Original Article

Can CBC Profile and Liver Function Test Predict Chronic Kidney Disease among a Normal Population?

Mahmood Moosazadeh, Fatemeh Espahbodi[1], Mahdi Afshari[2], Arman Eslami

Gastrointestinal Cancer Research Center, Non-Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran, [1]Department of Internal Medicine, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran, [2]Pediatric Gastroenterology and Hepatology Research Center, Zabol University of Medical Sciences, Zabol, Iran

Abstract

Background: Kidney disorders are mainly diagnosed after a major decline in the renal function. Chronic kidney disease (CKD) is one of the most common disorders of the urinary system defined by gradual reduction of renal function. Considering the silent nature and late diagnosis of this problem, this study aims to investigate the prevalence of CKD and its association with Complete Blood Count (CBC) profile and liver function tests. **Methods:** Out of the total population enrolled in the Tabari cohort study, 5822 subjects without history of diabetes mellitus, hypertension, cardiac disease, renal failure, cancer, and pathologic obesity were selected. Glomerular filtration rate (GFR) was calculated using creatinine clearance as well as Modification of Diet in Renal Disease (MDRD) equation. CKD was defined as GFR decline less than 60 ml/min/1.73 m^2 regardless of its main cause. **Results:** Prevalence of CKD in total population as well as men and women was 20.2%, 16.8%, and 23.1%, respectively. Multivariate models showed the odds ratios for third and fourth quartiles of Mean corpuscular volume (MCV) and also for the fourth quartile of the lymphocyte count as of 0.78 (0.64, 0.95), 0.81 (0.67, 0.99), and 1.22 (1.01, 1.47), respectively. Corresponding odds ratios for the fourth, third, and second quartiles of Blood Urea Nitrogen (BUN) were 1.42 (1.14, 1.77), 1.76 (1.42, 2.19), and 2.79 (2.27, 3.43), respectively. **Conclusions:** This study showed a high prevalence of CKD among the normal residents (without major underlying diseases and excessive obesity) in the north of Iran, especially among women. In addition, low MCV, low lymphocyte, and high BUN were detected as predictors of this disorder.

Keywords: *Blood cell count, chronic, cohort studies, liver function tests, renal Insufficiency*

Introduction

Chronic kidney disease (CKD) is one the most prevalent renal disorders in the world defined as a gradual loss of renal function.[1-6] According to the global burden of the disease study in 2015, 1.2 million deaths, 19 million disability-adjusted life-years, and 18 million life-years lost due to cardiovascular disorders are directly associated with the reduction in the glomerular filtration rate (GFR).[7]

Incidence and prevalence of CKD in different countries vary based on different ethnicities, social determinants, and genetic factors. CKD has been estimated to affect approximately 10% of the general population and more than 50% of the high-risk population.[3,8]

CKD is developed following a complex of various factors and chronic diseases such as hypertension, diabetes mellitus, hypercholesterolemia, aging, smoking, obesity, urinary infections, glomerulonephritis, pyelonephritis, polycystic kidney disease, urinary tract obstruction, renal stones, chronic use of special drugs (lithium, Non-steroidal anti-inflammatory drugs NSAIDS, opium) and severe renal trauma.[1,3,6,8-11]

Erythropoietin is produced by the kidneys for bone marrow stimulation for red blood cell production. During the severe kidney damage, erythropoietin will be decreased leading to RBC reduction. Hematologic parameters especially the RBC are the most affected markers following CKD.[3] Moreover, liver enzymes, such as ALT, AST, and GGT, are considered as markers for detection of aggression against hepatocytes. However, low serum levels of the liver enzymes can be seen in CKD patients with renal failure receiving hemodialysis. Such patients might be falsely diagnosed as liver damage.[12,13]

There are few evidences regarding the association between blood cells and liver

How to cite this article: Moosazadeh M, Espahbodi F, Afshari M, Eslami A. Can CBC profile and liver function test predict chronic kidney disease among a normal population? Int J Prev Med 2023;14:2.

Address for correspondence:
Prof. Mahmood Moosazadeh, Associate Professor of Epidemiology, Gastrointestinal Cancer Research Center, Non-Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran. E-mail: mmoosazadeh1351@gmail.com

Access this article online

Website: www.ijpvmjournal.net/www.ijpm.ir

DOI: 10.4103/ijpvm.ijpvm_9_22

Quick Response Code:

parameters and CKD. The available literature focuses mainly on the patients with hemodialysis or predialysis condition. The silent nature of the kidney disease and its delayed diagnosis makes it necessary to investigate the role of CBC profile and liver function tests in predicting the CKD among a healthy population without comorbidity with important chronic disease.

