

Original Article

Sex differences in the incidence of complications among people with diabetes in a South Indian population: 12 years follow up of CURES study (CURES-159)

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Background & objectives: Little data exist on population-based incidence of diabetes related complications in developing countries. We assessed sex-specific incidence of complications among Asian Indians with type 2 diabetes (T2D) based on follow up assessments from a community-based cohort.

Methods: We evaluated incident complications among individuals with T2D identified in the Chennai urban rural epidemiological study (CURES) conducted in 2001–03, who were complication-free at baseline and re-assessed once during a follow up survey in 2012–14. Diabetic retinopathy was assessed using retinal photography, diabetic peripheral neuropathy using biothesiometry, diabetic kidney disease using urinary albumin excretion and estimated glomerular filtration rate (eGFR), peripheral artery disease by ankle-brachial index, and coronary artery disease using medical history of coronary artery disease and/or Minnesota coding of ECGs. Cumulative incidence reflected the proportion developing each complication during a specified period of time, and relative risk analysis identified associated risk factors.

Results: Among 1,053 participants [men= 453(43%)], assessed in a cross-sectional manner about a decade later, the cumulative incidence rates differed by sex: women showed higher rates of diabetes kidney disease (36.1 vs. 31.4%) and peripheral artery disease (35.4 vs. 23.9%) whereas men had higher rates of diabetic retinopathy (37.0 vs. 27.3%) and coronary artery disease (36.2 vs. 34.5%). The incidence of peripheral neuropathy was comparable between men (63%) and women (62.7%). After adjusting for confounding variables compared to men, women had higher risk for peripheral artery disease [range (RR:1.62, 95% confidence interval (CI):1.20-2.17)] but a lower risk for diabetic retinopathy (RR:0.75,95% CI:0.59-0.97) and coronary artery disease (RR:0.60, 95% CI:0.49-0.75).

Interpretation & conclusions: Women have a higher risk of peripheral arterial disease and lower risk of diabetic retinopathy and coronary artery disease, while there were no sex differences for developing kidney disease and peripheral neuropathy.

Key words Asian Indians - diabetes complications - incidence microvascular complication - macrovascular complication - South Asians

[#]Equal contribution

Diabetes affects over 589 million individuals worldwide¹. In India, 101 million people have diabetes, accounting for nearly 20 per cent of the global burden, and 136 million have prediabetes². Type 2 diabetes (T2D) poses a major global health burden and is a leading contributor to morbidity and mortality due to its tendency to cause chronic complications involving the microvasculature (eyes, kidney, and nerves) and the macrovasculature (coronary, cerebral, and peripheral vessels). Maintaining strict control of blood glucose levels and effectively managing comorbidities such as hypertension and dyslipidaemia can delay or prevent most of these complications³. Data from high-income nations suggests that the development of macrovascular complications caused by diabetes has declined in recent years, most likely on account of earlier detection and institution of aggressive management modalities^{4,5}. There are, however, few data on the incidence (*i.e.*, new onset) of diabetes complications from developing countries such as India, although there are cross-sectional studies assessing their prevalence^{6,7}. Understanding the occurrence of diabetes related complications and the factors that contribute to their development is essential for designing and implementing more effective preventive strategies.

We report on the incidence of both microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular complications (coronary artery disease and peripheral artery disease) in a population from South India with T2D based on a population-based study in Chennai that assessed the outcomes in a cross-sectional manner after a decade. We also compare the incidence rates and predictors of micro- and macrovascular complications in men and women with T2D.

Materials & Methods

This study was undertaken by the department of Clinical Epidemiology, Madras Diabetes Research Foundation, Chennai, Tamil Nadu after obtaining the ethical clearance from Institutional Ethics Committee and all study participants gave informed consent.

