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ORIGINAL ARTICLE

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

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ABSTRACT

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

Methods: A cross sectional study was conducted from September to November 2017, on 163 CV patients attending emergency department (ED) of TASH.

Results: CKD, defined as estimated Glomerular Filtration Rate (eGFR) < 60 ml/min/1.73 m^2, was found in 39 (23.9%) and 35 (21.5%) participants with reference to the Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease- Epidemiological Collaboration (CKD-EPI) equations, respectively. CKD was significantly associated with hypertension (p= 0.019), systolic blood pressure (SBP), (p = 0.009), serum creatinine (SCr), (p = 0.001) and blood urea nitrogen (BUN), (p = 0.001) when defined by CKD-EPI equation and with SBP (p = 0.023), SCr (p = 0.001) and BUN (p = 0.001) when defined by MDRD equation. In serum electrolyte disorders, 80 (49.1%) patients had serum Cl^- imbalance, 59 (36.2%) had serum Na^+ imbalance and 37 (22.7%) had serum K^+ imbalance. Loop diuretic was significantly related with hypochloremia (p = 0.001) while potassium sparing diuretic was associated with the presence of hyponatremia (p = 0.036) and hypochloremia (p = 0.003).

Conclusion: CKD was present in 21.5– 23.9% of CV patients, but it is usually undiagnosed using SCr alone. Therefore, GFR should be considered as an assessment of renal insufficiency in any case of SCr levels. In addition, electrolyte disorders were also higher among CV patients.

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INTRODUCTION

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels and they contain 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]. 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, 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 infraction (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, 4, 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 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 expose 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 m^2) [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 not enough sensitive to detect CKD on its own, and might remain in the normal range despite impaired renal function[11, 12, 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, 17, 18, 19].

Although the high prevalence of CKD and electrolyte imbalance are known in patients with CVD and cause extra morbidity and mortality [20, 21, 22, 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 explain normal SCr levels as proof 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 base line data for further researches in the future.

MATERIALS AND METHODS

Study area and period

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

Study design and population

A cross sectional study design was conducted among new CV patients attending adult ED of TASH during 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.

Sample size determination and technique

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

$$n = \frac{(Z\alpha/2)^2\, p*q}{d^2}$$

where,

n = minimum number of sample size

Z = level of confidence (95%) = 1.96

p = 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 = margin of error (5%)

$$n = \frac{(1.96)^2 *0.12*0.88}{(0.05)^2} = 163$$

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

Data collection and measurements

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

Body mass index (BMI) was calculated as weight divided by height squared (Kg/m^2). Weight of participants were measured using electronic weighing scale with removing their heavy outer garments. Height

was measured using Stanley measuring tape (5m length), with the patients bare footed and head upright. Values of BMI was classified as follows: BMI ≤ 18.5 Kg/m^2 underweight, BMI = 18.5-24.9 Kg/m^2 normal weight, BMI = 25-29.9 Kg/m^2 overweight and BMI ≥ 30 Kg/m^2 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 a five minutes between measurements and an average was recorded. Systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥ 80 mmHg or current use of blood pressure-lowering medication was applied to define hypertension [26].

Laboratory measurements: Five milliliter of blood sample was collected using disposable syringe in ED. Serum electrolytes tests including K^+, Na^+, and Cl^- values were analyzed by Humalyte Plus[5] 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 m^2) = 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 x $(Scr/0.7)^{-0.329}$ x $(0.993)^{age}$, for female with SCr > 0.7 mg/dl: GFR = 166 × $(Scr/0.7)^{-1.209}$ x $(0.993)^{age}$, for male with SCr ≤ 0.9 mg/dl: GFR = 163 x $(Scr/0.9)^{-0.411}$ x $(0.993)^{age}$, and for male with SCr > 0.9 mg/dl: GFR = 163 × $(Scr/0.9)^{-1.209}$ x $(0.993)^{age.}$. These formulas, despite their mathematical complexity, were calculated by mobile application (pocket GFR calculator).

The participants who had eGFR < 60 ml/min/1.73 m^2 were advised to have their SCr checkup after a month. CKD was categorized based on 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 m^2): with stage 3A (eGFR 45-59.9), 3B (30–44.9), 4 (15–29.9) and 5 (< 15) ml/min/1.73 m^2, respectively [10].

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. 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.

Statistical Analysis

Data entry and analysis was done using SPSS software version 22.The descriptive statistics was calculated & logistic regression analysis was done. Categorical variables were expressed as frequencies and percentages. Chi-square (x^2) 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 $p < 0.05$.

