Assessment of Renal Function and Electrolyte Balance in Patients with Cardiovascular Disease at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

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Authors’ contributions

This work was carried out in collaboration among all authors. Author GCD designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author YAK managed the analyses of the study. Author SGA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Chronic kidney disease (CKD) and electrolyte imbalance are known in patients with cardiovascular disease (CVD), and cause extra morbidity and mortality. However, there is no published study on renal disease and electrolyte imbalance among cardiovascular (CV) patients in Ethiopia.

Objective: To assess the renal function and electrolyte balance in patients with CVD at Tikur Anbessa Specialized Hospital (TASH).

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1. INTRODUCTION

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels and they include coronary artery disease (CAD), cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease (CHD), deep vein thrombosis (DVT) and pulmonary embolism. CVDs are the number one cause of death globally [1]. Global Burden of Disease (GBD) study estimated that CVD caused 17.7 million deaths globally in 2016 [2]. It accounted for 32.3% of all deaths and twice that caused by cancer, as well as more than all communicable, maternal, neonatal and nutritional disorders combined. However, in Ethiopia, the GBD study reported that the mortality in CVD is 18.3% of all deaths in 2016 [2]. The reason why it is decreased is due to the nature of the diseases (for instance silent myocardial infarction (MI) or asymptomatic ischemic heart disease (IHD)) and the less attention given to chronic diseases in general.

CVDs are mostly precipitated by chronic kidney disease (CKD), [3-5]. Both CVD and kidney disease are closely interrelated and disease of one organ cause dysfunction of the other [6], ultimately leading to the failure of both organs and this is often referred as a cardiorenal syndrome (CRS), [3]. These two organs act in tandem to regulate blood pressure, vascular tone, diuresis, natriuresis, intravascular volume homeostasis, and peripheral tissue perfusion. Changes in the renin-angiotensin-aldosterone system (RAAS), sympathetic nervous system (SNS), and inflammation are the cardiorenal connectors to develop CRS [7].

CKD is defined as structural or functional abnormalities of the kidney that persist for at least 3 months and is manifested by either kidney damage (most frequently detected as persistent albuminuria or proteinuria (> 30 mg/24 h or > 1 on specific dipstick); or a decreased glomerular filtration rate (GFR), (< 60 ml/min per 1.73 m²), [8]. Early CKD has no sign or symptom [9], this is why CKD usually remains undetected for a longer period until a screening test identifies the silent problem. CKD in many patients remains unidentified because of screening for albuminuria is not regularly performed.

GFR specifically estimates how much blood passes through the glomeruli. It is accepted as the best index of overall kidney function [10]. Serum creatinine (SCr) is the most frequently used endogenous marker of GFR in clinical practices. However, SCr level, which is affected by factors other than the GFR, is insufficiently sensitive to detect CKD on its own and might remain in the normal range despite impaired renal function [11-13]. The National Kidney Disease Education Program (NKDEP) has recommended the routine use of the estimated GFR (eGFR) instead of the SCr alone to more accurately assess kidney function in adults over the age of 18 [14].

Electrolytes perform a variety of functions in the human body. Disorders of these electrolytes can cause multiple problems for cardiac patients
because the functioning heart is dependent on normal levels of electrolytes [15]. Especially in patients with Heart failure, electrolyte disorder frequently causes dangerous complication. Several factors like hormonal and physiological stress also interact to produce these changes [16-19].

Although the high prevalence of CKD and electrolyte imbalance are known in patients with CVD and cause extra morbidity and mortality [20-23], there is no published study on renal disease and electrolyte imbalance among CV patients in Ethiopia. In addition, many researchers recommended screening for evidence of kidney disease in all patients with CVD by using eGFR and albuminuria [8,24], but many physicians relay only on SCr as a measurement of renal function and interpret normal SCr levels as evidence of normal renal function. Therefore, the present study was undertaken to assess the renal function by using eGFR equations and proteinuria, and serum electrolyte balance in patients with CVD. In addition, the findings of the study will help as baseline data for further researches in the future.