The Chennai Urban Rural Epidemiological Study (CURES), a community-based study, was carried out between 2001 and 2003 in Chennai, South India. Its baseline survey was conducted among 26,001 individuals aged 20 yr and above (representative sample), and the methodological details have been published elsewhere^{8,9}. A total of 1900 individuals were

detected to have T2D in Phase-1 of CURES, and these individuals underwent more detailed investigations (including screening for complications) in Phases 2 and 3 of the study. The present paper presents the findings from a single follow up of the CURES conducted between 2012 and 2014. Of the 1900 individuals identified with T2D at baseline, follow-up information was available for 1,492 individuals (alive: 1,053; deceased: 439). The remaining 408 (21.5%) individuals were either untraceable even after multiple attempts at contact including at least three visits which included one weekend visit, or refused participation (21.5% non-responders, 2.0% were not available/refused, while 19.5% either shifted or were not traceable). Thus, the current analysis includes the 1,053 individuals available for outcome assessment, corresponding to a response rate of 55.4 per cent. The mean duration of follow up was 9.1 ± 1.5 yr. No significant differences were observed in baseline age, weight, LDL cholesterol, systolic and diastolic blood pressure between the responders ($n=1,053$) and the non-responders ($n=847$) of the study population. Figure provides the details of the follow up study of participants with known diabetes to look for microvascular and macrovascular complications.

Demographic, anthropometric and clinical assessment: Demographic details and anthropometric and blood pressure measurements were obtained during the baseline and follow up visits. Data on demographic and socioeconomic details, family history, medical details, smoking and alcohol consumption were collected using a pretested, and reliable interviewer-administered questionnaire. Anthropometric measurements (weight, waist circumference and height) and clinical assessments [blood pressure (BP)] were performed using standardised methods⁸.

Biochemical assessment: Biochemical assessments were performed in all participants with T2D as part of their follow-up evaluations. All assessments were done on a Hitachi 912 autoanalyser (Hitachi, Mannheim, Germany) with kits from Roche Diagnostics (Basel, Switzerland). Plasma glucose levels were measured using the GOD-POD method, while the CHOD-PAP, GPO-PAP, and direct methods were used to measure serum cholesterol, HDL cholesterol and triglycerides respectively. HbA1c (glycated haemoglobin) was measured using the Bio-Rad Variant system (Hercules, CA) *via* high-performance liquid chromatography, with intra- and inter-assay coefficients of variation ranging from 0.59 to 1.97 per cent. A fasting urine

