a result of infection and inflammation.

Erythropoietin (EPO) levels were considerably elevated in patients relative to the control group, with mean levels of 4.00 ± 0.87 mlu/ml and 17.16 ± 8.26 mlu/ml, respectively. This aligns with prior research indicating EPO deficit in chronic kidney illness, which is a physiological response to reduced glomerular filtration rate and the partial or total depletion or damage of specialized peritubular cells responsible for EPO production (Shih, H. M., et al., 2018).

Serum potassium levels were markedly elevated in patients relative to the control group, corroborating prior research that identified hyperkalemia in predialysis individuals with chronic kidney disease (CKD). The research identified a substantial positive association between hemoglobin (Hb) levels and

glomerular filtration rate (GFR) in patients not undergoing renal replacement treatment. (MacIsaac et al., 2021)

The research indicated that anorexia was observed in 44% of patients, but occult blood in stool was positive in 6% of patients. Elevated levels of CRP, ESR, and serum ferritin as markers of inflammation were observed in 50%, 100%, and 80% of patients, respectively. Furthermore, signs of "uremic milieu" were observed in all patients, characterized by elevated blood urea and serum creatinine levels, alongside diminished GFR levels (Rosner et al., 2021).

The study demonstrated a substantial inverse link between the number of risk factors and hemoglobin levels, indicating that an increase in risk factors associated with anemia corresponds to a decrease in hemoglobin levels. This data corroborates other research indicating that anemia is a prevalent consequence of chronic renal disease and must be factored into the therapy of CKD patients. (Hanna et al., 2021).

Conclusion

A study including 70 Egyptian volunteers, comprising 50 individuals with pre-end-stage CKD and 20 healthy controls, revealed that anemia is prevalent among pre-ESRD patients. The primary classification was normocytic-normochromic anemia (72%), succeeded by normocytic-hypochromic (14%) and microcytic-hypochromic (14%). Diabetes and hypertension were recognized as the principal causes of CKD. Marked disparities were observed between CKD patients and controls regarding critical markers, including hemoglobin, hematocrit, red blood cell count, platelet counts, inflammatory markers, renal function indicators, elevated serum potassium, diminished serum albumin, total protein, and erythropoietin (EPO) levels. The study additionally disclosed various problems, including proteinuria in 70% of chronic kidney disease patients and anorexia in 44%. The results underscore the necessity for ongoing research to elucidate the underlying causes of CKD and to formulate tailored therapies for related anemia and other consequences.

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