2. MATERIALS AND METHODS

2.1 Study Area and Period

The study was conducted from September to November 2017 at the adult emergency department (ED) of TASH, Addis Ababa, Ethiopia.

2.2 Study Design and Population

The cross-sectional study design was conducted among new CV patients attending adult ED of TASH during the study period. Patients were excluded if they were less than 18 years old, diabetic, pregnant, suffering from malnutrition and taking creatine dietary supplements. All new CV patients who were attending adult ED of TASH at the time of data collection and who were willing to participate in the study were included.

2.3 Sample Size Determination and Technique

Using the sample size formula for a single population proportion, the sample size was calculated as follows:

\[ n = \frac{(Z \alpha/2)^2 \times p \times q}{d^2} \]

where,
\[ n = \text{minimum number of sample size} \]
\[ Z = \text{level of confidence (95%) = 1.96} \]
\[ p = \text{Renal diseases accounted for 6% of adult hospital medical admissions in reports from various parts of the country [25]. However, the prevalence of renal disease in CV patients is approximately twice of community based study (approximately 12%).} \]
\[ q = 1-p = 0.88, \ d = \text{margin of error (5%)} \]
\[ n = \frac{(1.96)^2 \times 0.12 \times 0.88}{(0.05)^2} = 163 \]

Thus, the study was conducted among 163 CV patients and convenient sampling technique was employed.

2.4 Data Collection and Measurements

2.4.1 Data collection

Sociodemographic and risk factor variables were collected using a structured questionnaire by trained nurses. Clinical assessment and categorization of the CV patients were done by physicians.

Body mass index (BMI) was calculated as weight divided by height squared (Kg/m²). Weight of participants was measured using an electronic weighing scale with removing their heavy outer garments. Height was measured using Stanley measuring tape (5m length), with the patients barefooted and head upright. Values of BMI was classified as follows: BMI \( \leq 18.5 \) Kg/m² underweight, BMI = 18.5-24.9 Kg/m² normal weight, BMI = 25-29.9 Kg/m² overweight and BMI \( \geq 30 \) Kg/m² obese. Blood pressure was measured using aneroid sphygmomanometer in the right upper arm in the sitting posture after a 30 minutes rest. It was measured two additional times, waiting five minutes between measurements and an average was recorded. Systolic blood pressure \( \geq 130 \) mmHg and/or diastolic blood pressure \( \geq 80 \) mmHg or current use of blood pressure-lowering medication was used to define hypertension [26].

2.4.2 Laboratory measurements

Five milliliters of the blood sample was collected using a disposable syringe in the ED. Serum
electrolytes tests including K⁺, Na⁺, and Cl⁻ values were analyzed by Humalyte Plus® electrolytes analyzer by using direct Ion-Selective Electrode (ISE) method. Patients were classed as having an electrolyte disorder or not based on the reference ranges of TASH central laboratory: Na⁺: 135-145 mmol/L, K⁺: 3.5-5.0 mmol/L and Cl⁻: 95-105 mmol/L. Serum urea and creatinine were analyzed in the clinical laboratory using Mindray200BS which is an automatic biochemistry analyzer. A urine specimen was collected in a clean and dry container in ED, and urinalysis was done immediately using dipstick dry reagent test strip. The result of 1+ or more was regarded as proteinuria.

An eGFR was calculated separately for men and women through two methods (equations): Modification of Diet in Renal Disease (MDRD) study equation [27]: GFR (expressed in ml/min/1.73 m²) = 186 × [Scr (mg/dl)]⁻¹.¹⁵⁴ × (age)⁻⁰.₂⁰³ × (0.742 if female) × 1.²¹² (if black), and Chronic Kidney Disease- Epidemiological Collaboration (CKD-EPI) formula [28] using the following equations: for female with Scr ≤ 0.7 mg/dl: GFR = 166 × (Scr/0.7)⁻⁰.³²⁹ × (0.⁹⁹³)⁻age, for female with Scr > 0.7 mg/dl: GFR = 166 × (Scr/0.7)⁻¹.²⁰⁹ × (0.⁹⁹³)⁻age, for male with Scr ≤ 0.9 mg/dl: GFR = 163 × (Scr/0.9)⁻⁰.⁴¹¹ × (0.⁹⁹³)⁻age, and for male with Scr > 0.9 mg/dl: GFR = 163 × (Scr/0.9)⁻¹.²⁰⁹ × (0.⁹⁹³)⁻age. These formulas, despite their mathematical complexity, were calculated by mobile application (pocket GFR calculator).

