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Original Article

Evaluation of Liver Enzymes, Hematologic and Coagulation Factors in Patients with Chronic Kidney Disease

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HIGHLIGHTS

• In patients with CKD renal markers (creatinine and BUN) were higher than normal.

• In patients with CKD coagulation factors (PT, PTT, and INR) were higher than normal.

• Patients with CKD are prone to anemia because a decrease in the mean hemoglobin and hematocrit and an increase in RDW-CV were observed..

ABSTRACT

Introduction
Chronic Kidney Disease (CKD) is a condition where the kidneys have abnormal structure or function that lasts for more than three months, can have negative health effects, and often does not show symptoms in the beginning. In that research, we tried to examine the diagnostic markers from the laboratory to find clues for a faster diagnosis of this disease.

Methods
This paper is a cross-sectional analytical study on 107 patients with CKD hospitalized in Abadan University of Medical Sciences educational hospitals from March 21, 2017, to March 19, 2020. Once the necessary permits were obtained, the laboratory information of patients was received from HIS. The data was analyzed by SPSS version 16 software. Statistical significance is considered when P-value>0.05.

Results
Out of 107 patients with CKD in the study, 55 (51.4%) were female and 52 (48.6%) were male. The mean age of the group was 57.9±17.42 years. The means of renal diagnostic markers such as creatinine 7.42±4.55 and BUN 56.97±36.78 were higher than normal. Also, the mean coagulation markers, including PT (15.86±9.89), PTT (47.65±29.11), and INR (1.54±1.07), were higher than normal. The mean of hematological diagnostic markers, including hemoglobin and hematocrit, was lower than normal. The mean RDW-CV (16.97±4.19) and white blood cells (11.19±9.01) were higher than normal.

Conclusions
This study showed that renal markers (creatinine and BUN) and coagulation factors (PT, PTT, and INR) were higher than normal. In this study, it was observed that people with CKD are prone to anemia because a decrease in the mean hemoglobin and hematocrit and an increase in RDW-CV were observed.

Keywords: Kidney; Coagulation factors; Hemoglobin; Creatinine

Introduction

More than 750 million people around the world are affected by kidney disease (1). Although cardiac and cerebrovascular diseases and cancer are the primary causes of mortality related to chronic illnesses, kidney diseases have now become widespread. They are also one of the top causes of death in industrialized nations (2). In high-income countries, non-communicable diseases, such as diabetes and hypertension, are the leading causes of CKD. While in low- and middle-income countries, this disease has additional potential etiologies, including infectious diseases and environmental toxins (3).

Chronic Kidney Disease is a condition where the kidneys have abnormal structure or function for over 3 months, with associated health implications (4). Diabetes mellitus (DM) is the most common cause of CKD (5). CKD is frequently clinically silent in the early stages, resulting in most patients being detected shortly before or with the onset of symptomatic disease when the impact of available therapeutics is markedly reduced (6).

CKD may have asymptomatic metabolic complications like metabolic acidosis, anemia, and mineral and electrolyte disorders (7). Kidney disease is usually asymptomatic in the early stages, so early diagnosis is essential to reduce the risk of subsequent complications (8). Therefore, early diagnosis of this disease is necessary for effective treatment of CKD. In that research, we tried to examine the diagnostic markers from the laboratory to find clues for a faster diagnosis of this disease.

Methods

This investigation is a cross-sectional analytical study on patients with CKD hospitalized in educational hospitals of Abadan University of Medical Sciences from March 21, 2017, to March 19, 2020. The criteria for inclusion in the article were patients with CKD hospitalized in the educational hospitals of Abadan from March 21, 2017, to March 19, 2020, whose laboratory information was available. Exclusion criteria were people with chronic kidney disease hospitalized in educational hospitals of Abadan, whose laboratory information was unavailable. This study was approved by the Ethics Committee of Abadan University of Medical Sciences, Abadan, Iran (Ethical Approval ID: IR.ABADANUMS. REC.1399.043).

