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Predictors of Chronic Kidney Disease in Hypertensive Patients: A One-Year Prospective Study at Hamad General Hospital, Qatar

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Abstract

Background: Hypertension is a major risk factor of chronic kidney disease. With the rising prevalence of hypertension worldwide, the burden of patients with chronic kidney disease is expected to be higher. Early detection and treatment of hypertensive patients with renal impairment is therefore critically important and would prevent progression of kidney disease. This study aims to identify the predictors of chronic kidney disease (CKD) among patients with diagnosis of essential hypertension.

Methods: This prospective, descriptive study, which was conducted at Hamad General Hospital involved patients with a diagnosis of essential hypertension, admitted to the medical ward during the periods from June 2013 till June 2014.

Results: A total of 112 patients were enrolled in the study and the prevalence of CKD was 49.1%. Univariate analysis revealed that long standing hypertension (> 5 years), alcohol consumption, history of TIA/stroke, presence of proteinuria, history of CAD, ECG-determined left ventricular hypertrophy (LVH) and hyperlipidemia were probable predictors of CKD. Using multivariable logistic regression analysis we found long standing hypertension (≥ 5 years), presence of proteinuria and ECG-determined LVH to be independent predictors of CKD.

Conclusions: CKD was found in 49.1% of our patients. Long standing hypertension, presence of proteinuria and ECG-determined LVH were independent predictors of CKD. We recommend utilizing resources to initiate CKD screening programs to assist in early diagnosis of CKD among hypertensive patients.

Keywords: Chronic kidney disease; Proteinuria; Essential hypertension; Hypertensive retinopathy

Introduction

Hypertension is the most common condition seen in primary care and leads to myocardial infarction, stroke, heart failure, renal failure, and death if not detected early and treated appropriately [1]. It is reported to be the fourth contributor to premature death in developed countries and the seventh in developing countries. Out of total 58.8 million deaths worldwide in year 2004, high blood pressure was responsible for 12.8% (7.5 million deaths) [2]. In 2011-2012, the overall prevalence of hypertension among U.S. and Australian adults aged 18 and over was 29.1% and 32% respectively [3,4]. In Qatar, hypertension prevalence was estimated to be 18.69% [5].

Hypertension (systolic more than diastolic) is a major promoter of the decline in glomerular filtration rate (GFR) and a strong independent risk factor for chronic kidney disease (CKD) in both diabetic and nondiabetic kidney disease [6]. Therefore, identifying predictors of CKD in hypertensive patients allow health care systems to implement effective measures to counteract and possibly slow disease progression.

In Qatar, Data are sparse regarding CKD in hypertensive patients. This prompted us to conduct this study to evaluate the predictors for CKD in patients with systemic hypertension at Hamad General Hospital.

Materials and Methods

This prospective cross sectional study, which involved all adult patients (18 years of age or older) who were diagnosed with essential hypertension was conducted at Hamad General Hospital, Qatar from June 2013 to June 2014. This hospital is a 603-bed tertiary care center that covers all specialties except for hematology-oncology, cardiology and obstetrics and it has been Joint Commission International (JCI) accredited since 2006 and is the first hospital system in the region to achieve institutional accreditation from the Accreditation Council for Graduate Medical Education - International (ACGME-I).

The Inclusion criteria of the study included all patients above 18 years of age diagnosed and treated for essential hypertension admitted to Hamad General Hospital. All patients less than 18 years of age, with diagnosis of Diabetes Mellitus, accelerated or malignant hypertension within 6 months, and secondary hypertension together with pregnant

ladies and patients unable or unwilling to provide informed consent were excluded from the study.

A well-structured data capture form (DCF) was designed to collect all required data in view of study design and objectives. The following data were collected using data capture form (DCF) and included demographic, anthropocentric, clinical, biochemical, laboratory features and presence or absence of left ventricular hypertrophy (LVH) and history of coronary artery disease, cerebrovascular and peripheral vascular disease. All patients underwent proper retinal examination by an ophthalmologist in the retina clinic.

Procedures for data collection, entry, storage with password-protected access and data validation were established. Original DCF hard copies were maintained securely with patient unique identifying number. Once all data had been entered into database to be used for statistical analysis, it was audited by investigators and the research coordinators. Data verification, validation and evaluation of accuracy were performed at regular intervals. Quality of data (review of completeness, accuracy, security, and confidentiality of data) was maintained by lead investigators and assigned research coordinators. All missing fields were verified as truly not available.