The participants who had eGFR < 60 ml/min/1.73 m² were advised to have their Scr checkup after a month. CKD was categorized based on the Kidney Disease Outcomes Quality Initiative (K/DOQI) classification system guideline. For the purposes of this study, CKD was defined as stages 3–5 CKD (eGFR < 60 ml/min/1.73 m²); with stage 3A (eGFR 45-59.9), 3B (30–44.9), 4 (15–29.9) and 5 (< 15 ) ml/min/1.73 m², respectively, [10].

2.5 Data Quality Management and Control

The data collection tool was prepared in English and translated to Amharic with the intention that the respondents will understand it and provide an accurate response, and then back to English. The pretest was conducted among ten postgraduate students. To assure the quality of laboratory analysis the standard operating procedures (SOPs) of the TASH clinical chemistry laboratory was strictly followed. In addition, the laboratory analysis was performed by well trained and experienced two laboratory technologists.

2.6 Statistical Analysis

Data entry and analysis was done using SPSS software version 22. The descriptive statistics were calculated & logistic regression analysis was done. Categorical variables were expressed as frequencies and percentages. Chi-square (x²) analysis was used for between-group comparisons of CKD proportions. Multinomial logistic regression was performed by including variables that were significant at p < 0.05. Adjusted odds ratio (AOR) and their corresponding 95% confidence intervals (CI) were expressed to describe the association of risk factors with CKD (dependent variable). Statistical significance was considered at p < 0.05.

3. RESULTS

3.1 Sociodemographic and Clinical Characteristics of the Participants

A total of 163 CV patients participated in the study, 91 (55.8%) were females. The mean age of the study participants was 42 ± 18 years with 45 ± 18 for male and 40 ± 17 for female. Out of the total patients, 60 (36.8%) were between 25–44 years age group and 22 (13.5%) were 65 and above years old, ranging from 18 to 86 years old. One hundred ten (67.5%) patients were married and 51 (31.3%) were illiterate. One hundred thirteen (69.3%) patients were urban residents and 74 (45.4%) earned a monthly income of less than 1000 Ethiopian Birr.

Mean BMI of participants was 21.30 ± 4.05 Kg/m² and 26 (16.0%) participants were overweight with BMI 25-29.9 Kg/m². Mean SBP and DBP were 105 ± 20 and 67 ± 12 mmHg, respectively, and 52 (31.9%) patients had hypertension. Mean BUN was normal with 18.96 ± 12.54 mg/dl while mean Scr was increased with 1.30 ± 0.96 mg/dl. Mean eGFR values according to MDRD and CKD-EPI equations were indicated stage 2 CKD with 78 ± 30 and 82 ± 31 ml/min/1.73 m², respectively. Among patients diagnosed urinalysis, 41 (25.2%) had proteinuria. Mean serum Na⁺, Cl⁻ and K⁺ in all patients were found within normal range with 138.5 ± 7.2 mmol/L, 100.8 ± 7.7 mmol/L and 4.1 ± 0.7 mmol/L, respectively.
Regarding distribution of the types of CVDs, chronic rheumatic valvular heart disease (CRVHD) was the most commonly diagnosed which accounted for 75 (46.0%) followed by DVT 32 (19.6%), IHD 19 (11.7%), Stroke 14 (8.6%), hypertension 13 (8.0%), CHD 3 (1.8%) and others 7 (4.3%) during study period.

