

# Assessment of the relationship between CVD and CKD in a community based survey

## Abstract

**Objective:** The aim of this study was to assess the relationship between Chronic Kidney Disease (CKD) and cardiovascular Diseases (CVD) in a community based Survey.

**Methodology:** This was a community based survey, investigated 2944 individuals for CKD and CVD in Northern Saudi Arabia.

**Results:** Of the 2944 Glomerular filtration rate was measured for 2700/2944 (91.7%). Of the 2700, Congestive heart failure (CHF), Heart attack, Stroke and Peripheral vascular disease (PVD), were identified in 27, 52, 41 and 58 patients, respectively.

**Conclusion:** CVDs were highly connected to CKD among general population. There is strong relationship between CVD and CKD among those with undetected CKD. The most common CVDs were CHF, Heart Attack, Stroke and PVD.

**Keywords:** CVD, CKD, Stroke, heart attack, PVD, GFR

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## Introduction

Chronic kidney disease (CKD) is a progressively common disorder, with estimated prevalence of 8-16% worldwide.<sup>1</sup> It is defined as reduced kidney function, verified by declined level of glomerular filtration rate (eGFR), or evidence of kidney damage, such as increased proteinuria.<sup>2</sup>

The prevalence of CKD and/or renal function impairment in the general Saudi population is considerably high, since there is close homology within Saudi population in different regions. The prevalence of CKD was 9.4% in northern Saudi Arabia.<sup>3</sup> CKD is commonly associated with considerable co-morbidity, particularly in the elderly population.<sup>4,5</sup> The development and progress of cardiovascular disease (CVD) and chronic kidney Disease are very closely related.<sup>6</sup> CKD is strongly connected to early cardiovascular disease, which is the most important cause of death before end-stage renal disease in these patients.<sup>7</sup> About half of all deaths in patients with CKD arise from cardiovascular causes of which the most frequent is CHF.<sup>8</sup> Patients with CKD are three times more expected to have myocardial infarction (MI) and suffer from increased morbidity and higher mortality. CKD appears to affect the management of patients with acute MI; percutaneous coronary angiography is not uniformly did in patients with CKD and ESRD when matched with patient's normal kidney function.<sup>9</sup> Ischemic strokes resultant from atrial fibrillation (AF) set up an upsetting condition for patients and their care givers with massive burden on health care systems.<sup>10</sup> CKD has been reported to be independently linked to cerebral microbleeds (CMB). Since both glomerular afferent arterioles and cerebral perforating arteries are strain vessels, CKD and CMB may share similar dynamic abnormalities.<sup>11</sup> CKD is associated with a greater occurrence and number of CMB in intracerebral hemorrhage (ICH) patients, particularly in patients.<sup>12</sup> Declined eGFR predicts deprived outcome in acute ICH. Premature intensive BP lowering delivers similar treatment effects in patients with ICH with declined eGFR.<sup>13</sup> The prevalence of PVD was significantly high in patients with CKD particularly among those with stage IV.<sup>14</sup> The huge burden of PVD inpatients who have CKD contributes significantly to increased morbidity and mortality. The elevated risk of vascular disease witnessed in CKD patients

is likely to be multifactorial, with influences from traditional and nontraditional cardiovascular factors.<sup>15</sup>

However, most studies of CKD focus on mortality and End Stage Renal Disease (ESRD), with limited data on other adverse outcomes, particularly from KSA. Therefore, the aim of this study was to examine the associations CKD and CVD, specifically, CHF, Heart attack, Stroke and PVD.

## Materials and methods

This was a community based cross-sectional survey involved randomly selected samples collected from northern Kingdom of Saudi Arabia (KSA), Hail Region. Data was collected as a part of a comprehensive campaign about CKD in the area. Data regarding CVD was assessed for 2944 patients, of whom 2700 has responded to the blood sample to estimate GFR level and subsequent CKD stage. Data were collected by a professional medical team from College of Medicine, and College of Applied Medical Science, University of Hail. A form was design to collect the demographic information, such as previously diagnosed CVD, age and sex. Blood and urine specimens were collected for estimation of creatinine and proteinuria.

GFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation.<sup>16</sup> CKD was indicated based on the presence of protein urea and level of GFR. All individuals with a glomerular filtration rate (GFR) <60ml/min/1.73m<sup>2</sup>, were considered as having CKD. CKD stages were categorized according to the following: Stage I: Kidney with normal GFR ( $\geq 90$ ml/min/1.73m<sup>2</sup>). Stage II: Kidney with mild decrease in GFR (60 - 89ml/min/1.73m<sup>2</sup>). Stage III: Kidney with moderate decrease in GFR (30 - 59ml/min/1.73m<sup>2</sup>). Stage IV: Kidney with severe reduction in GFR (15 - 29ml/min/1.73m<sup>2</sup>). Stage V: Kidney failure (< 15ml/min/1.73m<sup>2</sup>).

