Original Article

An observational, cross-sectional study to assess the prevalence of chronic kidney disease in type 2 diabetes patients in India (START -India)

M. Prasannakumar, Rajesh Rajput[1], Krishna Seshadri[2], Pradeep Talwalkar[3], Pankaj Agarwal[4], G. Gokulnath[5], Bhavesh Kotak[6], Ammar Raza[6], Hardik Vasnawala[6], Chirag Teli[6]

Senior Consultant Endocrinologist, Center for Diabetes and Endocrine Care, Bangalore, Karnataka, [1]Senior Professor and Head, Department of Endocrinology, PGIMS, Rohtak, Haryana, [2]Head, Department of Endocrinology, Sri Ramchandra Medical College, Chennai, Tamil Nadu, [3]Consultant Diabetologist, Talwalkar Diabetes Clinic, Mumbai, Maharashtra, [4]Consultant Endocrinologist, Hormone Care and Research Centre, Ghaziabad, Uttar Pradesh, [5]Head, Department of Nephrology, Vydehi Institute of Medical Sciences and Research Centre, [6]Medical Affairs, AstraZeneca Pharma India Limited, Bangalore, Karnataka, India

ABSTRACT

Objective: The primary objective of this study is to estimate the prevalence of chronic kidney disease (CKD) among type 2 diabetes mellitus (T2DM) patients in India. **Materials and Methods:** This cross-sectional, observational, epidemiological, multi-center, study is enrolling T2DM patients of either gender aged 30 years or above. This study aimed to enroll a total of 3000 T2DM patients at 30 participating hospitals/clinics across India and the data from a planned interim analysis of 1500 patients are presented here. The primary endpoint of the study is to estimate proportion of T2DM patients with CKD (glomerular filtration rate [GFR] <60 ml/min/1.73 m^2 or albumin creatinine ratio [ACR] ≥30 mg/g or ≥3 mg/mmol or both). Routine treatment, as administered by the treating physician, was continued without any study specific intervention. Patients' data pertaining to demographic characteristics, medical history, current medication and physical examination were recorded. The blood/plasma and urine samples, were collected for estimation of hemoglobin A1c, microalbuminuria, serum creatinine, urine creatinine, and routine urine analysis. ACR was calculated from urine creatinine and albumin while GFR was estimated by using a modification of diet in the renal disease equation. **Results:** Study recruited 1500 patients from 18 centers across India. The study population included 840 (56.05%) males. Mean age, body mass index and systolic blood pressure were 55.1 years, 27.4 kg/m^2 and 134.5 mmHg respectively. The mean duration of diabetes was 102.2 months. History of co-morbid diseases such as dyslipidemia, hypertension, microvascular complications and macrovascular complications was present in 657 (43.8%), 655 (43.7%), 268 (17.9%) and 104 (6.93%), respectively. This interim analysis revealed that about 46% of the T2DM patients had CKD (urinary albumin creatinine ratio (UACR) ≥30 mg/g and/or estimated GFR [eGFR] <60 mL/min/1.73 m^2). The renal dysfunction as per eGFR criteria (<60 mL/min/1.73 m^2) was reported in about 23% while as per UACR criteria (≥30 mg/g) it was reported in about 35% patients. **Conclusion:** This interim analysis results suggests that over 40% of T2DM patients have CKD. Despite this high number of T2DM patients with CKD, eGFR analysis shows there are almost 80% of T2DM patients still have reasonably good renal function (eGFR above 60 ml/min), which ensures less restrictions in selecting oral anti-diabetic drugs. Full study results from Start-India study will provide detail insights into the occurrence of CKD in patients with T2DM in India.

Key words: Albumin creatinine ratio, chronic kidney disease, diabetes mellitus, glomerular filtration rate, renal dysfunction

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Corresponding Author: Dr. Hardik Vasnawala, AstraZeneca Pharma India Ltd., Block N1, 12th Floor, Manyata Embassy Business Park, Rechenahalli, Outer Ring Road, Bengaluru - 560 045, Karnataka, India. E-mail: hardik.vasmawala@astrazeneca.com

Introduction

Diabetes mellitus is a major cause of concern because of its increasing prevalence rate globally. The increase in burden is highest in the Asian and African countries.[1] As per estimates, in year 2013, worldwide, 382 million people aged 20–79 years were living with diabetes, 46% of them being undiagnosed. This number is expected to increase to 592 million by the year 2035. India plays host to a 65.1 million patients with diabetes, second only to China as per estimates in International Diabetes Federation Atlas 2013.[2] Furthermore, the average age at which Asian Indian develops diabetes is now estimated to be about 10 years lower than that of their western counterparts.[3,4]