Methods

All necessary information in this cross-sectional (descriptive-analytic) study was obtained from the TABARI cohort data registry in the enrolment phase. This cohort is a part of the Prospective Epidemiological Research Studies in Iran (PERSIAN).[14,15] Methodological details of the TABARI and PERSIAN cohorts have been explained elsewhere.[14-16] At the first phase of the TABARI cohort, 10,255 individuals including urban and mountainous residents of Sari (capital of Mazandaran province: north of Iran) district were investigated by a group of trained staff.

This study was approved by the National Institutes for Medical Research Development (NIMAD) ethical committee (IR.NIMAD. REC.1398.350). All ethical principles of the Helsinki ethical declaration have been met and written informed consent was obtained from all the participants.

The target group of the present study was healthy population without comorbidity with important chronic disease and excessive obesity. Therefore, patients with diabetes mellitus, cardiovascular diseases, renal failure, different cancers, and body mass index more than 34 were excluded from the study. Evidences for detection of any background disorders among study subjects were investigated using health insurance booklets, self-reporting questionnaires regarding previous history of having disease or relevant drug consumption, measurement of fasting blood sugar, systolic/diastolic pressure, and body mass index. Consequently, CBC, liver function tests, and lipid profiles were measured in all included subjects.

CKD was determined based on GFR which was calculated using MDRD formula.[17]

$$GFR = 186 \times (S_{Cr})^{-1.154} \times (age)^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if Black}).$$

CKD was classified to five stages based on the GFR including renal damage with normal or increased GFR (GFR >90), renal damage with mild reduction in GFR (GFR between 60 and 89), renal damage with moderate reduction in GFR (GFR between 30 and 59), renal damage with severe reduction in GFR (GFR between 15 and 29), and renal failure (dialysis) with GFR less than 15.[17]

CKD was defined based on the National Kidney Foundation Kidney Disease Outcomes Quality Initiative as renal damage if GFR was less than 60 ml/min per 1.73 m^2.[8,18]

Data analyses were performed using STATA version 16 (Stata Corp LP, College Station, TX, USA) and SPSS version 24 (IBM Corp., Armonk, NY, USA) software. Variables were described by mean, median, standard deviation, and quartiles. Categorical variables were compared between subjects with and without CKD using Chi-square test. Logistic regression models were applied using CBC, liver function tests, BUN, waist circumference, and BMI which had *P* values less than 0.2 in the univariate models. Consequently, the odds ratios (95% confidence intervals) for White Blood Count (WBC), Red Cell Distribution Width (RDW), Platelet distribution width (PDW), Gamma Glutamyltransferase (GGT), BUN, Lymphocytes (LY), Monocytes (MO), waist circumference, and BMI were estimated.

Results

Of 10,255 subjects enrolled in the TABARI cohort, 4429 were excluded due to comorbidities and also 4 people were excluded because they did not have the results of the required laboratory exams. Finally, 5822 subjects were entered into the current study.

Frequencies of patients with normal or increased GFR as well as mild and moderate reduction in GFR were 328 (5.6%), 4318 (74.2%), and 1175 (20.2%), respectively. Just one of the patients had severe reduction in GFR. Totally, prevalence of CKD among normal population of the TABARI cohort was 20.2% (1176/5822).

Mean, standard deviation, median, minimum, and maximum GFR of the participants were 69.6, 11.8, 68.5, 26.6, and 138.7, respectively. Moreover, the first and third quartiles of GFR among the participants were 61.5 and 76.7, respectively. Therefore, 25% of the participants had GFR less than 61.5 while 25% of them had GFR more than 76.7. In addition, 50% of the study subjects had GFR between 61.5 and 76.7.

Prevalence of CKD among men and women was 16.8% (443/2642) and 23.1% (733/3180), respectively. In addition, prevalence of CKD among those aged 35–39, 40–49, 50–59, and 60–70 was 11.1% (144/1294), 17.1% (391/2291), 27.5% (428/1559), and 31.4% (213/678), respectively. Moreover, 21.4% (868/4062) and 17.5% (308/1760) of the population, respectively, living in urban and mountainous areas had CKD. Frequencies of the other clinical and epidemiological factors among subjects with and without CKD are illustrated in Table 1.