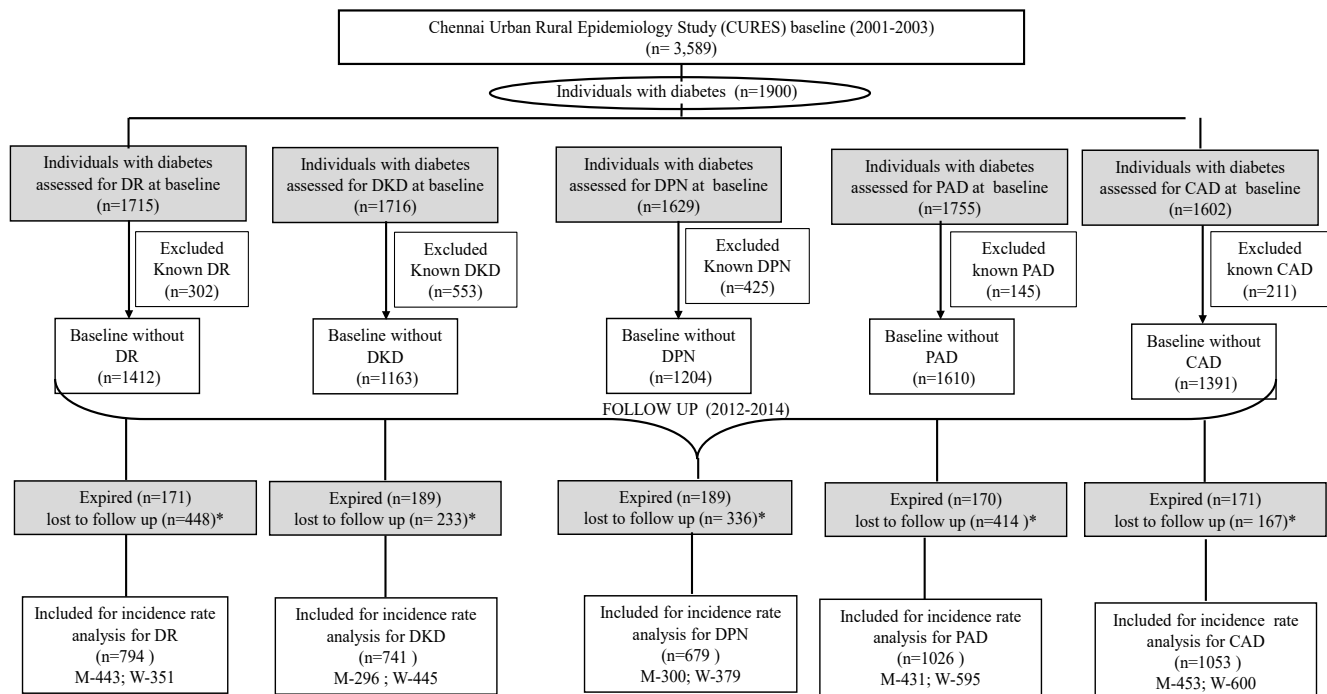


Figure. Study flow chart. Here, *Lost to follow up includes those who had migrated and were not traceable and those who refused to participate even after repeated attempts. DR, diabetic retinopathy; DPN, diabetic peripheral neuropathy; PVD, peripheral vascular disease; CAD, coronary artery disease; M, men; W, women.

sample was also collected to measure the concentration of albumin by means of an immunoturbidimetric assay test on a Beckman Coulter AU2700 (Fullerton, CA, USA) chemistry analyser. All biochemical analyses were performed in a laboratory accredited by both the College of American Pathologists (CAP) and the National Accreditation Board for Testing and Calibration Laboratories (NABL).

Screening for complications:

Retinal photography: Retinal photography was used to assess diabetic retinopathy. All participants underwent a detailed eye examination which involved measuring visual acuity, checking intraocular pressure, examining the eye using a slit-lamp, fundus examination with pupils dilated and ophthalmoscopy (direct/indirect) by ophthalmologists. Digital colour fundus photography was performed following pupil dilation using a mydriatic FF 450 Plus fundus camera (Carl Zeiss, Jena, Switzerland).

Estimated glomerular filtration rate (eGFR): To assess diabetic kidney disease, eGFR was estimated using the chronic kidney disease-Epidemiology Collaboration (CKD-EPI) formula¹⁰. The eGFR level was reported

in mL/min/1.73m² according to the KDIGO (kidney disease: Improving Global Outcomes) guidelines¹¹.

Biothesiometry studies: Diabetic peripheral neuropathy was evaluated by means of a biothesiometre. The vibratory perception threshold of the great toes was measured using a standardised method as previously described¹². The mean of three measurements from each leg was used for analysis.

Doppler studies: Peripheral artery disease was screened using doppler probe (KODY Vaslab Machine, Kody Labs, Chennai, India) for calculating ankle-brachial index. Blood pressure was measured in the upper limb at the brachial pulse, while in the lower limb, it was measured at the dorsalis pedis and posterior tibial pulses by inflating the cuff above the ankle. The ankle pressure was determined by taking the average of these two readings. Ankle-brachial index was calculated as the ratio of the higher of the two brachial pressures to the mean ankle pressure of the corresponding limb. The lower ABI value between the two legs was used as the participant's overall Ankle-brachial index.

Electrocardiogram (ECG): Coronary artery disease was assessed using a resting standard 12-lead ECG

was recorded utilising a Myocard R electrocardiograph (Marks Electronics, Chennai, India).

Definitions:

Diabetes: Diagnosed in individuals with a fasting venous plasma glucose level of ≥ 126 mg/dL (7.0 mmol/L) and/or a 2 h plasma glucose (2hr PG) level of ≥ 200 mg/dL (11.1 mmol/L) following an oral glucose load, and/or those who were on antidiabetic agents¹³. A history of diabetes was collected through self-report and verified against medical records for accuracy, which also provided the date and year of diagnosis.

Hypertension: Diagnosed in individuals with a systolic blood pressure 140 mmHg and above or diastolic blood pressure ≥ 90 mmHg or those taking antihypertensive medication¹⁴.

Body mass index (BMI): Weight (kg) divided by the square of height (m^2).

Family history of diabetes: Defined as at least one first-degree relative with diabetes.

Smoking: Individuals were categorised as current and non-smokers.

Current alcohol use: Defined as self-reported consumption of alcohol regardless of the duration and quantity consumed.

Poor glycaemic control: Defined as HbA1c ≥ 7.0 per cent¹⁵.

Poor blood pressure control: Defined as $\geq 140/90$ mm Hg¹⁴.

Poor lipid control: Defined as total cholesterol of ≥ 200 mg/dL or triglycerides of ≥ 150 mg/dL or LDL cholesterol of ≥ 100 mg/dL¹⁶.

