International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 8, Issue 12, 2016

Original Article

IS RENAL IMPAIRMENT CONCEALED IN ELDERLY DIABETICS????

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Received: 25 Aug 2016 Revised and Accepted: 14 Oct 2016

ABSTRACT

Objective: To compare and evaluate the renal profile of elderly and younger diabetics.

Methods: This cross sectional study was conducted in a tertiary care teaching hospital. Patients with type-2-diabetes were grouped into elderly (age≥60years) and younger diabetics. Patients' demographics, duration of diabetes and serum creatinine were recorded. Cockcroft-Gault formula was used to calculate creatinine clearance (Clcr). Statistical analysis was done using Students''t' test and Pearson's correlation. Regression analysis to adjust for covariables was done wherever required.

Results: A total of 477 diabetics were included (elderly *n*=320, young *n*=157). Body mass index (BMI) was significantly lower (p=0.003) and duration of diabetes was significantly longer (p=0.001) among elderly. Significant difference was noted in serum creatinine (1.06±0.32 vs 0.95±0.29 mg/dl; p=0.0002) and Clcr (57.82±17.41 vs 88.07±24.60 ml/min; p=0.001) between elderly and younger diabetics. Only 4.7% of elderly, whereas 47.8% of young had normal Clcr. Clcr showed a negative correlation with age in elderly (r=-0.389, p<0.001) and young (r=-0.396, p<0.001) and positive correlation with BMI in elderly (r=0.401, p<0.001) and young(r=0.337, p<0.001). Regression analysis of Clcr in elderly and young showed a positive correlation for BMI and inverse relationship for age and duration of diabetes mellitus.

Conclusion: Almost 95% of the elderly and 50% of younger diabetics had impaired creatinine clearance. Renal impairment was concealed in most of them since mean serum creatinine was 1 mg/dl. Indian elderly diabetics should be considered renally impaired and drugs for all conditions need adjustment for creatinine clearance.

Keywords: Diabetes Mellitus, Creatinine clearance, Younger diabetics

DOI: http://dx.doi.org/10.22159/ijpps.2016v8i12.14887

INTRODUCTION

In the 21st-century diabetes mellitus is a major threat to human health [1]. Diabetes mellitus is associated with increased morbidity from macro-and microvascular complications. It is well known that chronic complications of diabetes mellitus involve both large vessels and small vessels. Macrovascular complications include cardiovascular disease, cerebrovascular disease, and peripheral vascular diseases, while the microvascular diseases include diabetic nephropathy, neuropathy and retinopathy. The risk of microvascular complication is also increased in elderly persons [2]. Diabetic nephropathy (DN) is more common in elderly diabetics with type 2 diabetes than with type 1 diabetes mellitus [3]. Nephropathy in elderly diabetics is heterogeneous because of diabetic lesions and other lesions like vascular lesions [4]. Worldwide DN is the major cause of end-stage renal disease, due to the fact that (a) rapidly increasing prevalence of diabetes and (b) diabetics now live longer [5]. In diabetics, the volume of the whole kidney and of individual glomeruli is increased at diagnosis [6] and glomeruli continue to enlarge later in the disease [7]. At present two general classes of tests are used to screen DN. (1) GFR: Can be estimated conveniently with a creatinine value incorporating into prediction equations. GFR decline is a late index of kidney damage, especially in diabetic renal disease. (2) Albuminuria: Urine albumin excretion rate (UAER) remains the cornerstone of early detection of diabetic nephropathy and is the recommended screening test for the diagnosis of DN [8].

Serum creatinine is frequently normal in elderly patients in spite of decline in renal function. Several formulae have been developed to calculate the creatinine clearance using individual's age, sex, and serum creatinine levels [9-10].

Due to age-related reduction in renal function, the pharmacokinetics of many drugs are changed in elderly patients. Hence the most important tool for monitoring renal function with advanced age is creatinine clearance [11]. In clinical practice, screening of chronic renal dysfunction by using GFR formula may help the clinicians to identify patients who are at the risk of developing end-stage renal disease and also ADRs to water soluble drugs.

The National Kidney Foundation [12] has staged chronic kidney disease (CKD) which helps to understand the renal status of the patient, to plan treatment and predict outcomes.

If CKD is undetected, can lead to kidney failure, dialysis or transplantation and result in premature death due to cardiovascular events [13]. Recent data have high-lightened that even a small increase in serum creatinine levels has a great impact on cardiovascular mortality [14]. The population who are at high risk are those with DM [15], hypertension, kidney stones, old age and family history of kidney diseases. In India, around 30% of chronic renal failures are due to DN [16] and type 2 diabetes is considered to be a disease of the middle-aged and elderly [17]. There are no Indian studies comparing elderly diabetics with younger diabetics, hence the present study was designed to compare and evaluate the renal profile of elderly and younger diabetic patients.