Based on the results of univariate analyses, the odds of having CKD among subjects with WBC more than the fourth quartile were significantly 20% lower than that among those with WBC lower than the first quartile (OR: 0.80; CI 95%: 0.67, 0.96). The corresponding odds ratios for MCV at the third and fourth quartiles were 0.80 (0.67, 0.96) and 0.76 (0.63, 0.91), respectively. In addition, the odds ratios for the third and fourth quartiles of lymphocyte

Table 1: Epidemiological and preclinical characteristics of participants with and without CKD

Variables	CKD; %		*P*
	No; *n*=4646	Yes; *n*=1176	
Gender			
Male	83.2	16.8	<0.001
Female	76.9	23.1	
Residence area			
Urban	78.6	21.4	0.001
Rural	82.5	17.5	
Tobacco use			
No	79.6	20.4	0.277
Yes	81.4	18.6	
Age group			
35-39	88.9	11.1	<0.001
40-49	82.9	17.1	
50-59	72.5	27.5	
60-70	68.6	31.4	
Education level			
University/College	77.7	22.3	<0.001
9-12 years in school	79.5	20.5	
6-8 years in school	85.2	14.8	
1-5 years in school	82.2	17.8	
No schooling	75.7	24.3	
Social-economic level			
1	19.4	16.2	<0.001
2	19.5	15.2	
3	20.5	18.4	
4	21.4	23.0	
5	19.2	27.2	
Waist circumference			
<102 for male and <88 for female	81.8	18.2	<0.001
≥102 for male and ≥88 for female	76.3	23.7	
BMI			
<25	85.8	14.2	<0.001
25-29.9	77	23	
≥30	77.1	22.9	
HDL			
>40 for male or >50 for female	79.3	20.7	<0.001
≤40 for male or ≤50 for female	80.8	19.2	
TC			
<200	83.6	16.4	<0.001
≥200	72.7	27.3	
TG			
<150	81.5	18.5	<0.001
≥150	77	23	
WBC			
<5.30	77.9	22.1	0.106
5.30-6.09	79.4	20.6	
6.10-7.09	80.3	19.7	
≥7.10	81.4	18.6	
RDW			
<10.50	81.2	18.8	0.357
10.51-10.79	79.4	20.6	
10.80-11.09	78.6	21.4	
≥11.20	80.1	19.9	
RBC			
<4.45	78.4	21.6	0.446
4.45-4.77	79.8	20.2	
4.78-5.15	80.3	19.7	
≥5.16	80.7	19.3	
MCV			
>82.40	77.8	22.2	0.002
82.40-86.79	77.7	22.3	
86.80-90.19	81.4	18.6	
≥90.20	82.2	17.8	
MPV			
<7.50	80.3	19.7	0.701
7.50-7.89	79.7	20.3	
7.90-8.29	79.0	21.0	
≥8.30	80.6	19.4	
PLT			
<214	78.8	21.2	0.730
214-248	80.4	19.6	
249-248	79.7	20.3	
249–285	80.2	19.8	
PDW			
<16.40	80.8	19.2	0.147
16.40-16.89	80.0	20.0	
16.90-17.49	80.7	19.3	
≥17.50	77.8	22.2	
BUN			
<14	87.8	12.2	<0.001
14-16.9	82.9	17.1	
17-21.9	79.1	20.9	
≥22	70.2	29.8	
Ly			
<32.30	82.0	18.0	0.006
32.30-37.69	80.8	19.2	
37.70-42.99	79.4	20.6	
≥43	77.0	23.0	
MO			
<2.70	82.2	17.8	0.014
2.70-3.49	79.9	20.1	
3.50-4.29	80.0	20.0	
≥4.30	77.3	22.7	
GGT			
<14	80.6	19.4	0.092
14-18.9	81.3	18.7	
19-26.9	77.9	22.1	
≥27	79.6	20.4	

Contd...

Contd...

Table 1: Contd...

Variables	CKD; %		*P*
	No; *n*=4646	Yes; *n*=1176	
ALP			
<163	78.4	21.6	0.282
163-197	80.3	19.7	
198-238	79.4	20.6	
≥239	81.1	18.9	
AST (SGOT)			
<15	79.7	20.3	0.512
15-17	81.0	19.0	
18-21	79.9	20.1	
≥22	78.7	21.3	
ALT (SGPT)			
<12	80.5	19.5	0.515
12-16	78.9	21.1	
17-23	79.3	20.7	
≥24	80.8	19.2	

Index unit: WBC: $10^3/\mu l$

were 1.19 (0.99, 1.43) and 1.36 (1.13, 1.63), respectively. Corresponding figures for monocytes were 1.15 (0.95, 1.39) and 1.36 (1.13, 1.63), respectively. Subjects with BUN in the second, third, and fourth quartiles had 1.49 (1.20, 1.84), 1.90 (1.55, 2.32), and 3.06 (2.53, 3.72)-folds higher chance of developing CKD compared to those with the first quartile of BUN [Table 2].