Ethical Consideration

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.

RESULTS

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 monthly income of less than 1000 Ethiopian birr.

Mean BMI of participants was 21.30 ± 4.05 Kg/m^2 and 26 (16.0%) participants were overweight with BMI 25-29.9 Kg/m^2. Mean SBP and DBP were 105 ± 20 and 67 ± 12 mmHg, respectively, and 52 (131.9%) 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 an eGFR values according to MDRD and CKD-EPI equations were indicated stage 2 CKD with 78 ± 30 and 82 ± 31 ml/min/1.73 m^2, 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 ± 7.2mmol/L, 100.8 ± 7.7mmol/L and 4.1 ± 0.7mmol/L, respectively.

Regarding distribution of the types of CVDs, chronic rheumatic valvular heart disease (CRVHD) was the most common 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.

Prevalence of CKD

A total of 124 (76.1%) patients had a normal renal function (eGFR of ≥ 60 ml/min/1.73m^2); 23 (14.1%) patients had stage 3a CKD (eGFR 45–59 ml/min/1.73m^2); 8 (4.9%) patients had stage 3b CKD (eGFR 30–44 ml/min/1.73m^2); and 6 (3.7%) patients had stage 4 or 5 CKD (eGFR <30 ml/min/1.73m^2) 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/1.73m^2); 71 (43.6%) patients had stage 2 CKD (eGFR 60-89 ml/min/1.73m^2); 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 4, 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 m^2), (Table 1).

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.

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

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

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

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 significant association between CKD (eGFR < 60 ml/min/1.73 m^2) 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).

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, hyperkalemia and hypernatremia, 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%) hyponatremia and 17 (10.4%) hypernatremia] and 37 (22.7%) had serum K^+ imbalance [22 (13.5%) hypokalemia and 15 (9.2%) hyperkalemia], (Table 4).

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**

Variables		MDRD		*p*-value	CKD-EPI		*p*- value
		CKD	no CKD		CKD	no CKD	
Sex	Female	15.3	40.5	0.235	12.9	42.9	0.578
	Male	8.6	35.6		8.6	35.6	
Age	≥60years	6.7	13.5	0.160	6.7	13.5	0.067
	<60years	17.2	62.6		14.7	65.0	
BMI	≥25Kg/m2	6.1	12.3	0.183	5.5	12.9	0.210
	<25Kg/m2	17.8	63.8		16.0	65.6	
Diuretics	Yes	17.2	45.4	0.175	16.0	46.6	0.108
	NO	6.7	30.7		5.5	31.9	
Duration of diuretics	< 1month	4.9	8.8	0.763	4.9	8.8	0.623
	1m-1year	4.9	13.7		4.9	13.7	
	> 1 year	17.6	50.0		15.7	52.0	
Hypertension	Yes	10.4	21.5	0.075	10.4	21.5	0.019*
	NO	13.5	54.6		11.0	57.1	
SBP	≥130mmHg	5.5	6.7	0.023*	1.8	3.7	0.009*
	<130mmHg	18.4	69.3		19.6	74.8	
DBP	≥80mmHg	4.9	16.6	0.867	4.3	3.1	0.822
	<80mmHg	19.0	59.5		17.2	75.5	
SCr	>1.2mg/dl	21.5	8.6	0.001*	19.0	11.0	0.001*
	≤ 1.2mg/dl	2.5	67.5		2.5	67.5	
BUN	>20mg/dl	16.6	14.7	0.001*	16.6	14.7	0.001*
	≤20mg/dl	7.4	61.3		4.9	63.8	
Proteinuria	Positive	7.4	17.8	0.357	6.7	18.4	0.337
	Negative	16.6	58.3		14.7	60.1	

*: 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 3: **Factors associated with CKD according to the MDRD and CKD-EPI equations among CV patients at ED of TASH, Addis Ababa, Ethiopia, 2017**

Factors		MDRD equation	*p*-value	CKD-EPI	*p*-value
		AOR (95% CI)		AOR (95% CI)	
HTN	Yes	----------		0.61(0.16-2.34)	0.480
	NO	----------		1	
SBP	≥130mmHg	3.60(0.69-18.75)	0.128	7.45(1.02-54.22)	0.047*
	<130mmHg	1		1	
SCr	≥ 1.2mg/dl	47.57(13.72-164.89)	0.001*	31.13 (8.67-111.77)	0.001*
	<1.2mg/dl	1		1	
BUN	>20mg/dl	3.09(1.00-9.37)	0.050	6.75 (2.14-21.27)	0.001*
	≤20mg/dl	1		1	

