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Original Article

Prevalence of Reduced Renal Function among Diabetic Hypertensive Patients

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Abstract: Patients with diabetes mellitus and hypertension are at high risk of vascular complications, particularly, renal deterioration. This study aimed to evaluate the prevalence and the risk factors of reduced renal function corresponding to chronic kidney disease (CKD) stages 3 – 5 among diabetic hypertensive patients. This is a retrospective cohort study of diabetic hypertensive patients attending A-Watani governmental medical center from August 2006 until August 2007. Creatinine clearance (CrCl) was estimated using the Cockcroft–Gault equation. Those with CrCl< 60 ml/ min, corresponding to CDK stages 3 – 5, were considered to have reduced renal function. The prevalence of reduced renal function was calculated, and the risk factors associated with it were evaluated using multiple logistic regression. The following were the results found in this study: (a) the prevalence of reduced renal function among the study patients was 35.5% distributed as follows: (63.5%) had stage 3 CKD, 21.7% had stage 4 and 13% had stage 5 CKD. (b) Patients with reduced renal function were elderly, had a higher number of chronic diseases and had a longer duration of diabetes and hypertension than those with CrCl≥ 60ml/ min. (c) Men had a higher prevalence of reduced renal function than women. (d) Significant predictors of reduced renal function were older age, duration of diabetes and the number of chronic diseases based on logistic regression analysis. Early and continuous screening of renal function among diabetic hypertensive patients is required to implement preventable strategies of end stage renal disease (ESRD). Better control of blood pressure and diabetes mellitus are important.

Key Words: Prevalence, reduced renal function, diabetic hypertension, diabetes mellitus

Introduction

It is estimated that 2.7% of Palestinians living in West-Bank have hypertension (HTN) and 2.1% have diabetes mellitus (DM) [1]. Although, no epidemiological data are available about Palestinians who have DM and HTN together, the prevalence of HTN, in general, is a few times greater in patients with DM than in matched non-diabetic individuals [2]. The major adverse outcomes of DM are a result of vascular complications, both, at the microvascular (retinopathy, nephropathy or neuropathy) and macrovascular levels (coronary artery disease, cerebrovascular and peripheral vascular disease) [3,4]. These complications, particularly renal damage, are augmented by the co-existence of HTN [5]. To minimize and delay renal complications, early screening of renal function, appropriate antihypertensive therapy and tight BP and glucose control are required. Recent audit data suggest that existing guidelines on screening for renal disease in hypertensive and diabetic populations are frequently not followed, and when they are, action is not always taken [6]. Unfortunately, late referrals of renal disease are associated with increased morbidity and mortality. This study provides some data as to the likely prevalence and risk factors of reduced renal function corresponding to chronic kidney disease (CKD) stages 3 – 5 among diabetic hypertensive patients.

Methodology

Table 1. Clinical and lab characteristics of patients with and without reduced renal function

Variable	CrCl <60	CrCl≥60	P value
Age:(years)	67±13	63.4±9.5	0.004
Gender: Men	53(46.1)	88(41.9	0.27
Atrial fibrillation, n (%)	7(6.1)	24(11.4)	0.08
Ischemic heart disease, n (%)	45(39.1)	100(47.6)	0.08
Congestive heart failure, n (%)	21(18.3)	34(16.2)	0.37
Systolic blood pressure (mmHg)	148.2±28.5	151.9±29.2	0.27
Diastolic blood pressure(mmHg)	83.8±12.7	86.6±12.9	0.058
Patients on target BP (< 130/ 80 mmHg)	33(28.7)	48(22.9)	0.25
Serum Blood glucose (mg/dl)	256±152	257.8±116.8	0.94
Creatinin Clearance (ml/min)	34.9±15.8	125.1±70.2	<0.001
No of diagnosis	3.2±0.8	2.9±0.8	0.003
Duration of DM(years)	14.9±8.6	10.7±8.5	<0.001
Duration of HTN(years)	9.1±8.5	6.8±7	0.03

CrCl: creatinine clearance; BP: blood pressure; DM: diabetes mellitus; HTN: Hypertension.