After obtaining the necessary permissions, by referring to the medical records department of Abadan and Khorramshahr hospitals, the laboratory information of 107 hospitalized CKD patients from March 21, 2017, to March 19, 2020, available in HIS was obtained. The selection of samples was done randomly and only based on their diagnosis.

The information included renal factors (Creatinine (Cr), Blood Urea Nitrogen (BUN), serum potassium (K) and serum sodium (Na); liver factors (SGOT or AST and SGPT or ALT); hematologic factors White Blood Cell (WBC), Red Blood Cells (RBC), Mean Corpuscular Hemoglobin Concentration (MCHC), Lymphocytes (lymph), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Red Cell Distribution Width (RDW-CV) and coagulation factors (PT, PTT, Platelets and INR).

When describing the data, we utilize mean and standard deviation for quantitative variables and frequency and percentage for qualitative variables. We also check the normality of quantitative variables using the Kolmogorov-Smirnov test. We analyzed the data using a T-test and one-way ANOVA with SPSS version 16 software. Statistical significance is considered when P-value>0.05.

Results

Out of 107 patients with CKD in the study, 55 (51.4%) were female and 52 (48.6%) were male. The group's mean was 57.9±17.42 years, with the youngest and the oldest being 20 and 88 years old, respectively.

In CKD patients, the highest frequency was related to the age group of 60-69 years 31(29%) (Table 1). Among the investigated factors, the mean BS 172.98±135.24 was higher than normal. The means of renal diagnostic markers such as creatinine 7.42±4.55 and BUN 56.97±36.78 were higher than normal. Also, the mean coagulation markers, including PT (15.86±9.89), PTT (47.65±29.11), and INR (1.54±1.07), were higher than normal. The mean of hematological diagnostic markers, including hemoglobin and hematocrit, was lower than normal. The mean RDW-CV (16.97±4.19) and white blood cells (11.19±9.01) were higher than normal. Liver enzymes, including ALT and AST, were in the normal range (Table 2). There was no significant difference in laboratory diagnostic factors in this study between men and women (Table 3) and different age groups (Table 2).

Discussion

In this study, laboratory diagnostic markers were investigated in patients with CKD. The renal diagnostic markers (creatinine and BUN) were observed to be higher than normal in these patients. Also, by examining the hematological factors, it was observed that the mean hematocrit and hemoglobin are lower than normal in these patients, and the mean white blood cell and RDW-CV are higher than normal.

Table 1. Frequency of patients with CKD by age group

Age, year	N (%)
≤ 49	28 (26.2)
50-59	21 (19.6)
60-69	31 (29)
≥70	27 (25.2)

Table 2. The mean and standard deviation of the investigated factors in patients with CKD based on age group