### 3.2 Prevalence of CKD

A total of 124 (76.1%) patients had a normal renal function (eGFR of ≥ 60 ml/min/1.73m²); 23 (14.1%) patients had stage 3a CKD (eGFR 45–59 ml/min/1.73m²); 8 (4.9%) patients had stage 3b CKD (eGFR 30–44 ml/min/1.73m²); and 6 (3.7%) patients had stage 4 or 5 CKD (eGFR <30 ml/min/1.73m²) using MDRD equation. When renal function estimated by CKD-EPI equation, 57 (35.0%) patients had a normal renal function (eGFR of ≥ 90 ml/min/1.73m²); 71 (43.6%) patients had stage 2 CKD (eGFR 60-89 ml/min/1.73m²); 18 (11.0%) patients had stage 3a CKD; 9 (5.5%) patients had stage 3b CKD; and 8 (4.9%) patients had stage 4 or 5 CKD. As shown in Table 1, 39 (23.9%) patients based on MDRD equation and 35 (21.5%) patients based on CKD-EPI equation had CKD (defined as eGFR < 60 ml/min/1.73 m²).

Out of the total study participants, 114 (69.9%) had normal SCr (SCr ≤ 1.2 mg/dl). When these participants were assessed using MDRD formula, stage 2 CKD was found in 71 (62.3%) participants and stage 3 CKD was found in 4 (3.5%) participants. When assessed using CKD-EPI formula, stage 2 CKD was found in 54 (47.4%) of these participants and stage 3 CKD was found in 4 (3.5%) of these participants.

### 3.3 Factors Associated with CKD

CKD was significantly associated with hypertension when renal function defined by CKD-EPI (p = 0.019) but not by MDRD formula (p = 0.075). SBP was significantly associated with CKD defined by MDRD (p = 0.023) and CKD-EPI equations (p = 0.009). Although no significant differences between male and female, CKD was higher in females compared to males. By age group, older age was not significantly associated with CKD defined by MDRD (p = 0.160) and CKD-EPI equations (p = 0.067). CKD was significantly higher among patients with high SCr when compared with low SCr: 21.5% vs. 2.5%, p = 0.001 by MDRD and 19.0% vs. 2.5%, p = 0.001 by CKD-EPI. CKD was also significantly higher in patients with high BUN compared with low BUN: 16.6% vs. 7.4%, p = 0.001 by MDRD and 16.6% vs. 4.9%, p = 0.001 by CKD-EPI (Table 2).

The univariate analysis showed a significant association between CKD (eGFR < 60 ml/min/1.73 m²) and the following variables: hypertension, elevated SBP, high SCr, and high BUN. After incorporating all significant (p < 0.05) variables in the univariate analysis, multivariate logistic regression was performed to identify risk factors independently associated with CKD.

In multivariate analysis, only high SCr (AOR = 47.57, CI 13.72-164.89) was independently associated with CKD defined by MDRD equation. But, high SBP (AOR = 7.45, CI 1.02-54.22), high SCr (AOR = 31.13, CI 8.67-111.77) and high BUN (AOR = 6.75, CI 2.14-21.27) were independently associated with CKD defined by CKD-EPI equation (Table 3).

### 3.4 Serum Electrolyte Imbalance in CV Patients

From eighty five heart disease (HD) patients, 44 (51.8%), 22 (37.7%) and 16 (20.0%) had serum Cl⁻, Na⁺ and K⁺ imbalance, respectively. Among these patients, 23 (27.1%), 22 (25.9%) and 11 (12.9%) had hyponatremia, hypochloremia and hypokalemia, respectively. On the other hand, 22 (25.9%), 9 (10.6%) and 6 (7.1%) patients had hyperchloremia, hypernatremia and hyperkalemia, respectively. As shown in Table 4, among 78 vascular disease (VD) patients, 36 (46.1%), 27 (34.7%) and 20 (25.5%) had serum Cl⁻, Na⁺ and K⁺ imbalance, respectively. Out of these patients, 19 (24.4%), 14 (17.9%) and 11 (14.1%) had hyponatremia, hypochloremia and hypokalemia, respectively. But, 22 (28.2%), 9 (11.5%) and 8 (10.3%) patients had hyperchloremia, hypernatremia and hyperkalemia, respectively.