Multivariate analyses showed that the odds ratios for having MCV more than the third and fourth quartiles were 0.78 (0.64, 0.95) and 0.81 (0.67, 0.99), respectively. Corresponding odds ratio for lymphocyte higher than the fourth quartile was 1.22 (1.01, 1.47) and for the second, third, and fourth quartiles of BUN was 1.42 (1.14, 1.77), 2.79 (2.27, 3.43), and 2.79 (2.27, 3.43), respectively [Table 2].

Discussion

Due to the importance of the primary and secondary levels of prevention, it was crucial to investigate the prevalence of CKD and its laboratory predictors among general population. In the current study, we found that more than one-fifth of the TABARI cohort general population particularly women (female-male ratio = 1.4) were suffered from CKD. CKD prevalence was directly associated with age. Patients with MCV higher than 86.80–90.19 compared to those with MCV lower than 82.40 had higher chance of developing CKD. Having lymphocyte count more than the fourth quartile increased the chance of developing CKD about 22%. In addition, subjects with BUN more than the second quartile had higher chance of CKD compared to those with BUN less than the first quartiles.

The available literature did not show any evidence for investigating the CKD among a healthy population free of any comorbidities. Such difference between the study populations in the present study and similar evidences indicates that the risk of CKD in those populations might be higher than that of the current study. Results of a meta-analysis showed the prevalence of stages 3–5 as of 7.6% (6.4–8.9%), 0.4% (0.3–0.5%), and 0.1% (0.1–0.1%), respectively, which was considerably lower than that estimated in our study.[5]

Wang *et al*.[4] showed that patients with high RDW had more than 50% higher chance of developing acute renal injury. In the study carried out by Sun *et al*.[19] RDW level was significantly higher among dead patients with peritoneal dialysis compared to those survived. However, there was no difference between the two groups in the case of platelet count. Yonemoto *et al*.[20] found that the adverse renal outcomes among patients with high RDW were approximately 50% higher than that among those with low RDW. They also observed a negative association between RDW level and eGFR. That was similar to the results reported by Lippi *et al*.[21] RDW was also found to have a direct correlation with failure of the arteriovenous fistula among patients on hemodialysis. It seems that RDW is increased following the unknown inflammatory responses associated with erythropoiesis. Therefore, it can be considered as a marker for prediction of mortality among patients with CKD.[19,22-24]

Lopes and Sette[13] reported that serum AST and ALT levels had a negative correlation with serum creatinine levels and a direct association with GFR. They also found higher liver enzymes among patients with lower stages of CKD; however, their observed associations were borderline significant. Dyab Allawi *et al*.[25] reported that mean ALT and AST levels were significantly lower among patients on dialysis as well as CKD cases which is in contrast to the findings of the present study.

One of the strengths of the current research is selection of a study population without underline diseases such as diabetes mellitus, cardiac disorders, hypertension, renal failure, cancer, and high body mass index. In addition, we used laboratory parameters which are performed as routine tests for many patients, for early prediction of CKD as an asymptomatic disease in the first stages. Although previous evidences reported the effect of these parameters in special target populations (with comorbidities), our study subjects were a normal population.

Our study was prone to some limitations. For example, since our study population was normal/healthy population, as expected, the estimated ranges were narrow. Even those in the first and fourth quartiles had normal ranges for many parameters. However, it seems that using quartiles as our specific approach slightly improved this limitation. Another limitation of the current study is limitation of the LR test results for clinical judgment. But it is possible to apply this indicator for primary assessment and early diagnosis. Further studies are recommended to

Table 2: Crude and adjusted associations of blood count indices and liver function tests with CKD among normal population of TCS