Diabetic retinopathy: The existence of distinct microaneurysm (at least one) in any photographed field was the minimum requirement for diagnosis. The fundus photographs were assessed by trained retina specialists, and the final diagnosis was determined based on the grading of the more severely affected eye, according to the Early Treatment Diabetic Retinopathy Study (ETDRS) criteria¹⁷.

Diabetic kidney disease: It was defined as eGFR < 60 mL/min/1.73m² and/or albuminuria ≥ 30 μ g/mg (kidney failure was defined as eGFR < 30 mL/min/1.73m²)¹¹.

Diabetic peripheral neuropathy: It was defined as an average VPT greater than or equal to 20 V¹².

Peripheral artery disease: An ankle-brachial index of less than 0.9 was regarded as diagnostic cutoff for peripheral artery disease¹⁸.

Coronary artery disease: It was diagnosed based on a recorded history of myocardial infarction or previous revascularisation or angina pectoris validated by ischemic changes including ST segment changes (Minnesota codes 1-1-1 to 1-1-7) in the ECG¹⁹.

Statistical analyses: Statistical Package for Social Sciences version 24.0 (SPSS Inc., Chicago, IL) was used for performing analyses, with estimates expressed as mean \pm SD and categorical variables as proportions. For categorical variables, a Chi-square test was used while to compare continuous variables a Student's t-test was used. $P < 0.05$ was considered statistically significant. The cumulative incidence (incidence proportion) was calculated as the proportion of the population that developed the complication over a defined period of time. Generalised linear models (GLMs), treating sex as the primary exposure and each diabetic complication as the outcome of interest were carried out. To enhance the validity of the estimates, the models were adjusted for key confounding variables, including baseline age, HbA1c (as a marker of glycaemic control), systolic blood pressure, cholesterol levels, BMI, and smoking status (as a behavioural factor). Relative risks (RRs) and 95 per cent confidence intervals (CIs) were calculated to assess the association between baseline risk factors and the incidence of diabetes-related complications over the follow up period.

Results

A total of 1053 individuals with T2D (453 men and 600 women) were included in the CURES follow-up study. The mean age of study participants at follow-up was 57.8 ± 10.3 yr. Table I shows the clinical and biochemical characteristics of responders (baseline participants as well as those followed up) and non-responders, stratified by sex. Body mass index (BMI), diastolic blood pressure, fasting plasma glucose and HbA1c significantly increased in both sexes over the