In total, this study showed that 80 (49.1%) patients had serum Cl⁻ imbalance [36 (22.1%) hypochloremia and 44 (27.0%) hyperchloremia], 59 (36.2%) had serum Na⁺ imbalance [42 (25.8%) hypokalemia and 17 (10.4%) hyperkalemia] and 37 (22.7%) had serum K⁺ imbalance [22 (13.5%) hypokalemia and 15 (9.2%) hyperkalemia], (Table 4).

### 3.5 Association of Diuretics Therapy with Serum Electrolyte Disorders

Hyponatremia was significantly found in patients on potassium-sparing diuretic treatment
(spironolactone) ($p = 0.036$). There was no significant difference between all types of diuretics and duration of diuretics used, and hypernatremia ($p > 0.05$). All types of diuretics (furosemide and spironolactone) and duration of diuretics used were not significantly associated with hypokalemia and hyperkalemia ($p > 0.05$). Hypochloremia was significantly more common in patients on loop (furosemide), (19.0% vs 3.1%, $p = 0.001$) and potassium-sparing (spironolactone) diuretic therapy (12.3% vs 9.8%, $p = 0.003$) compared with those without treatment. But, there was no significant difference between the duration of diuretics used and hypochloremia ($p > 0.05$). All types of diuretics and duration of diuretics used were not significantly associated with hyperchloremia ($p > 0.05$).

Table 1. GFR category according to K/DOQI classification using equations among CV patients at ED of TASH, Addis Ababa, Ethiopia, 2017

<table>
<thead>
<tr>
<th>GFR category (ml/min/1.73m$^2$)</th>
<th>Description</th>
<th>MDRD N (%)</th>
<th>CKD-EPI N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 (90)</td>
<td>Normal or high GFR</td>
<td>39 (23.9)</td>
<td>57 (35.0)</td>
</tr>
<tr>
<td>G2 (60-89)</td>
<td>Mildly ↓GFR</td>
<td>85 (52.2)</td>
<td>71 (43.6)</td>
</tr>
<tr>
<td>G3a (45-59)</td>
<td>Mildly to moderately ↓GFR</td>
<td>23 (14.1)</td>
<td>18 (11.0)</td>
</tr>
<tr>
<td>G3b (30-44)</td>
<td>Moderately to severely ↓GFR</td>
<td>8 (4.9)</td>
<td>9 (5.5)</td>
</tr>
<tr>
<td>G4 (15-29)</td>
<td>Severely ↓GFR</td>
<td>6 (3.7)</td>
<td>6 (3.7)</td>
</tr>
<tr>
<td>G5 (&lt; 15)</td>
<td>Kidney failure</td>
<td>2 (1.2)</td>
<td>2 (1.2)</td>
</tr>
</tbody>
</table>

CKD: Chronic Kidney Disease; GFR: Glomerular Filtration Rate; MDRD: Modification of Diet in Renal Disease; CKD-EPI: Chronic Kidney Disease-Epidemiological Collaboration; G: Group; N: Number

Table 2. Distribution of CKD by characteristics of study participants using MDRD and CKD-EPI equation among CV patients at ED of TASH, Addis Ababa, Ethiopia, 2017