Increase in prevalence of type 2 diabetes mellitus (T2DM) is associated with a consequent increase in the incidence of related microvascular as well as macrovascular complications, including kidney disease.[5] Diabetes has been found to be the primary cause of kidney failure in nearly 45% of patients undergoing dialysis.[6,7] Diabetic nephropathy is one of the common microvascular complications of T2DM. Data from the US population suggests that nearly 15–23% of diabetic patients suffer from moderate to severe chronic kidney disease (CKD) with a potential to progress to end-stage renal disease (ESRD). Furthermore cardiovascular (CV) diseases have been found to be related to diabetic nephropathy. CV events have been found to increase by 19–40% as the glomerular filtration rate (GFR) declines from ≥90 mL/min/1.73 m^2 to <45 mL/min/1.73 m^2.[8]

Type 2 diabetes mellitus requires life-long management and the development of CKD complicates the scenario further by adding to the already elevated risk of morbidity and mortality with a significant impact on the health care infrastructure.[9] Besides, CKD introduces many constraints in the management of diabetes. Declining GFR limits OAD options available for achieving optimal glycemic control resulting in higher tendency to initiate Insulin to overcome this issue.[10,11] Therefore, it is important to know the level of renal impairment and current prevalence of CKD in T2DM patients. In our country, currently there is no nationwide data or registry available, looking at the burden of renal impairment in patients with T2DM with various durations of disease. This study, therefore, aims at collecting useful information in a large multi-centric setting, estimating the prevalence of CKD in such patients.

Materials and Methods

This observational, multi-center, cross-sectional study enrolled T2DM patients of either gender aged 30 years or above. Patients with diagnosis of T1DM, acute kidney injury, symptomatic urinary tract infection, history of hematuria, known renal transplant, on maintenance dialysis, participation in any interventional study within past 3 months and pregnant women were excluded from the study. The study is aiming to enroll a total of 3000 T2DM patients, and the data from a planned interim analysis of 1500 patients is presented in this paper.

This is a cross-sectional, epidemiological study, and the routine treatment as administered by the treating physician was continued without any study specific medication being administered. Patient data pertaining to demographic characteristics, disease characteristics, medical history, current medication, physical examination, and vital parameters was recorded. Data regarding diabetes complications both micro- and macro-vascular were captured as a part of history taking independent of glucose control in those patients. Blood/plasma and urine samples were collected for assessing hemoglobin A1c levels, presence of microalbuminuria, serum creatinine, urine creatinine, and routine urine analysis.

The study is being performed in accordance with Ethical principles that are consistent with the declaration of Helsinki, international conference on harmonization of technical requirements for registration of pharmaceuticals for human use - good clinical practices and guidelines issued by Indian regulatory authorities for noninterventional studies.

The primary objective of the START India study was to estimate the proportion of T2DM patients with CKD (GFR <60 ml/min/1.73 m^2 or albumin creatinine ratio [ACR] ≥30 mg/g or ≥3 mg/mmol or both) as defined by Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines.[12] ACR was calculated from urine creatinine and albumin, while GFR was estimated by using modification of diet in renal disease equation:

$$eGFR\ (mL/min/1.73\ m^2) = 175 \times (Serum\ creatinine\ [\mu mol/L])^{-1.154} \times age\ (years)^{-0.203} \times 0.742\ (if\ female)$$

Statistical analysis was performed using SAS version 9.2 (SAS Institute, Cary, NC, USA). This paper summarizes findings of an observational study and presents primary endpoint data from the interim analysis.

Results

As planned we recruited 1500 patients meeting the inclusion criteria from 18 centers across the country. Mean age of the

study population was 55.1 years. The other demographic details are presented in Table 1. Mean duration of T2DM was 102 months. Summary of the incidence and history of diabetes-induced complications is presented in Table 2. Almost 44% of the study population was reported dyslipidemia and hypertension each, whereas the low percentage of patients had microvascular and macrovascular complications. This analysis revealed that 697 (46.47%) of the T2DM patients had CKD (Urinary ACR [UACR] ≥30 mg/g and/or estimated GFR (eGFR) <60 mL/min/1.73 m^2). Renal dysfunction was found as per eGFR criteria (<60 mL/min/1.73 m^2) and UACR criteria (≥30 mg/g) in 22.60% and 34.5% of study population respectively. Further details of the analysis are presented in Table 3.