We conducted this study at Al-Watani governmental hospital and medical center, the largest non-surgical medical center in north Palestine with in and out-patient community medical services. We used the medical records of the patients to obtain demographic, diagnostic information, laboratory test results and medication history. Data was collected from August 1, 2006 to August 1, 2007. All aspects of the study protocol, including access to and use of the patient clinical information, were authorized by the medical ethics committee and the local health authorities. All in and outpatients with a history of both diabetes mellitus and hypertension were investigated. Patients are considered to have DM and HTN if these diagnoses were present in their medical records and they were on antihypertensive and antidiabetic medications. Creatinine clearance was calculated using Cockcroft-Gault equation [7]. Reduced renal function was defined as creatinine clearance (CrCl)< 60 ml/min. This cut-off point has been previously validated against insulin clearance [8]. This corresponds to the newly proposed National Kidney Foundation Kidney Dialysis Outcomes Quality Initiative (K/DOQI) guidelines for defining chronic kidney disease

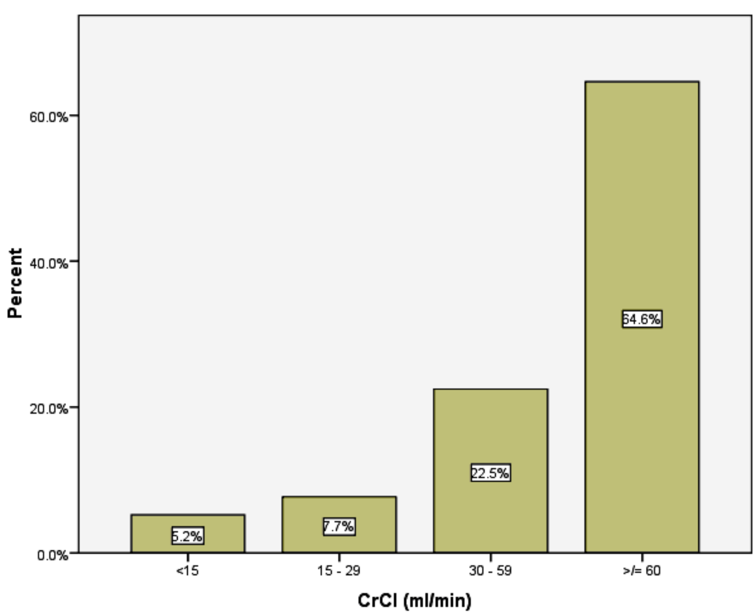

Figure 1: Prevalence of reduced renal function among the total sample using CrCl< 60 ml/ min as a cut-off point.

Table 2. Clinical and lab characteristics of the patients stratified by gender and renal function

Variable	Men n=141			Women n=184		
	CrCl <60 n=53	CrCl≥60 n =88	P value	CrCl <60 n=62	CrCl≥60 n =122	P value
Age:(years)	66.2±13.3	62.8±9.4	0.07	67.7±12.8	63.8±9.5	0.02
Atrial fibrillation, n (%)	3(5.7)	4(4.5)	0.52	4(6.7)	20(16.4)	0.06
IHD, n (%)*	24(45.3)	47(53.4)	0.22	21(33.9)	53(43.4)	0.13
CHF, n (%)	10(18.9)	14(15.9)	0.41	11(17.7)	20(16.4)	0.48
SBP (mmHg)*	146.1±28.4	149.2±26.6	0.51	150.1±28.7	153.8±30.8	0.43
DBP (mmHg)*	82.1±11.4	86.6±13.4	0.06	85.3±13.7	86.6±12.5	0.51
POTBP (< 130/ 80 mmHg)*	17(32.1)	19(21.6)	0.17	16(25.8)	29(23.8)	0.76
SBG (mg/dl)*	264.8±157.7	254.2±98.9	0.62	249.9±149.1	260.4±128.5	0.61
CC (ml/min) *	34.4±15.8	118.7±48.9	<0.001	35.3±15.9	129.7±82	<0.001
No of diagnosis	3.4±0.8	2.9±0.7	0.001	3.1±0.8	2.9±0.9	0.32
Duration of DM(years)	15±9.9	10.9±9.4	0.043	14.7±7.5	10.5±8	0.003
Duration of HTN(years)	9.6±8.2	6±6	0.022	8.7±8.8	7.3±7.5	0.37