Variables	Univariate logistic regression			Multiple logistic regression		
	OR	CI 95%	*P*	OR	CI 95%	*P*
WBC*						
<5.30	–	–	–	–	–	–
5.30-6.09	0.91	0.76-1.10	0.331	0.90	0.75-1.09	0.302
6.10-7.09	0.86	0.72-1.03	0.108	0.87	0.72-1.05	0.160
≥7.10	0.80	0.67-0.96	0.017	0.87	0.72-1.05	0.139
RDW*						
<10.50	–	–	–	–	–	–
10.51-10.79	1.12	0.93-1.36	0.237	1.01	0.83-1.24	0.893
10.80-11.09	1.17	0.98-1.41	0.085	1.02	0.84-1.23	0.871
≥11.20	1.07	0.89-1.29	0.472	0.90	0.74-1.09	0.292
PDW*						
<16.40	–	–	–	–	–	–
16.40-16.89	1.05	0.87-1.27	0.601	1.05	0.86-1.28	0.631
16.90–17.49	1.00	0.83-1.20	0.994	0.99	0.82-1.21	0.961
≥17.50	1.20	0.99-1.43	0.054	1.16	0.96-1.41	0.126
MCV*						
>82.40	–	–	–	–	–	–
82.40-86.79	1.01	0.85-1.20	0.921	1.00	0.83-1.21	0.964
86.80-90.19	0.80	0.67-0.96	0.018	0.78	0.64-0.95	0.012
≥90.20	0.76	0.63-0.91	0.003	0.81	0.67-0.99	0.042
GGT*						
<14	–	–	–	–	–	–
14-18.9	0.96	0.79-1.16	0.661	0.90	0.73-1.11	0.318
19-26.9	1.18	0.98-1.43	0.083	1.12	0.91-1.38	0.283
≥27	1.07	0.88-1.30	0.513	0.99	0.79-1.25	0.959
BUN*						
<14	–	–	–	–	–	–
14-16.9	1.49	1.20-1.84	<0.001	1.42	1.14-1.77	0.002
17-21.9	1.90	1.55-2.32	<0.001	1.76	1.42-2.19	<0.001
≥22	3.06	2.53-3.72	<0.001	2.79	2.27-3.43	<0.001
Ly*						
<32.30	–	–	–	–	–	–
32.30-37.69	1.09	0.90-1.31	0.384	1.01	0.83-1.23	0.886
37.70-42.99	1.19	0.99-1.43	0.067	1.09	0.90-1.32	0.387
≥43	1.36	1.13-1.63	0.001	1.22	1.01-1.47	0.043
MO*						
<2.70	–	–	–	–	–	–
2.70-3.49	1.61	0.96-1.40	0.118	1.08	0.89-1.31	0.428
3.50-4.29	1.15	0.95-1.39	0.147	1.01	0.83-1.24	0.894
≥4.30	1.36	1.13-1.63	0.001	1.15	0.94-1.40	0.162
Waist**						
<102 for male and <88 for female	–	–	–	–	–	–
≥102 for male and ≥88 for female	1.40	1.23-1.59	<0.001	0.87	0.72-1.04	0.135
BMI***						
<25	–	–	–	–	–	–
25-29.9	1.80	1.53-2.10	<0.001	1.67	1.40-1.99	<0.001
≥30	1.79	1.48-2.16	<0.001	1.59	1.25-2.01	<0.001

*Adjusted by gender, area residence, social-economic level, age, education level, waist, BMI, HDL, TC, and TG. **Adjusted by gender, area residence, social-economic level, age, education level, BMI, HDL, TC, and TG. ***Adjusted by gender, area residence, social-economic level, age, education level, waist, HDL, TC, and TG

find new strategies for early detection of CKD within the community.

Our study showed clear evidences that CKD is a common problem among the healthy population of the northern part

of Iran, especially among women and elder people. We also found that low MCV, high lymphocyte, and elevated BUN can be predictors of CKD. Considering the silent nature of CKD in the early phases, CBC indices as well as liver enzymes and BUN can be applied for the primary assessment for CKD.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the NIMAD ethical committee (IR.NIMAD. REC.1398.350). All ethical principles of the Helsinki ethical declaration have been met and written informed consent were obtained from all the participants.

Acknowledgments

We would like to thank all the members of TABARI and PERSIAN cohort study, the Ministry of Health and Medical Education and Mazandaran University of Medical Sciences.

Financial support and sponsorship

Research reported in this publication was supported by Elite Researcher Grant Committee under award number (grant no. 988198) from the National Institutes for Medical Research Development (NIMAD), Tehran, Iran. The funding body played no role in the design of the study and collection, analysis, and interpretation of data and in writing or decision to publish this manuscript.

Conflicts of interest

There are no conflicts of interest.

Received: 07 Jan 22 **Accepted:** 28 Apr 22
Published: 20 Jan 23

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