Variables	Age group					F**	P-value
	≤49	50-59	60-69	≥70	Total		
BS (mg/dL)	153.93±82.94	227.40±258.52	180.93±95.49	141.73±47.39	172.98±135.24	1.79	0.15
BUN (mg/dL)	54.21±44.43	54.47±28.54	62.57±34.10	55.15±38.62	56.97±36.78	0.33	0.79
Cr (mg/dL)	8.95±5.67	7.92±4.73	7.20±3.76	5.71±3.39	7.42±4.55	2.44	0.06
Na (mEq/L)	137.93±5.17	136.35±4.18	138.06±4.24	139.08±4.75	137.95±4.64	1.31	0.72
PT (s)	17.53±12.24	13.06±2.04	13.71±3.74	19.82±15.39	15.86±9.89	1.99	0.12
PTT (s)	51.37±32.28	44.29±23.28	42.38±20.84	55.20±40.83	47.65±29.11	0.77	0.51
INR	1.70±1.24	1.22±0.40	1.31±0.63	2.00±1.58	1.54±1.07	2.18	0.09
WBC (/mm3)	13.28±9.81	9.27±4.65	10.81±11.99	11.01±6.62	11.19±9.01	0.81	0.48
RBC (million/mm3)	3.68±1.26	4.20±1.63	4.08±1.11	4.28±1.95	4.05±1.50	0.83	0.47
MCV (µm³)	86.61±8.03	83.70±9.23	87.53±9.85	89.92±10.62	87.14±9.59	1.73	0.16
Hb (g/dL)	9.88±3.24	13.20±14.38	10.77±2.46	10.61±2.44	10.99±6.88	0.98	0.40
Hematocrit (%)	31.56±9.83	32.91±7.67	35.05±8.25	34.96±6.84	33.66±8.28	1.11	0.34
MCH (pg/cell)	27.94±3.53	26.71±3.90	28.13±3.85	27.55±4.09	27.65±3.82	0.63	0.59
PLT (mm³)	227.46±98.65	22.47±99.60	217.07±113.13	201.92±97.93	217.03±101.96	0.30	0.81
RDWCV (%)	17.80±6.88	16.98±3.61	16.80±2.44	16.32±2.38	16.97±4.19	0.56	0.64
ALT (IU/L)	13.13±10.16	9.60±5.06	13.65±7.76	19.53±21.89	14.47±13.55	1.43	0.24
AST (IU/L)	15.92±10.70	12.00±5.27	22.70±30.43	35.90±45.22	22.48±29.68	2.33	0.08
LYMPH (%)	21.10±12.65	26.10±14.41	25.52±14.38	21.69±15.32	23.52±14.08	0.70	0.55
Neutrophil (%)	78.24±13.52	74.14±15.21	71.67±18.28	77.84±15.33	75.37±15.80	0.89	0.45
K (mEq/L)	5.02±0.96	4.77±0.95	5.13±1.30	4.92±0.99	4.98±1.07	0.96	0.41

*Standard deviation
**: F-value conducted from ANOVA test.
BS: Blood sugar, BUN: blood urea nitrogen, Cr: creatinine, Na: sodium, PT: prothrombin time, PTT: partial thromboplastin time, INR: international normalized ratio, WBC: white blood cell, RBC: red blood cell, MCV: Mean corpuscular volume, Hb: hemoglobin, RDWCV: Red cell distribution width, MCH: mean corpuscular hemoglobin, PLT: platelet, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LYMPH: lymphocyte

Table 3. The mean and standard deviation of the investigated factors in patients with CKD based on the gender of the patients

Variables	Sex		T*	P-value
	Male	Female		
BS (mg/dL)	176.45±145.74	169.58±125.42	0.25	0.79
BUN (mg/dL)	53.12±30.17	60.61±42.05	-1.05	0.29
Cr (mg/dL)	7.63±5.09	12.99±43.14	-0.87	0.38
Na (mEq/L)	138.66±3.93	137.3±5.16	1.49	0.13
K (mEq/L)	4.92±1.00	5.04±1.14	-0.99	0.32
Ca (mEq/L)	8.91±0.87	8.75±1.04	0.76	0.44
PT (s)	14.94±8.04	16.66±11.31	-0.75	0.45
PTT (s)	46.34±25.79	48.80±32.03	-0.36	0.71
INR	1.44±0.87	1.63±1.21	-0.77	0.44
WBC (/mm3)	12.18±10.91	10.25±6.72	1.09	0.27
RBC (million/mm3)	4.20±1.86	3.91±1.06	0.98	0.32
MCV (µm³)	86.76±8.51	87.47±10.54	-0.37	0.70
Hb (g/dL)	10.50±2.78	11.44±9.18	-0.70	0.48
Hematocrit (%)	33.82±8.37	33.52±8.27	0.18	0.85
MCH (pg/cell)	28.19±3.58	27.15±4.01	1.40	0.16
PLT (mm³)	211.47±89.04	222.18±113.21	-0.53	0.59
RDWCV (%)	16.56±2.95	17.36±5.09	-0.96	0.33

ALT (IU/L)	13.35±11.66	62.19±242.35	-1.22	0.22
AST (IU/L)	19.44±20.30	80.16±279.63	-1.33	0.19
LYMPH (%)	23.51±13.69	23.52±14.62	-0.00	0.99
Neutrophil (%)	76.26±13.47	268.10±1240.26	-0.99	0.32