*IHD: Ischemic heart disease, CHF: congestive heart failure; DBP: diastolic blood pressure; SBP: systolic blood pressure; CC: creatinin clearance; POTBP: patients on target BP; SBG: Serum Blood glucose; CrCl: creatinine clearance; BP: blood pressure; DM: diabetes mellitus; HTN: Hypertension.

(CKD) stages 3 – 5 [9]. Elevated or non-target BP was defined as greater than or equal to 130/80 mmHg, according to the Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [10].

Statistical analysis

Data was entered and analyzed using Statistical Package for Social Sciences program version 16 (SPSS). Chi square or Fischer's exact test, whichever appropriate, was used to test significance between categorical variables. Independent samples t test was used to compare means of continuous variables. Multiple logistic regression analysis was used to identify risk factors associated with reduced renal function. Variables included in the regression were those with significant P value (< 0.05) in the univariate analysis. Data was expressed as mean ± SD for continuous variables and as frequency for categorical variables.

Results

A sample of 325 consecutive diabetic hypertensive patients was investigated. There were 141 (43.4%) men and 184 (56.6%) women patients. The mean age of the patients was 64.7 ± 11 years. The mean creatinine clearance (CrCl) of the patients was 93.1 ± 71.6 ml/ min. The mean duration of DM was 12.1±8.8 and that for hypertension was 7.6±7.6 years. There was a significant negative correlation between CrCl and duration of DM (r= -0.175, P = 0.007) but not with that of HTN (r = - 0.12, P= 0.08). When the patients were categorized based on CrCl level, there was 115 (35.4%) patients having CrCl< 60 ml/ min and 210 (64.6%) patients having CrCl≥ 60 ml/min. **Table 1** compares the demographic and clinical characteristics of patients in both groups and shows that patients with CrCl< 60ml/ min were elderly (67±13 versus 63.4±9.5 years, P= 0.004), had significantly longer durations of HTN (9.1±8.5 versus 7.3±7.5 years, P = 0.03), DM

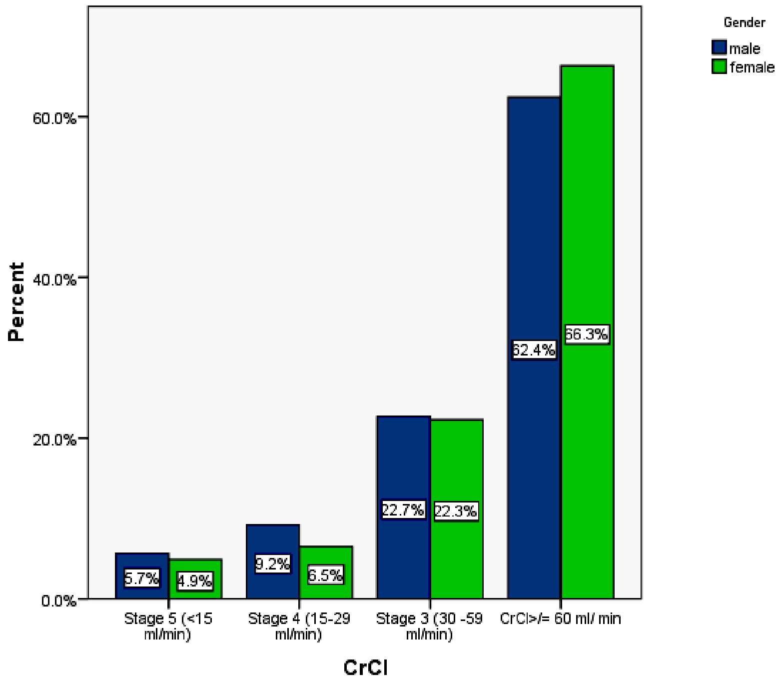

Figure 2: Prevalence of reduced renal function stratified with gender.