Regarding data analysis, categorical and continuous values were expressed as frequency (percentage) and mean ± SD or median and interquartile range (IQR) as appropriate. Descriptive statistics were used to summarize demographic, clinical sign and symptoms, physical examination and radiological findings of the patients. The Kolmogorov-Smirnov (K-S) test or Q-Q Plot as appropriate was used to test for normality of the data. The primary outcome variable is the prevalence of HCV was estimated and presented along with 95%CI.

Associations between two or more qualitative variables were assessed using chi-square test and Fisher Exact test as appropriate. Quantitative variables means between the two independent groups were analyzed using unpaired't' and Mann Whitney U tests as appropriate depending on the results of the normality test. The results were presented with the associated 95% confidence interval. Relationship between various quantitative variables with GFR was examined using Pearson's and Spearman's correlation coefficients. A two-sided P value <0.05 were considered to be statistically significant.

In identifying the predictors of CKD, logistic regression analysis was used. Univariate logistic regression was performed to determine the probable predictors of CKD. All potential risk factors significant at the 0.1 level in the univariate analysis were entered in the multiple logistic regressions to identify the independent predictors of CKD at $P < 0.05$. Statistical analysis was carried out using the software package SPSS 22.0 (SPSS Inc. Chicago, IL) and Epi Info 2000 (Centers for Disease Control and Prevention, Atlanta, GA).

The study was approved by the Research Committee and Medical Research Centre at the Hamad Medical Corporation (Ref # 13203/13). Informed consent was obtained in all cases, from each participant (or their closest relatives in instances where the patient was unable to give the consent), before any interview or physical examination was conducted.

Clinical Definitions

Chronic kidney disease: it is defined as GFR of ≤ 60 ml/min/1.73 m2 [7].

Hypertension: it is defined as systolic blood pressure of 140mm Hg or greater or diastolic blood pressure of 90mmHg or greater [8].

Smoking status: Smoking is the inhalation of the smoke of burning tobacco encased in cigarettes, pipes, and cigars. The standard NHIS current smoking definition, which screens for lifetime smoking ≥100 cigarettes, was used [9].

Alcoholism: moderate alcohol consumption is defined as having up to 1 drink per day for women and up to 2 drinks per day for men [10].

Cardiovascular disease: Disease affecting the heart or blood vessels. Cardiovascular diseases include arteriosclerosis, coronary artery disease, heart valve disease, arrhythmia, heart failure, heart failure, diseases of the aorta and its branches, disorders of the peripheral vascular system, and congenital heart disease.

Body mass index (BMI): It is a simple index obtained by dividing the weight in kilograms by height in meters squared.

Obesity: It is defined by the WHO as body mass index (BMI) greater than or equal to 30 [11].

Results

Demographic and clinical data

During the study period, from June 2013 to June 2014, a total of 112 patients with essential hypertension were enrolled and recruited. The mean age of the patients was 54.9 ± 9.0 years (range 30 to 87 years), 43.8% were male and 13.3% were aged 65 years or more. The mean body mass index (BMI) was 26.7 ± 6 kg/m^2. Median proteinuria was 0.20 g/24 hours, with levels ≥ 1.0 g/24 hours in 23% of patients. Majority of the patients were on antihypertensive therapy (1 or 2 medications). 81% of the patients were non-alcohol consumers and 51% of them had exposure to cigarette smoke (current smokers and ex-smokers). The baseline demographic, clinical, biochemical, laboratory and other related characteristics are shown in Table 1. The overall percentage of CKD (low GFR <60 ml/min/1.73 m^2) in this cohort was 49.1% (95% CI: 39.9 to 58.3).

Characteristics	Mean ± SD [median (min-max)] N (%)
Age of diagnosis of Hypertension	
≤ 65 years	97(86.6%)
>65 years	15 (13.4%)
Cholesterol	4.5 ± 1.33[4.4(0.94-8.6)]