MATERIALS AND METHODS

A cross-sectional study was conducted in an outpatient department of a tertiary care teaching hospital where patients with type 2 diabetes mellitus were grouped into elderly (age≥60years) and younger diabetics (age<60years). The study protocol was approved by the institutional ethics committee and then patients were included in the study after obtaining written informed consent. Patients' age, duration of diabetes and serum creatinine were noted. Body mass index (BMI) was calculated. Creatinine clearance (Clcr) was calculated using Cockcroft-Gault formula. Based on Clcr, patients were distributed as normal (90 ml/min), mild renal impairment (60-89 ml/min), moderate renal

impairment (30-59 ml/min), severe renal impairment (15-29 ml/min) and renal failure (<15 ml/min). Results were analyzed using statistical package for the social sciences version 11.5. Student's unpaired t-test (t-test) for variable with normal distribution and Mann-Whitney U test (Z test) for variable with non-normal distribution was used. Chi-square test for distribution of patients with regard to Clcr. Pearson's correlation coefficient was used to correlate different parameters. Regression analysis to adjust for the covariables was done wherever required. All the analyses were done at the 5 % significance.

RESULTS

Four hundred and seventy-seven diabetic patients were included in the study (elderly *n*=320, young *n*=157). The mean age of elderly and younger diabetics was 68.31±6.06 and 49.91±6.93 y respectively. There is statistically significant difference in body mass index (BMI) (24.78±3.81 vs 25.89±4.11; p=0.003) and duration of diabetes mellitus (11.38±8.90 vs 6.52±5.71; p=0.001) between elderly and younger diabetics respectively.

Table 1 shows a comparison of renal profile between elderly and young diabetics.

Table 1: Comparison of renal profile

Renal parameters	Elderly (n=320)	Young (n=157)	P value
S. Creatinine (mg/dl)	1.06±0.32	0.95±0.29	0.0002 *
Clcr (ml/min)	57.82±17.41	88.07±24.60	0.001 *

Values are expressed as mean±SD; * significant. Table 2 gives the distribution of patients, according to creatinine clearance (Clcr). The majority of elderly diabetics had a moderate renal impairment (54.1%), while the majority of younger diabetics had normal creatinine clearance (47.8%).

Table 2: Comparison of creatinine clearance (Clcr)

Clcr grading	Elderly n=320 (%)	Young n=157 (%)	X^2 value	p value
Normal	15 (4.7)	75 (47.8)	124.91	0.0001 **
Mild	120 (37.5)	61 (38.9)	0.03	0.85
Moderate	173 (54.1)	21 (13.4)	70.58	0.0001 **
Severe	12 (3.8)	0 (0)	4.61	0.032 *

*Significant; Clcr in ml/min: Normal>90; Mild 60-89; Moderate 30-59; Severe 15-29, As shown in table 3 correlation analysis showed statistically significant negative correlation of age with creatinine clearance for elderly (r=-0.389, p<0.001), young (r=-0.396, p<0.001) and total population (r=-0.655, p<0.001). Statistically significant positive correlation of BMI with Clcr for elderly (r=0.401, p<0.001), young (r=0.337, p<0.001) and total population (r= 0.376, p<0.001) was seen.

Table 3: Correlation of creatinine clearance vs age, BMI

	Total population n=477		Elderly n=320		Young n=157	
	r value	p value	r value	p value	r value	p value
Age	-0.66	<0.001	-0.39	<0.001	-0.39	<0.001
BMI	0.38	<0.001	0.40	<0.001	0.34	<0.001

r = Pearson correlation.

Regression analysis of creatinine clearance (Clcr) in elderly and younger diabetics showed a positive correlation for BMI and inverse relationships for age and duration of diabetes mellitus (table 4).

Table 4: Group wise regression analysis: Clcr as dependent variable

Variables	β coefficients±standard error	p-value
Elderly n =320, R=0.385, R^2= 0.148		
Constant	84.42±12.10	
Age	-1.08±0.13	<0.001*
BMI	1.71±0.22	<0.001 *
DM duration (Yrs)	-0.26±0.09	0.007*
Younger n =157, R=0.397, R^2= 0.158		
Constant	99.15±15.92	
Age	-1.71±0.25	<0.001*
BMI	2.80±0.40	<0.001*
DM duration (Yrs)	-0.64±0.30	<0.03*

*Significant

DISCUSSION

Our study showed that elderly diabetics had significantly lower BMI compared to younger diabetics and this lower BMI in the elderly could be due to malnutrition, age-related changes in taste and appetite suppression or/and age-related weight reduction [18-20]. Simultaneously, adherence to lifestyle modification and better insulin sensitivity could also play a role in lowering BMI. Shorter duration of disease, insulin resistance and poor adherence to lifestyle probably accounted for high BMI in younger diabetics.