<table>
<thead>
<tr>
<th>Variables</th>
<th>MDRD CKD</th>
<th>MDRD No CKD</th>
<th>p-value</th>
<th>CKD-EPI CKD</th>
<th>CKD-EPI No CKD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Female</td>
<td>15.3 40.5</td>
<td>0.235</td>
<td>12.9 42.9</td>
<td>0.578</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>8.6 35.6</td>
<td></td>
<td>8.6 35.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>≥60 years</td>
<td>6.7 13.5</td>
<td>0.160</td>
<td>6.7 13.5</td>
<td>0.067</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;60 years</td>
<td>17.2 62.6</td>
<td></td>
<td>14.7 65.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>≥25 Kg/m$^2$</td>
<td>6.1 12.3</td>
<td>0.183</td>
<td>5.5 12.9</td>
<td>0.210</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;25 Kg/m$^2$</td>
<td>17.8 63.8</td>
<td></td>
<td>16.0 65.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretics</td>
<td>Yes</td>
<td>17.2 45.4</td>
<td>0.175</td>
<td>16.0 46.6</td>
<td>0.108</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>6.7 30.7</td>
<td></td>
<td>5.5 31.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of diuretics</td>
<td>&lt; 1 month</td>
<td>4.9 8.8</td>
<td>0.763</td>
<td>4.9 8.8</td>
<td>0.623</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1m-1 year</td>
<td>4.9 13.7</td>
<td></td>
<td>4.9 13.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt; 1 year</td>
<td>17.6 50.0</td>
<td></td>
<td>15.7 52.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>Yes</td>
<td>10.4 21.5</td>
<td>0.075</td>
<td>10.4 21.5</td>
<td>0.019*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>13.5 54.6</td>
<td></td>
<td>11.0 57.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>≥130 mmHg</td>
<td>5.5 6.7</td>
<td>0.023*</td>
<td>1.8 3.7</td>
<td>0.009*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;130 mmHg</td>
<td>18.4 69.3</td>
<td></td>
<td>19.6 74.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBP</td>
<td>≥80 mmHg</td>
<td>4.9 16.6</td>
<td>0.867</td>
<td>4.3 3.1</td>
<td>0.822</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;80 mmHg</td>
<td>19.0 59.5</td>
<td></td>
<td>17.2 75.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCr</td>
<td>&gt;1.2 mg/dl</td>
<td>21.5 8.6</td>
<td>0.001*</td>
<td>19.0 11.0</td>
<td>0.001*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤1.2 mg/dl</td>
<td>2.5 67.5</td>
<td></td>
<td>2.5 67.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BUN</td>
<td>&gt;20 mg/dl</td>
<td>16.6 14.7</td>
<td>0.001*</td>
<td>16.6 14.7</td>
<td>0.001*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤20 mg/dl</td>
<td>7.4 61.3</td>
<td></td>
<td>4.9 63.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteinuria</td>
<td>Positive</td>
<td>7.4 17.8</td>
<td>0.357</td>
<td>6.7 18.4</td>
<td>0.337</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>16.6 58.3</td>
<td></td>
<td>14.7 60.1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*: Significant ($p<0.05$); MDRD: Modification of Diet in Renal Disease; CKD-EPI: Chronic Kidney Disease-Epidemiological Collaboration; CKD: Chronic Kidney Disease; BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; SCr: Serum Creatinine; BUN: Blood Urea Nitrogen; m: month
### Table 2. Factors associated with CKD according to the MDRD and CKD-EPI equations among CV patients at ED of TASH, Addis Ababa, Ethiopia, 2017

<table>
<thead>
<tr>
<th>Factors</th>
<th>MDRD equation</th>
<th>p-value</th>
<th>CKD-EPI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AOR (95% CI)</td>
<td></td>
<td>AOR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>HTN Yes</td>
<td>0.61 (0.16-2.34)</td>
<td>0.480</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>SBP ≥130 mmHg</td>
<td>3.60 (0.69-18.75)</td>
<td>0.128</td>
<td>7.45 (1.02-54.22)</td>
<td>0.047*</td>
</tr>
<tr>
<td>&lt;130 mmHg</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>SCr ≥1.2 mg/dl</td>
<td>47.57 (13.72-164.89)</td>
<td>0.001*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1.2 mg/dl</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>BUN &gt;20 mg/dl</td>
<td>3.09 (1.00-9.37)</td>
<td>0.050</td>
<td>6.75 (2.14-21.27)</td>
<td>0.001*</td>
</tr>
<tr>
<td>≤20 mg/dl</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

*: Significant (p < 0.05); MDRD: Modification of Diet in Renal Disease; CKD-EPI: Chronic Kidney Disease Epidemiological Collaboration; HTN: Hypertension; SBP: Systolic Blood Pressure; SCr: Serum Creatinine; BUN: Blood Urea Nitrogen; AOR: Adjusted Odds Ratio; CI: Confidence Interval