Triglycerides	1.56 ± 0.94[1.3(0.4-6.0)]
HDL	1.12 ± 0.56[1.0(0.14-4.29)]
LDL	2.7±1.1 [2.7 (0.47-6.13)]
PCR	88.67 ± 141.8[21.5 (3-820)]
Echo	54.5 ± 8.1 [55.0 (25-65)]
Duration of Hypertension	
<5years	42 (37.5%)
≥5years	70 (62.5%)
Gender	
Male	84 (75%)
Female	28 (25%)
Hypertension treatment	
Not on medications	27 (24.1%)
One medication	32 (28.6%)
Two medication	38 (33.9%)
Three medications	15 (13.4%)
Alcohol	
Consumer	21(18.8%)
Non- consumer	91 (81.3%)
Smoking	
Non smoker	54 (48.2%)
X- Smoker	30 (26.8%)
Current smoker	28 (25%)
BMI	
Underweight (<18.5	3 (2.7%)
Normal (18.5-25)	45(40.2%)
Overweight (25-30)	41(36.6%)
Obese (>30)	23 (20.5%)
History of stroke/TIA	
Yes	29 (25.9%)
NO	83 (74.1%)
History of CAD	
Yes	19 (17%)
NO	93 (83%)
History of Peripheral vascular disease	
Yes	1(0.9%)

No	111(99.1%)
History of hyperlipidemia	
Yes	25(22.3%)
No	87 (77.7%)
GFR	
<60	55 (49.1%)
≥60	57(50.9%)
LVH in ECG	
Yes	57(52.3%)
No	52 (47.7%)
Retinopathy	
Yes	52(53.6%)
No	45 (46.4%)
Echocardiography	
normal	19(20.4%)
LVH	16 (14.3%)
Diastolic dysfunction	43 (46.2%)
Both LVH and diastolic dysfunction	6 (6.5%)
Systolic dysfunction	9 (9.7%)

Table 1: Baseline characteristics.

Logistic regression analysis shown in Table 2 revealed long standing hypertension more or equal to 5 years (OR 2.04; 95%CI 0.94, 4.47; P=0.073, alcohol consumption (OR 3.19; 95% CI 1.13, 8.95; P=0.028), history of TIA/stroke (OR 0.44; 95% CI 0.19, 1.07; P=0.071), presence of proteinuria (OR 11.25; 95% CI 4.39, 28.83; P<0.0001), history of CAD (OR 1.99; 95% CI 0.72, 5.51; P=0.184), ECG-determined LVH (OR 1.63; 95% CI 0.76, 3.47; P=0.109) and hyperlipidemia (OR 0.40; 95% CI 0.16, 1.03; P=0.056 were probable predictors of CKD. Although a higher percentage of male patients had CKD, the result was not statistically significant (OR 1.39; 95% CI 0.59, 3.31; P=0.446). There was also no correlation between prevalence of retinopathy (OR 1.37; 95% CI 0.16, 3.06; P=0.444), and history of smoking (OR 1.24; 95% CI 0.59, 2.61; p=0.566) with CKD.

Variable	Percentage of CKD (GFR<60)	Unadjusted Odds ratio (OR)	95% CI for OR	P-value
Gender				
Male	43 (51.2%)	1.39	0.59, 3.31	0.445
Female	12 (42.9%)	1.0 (reference)		
Age at diagnosis hypertension				
<65 years	49 (50.5%)	1.53	0.51, 4.63	0.451
≥65 years	6 (40.0%)	1.0 (reference)		
Duration of hypertension				
≥5years	39 (55.7%)	2.04	0.94, 4.47	0.073
<5 years	16 (38.1%)	1.0 (reference)		

Alcohol				
Consumer	15 (71.4%)	3.19	1.13, 8.95	0.028
Non Consumer	40 (44.0%)	1.0 (reference)		
Smoking				
Yes	30 (51.7%)	1.24	0.59, 2.61	0.566
No	25 (46.3%)	1.0 (reference)		
History of stroke/TIA				
Yes	10 (34.5%)	0.44	0.19, 1.07	0.071
No	45 (54.2%)	1.0 (reference)		
History of CAD				
Yes	12 (63.2%)	1.99	0.72, 5.51	0.184
No	43 (46.2%)	1.0 (reference)		
Proteinuria				
Yes	36 (81.8%)	11.25	4.39, 28.83	<0.0001
No	18 (28.6%)	1.0 (reference)		
LVH in ECG				
Yes	31 (54.4%)	1.63	0.76, 3.47	0.109
No	22 (42.3%)	1.0 (reference)		
Retinopathy				
Yes	26 (50.0%)	1.37	0.61, 3.06	0.444
No	19 (42.2%)	1.0 (reference)		
Hyperlipidemia				
Yes	8 (32.0%)	0.4	0.16, 1.03	0.056
No	47 (54.0%)	1.0 (reference)		

Table 2: Association of various predictors with CKD: Univariate logistic regression analysis.