As expected the duration of diabetes was longer in elderly. Creatinine clearance was significantly lower in elderly diabetics with a mean GFR of 57.82±17.41 ml/min which suggests moderate renal impairment in almost all the elderly diabetics. Almost 95% of the elderly diabetics had impaired creatinine clearance while

50% of the younger diabetics had the same. This has significant implications for drug dosage and excretion. In view of 95% of the elderly diabetics being renally impaired we recommend that Indian elderly diabetics must be treated as renally impaired unless otherwise proven. This impairment of renal function could be due to the effects of aging, lower BMI, long duration of diabetes, presence of hypertension and could also be related to increased use of ACE inhibitors and angiotensin receptor blockers. No Indian data are available on the correlation between aging, diabetes and creatinine clearance.

However, there is a western study of concealed renal failure and adverse drug reaction in older patients with type 2 diabetes, which is a part of a major study, Gruppo Italiano di Farmacovigilanza nell' Anziano (GIFA) [21]. In the GIFA study, among 11,687 hospitalized elderly patients, the normal renal function was found in 7195 (61.6%) patients, overt renal insufficiency was seen in 2861 (24.5%) patients and concealed renal insufficiency was found in 1631 (14%) patients. Among the 2257 diabetic patients, 1891 (83.8%) had impaired renal function of which 1528 (67.7%) had an overt renal failure and 363 (16.1%) had concealed renal impairment. Our study agrees with their study. However, their study is on hospitalized patients where renal impairment can occur due to acute illnesses. Ours is purely an outpatient study of stable elderly diabetics and hence the higher fig. seen in our study indicates that Indian diabetics are definitely more renally impaired than the western diabetics.

In yet another study by Kurtal H, *et al.*, [22] in 221 hospitalized geriatric patients a reduced renal function (<60 ml/min) was found in 61% of the elderly patients. However, this study included patients with GFR<60 ml/min alone as renally impaired while in our study the 95% prevalence of renal impairment included 37.5% patients of mild renal impairment with creatinine clearance of 60–90 ml/min, 54.1% patients of moderate renal impairment with creatinine clearance of 30–59 ml/min and 3.8% patients of severe renal impairment with creatinine clearance<30 ml/min in elderly diabetics. Thus a total of 57.9% of patients had GFR<60 ml/min which is comparable, however, their study too was on hospitalized patients while ours is an outpatients based study.

In a study by Wasen E, *et al.*, [23] on the estimation of prevalence of decreased kidney function in an elderly population of 1246 residents, it was found that 58.6% had moderate or severely decreased renal function. Our study showed 57.9% of elderly patients had moderate or severe renal impairment.

No authentic Indian data are available on diabetic or nondiabetic elderly population regarding GFR. However, there is a single study of 10 patients with benign prostatic hypertrophy with a mean age of 70.5 y, where a mean GFR of 60.45 ml/min has been reported by the CG formula [24].

In the present study, mean serum creatinine of elderly diabetics was 1.06±0.32 mg/dl, which is within the normal limits; but mean creatinine clearance was 57.82 ml/min. This shows that renal impairment was concealed in elderly. The same trend was noted in GIFA study where they referred to such renal impairment as a concealed renal failure [21]. Serum creatinine values may mislead clinicians in recognizing renal impairment, hence creatinine clearance should be calculated for every elderly person and more so if he/she is a diabetic. Since the mean creatinine clearance of elderly diabetics was 57.82 ml/min (i.e.,<60 ml/min) every elderly diabetic should be treated as a person with moderate renal impairment and drug dosage needs to be adjusted.

Creatinine clearance negatively correlated with age and BMI, both of which are incorporated in the creatinine clearance formula. In regression analysis, duration of diabetes emerged as the single most significant factor negatively correlating with creatinine clearance. This factor remained significant in both the elderly and younger population. The limitations of the study are that creatinine clearance alone may not be adequate to assess renal function, it is necessary to consider microalbuminuria, albuminuria or proteinuria in diabetics. Authors could not perform these investigations because of the financial constraints. To extrapolate the study results, larger sample is required.

CONCLUSION

Almost 95% of the elderly and 50% of younger diabetics had impaired creatinine clearance. Renal impairment was concealed in most of them since mean serum creatinine was 1 mg/dl. Indian elderly diabetics should be considered renally impaired and drugs for all conditions need adjustment for creatinine clearance.

CONFLICTS OF INTERESTS

Declared none

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How to cite this article

- Rajeshwari Shastry, Prabha Adhikari MR, Shashidhar Kotian M. Is renal impairment concealed in elderly diabetics????. Int J Pharm Pharm Sci 2016;8(12):163-166.