(14.9±8.6 versus 10.7±8.5 years, P < 0.001), and had a higher number of chronic diseases (3.2±0.8 versus 2.9±0.8, P= 0.003). No significant correlation between CrCl < 60ml/ min and gender was revealed (P= 0.27). The average number of antihypertensive medications utilized by the two groups was not significantly different (1.83 ± 1.0 versus 1.80 ±1.2). Among the 115 patients with reduced renal function, 73 (63.5%) had CrCl = 30 – 59.9 ml/ min (stage 3 CKD), 25 (21.7%) had CrCl = 15 – 29.9 ml/ min (stage 4 CKD) and 15 (13%) had CrCl< 15 ml/ min (stage 5 CKD). Of the total sample, 5.2% had stage 5, 7.7% had stage 4 and 22.5% had stage 3 (**Figure 1**). Men and women in the total sample had comparable demographic and clinical characteristics except for the presence of IHD where men had higher proportions of IHD than women (50.4% versus 40.2%, P = 0.04). No significant difference in congestive heart failure (CHF) (P = 0.54) or number of patients at the target BP (P=0.82) between men and women was found. **Table 2** shows the clinical characteristics for men and women stratified with renal function. Within the men group, there were 53 (37.6%) patients with CrCl< 60ml/min who significantly had higher numbers of chronic diseases (3.4± 0.8 versus 2.9± 0.7; P <0.001), longer duration of DM (15±9.9 versus 10.9±9.4 years, P=0.043) and HTN (9.6±8.2 versus 6±6, P=0.022) than men with CrCl≥ 60ml/ min. Among the women group, there was 62 (33.7%) patients with reduced renal function. Women with CrCl< 60ml/min were significantly older (67.7±12.8 versus 63.8±9.5 years, P= 0.02) and had significantly longer durations of DM (14.7±7.5 versus 10.5±8 years, P = 0.003) than women with CrCl≥ 60 ml/ min. In general, men had higher prevalence of reduced renal function than women (37.6% versus 33.7%). Women had lesser proportions of stages 4 and 5 while comparable proportions of stage 3 to that in men (**Figure 2**). In both men and women, the prevalence of reduced renal function tends to increase with age, with the highest prevalence being among men and women in the eighth decade. The overall prevalence of reduced renal function among the total sample was 35.4% (**Table 3**).

Table 4 shows the multivariate logistic regression analysis of reduced renal function. The following were taken as independent variables in the analysis: the number of chronic diseases, duration of DM, duration of HTN, and age. All included variables had a significant P value in the univariate analysis between patients with and without reduced renal function. Multiple logistic regression showed that increased risk factors for reduced renal function were seen with the number of chronic diseases (P= 0.001), duration of DM (P= 0.005) and age (P= 0.039). However, duration of HTN (P= 0.69) was not a significant

Table 3. Prevalence of reduced renal function stratified with age and gender

Age category (Years)	Men (N)	Prevalence of CrCl<60ml/min Among men n (%)	Women (N)	Prevalence of CrCl<60ml/min Among women n (%)	Prevalence of CrCl< 60ml/min in the total sample (%)
<50	13	5 (38.5)	15	4 (26.7)	32.1
50-59	32	12 (37.5)	32	9 (28.1)	32.8
60-69	48	13 (27.1)	67	16 (23.9)	25.2
70-79	37	15 (40.5)	52	22 (42.3)	41.6
≥ 80	11	8 (72.7)	18	11 (61.1)	65.5
Total	141	53 (37.6)	184	62 (33.7)	35.4

CrCl: creatinine clearance.