### Table 3. Serum electrolyte level according to heart and vascular disease at ED of TASH, Addis Ababa, Ethiopia, 2017

<table>
<thead>
<tr>
<th>Serum electrolyte level</th>
<th>Cardiovascular disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HD (n = 85)</td>
</tr>
<tr>
<td>K⁺ (Hypokalemia &lt; 3.5 mmol/L)</td>
<td>11 (12.9)</td>
</tr>
<tr>
<td>(Normokalemia 3.5-5.0 mmol/L)</td>
<td>68 (80.0)</td>
</tr>
<tr>
<td>Hyperkalemia &gt; 5.0 mmol/L</td>
<td>6 (7.1)</td>
</tr>
<tr>
<td>Na⁺ (Hyponatremia &lt; 135 mmol/L)</td>
<td>23 (27.1)</td>
</tr>
<tr>
<td>(Normonatremia 135-145 mmol/L)</td>
<td>53 (62.4)</td>
</tr>
<tr>
<td>Hypernatremia &gt; 145 mmol/L</td>
<td>9 (10.6)</td>
</tr>
<tr>
<td>Cl⁻ (Hypochloremia &lt; 95 mmol/L)</td>
<td>22 (25.9)</td>
</tr>
<tr>
<td>(Normochloremia 95-105 mmol/L)</td>
<td>41 (48.2)</td>
</tr>
<tr>
<td>Hyperchloremia &gt; 105 mmol/L</td>
<td>22 (25.9)</td>
</tr>
</tbody>
</table>

HD: Heart Disease; VD: Vascular Disease; K⁺: Serum potassium ion; Na⁺: Serum sodium ion; Cl⁻: Serum chloride ion; N: Number

### 4. DISCUSSION

CKD is a global health burden with a high economic cost to health systems [29] and higher among patients with CVD [30,31]. All stages of CKD are associated with increased risks of CV morbidity, premature mortality, and/or decreased quality of life [8,21,23]. Thus, early detection and recognition of CKD are important in patients with CVD to improve adverse outcomes, delay the progression to end-stage renal disease (ESRD) and encourage early referral to the nephrologist [32].

In this study, CKD (eGFR < 60 ml/min/1.73 m²) was found in 23.9% (using MDRD) and 21.5% (using CKD-EPI) of participants based on the formula used to estimate GFR, with stage 3 being dominant (16.5 to 19.0%). The estimated prevalence of CKD using the MDRD equation was lower than reported by Amenos et al. [2010] and Yang et al. [2010]. These differences might be due to the study design and sample size. The estimated prevalence of CKD using the CKD-EPI equation was lower than reported by Lofman et al. [2016] and higher than reported by Wang et al. [2014]. These differences might be due to the study design and sample size.

The NKDEP suggests the use of eGFR as a superior measure of renal function compared with SCr alone. In this study, a number of participants ranging from 50.9-65.8% have shown to have mild to moderate RI (stages 2 to 3CKD) despite normal SCr levels using eGFR equations. Clinically significant CKD was found in 3.5% based on the formula used to estimate GFR. The estimated prevalence of undiagnosed CKD using the MDRD equation was closer to reported by Bachoerzewska-Gajewska [2006]. Due to the lack of information on the estimated prevalence of undiagnosed CKD assessed by the CKD-EPI equation, it is difficult to compare.
Therefore, the current guidelines stated that SCR alone should not be used to assess kidney function, because SCR is affected by several factors, including age, sex, race and body size. It also fails to identify many patients whose kidney function is reduced while their SCR remains within the normal range. A marked reduction in GFR can be presented before a rise in SCR is reflected (up to 50% of kidney function has already been lost before creatinine might change). Thus, an estimation of GFR using prediction equations is recommended to avoid the misclassification of individuals on the basis of SCR alone [11,12,14, 27]. The CKD-EPI formula may currently be the best means of estimating GFR. This equation reduces the bias or underestimation of the MDRD formula, above all in GFR > 60 ml/min/1.73 m² [28,29].