Table I. Clinical and biochemical characteristics of individuals with diabetes

Variables	Nonresponders (n=847)			Responders (n=1053)					
	Men	Women	P value	Men			Women		
				All participants	Follow up participants		All participants	follow up participants	
					Baseline	Baseline		Follow up	Baseline
N	371	476		834	453	453	1066	600	600
Age (yr)	54.7±12.4	52.7±11.3	0.024	51.7±11.3	49.1±9.9	58.2±9.9*	51±11	48.3±10.6	57.5±10.7**
Body mass index (kg/m ²)	23.4±3.6	25.3±4.8	<0.001	24.1±3.7	24.5±3.7	25.7±4.1*	26.1±4.1*	26.3±4.1	28.1±4.6*
Systolic blood pressure (mmHg)	130±23	133±23	0.049	128±21	124±14	127±16	130±21**	122±12	125±16
Diastolic blood pressure (mmHg)	78±12	77±13	0.565	78±11	77.1±10.2	84±8**	77±11**	74±9	85.8±10*
Fasting plasma glucose (mg/dL)	162±70	178±85	0.006	161±69	158±64	169.2±75.7*	164±75	154±63	178±80*
Glycated haemoglobin (%)	8.9±2.3	9.0±2.7	0.451	8.8±2.2	8.7±2.1	8.9±2*	8.6±2.3**	8.3±2	9.2±2.3*
Creatinine (mg/dL)	0.87±0.11	0.89±0.14	0.205	0.96±0.39	0.92±0.14	0.94 ±0.89	0.77±0.16*	0.75±0.12	0.92±0.39*
Total cholesterol (mg/dL)	195±41	208±48	<0.001	194±40	193±38	174±40*	206±43*	203±38	194±45*
Serum triglycerides (mg/dL)	183±157	175±111	0.456	188±152	189±143	165±114*	174±111**	169±99	175±110*
LDL cholesterol (mg/dL)	118±39	128±42	<0.001	117±38	118±33	103±34*	128±38*	126±33	118±38*
HDL cholesterol (mg/dL)	41±9	44±10	<0.001	40±8	39±8	38±9*	44±9*	44±9	43±9*
Smoking, n (%)	139 (38.9)	-	-	362 (44.2)	224 (49.4)	254 (56.1)*	NA	NA	NA
Alcohol, n (%)	317 (85.4)	-	-	311(37.9)	163 (36.0)	209 (46.1)*	NA	NA	NA
Family history of diabetes, n (%)	203 (59.0)	260(59.1)	0.520	618 (75.4)	290 (64.0)	346 (76.4)*	786 (74.7)	380 (63.3)	477 (79.5)*
Hypertension, n (%)	161 (48.3)	215 (58.3)	0.005	328 (40)	169(37.8)	295(65.0)	411(39.1)	174 (29)	442(73.6)
On HTN drugs, n (%)	180 (54.1)	251 (68.0)	<0.001	204 (24.9)	104 (23)	184 (40.6)*	311 (29.5)	162 (27)	259 (43.1)*
On lipid lowering drugs, n (%)	34 (10.3)	69 (18.8)	0.002	53 (6.5)	31 (6.8)	94(20.8)*	68(6.5)	45 (7.5)	113 (18.8)*
Poor glycemic control, n (%)	208 (62.7)	222 (60.2)	0.535	509(62.1)	264 (58.8)	327 (72.3)	612 (58.2)	305(51)	425(70.6)
Poor BP control n (%)	161 (48.3)	251 (68.0)	<0.001	289 (35.2)	102 (23.3)	171 38.6)	282 (26.8)	14 (2.3)	386(64.2)
Hypercholesterolemia n (%)	141 (42.7)	199 (54.1)	0.003	330 (40.3)	174 (37.0)	101 (24.6)	571 (54.3)	323(53.4)	218(41.9)
Hypertriglyceridemia n (%)	154(46.7)	189 (51.4)	0.226	406 (49.6)	235 (52.1)	160 (39.5)	519 (49.4)	294 (48.9)	249 (47.8)
High LDL cholesterol n (%)	234 (70.9)	282 (76.6)	0.101	560 (68.4)	316 (71.4)	220 (56.5)	819 (77.9)	477 (78.8)	338 (67.3)

Data presented as mean standard ± deviation; Generalized linear Model (GLM) for between group difference; Paired 't' test for with in group difference; P* < 0.001; ** < 0.05; #Difference between Women and Men (W-M)

Table II. Cumulative incidence of diabetes related complications

Variables		Diabetic retinopathy	Diabetic peripheral neuropathy	Diabetic kidney disease	Peripheral artery disease	Coronary artery disease
Men	Number at risk at baseline (free of complication) (n)	351	300	296	431	453
	Outcome (Number who developed the complication)	130	189	93	103	164
	9-year Cumulative incidence rate (%)	37.0	63.0	31.4	23.9	36.2
Women	Number at risk at baseline (free of complication) (n)	443	379	445	595	600
	Outcome (Number who developed the complication)	121	238	161	211	207
	9-yr Cumulative incidence rate (%)	27.3	62.7	36.1	35.4	34.5
Overall	Number at risk at baseline (free of complication) (n)	794	679	741	1026	1053
	Outcome (Number who developed the complication)	251	427	254	314	371
	9-yr Cumulative incidence rate (%)	31.6	62.8	34.2	30.6	35.2

follow up period and the increase was more significant in women compared to men. Significant decreases in total cholesterol (TC) and LDL cholesterol were noted, with men exhibiting larger decreases than women. Serum triglycerides (TG) decreased significantly in men, while women showed a slight increase over the follow up period. HDL cholesterol decreased marginally in both sexes. There was a substantial increase in hypertension prevalence and poor blood pressure control, while lipid control improved over time with the frequency of hypercholesterolemia, hypertriglyceridemia and high LDL cholesterol levels decreasing at follow-up compared to baseline. Among the 847 non-responders (371 men and 476 women) men were slightly older than women, while women had significantly higher body mass index, systolic blood pressure, fasting plasma glucose compared with men, although HbA1c levels did not differ significantly between the groups.