Table 4. Multivariate logistic regression analysis of reduced renal function

Variable	β	β S.E	P value	95% CI for β
Age	-0.006	0.003	0.039	- 0.01 – 0.0
Number of chronic diseases	-0.0127	0.037	0.001	-0.02 - -0.054
Duration of DM	-0.011	0.004	0.005	-0.019 - -0.004
Duration of HTN	-0.002	0.004	0.692	-0.011 -0 .007

S.E: standard error, CI: confidence interval; DM: diabetes mellitus; HTN: Hypertension.

predictor in the model.

Discussion

Early identification of renal disease is important. People with renal impairment are more likely than the general population to have cardiovascular disease and thus suffer extra morbidity and mortality. There is increasing evidence that some adverse outcomes of CKD can be prevented or delayed by early detection and treatment [11]. Unfortunately, CKD is underdiagnosed and undertreated, resulting in lost opportunities for prevention [12-14]. A study in London/ UK that investigated the prevalence of renal impairment in individuals with known hypertension or diabetes aged 50 -70 years has found the prevalence of renal disease to be 6.1% in hypertensives, 12.6% in the diabetics and 16.9% in those with both suggesting that diabetics hypertensive patients are at higher risk of renal disease than patients with either disease alone [15]. Our study indicated that 35.4% of the diabetic hypertensive patients attending a major medical center had reduced renal function corresponding to CKD stages 3 – 5. A study in Italy showed that GFR<60 ml/min/1.73 m2 was revealed in 41% of diabetic patients (16). Among Americans with diabetes, the prevalence rate of those with GFR<60 ml/min was 27.5% [17]. A Chinese study showed that the prevalence of reduced renal function (GFR< 60 ml/ min) among diabetic patients was 32.8% [18]. In a cohort of 721 patients who had essential hypertension, a GFR< 60 ml/min was observed in 16.2% of the patients [19]. In another recently published study [20], the prevalence of a GFR< 60 ml/min in 13,687 patients who had hypertension and were seen in primary care in Spain was 27.7%. Our results showed a similar high prevalence of the CKD Stages 3–5 to that reported in Western and Chinese diabetic patients. Our prevalence rate was higher than that reported among hypertensives and closer to that reported among diabetic patients.

In this study, less than one third of the patients with or without reduced renal function were at the target blood pressure. Good blood pressure management is important in preventing the progression of renal disease. Guidelines on suitable target BP for diabetic hypertensive patients are available at the JNC 7th report. Similar results were obtained by other researchers who reported target blood pressures are seldom achieved among this category of patients [21]. In our study, there was no correlation between gender and reduced renal function. However, some studies including those from the United States, Taiwan, and Australia showed that female sex was one of the risk factors of CKD [22-24]. Such differences in the impact of gender could be due to genetic or social differences between Middle Eastern communities and other communities.

Although this study is the first one of its type in Palestine, it has a few limitations. It is limited by the fact that the K/DOQI proposed using GFR and proteinuria to evaluate and classify the stages of chronic kidney diseases. The lack of information in this study regarding proteinuria made it difficult to confirm whether patients with CrCl> 60 ml/ min were having CKD or not. Furthermore, there was a lack of information regarding the prevalence of reduced renal function in patients with diabetes alone or hypertension alone.