BUN showed highly significant association with CKD defined by MDRD (p = 0.001) and CKD-EPI (p = 0.001) equations. This is consistent with the study of Amsalem et al. [2008]. Concomitant elevations of BUN implies renal excretory failure, but only at an advanced stage of kidney damage [33]. BUN is an imperfect measurement of kidney function and is influenced by factors other than GFR [34]. An elevated BUN can further reflect a state of renal hypoperfusion from hypovolemia, renovascular disease, or reduced cardiac output [35,36]. BUN may also be raised independently of a change in GFR or SCR due to enhanced urea reabsorption under the activation of the SNS and RAAS [37].

Regarding risk factors, this study found an insignificant association between older age and CKD defined by MDRD (p = 0.160) and CKD-EPI (p = 0.067) equations. This contradicts with the finding of studies [38,39]. This might be due to the small sample size used in our study. In fact, younger people have a higher SCR than older people, which may lead to a late diagnosis of kidney disease. As age increases, there is a gradual decrement in the number of nephrons and GFR. Thus, screening CKD in this age group is an important strategy to improve the outcomes [40].

In this study, hypertension was not independently associated with CKD (p = 0.480) even though elevated SBP was independently associated with CKD (p = 0.047) defined by the CKD-EPI equation. On the other hand, univariate analysis showed that hypertension was a significant risk factor for CKD (p = 0.019) defined by the CKD-EPI equation. This is in agreement with other related studies [21,38]. On the contrary, this study showed that hypertension was not significantly associated with CKD (p = 0.075) although SBP was significantly associated with CKD defined by MDRD equation (p = 0.023). This contradicts with the finding of Chen et al. [2016] and Amenos et al. [2010]. The differences might be due to the small sample size used in this study. Systemic hypertension is transmitted to intraglomerular capillary pressure leading to glomerulosclerosis and loss of kidney function [41]. Thus, the beneficial effects of controlling blood pressure in CVD has been described repeatedly in current guidelines [26].

Disorders of serum electrolytes are higher among CV patients than the other associated disease [42], and can cause multiple problems for cardiac patients [15]. Alterations in the level of serum electrolytes have also been associated with increased CV morbidity and mortality [20]. This study also showed that there was a high prevalence of serum electrolyte imbalance in CV patients.

The most prevalent electrolyte imbalance was serum Cl⁻ disorder. This serum chloride disorder was higher than study reported by Hasan [2013] in stroke patients. These differences might be due to the source population used in our study. Hyperchloremia may be caused by dehydration [43] or physiological saline used [44]. In this study, hyperchloremia was significantly associated with loop furosemide (p = 0.001) and potassium-sparing spironolactone (p = 0.003). There is a lack of study that associates diuretics with serum chloride levels. However, one study conducted in HF with preserved ejection fraction has shown that loop diuretic use, but not spironolactone, lead to a decrease in serum chloride level over time [45]. The lower chloride level in HF may also represent a broader homeostatic imbalance [46].

The second electrolyte imbalance in our study was hyponatremia with 25.8%. Its prevalence was lower than that found by Balci et al. [2013] and closer to reported by Ali et al. [2016]. These differences might be due to the small sample size used in the present study. Hyponatremia may occur due to potassium-sparing diuretic (spironolactone) usage [47] and it was also supported by our study (p = 0.036). The mechanism is probably by the direct effect of spironolactone on the collecting tubule, which increases sodium loss [48]. In addition, the non-osmotic release of vasopressin in CVD may
5. CONCLUSION

CKD was present in 21.5 – 23.9% of CV patients attending ED of TASH, Addis Ababa, Ethiopia, but it is usually undiagnosed using SCr alone. Furthermore, stage 2 to 3 CKD was higher in CV patients despite normal SCr levels using MDRD and CKD-EPI equations. Therefore, GFR should be considered as an estimate of renal insufficiency regardless of SCr levels. In addition, electrolyte disorders were higher among CV patients. Among electrolyte disorders, hyperchloremia, hyponatremia, and hypokalemia were the most common in CV patients.

ETHICAL APPROVAL AND CONSENT

Ethical approval for the research was obtained from Addis Ababa University, College of Health Science, and School of Medicine Department of Medical Physiology Research Ethics Review Committee. Participants were informed about the confidentiality of the information they gave and written consent was obtained from each participant immediately.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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