BS: Blood sugar, BUN: blood urea nitrogen, Cr: creatinine, P: phosphorus, Na: sodium, K: potassium, Ca: Calcium, PT: prothrombin time, PTT: partial thromboplastin time, INR: international normalized ratio, WBC: white blood cell, RBC: red blood cell, MCV: Mean corpuscular volume, Hb: hemoglobin, MCH: mean corpuscular hemoglobin, PLT: platelet, RDWCV: Red cell distribution width, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LYMPH: lymphocyte, K: potassium

*: T-value conducted from Independent T-test.

According to a study by Suresh M et al., in 2012, patients with chronic kidney disease often have lower blood indices due to a variety of factors including impaired erythropoietin production, increased hemolysis, suppression of bone marrow erythropoiesis, hematuria, blood loss from the digestive system. Hematological parameters are negatively correlated with serum creatinine concentration. The majority of individuals with chronic kidney disease who have abnormal levels of RBC, hemoglobin, and hematocrit have levels lower than normal, while the majority of those with abnormal levels of urea and creatinine have levels higher than normal (9).

Also, according to Afshan Zeeshan Wasti et al., chronic kidney patients have significantly lower mean indices of red blood cells, hemoglobin, MCH, and MCHC (10). Fatih KAMIŞ et al., (2021) reported a significant increase in blood serum creatinine levels in patients with chronic kidney disease. However, no significant differences were found in WBC, neutrophil, lymphocyte, and platelet indices (11). The present paper's results indicated that mean coagulation markers PT, PTT, and INR were higher than normal in CKD patients.

According to a study conducted by Xia and colleagues in 2023, there were no significant statistical differences in PT levels between patients with renal failure and the control group. However, male patients with renal failure stated significant differences in PTT levels in comparison with the control group. The research suggests that PTT levels may serve as an indicator of coagulation abnormalities in male patients with renal failure (12). In the present study, liver enzymes (AST and ALT) were within the normal range in patients with CKD.

Musazadeh et al., (2023) reported that patients with chronic kidney disease had lower ALT and AST serum levels than the control group. However, the two groups had no significant difference (13).

Sette et al., found that serum AST and ALT levels were negatively correlated with serum creatinine levels and positively correlated with GFR. They also observed higher liver enzyme levels in patients with lower stages of CKD (14). According to Dyab Allawi et al., Dialysis patients and CKD cases had significantly lower mean ALT and AST levels (15).

Among the limitations of this study were incomplete patient information in HIS and low sample size. It is suggested that in future studies, more extensive studies with larger sample sizes among different ethnic groups and comparisons with the control group should be conducted.

Conclusions
This study showed that renal markers (creatinine and BUN) and coagulation factors (PT, PTT, and INR) were higher than normal. In this study, it was observed that people with CKD are prone to anemia because a decrease in the mean hemoglobin and hematocrit and an increase in RDW-CV was observed.

Authors' contributions
Conceptualization: ER, Formal analysis: AZ, NK, Investigation: ER, AZ, and ABK, Methodology: ER, ABK, HMF, TEF, MMSh, and KhK, Project administration: ER, Validation: HMF, Writing–original draft: ABK, Writing–review & editing: ER.

Conflict of interest
All authors declare that there is no conflict of interest.

Ethics statement
The Ethics Committee of Abadan University of Medical Sciences approved this study (Ethical Approval ID: IR.ABADANUMS.REC.1399.043).

Data availability
Data will be provided on request.

Abbreviations

ALT	Alanine transaminase
AST	Aspartate aminotransferase
BS	Blood sugar
BUN	Blood urea nitrogen
Cr	Creatinine
INR	International normalized ratio
K	Potassium
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
Na	Sodium
PT	Prothrombin time
PTT	Partial thromboplastin time
RBC	Red blood cell
RDW-CV	Red Cell Distribution Width
WBC	White blood cell

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