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References

[1] Palestinian Central Bureau of Statistics. Detailed Statistics. Health survey 2000. Percentage of Persons Who Indicated Having Certain Chronic Diseases and Receiving Treatment by Disease and Selected Background Characteristics, 2000.
[2] Simonson DC. Etiology and prevalence of hypertension in diabetic patients. Diabetes Care. 1988; 11(10):821-827.
[3] Grundy SM, Benjamin IJ, Burke GL, Chait A, Eckel RH, Howard BV, Mitch W, Smith SC Jr, Sowers JR. Diabetes and cardiovascular disease: a statement for healthcare professionals from the American Heart Association. Circulation. 1999; 100(10):1134-1146.
[4] Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998; 352(9131):837-853.
[5] Epstein M, Sowers JR. Diabetes mellitus and hypertension. Hypertension. 1992; 19(5):403-418.
[6] Kissmeyer L, Kong C, Cohen J, Unwin RJ, Woolfson RG, Neild GH. Community nephrology: audit of screening for renal insufficiency in a high risk population. Nephrol Dial Transplant. 1999; 14(9):2150-2155.
[7] Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976; 16(1):31-41.
[8] Couchoud C, Pozet N, Labeeuw M, Pouteil-Noble C. Screening early renal failure: cut-off values for serum creatinine as an indicator of renal impairment. Kidney Int. 1999; 55(5):1878-1884.
[9] National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002; 39(2 Suppl 1):S1-266.
[10] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003; 42(6):1206-1252.
[11] Remuzzi G, Ruggenenti P, Perico N. Chronic renal diseases: renoprotective benefits of renin-angiotensin system inhibition. Ann Intern Med. 2002 ;136(8):604-615
[12] Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. Am J Kidney Dis. 2003 ;41(1):1-12.
[13] McClellan WM, Knight DF, Karp H, Brown WW. Early detection and treatment of renal disease in hospitalized diabetic and hypertensive patients: important differences between practice and published guidelines. Am J Kidney Dis. 1997 ;29(3):368-375
[14] Obrador GT, Ruthazer R, Arora P, Kausz AT, Pereira BJ. Prevalence of and factors associated with suboptimal care before initiation of dialysis in the United States. J Am Soc Nephrol. 1999; 10(8):1793-800.
[15]Ellis PA, Cairns HS. Renal impairment in elderly patients with hypertension and diabetes. QJM. 2001; 94(5):261-265.
[16] Sasso FC, De Nicola L, Carbonara O, Nasti R, Minutolo R, Salvatore T, Conte G, Torella R. Cardiovascular risk factors and disease management in type 2 diabetic patients with diabetic nephropathy. Diabetes Care. 2006; 29(3):498-503.
[17] Middleton RJ, Foley RN, Hegarty J, Cheung CM, McElduff P, Gibson JM, Kalra PA, O'Donoghue DJ, New JP. The unrecognized prevalence of chronic kidney disease in diabetes. Nephrol Dial Transplant. 2006; 21(1):88-92.

[18] Lu B, Song X, Dong X, Yang Y, Zhang Z, Wen J, Li Y, Zhou L, Zhao N, Zhu X, Hu R. High prevalence of chronic kidney disease in population-based patients diagnosed with type 2 diabetes in downtown Shanghai. J Diabetes Complications. 2008; 22(2):96-103.

[19] Jabary NS, Martín D, Muñoz MF, Santos M, Herruzo J, Gordillo R, Bustamante J. Serum creatinine and creatinine clearance to estimate renal function in essential hypertension. Nefrologia. 2006; 26(1):64-73.

[20] Redón J, Cea-Calvo L, Lozano JV, Fernández-Pérez C, Navarro J, Bonet A, González-Esteban J; ERIC-HTA 2003 Study Investigators. Kidney function and cardiovascular disease in the hypertensive population: the ERIC-HTA study. J Hypertens. 2006; 24(4):663-669.

[21] Dasgupta I, Madeley RJ, Pringle MA, Savill J, Burden RP. Management of hypertension in patients developing end-stage renal failure. QJM. 1999; 92(9):519-525.

[22] Chadban SJ, Briganti EM, Kerr PG, Dunstan DW, Welborn TA, Zimmet PZ, Atkins RC. Prevalence of kidney damage in Australian adults: The AusDiab kidney study. J Am Soc Nephrol. 2003; 14(7 Suppl 2):S131-S138.

[23] Kramer HJ, Nguyen QD, Curhan G, Hsu CY. Renal insufficiency in the absence of albuminuria and retinopathy among adults with type 2 diabetes mellitus. JAMA. 2003; 289(24):3273-3277.

[24] Lin S. Nephrology in China: A great mission and momentous challenge. Kidney Int Suppl. 2003 ;(83):S108-S110.