Table II presents the cumulative incidence of diabetes related complications. The overall cumulative incidence of diabetic retinopathy was 31.6 per cent (251/794), diabetic peripheral neuropathy 62.8 per cent (427/679), diabetic kidney disease 34.2 per cent (254/741), peripheral artery disease 30.6 (314/1026) and coronary artery disease 35.2 per cent (371/1053). The cumulative incidence rates varied by sex. Women had higher rates of diabetic kidney disease [36.1% (161/445) vs. 31.4% (93/296)] and peripheral artery disease [35.4% (211/595) vs. 23.9% (103/431)] compared to men. In contrast, men had a higher

incidence of Diabetic retinopathy [37.0% (130/351) vs. 27.3% (121/443)] and coronary artery disease 36.2 per cent (164/453) vs. 34.5 per cent (207/600)]. The incidence of Diabetic peripheral neuropathy was similar between sexes [63.0% (189/300) in men vs. 62.7 per cent (238/379) in women].

Table III shows the association of sex with diabetes-related complications after adjusting for baseline variables as well as covariates differences between baseline and follow up using generalised linear models. The model was controlled for potential confounders including age, BMI, systolic blood pressure, HbA1c, cholesterol, and smoking status. The risk for diabetes complications differed significantly between men and women. When adjusted for covariates differences between baseline and follow up, women showed a higher risk of peripheral artery disease, with an adjusted risk ratio (aRR) of 1.62 but had a significantly lower risk of diabetic retinopathy [aRR = 0.75 and coronary artery disease (aRR = 0.60) compared to men across all models. No significant sex differences were observed for diabetic kidney disease and diabetic peripheral neuropathy after adjusting for covariates.

Discussion

This prospective study conducted in urban Chennai, south India, reveals a higher incidence of microvascular compared to macrovascular complications among individuals with T2D over a 12-yr period, which aligns with findings of previous studies^{4,20}. There were

Table III. Sex differences in relative risk of microvascular and macrovascular complications in diabetes

Complications	Risk ratio	95% CI	P value	Risk ratio	95% CI	P value	Risk ratio	95% CI	P value
	Unadjusted			Adjusted for baseline values [#]			Adjusted for covariate differences between baseline and follow up [#]		
Diabetic retinopathy	0.74	0.60 - 0.90	0.003	0.66	0.52 - 0.83	<0.001	0.75	0.59 - 0.97	0.027
Diabetic peripheral neuropathy	1.00	0.89 - 1.12	0.957	1.18	1.02 - 1.37	0.027	1.10	0.92 - 1.31	0.306
Diabetic kidney disease	1.15	0.93 - 1.42	0.185	1.16	0.88 - 1.53	0.290	1.14	0.86 - 1.52	0.346
Peripheral artery disease	1.57	1.28 - 1.94	<0.001	1.88	1.43 - 2.48	<0.001	1.62	1.20 - 2.17	0.001
Coronary artery disease	0.74	0.62 - 0.87	<0.001	0.63	0.52 - 0.78	<0.001	0.60	0.49 - 0.75	<0.001

[#]Adjusted for age, HbA1c, systolic blood pressure, body mass index, cholesterol and smoking status; The risk ratio was calculated for women by taken men as reference = 1.0

sex-specific differences in the risk for complications, compared to men, women have higher risk of peripheral artery disease and lower risk of diabetic retinopathy and coronary artery disease, while there were no sex differences for diabetic kidney disease and diabetic peripheral neuropathy. Literature shows that gender-specific differences in diabetes complications may be attributed to hormonal and metabolic variations, which may be the case in our study population as well²¹.

The observed incidence rate of diabetic retinopathy in the present study 31.6 per cent was notably higher than rates previously reported in the UK Prospective Diabetes Study (UKPDS), which reported a 6-year incidence of 22 per cent²². Lower incidence rates have also been documented in other regions, including Brazil (17.3%)²³ and several Asian populations (20.3% in Hong Kong; 21.9% in Singapore; and 22% in Korea)²⁴⁻²⁶. Our findings are also consistent with those from a large diabetes cohort, which reported a higher incidence and risk among men compared to women²⁷.