Diagnosis of CVD based on the previous investigations that found within patient medical file in related primary health care center. For CHF mainly depend on the results of an electrocardiogram (ECG or EKG), an echocardiogram (cardiac echo), and cardiac catheterization. For Heart attack beside ECG and cardiac echo, cardiac enzymes

were also included. For stroke many test were considered together including; Physical examination, Blood tests, Computerized tomography (CT) scan, Magnetic resonance imaging (MRI), Carotid ultrasound, cerebral angiogram and Echocardiogram. For PVD, the diagnosis confirmed by these tests; measuring the pulses in legs and feet, Doppler ultrasound, ankle-brachial index (ABI), pulse volume recording (PVR), Angiography, magnetic resonance angiography (MRA) and computerized tomography angiography (CTA). However, not all of these test were previously performed for each patients. Some tests depended on the facilities available in the related primary health center or referral hospital.

## Results

This study investigated 2944 persons their age ranging between 13 to 99 years with a mean age of 44years old. Of the 2944 participants 1369 /2944(46.5%) were males and 1575/2944(53.5%), giving males' females' ratio of 0.86: 1.00. Of the 2944 participants, GFR was estimated in 2700/2944(91.7%). Congestive heart failure (CHF) was identified in 27 subjects. Of the 27 patients, 12/27(44.4%), 5/27(18.5%), and 3/27(11.1%), were stage II, III, and IV respectively. For the CHF, the adjusted odd Ratio (OR) and the 95% Confidence Interval (CI) were found to be 5.12 (2.22 - 11.85),  $P < 0.0001$ . Heart Attack was identified in 52 patients. Of the 52 patients, Stage II, Stage III, and Stage IV, were identified in 21/52(40%), 14/52(27%), and 3/52(5.8%), respectively. For the heart attack, the adjusted OR and the 95% CI were found to be 5.76 (3.17 - 10.47),  $P < 0.001$ .

Stroke was found in 41 participants of whom Stage II, Stage III, Stage IV, and Stage V were revealed in 19/41(46.3%), 6/41(14.6%), 2/41(4.9%) and 1/41(2.4%), in this order. For the stroke, the adjusted OR and the 95% CI were found to be 3.35 (1.58 - 7.11),  $P < 0.0017$ . PVD was detected in 58 participants of whom Stage II, and Stage III were revealed in 26/58(44.8%), and 8/58(13.8%), in this order, as indicated in Table 1 and Figure 1. For the PVD, the adjusted OR and the 95% CI were found to be 1.90 (0.89 - 4.07),  $P < 0.0972$ .

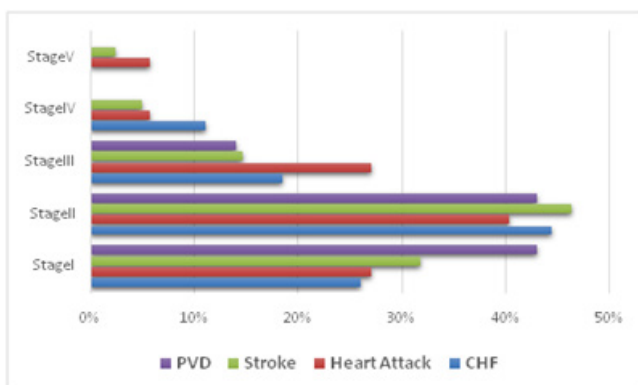


Figure 1 Study population by CVD and CKD stage.

Of the 27 cases of CHF, 10/27(37%) were males and 17/27(63%) were females. The risk of CHF is more associated with females than males and this relationship is statistically significant ( $P < 0.05$ ). Of the 52 cases with heart attack, 33/52(63.5%) were males and 19/52(36.5%).The risk of heart attack is more associated with males than females and this relationship is statistically significant ( $P < 0.006$ ). Of the 41 cases with stroke, 28/41(68.3%) were males and 13/41(31.7%).The risk of stroke is more associated with males than females and this relationship is statistically significant ( $P < 0.001$ ). Of the 58 cases with PVD, 12/58(20.7%) were males and 46/58(79.3%).

The risk of PVD is more associated with females than males and this relationship is statistically significant ( $P < 0.0001$ ), as indicated in Table 2 and Figure 2.

Table 3 summarizes the distribution of CVD and CKD by age. Although almost all CVD categories were associated with elderly individuals (over 40years old), but PVD was relatively associated with younger age (under 40years old). The description of the study CVD and CKD by age (within each age group) was shown in Figure 3.