*: 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 4: **Serum electrolyte level according to heart and vascular disease at ED of TASH, Addis Ababa, Ethiopia, 2017**

Serum Electrolyte Level		Cardiovascular Disease		
		HD (n = 85)	VD (n = 78)	Total (n = 163)
		N (%)	N (%)	N (%)
K^+	Hypokalemia (< 3.5 mmol/L)	11 (12.9)	11 (14.1)	22 (13.5)
	Normokalemia (3.5-5.0 mmol/L)	68 (80.0)	58 (74.4)	126 (77.3)
	Hyperkalemia (> 5.0mmol/L)	6 (7.1)	9 (11.5)	15 (9.2)
Na^+	Hyponatremia (< 135mmol/L)	23 (27.1)	19 (24.4)	42 (25.8)
	Normonatremia (135-145mmol/L)	53 (62.4)	51 (65.4)	104 (63.8)
	Hypernatremia (> 145 mmol/L)	9 (10.6)	8 (10.3)	17 (10.4)
Cl^-	Hypochloremia (< 95 mmol/L)	22 (25.9)	14 (17.9)	36 (22.1)
	Normochloremia (95-105 mmol/L)	41 (48.2)	42 (53.8)	83 (50.9)
	Hyperchloremia (> 105 mmol/L)	22 (25.9)	22 (28.2)	44 (27.0)

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

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 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).

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 is 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 m^2) 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 study design and sample size. The estimated prevalence of CKD using 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 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. This estimated prevalence of undiagnosed CKD using the MDRD equation was closer to reported by Bachoerzewska-Gajewska (2006). Due to lack of information on the estimated prevalence of undiagnosed CKD assessed by 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 [11, 12, 14, 27] SCr alone. 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 m^2 [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 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 independent of a change in GFR or SCr due to enhanced urea reabsorption under the activation of the SNS and RAAS [37].

Regarding to risk factors, this study found insignificant association between older age and CKD defined by MDRD (p = 0.160) and CKD-EPI (p = 0.067) equations. This contradicts with finding of studies [38, 39]. This might be due to small sample size used in our study. In fact, younger people have a higher GFR than older people, which may lead to 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 CKD-EPI equation. On the other hand, univariate analysis showed that hypertension was a significant risk factor for CKD (p = 0.019) defined by 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 finding of Chen *et al.* (2016) and Amenos *et al.* (2010). The differences might be due to 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 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 source population used in our study. Hyperchloremia may be caused by dehydration [43] or physiological saline used [44]. In this study, hypochloremia 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 represents 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 small sample size used in 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, non-osmotic release of vasopressin in CVD may occur due to acute development of left ventricular dysfunction, pain and stress resulting in reduced level of sodium [49, 50]. Moreover, one study showed that decrease in serum sodium level was due to hypoxia, ischemia and infarction, which cause increased permeability of sarcolemma to sodium [51].

The third serum electrolyte disorder was hypokalemia with 13.5%. This finding is in line with study reported by Balci *et al.* (2013) and Kjeldsen (2010). Although hypokalemia was not significant in present study (p = 0.765), it may be caused by loop furosemide [47]. The contradiction is might be due to differences in cut off value. The possible mechanism for loop induced hypokalemia is an increased delivery of sodium to the distal tubule results in reuptake of Na by epithelial Na channels, which causes a compensatory excretion of potassium to occur in order for cells to maintain their charge balance [52]. Moreover, hypokalemia may also be due to stress induced catecholamine and beta 2 adrenoceptor agonists linked to sodium-potassium ATPase pump that resulting in increased potassium uptake by the cells [15, 53], which were not studied in this study.

Although this study is the first of its type in Ethiopia, it has a few limitations. First, this study was a cross-sectional study, which does not enable those patients with temporary disorders in renal function to be distinguished from those with true CKD. Second, the dipstick provides only a semi-quantitative measurement of proteinuria, relatively insensitive and does not register as positive until total protein excretion is more than 300 mg/day. Third, influence of other medications and diet were also not taken into consideration during this study. Our study also has strengths, including assessing renal function by using eGFR and proteinuria, and serum electrolyte balance in CVD, because it is not studied and explored in Ethiopia.

Conclusions

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.

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