Discussion

Chronic kidney disease remains an important health issue worldwide and in India. CKD requires close patient monitoring and attention as it puts major restrictions on the patient's quality of life. It places a major strain on the nation's economy and health care infrastructure. It is attributable to a number of etiologies including kidney infections, glomerulonephritis, exposure to nephrotoxins including certain drugs, and the existence of one of several risk factors in a patient including hypertension. The leading cause of CKD however, is diabetes.[13]

In diabetic patients, in the absence of early diagnosis and appropriate management of CKD, kidney function can rapidly deteriorate to reach ESRD, when routine dialysis and eventually renal transplant could be the only treatment options.[14] Fortunately, some of the adverse outcomes of CKD can be prevented or delayed by early intervention, including optimal glycemic control.

Our study found that over 40% of study population suffers from CKD as defined by KDOQI guidelines. While there is no nationwide data available from India, our study results seem to be similar to the CKD rates reported from other countries. A report published in 2010 by the National Health and Nutrition Examination Survey for noninstitutionalized US population indicates that CKD prevalence was 32.9% in those with diagnosed diabetes.[15] In this survey, an eGFR of 15–59 ml/min/1.73 m^2 or an ACR ≥30 mg/g at a single measurement was taken as evidence of the existence of CKD. Similarly a national diabetes audit in the UK (2011–2012), covering a total of 2.5 million diabetics found that 42.9% suffer from early CKD defined as microalbuminuria and GFR between 60 and 90 ml/min/1.73 m^2.[16] Moreover, recently a large, multicentric international study, SAVOR-TIMI 53 reported that the proportion of patients with eGFR below 50 mL/min/1.73 m^2 was approximately 16% only despite the average duration of diabetes being 10 years. Our study has shown that the proportion of patients with eGFR below 60 mL/min/1.73 m^2 is around 22% only which is in line with the SAVOR data.

One of the limitations of our study is that a single laboratory assessment was done to define the presence of CKD whereas the recommendation from international bodies is to rely on data from two visits 3 months apart. Despite this limitation, our study provides meaningful insights into the level of renal dysfunction in the studied diabetes population. In India, eGFR is frequently used as

Table 1: Demographic characteristics of study patients (*n*=1500)

Parameter	Value
Age in years (mean±SD)	55.1±11.37
Gender (%)	
Female	660 (44.0)
Male	840 (56.0)
Weight in kg (mean±SD)	71.3±13.52
BMI in kg/m^2 (mean±SD)	27.4±4.82
BMI group (*n* %) (kg/m^2)	
Underweight: <18.50	20 (1.33)
Normal: 18.50-24.99	473 (31.5)
Overweight: 25.00-29.99	618 (41.2)
Obese: ≥30.00	389 (25.9)
Blood pressure (mmHg)	
Systolic (mean±SD)	134.5±16.60
Diastolic (mean±SD)	79.8±10.49

SD: Standard deviation, BMI: Body mass index

Table 2: Medical history of study patients (*n*=1500)

Condition	*n* %	Average duration in months mean±SD
T2DM	1500 (100)	102.2±87.78
Dyslipidemia	657 (43.8)	
Hypertension	655 (43.7)	
Microvasuclar complications	268 (17.9)	
Retinopathy	50 (2.81)	33.3±33.92
Neuropathy	167 (9.38)	30.0±33.04
Nephropathy	58 (3.26)	36.1±57.55
Other	25 (1.40)	34.7±41.14
Macrovascular complications	104 (6.93)	
Known CAD	90 (5.05)	46.4±40.02
Stroke	13 (0.73)	37.8±40.84
Peripheral arterial disease	1 (0.06)	120.0
Other	2 (0.11)	48.0±16.97

CAD: Coronary artery disease, SD: Standard deviation, T2DM: Type 2 diabetes mellitus

Table 3: Renal dysfunction analysis of study patients (*n*=1500)

	(*n*=1500)
T2DM patients having CKD as per (eGFR/UACR)	697 (46.47)
Renal dysfunction as per eGFR <60	339 (22.60)
Renal dysfunction as per UACR ≥30	518 (34.53)

CKD: Chronic kidney disease, eGFR: Estimated glomerular filtration rate, UACR: Urine albumin: Creatinine ratio, T2DM: Type 2 diabetes mellitus

a parameter to evaluate renal function. Our study results of approximately 80% patients having a reasonably good renal function with eGFR above >60 mL/min/1.73 m^2 appears reassuring.

Conclusion

The interim analysis of START India data provides valuable insights into the level of renal dysfunction in T2DM population in the country from a nationwide survey. Full study results will provide detailed insights into the occurrence of CKD in patients with T2DM in India.

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Conflict of interest

There are no conflicts of interest.

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