Using multivariable logistic regression analysis we found long standing hypertension (> 5 years) (OR 2.85; 95% CI 0.96, 8.7; p=0.056), presence of proteinuria (OR 15.45; 95% CI 4.97, 48.03; p<0.0001) and ECG-determined LVH (OR 3.73; 95% CI 1.2, 11.57; P=0.023) to be independent predictors of CKD (Table 3).

Variable	Percentage of CKD (GFR<60)	Adjusted Odds ratio (OR)	95% CI for OR	P-value
Duration of hypertension				
≥ 5years	39 (55.7%)	2.85	0.96, 8.7	0.056
<5 years	16 (38.1%)	1.0 (reference)		
Proteinuria				
Yes	36 (81.8%)	15.45	4.97, 48.03	<0.0001
No	18 (28.6%)	1.0 (reference)		

LVH in ECG				
Yes	31 (54.4%)	3.73	1.2, 11.57	0.023
No	22 (42.3%)	1.0 (reference)		

Table 3: Association of various predictors with CKD: Multivariate logistic regression analysis.

Discussion

To our knowledge, this is the first report to study predictors of CKD in hypertensive patients in our local settings. CKD is present in 49.1% of our patients with hypertension.

The relationship between abnormal blood pressure and kidney dysfunction was first established in the 19th century. Since then, many reports had been issued to describe the mechanism of kidney damage and to determine the predictors of chronic kidney disease in hypertensive patients. The Kidney Dialysis Outcomes Quality Initiative (KDOQI) classification provides a step-wise progressive definition of CKD ranging from albuminuria with preserved GFR (stage 1) to ESRD with GFR <15 ml/ min/1.73 m^2 (stage 5), [12] and many reports found that progression of CKD in hypertensive patients occurs at a variable rate, ranging from less than 1 to more than 12 ml/min per 1.73 m^2 per year, depending upon the level of blood pressure control, the degree of proteinuria, the previous rate of GFR decline, and the underlying kidney disease, including diabetes [12,13]. In line with previous studies [8,14,15] we found proteinuria as a strong independent risk factor for CKD. Reducing proteinuria reduces the risk of CKD progression [8]. As described by many reports [12,16] duration of hypertension also appears to have an effect on decline in renal function. Similarly, our study showed that longer duration of hypertension is also considered as independent risk factor for CKD. More than 50% of the patients belonged to the combined category of no treatment and more than 2 drugs for hypertension treatment. A higher prevalence of CKD was observed in patients with ECG-determined LVH [17]. Likewise we found ECG-determined LVH an independent predictor of CKD. Although alcohol consumption, hyperlipidemia, history of TIA/stroke, history of CAD and old age were probable predictors of CKD in univariate analysis, they fail to show any significance in multivariate analysis.

Patients with chronic kidney disease (CKD) are at increased risk for progression to ESRD and for premature cardiovascular disease (CVD). Therefore, efforts towards reducing the burden of hypertension and its clinical consequences should aim at early identification of risk factors that are potential targets for intervention. However, the early recognition of CKD is made difficult by its largely asymptomatic nature; because symptoms develop only if GFR decreases below 30 ml/ minute/1.73m^2. Therefore, early detection can only occur through laboratory testing of individuals. CKD screening programs, with a view to making early referrals and institute early interventions, have intensified in the last few years. The National Kidney Foundation (NKF) Kidney Early Evaluation Program (KEEP), initiated in 2000 to detect early kidney disease in at-risk patients [18]. Additionally, many programs had been established such as National Kidney Disease Education Program to increase patient and physician awareness of CKD. Although our study is not designed to describe patient-physician awareness of CKD, and hence we don't know how often patients with hypertension get kidney disease educational opportunities during physician office visits, we suggest to establish a similar programs in Qatar.

Our study has some limitations. First, the study was small, cross sectional and hospital based, thus the results may not be applicable to other hospitals in Qatar. Second, we did not assess the awareness of patient-physician for CKD. Despite these limitations, this study is the first step in highlighting the problem of CKD in the state of Qatar, and its implication is very important for planning health care interventions in the future.

In conclusion, CKD was found in 49.1% of our patients. Long standing hypertension, presence of proteinuria and ECG-determined LVH were independent predictors of CKD. We recommend conducting longitudinal prospective, large, population-based study to confirm this relationship. Moreover, launching educational programs for patient-physician awareness of CKD and CKD screening programs also are considered necessary for early diagnosis of CKD among hypertensive patients to intervene at the earliest possible stage.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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