The incidence of coronary artery disease in our study participants found a cumulative incidence of coronary artery disease of 35.2%, with men having a substantially higher incidence than women (36.2% vs. 34.5%). This finding aligns with a large body of epidemiological and prospective data. The European Prospective Investigation into Cancer-Norfolk (EPIC-Norfolk) study reported that the cumulative incidence ranged from 4.7 to 68.9 per cent for men and 3.2–57.4 per cent for women aged between 60 – 90 yr²⁸. While, Gibson *et al*²⁷ reported a cumulative incidence of 44.4 per cent among men and 30.9 per cent among women and a similar finding by An *et al*⁴. This is consistent with our finding that women are generally less likely

to develop coronary artery disease due to estrogen's protective effects; however, diabetes weakens this advantage, narrowing the coronary artery disease risk gap between sexes.

There are very few studies on the incidence of peripheral artery disease in T2D, based on ABI measurements. The current study reports a higher incidence of peripheral artery disease (30.6%) overall, with women exhibiting a substantially higher rate than men (35.4% vs. 23.9%). This sex difference in peripheral artery disease incidence is in line with, but somewhat higher than, estimates from several prospective cohort studies²⁹. The Chronic Renal Insufficiency Cohort (CRIC) study reported an overall cumulative incidence of peripheral artery disease to be 17.8 per cent (Women: 22.6% vs. Men: 13.8%)²⁹. In our study also, the risk for peripheral artery disease was greater in women compared to men. This aligns with longitudinal evidence from CRIC study, the Health, Aging, and Body Composition (Health ABC) study, which revealed that women had a significantly higher risk of subclinical peripheral artery disease^{29,30}.

We found that the incidence of diabetic kidney disease was higher in women than in men, consistent with findings from previous studies^{4,23}. An *et al*⁴, reported that women had a higher cumulative incidence of CKD compared to men, and Cardose *et al*²³, reported that the cumulative incidence of CKD ranged from 5.2 - 60.6 per cent among those aged between 20-80 yr. The National Health Examination V Survey conducted in Thailand found that female sex was associated with a twofold increased CKD risk compared to males³¹. Zhang *et al*³² also reported that compared to men, women with T2D had a higher risk of developing

diabetic nephropathy and tend to experience a more rapid decline in kidney function.

Peripheral neuropathy represents a key risk factor for the development of foot ulcers as well as amputation. In this context, it is concerning that our study reported a higher incidence of diabetic peripheral neuropathy (62.8%) compared to other reports^{4,23}. Earlier studies conducted in Iran reported a lower cumulative incidence of diabetic peripheral neuropathy (18%) while a Brazilian study reported the incidence to be 11.9 per cent²³. Earlier studies have indicated that the incidence of diabetic peripheral neuropathy was higher in women compared to men^{33,34}, whereas our study reports that the incidence rates are similar between the two genders. With regard to risk for developing diabetic peripheral neuropathy, a study which assessed the predictors of diabetic peripheral neuropathy among T2D reported that women have higher risk for neuropathy compared to men³⁵. In contrast, the present study found that the risk of diabetic peripheral neuropathy did not differ between men and women indicating comparable vulnerability in both sexes.

Our study has several strengths and limitations. The major strengths are the sample representative of urban India, the long follow up period, and the application of standardised methods for collecting data on diabetes complications from the population. To our knowledge, this is the first study to report on the incidence of microvascular and macrovascular complications among Asian Indians who contribute 20 per cent of global burden of diabetes, and one of the few from a developing country. However, we were unable to determine the exact time of development of complications due to lack of year-by-year follow up as we had conducted only one follow-up after a median period of 9.4 yr. In addition, for person-years calculation we did not include those who died or were lost to follow up, as we lacked information on the exact timing of events or whether the complication occurred at all and the follow up also occurred at different time points between 2012-2014. As only 55.4 per cent of the original study participants were available for outcome assessment, this introduces the possibility of selection and survivor bias, potentially inflating the calculated incidence rates. The reported figures should be interpreted as incidence among the followed-up participants rather than as representative of the entire baseline population. In addition, as the study was conducted in a city, generalisability of this study to rural areas is not clear.

In conclusion, the incidence of diabetes complications in this urban Asian Indian population is high compared to western populations. The incidence of diabetic retinopathy and coronary artery disease were higher in men compared to women, while the incidence of diabetic kidney disease and peripheral artery disease were higher among women, the incidence of diabetic peripheral neuropathy was similar among both sexes. These sex-specific patterns underscore the need for clinicians to incorporate individualised risk profiling into routine diabetes care, enabling timely screening and tailored management strategies to reduce the risk of complications.

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