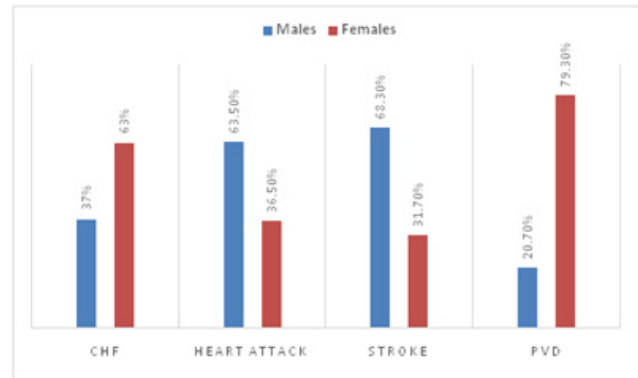


Figure 2 Description of the CVD and CKD stage by sex.

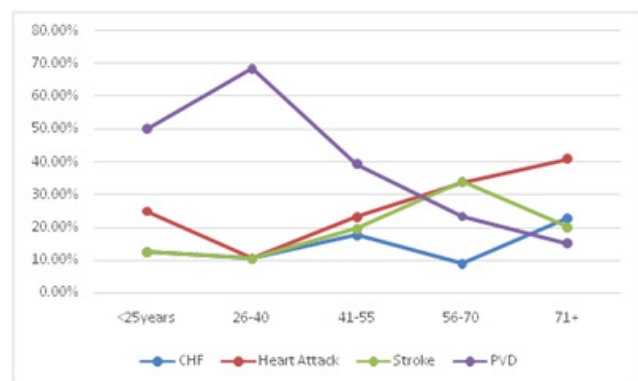


Figure 3 Description of the CVD and CKD stage by age (within each age group).

## Discussion

Most studies of CKD focus on mortality and ESRD, with inadequate data on other adverse comorbidities, particularly CVD. The present study was a part of a comprehensive survey investigation CKD and its risk factors, such as diabetes, hypertension and obesity. The covered a large area in northern KSA. In the current study, the burden of CVD was assessed in relation to CKD. The statistical significant values were produced by considering Stage III, Stage IV and Stage V merely.

The findings of the present study showed a significant relationship between CKD and CHF. It well known that Impaired renal function is a major risk factor of cardiovascular disease, particularly CHF,<sup>17</sup> but there is no study from KSA in this context. A number of studies have found a significant independent relationship between CKD and CVD events, such as, death, heart failure, myocardial infarction, ventricular arrhythmias and sudden cardiac death.<sup>18,19</sup> Furthermore, other studies suggest structural remodeling of the heart and electrophysiological alterations in this population. These progressions may clarify the increased risk of arrhythmia in CKD and support to detect patients who are at increased risk of sudden cardiac death. In CKD, the sympathetic hyperactivity appears to be expressed at the initial clinical stage of the

disease, showing a direct association with the severity of the state of renal failure.<sup>18</sup>

The relationship between heart attack and advanced stages of CKD was also found to statistically significant in this study. However, the most frequent conditions expressed as heart attack is myocardial

infarction. Although, myocardial infarction is frequently common in KSA, but no study investigate its relationship with CKD. Other condition also might be expressed as heart attack including acute coronary syndrome (ACS) and Ischemic heart disease (IHD). IHD is the most frequent cause of death in patients with CKD. CKD in ACS is independently associated with elevated morbidity and mortality.<sup>20</sup>

**Table 1** Distribution of the study population by CVD and CKD stage

| Variable     | Category | Stage I | Stage II | Stage III | Stage IV | Stage V | Total |
|--------------|----------|---------|----------|-----------|----------|---------|-------|
| CHF          | Present  | 7       | 12       | 5         | 3        | 0       | 27    |
|              | Absent   | 1510    | 960      | 180       | 12       | 11      | 2673  |
|              | Total    | 1517    | 972      | 185       | 15       | 11      | 2700  |
| Heart attack | Present  | 14      | 21       | 14        | 3        | 0       | 52    |
|              | Absent   | 1500    | 950      | 175       | 12       | 11      | 2648  |
|              | Total    | 1514    | 971      | 189       | 15       | 11      | 2700  |
| Stroke       | Present  | 13      | 19       | 6         | 2        | 1       | 41    |
|              | Absent   | 1502    | 951      | 183       | 13       | 10      | 2659  |
|              | Total    | 1515    | 970      | 189       | 15       | 11      | 2700  |
| PVD          | Present  | 25      | 25       | 8         | 0        | 0       | 58    |
|              | Absent   | 1516    | 941      | 179       | 15       | 11      | 2642  |
|              | Total    | 1541    | 967      | 187       | 15       | 11      | 2700  |

**Table 2** Distribution of the CVD and CKD stage by sex

| Variable     | Category | Stage I | Stage II | Stage III | Stage IV | Stage V | Total |
|--------------|----------|---------|----------|-----------|----------|---------|-------|
| CHF          | Males    | 2       | 6        | 2         | 0        | 0       | 10    |
|              | Females  | 5       | 6        | 3         | 3        | 0       | 17    |
|              | Total    | 7       | 12       | 5         | 3        | 0       | 27    |
| Heart attack | Males    | 8       | 17       | 8         | 0        | 0       | 33    |
|              | Females  | 6       | 4        | 6         | 3        | 0       | 19    |
|              | Total    | 14      | 21       | 14        | 3        | 0       | 52    |
| Stroke       | Males    | 8       | 13       | 5         | 1        | 1       | 28    |
|              | Females  | 5       | 6        | 1         | 1        | 0       | 13    |
|              | Total    | 13      | 19       | 6         | 2        | 1       | 41    |
| PVD          | Males    | 5       | 6        | 1         | 0        | 0       | 12    |
|              | Females  | 19      | 20       | 7         | 0        | 0       | 46    |
|              | Total    | 24      | 26       | 8         | 0        | 0       | 58    |

**Table 3** Distribution of the CVD and CKD stage by age

| Age      | CHF | Heart Attack | Stroke | PVD | Total |
|----------|-----|--------------|--------|-----|-------|
| <25years | 1   | 2            | 1      | 4   | 8     |
| 26-40    | 2   | 2            | 2      | 13  | 19    |
| 41-55    | 10  | 13           | 11     | 22  | 56    |
| 56-70    | 5   | 19           | 19     | 13  | 56    |
| 71+      | 9   | 16           | 8      | 6   | 39    |
| Total    | 27  | 52           | 41     | 58  |       |

PVD was also found to be a factor linked to CKD in this study. Although there are several studies showed a significant association between CKD and a high risk of ischemic events and mortality, but the association between CKD and PVD still need more evaluation.<sup>21</sup> However, patients with CKD and PVD had a higher mortality than patients with either CKD or PAD alone.<sup>22</sup> Lower extremity PAD has not been assessed in most previous epidemiological studies of CVD amongst patients with CKD<sup>23</sup> and very limited studies of PAD have considered CKD as a potential risk factor.<sup>24</sup> Consequently,

understanding of outcomes and treatment choices for PAD among patients with CKD stand behind that for other forms of CVD.

For the stroke, in the current the adjusted OR and the 95% CI were found to be 3.35 (1.58 - 7.11), P < 0.0017. Stroke is the second most common cause of death and the leading cause of neurological disability worldwide. CKD is associated with a considerably increased risk of stroke. Notably, there are numerous risk factors for stroke, such as hypertension, hypercholesterolemia, smoking and atrial fibrillation<sup>25</sup> which were not shared in this study. Cerebrovascular disease and

stroke are very common at all stages of CKD, likely demonstrating both shared risk factors and synergy amongst risk factors.<sup>26</sup> Stroke commonly followed by poor outcomes at all stages of CKD, and improving these outcomes requires future clinical trials.

In the present study CHF among women was found to be higher than men and such findings were previously reported.<sup>27</sup> Heart attack was significantly higher among males in the current study. It was well established that heart attack is more frequent among males compared to females.<sup>28</sup> Coronary heart disease (CHD), conventionally regarded as a male disease, but responsibly of high incidence of deaths in women. The prevalence of CHD is lower in women at all ages, and the clinical outcomes such as myocardial infarction mortality, worse in women with CVD than in men.<sup>29</sup> Stroke was more common among males in this study, which was similarly reported in some studies.<sup>30</sup> but some studies from Japan reported reverse results.<sup>31</sup> PVD was also found to be more among females than males, which was previously reported.<sup>32</sup> However, PVD was also reported more common among men compared to women.<sup>33</sup>

In regard to the age, all CVD and CKD were found to increase with age in the present study and these facts are well established in literature.<sup>34,35</sup> The strengths of the present study include; the reporting of findings that will add to the existing literature from Saudi Arabia, which might not be reported before. The relationship between CVD and CKD created in the present study will help health care givers to fill gaps in this context as well as, stimulating future research in this subject. The acquisition of data from community may give more apparent picture to the true situation and may give more sounded control measures, since those cases of CKD were undetected.

The study has some limitations, such as, information regarding other comorbidities, such as hypertension and diabetes. Detailed information regarding infections and subsequent patients' management.

## Conclusion

There is strong relationship between CVD and CKD among those with undetected CKD. The most common CVDs were CHF, Heart Attack, Stroke and PVD.

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## Ethical consent

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

## Conflicts of interest

Author declares there are no conflicts of interest.

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