

Chronic complications in newly diagnosed patients with Type 2 diabetes mellitus in India

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ABSTRACT

Background: Prevalence of diabetes is on an increase in India, currently there is limited nation-wide data regarding the prevalence of chronic complications in diabetic patients at diagnosis. This information will help health-care professionals approach management more aggressively to prevent complications. **Objective:** To determine the prevalence of chronic complications in newly-diagnosed Type 2 diabetic (T2D) patients in India. **Design and Methods:** This was a cross-sectional survey of T2D patients, diagnosed within 3 months of their first visit to the centers doing the survey. Each patient was screened for diabetic complications, hypertension, dyslipidemia, and body mass index. Family history was recorded. Standard protocols were used to make the diagnosis of retinopathy, neuropathy and nephropathy. Data analysis was carried out using the standard statistical techniques. **Results:** Of the total 4,600 (males 67%, females 33%) newly diagnosed patients with T2D, majority were from the age group 41-50 years (40%). 13.15% of newly detected India T2D had neuropathy 6.1% had retinopathy and 1.06% had nephropathy. Risk factors of macro vascular complication such as hypertension, obesity, and dyslipidemia were observed in 23.3%, 26%, and 27% of patients respectively. Ischemic heart disease was noticed in 6%. **Conclusion:** High prevalence of micro vascular complications was present at diagnosis along with association of CV cardiovascular risk factors among Indian T2D. In view of this, screening must be instituted for all diabetics for complications at the time of diagnosis itself.

Key words: Complications, dyslipidemia, hypertension, neuropathy, prevalence, retinopathy, type 2 diabetes mellitus

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is the most common form of diabetes constituting 90% of the diabetic population. The number of patients with diabetes in India is currently around 40.9 million and is expected to rise to 101 million by 2030.^[1]

The so-called “Asian Indian Phenotype” refers to certain unique clinical and biochemical abnormalities in Indians

which include increased insulin resistance, higher waist circumference despite lower body mass index (BMI), lower adiponectin and higher levels of highly sensitive

C-reactive protein levels. This phenotype makes Asians more prone to diabetes and premature coronary artery disease.^[2]

The course leading to complications related to diabetes starts with lingering dysglycemia. Chronic complications of diabetes, the major cause of morbidity and mortality, are often present at the time of diagnosis. The problem is further worsened as the diagnosis of diabetes is often delayed from months to years due to lack of symptoms, lack of awareness and the fear of unknown in spite of awareness.

A very high prevalence of complications at diagnosis has been reported from various studies across the globe and from parts of India. However, a nationwide Indian

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data for the same is not available. A high prevalence of such complications, if documented, will help to convince the physicians of the importance of screening for these complications in all Type 2 diabetics (T2D) at presentation, for appropriate implementation of treatment without delay.

The present study was designed to determine the prevalence of complications in newly-diagnosed T2D patients across various regions of India.

DESIGN AND METHODS

The present study was a cross-sectional survey done across 14 centers representing north, west, south and east region of India. In this study, adult patients aged 18 years and above, newly-diagnosed with T2DM for less than 3 months based on the American Diabetes Association criteria were included.^[3] Patients who have been diagnosed with diabetes for more than 3 months, patients on any drug therapy, gestational diabetics, and steroid-induced diabetics or those with co-morbid conditions that require prolonged steroid therapy were excluded. Cut-off of < 3 months duration was selected mainly because of the fact that some earlier studies had used the same criteria. The diagnostic criteria comprising standard methods were agreed upon by all investigators from 14 Indian centers; they were senior endocrinologists and physicians who had particular research interest in diabetes.

Physicians from all the 14 centers were contacted and informed about the protocol and criteria for making the diagnosis of diabetes and various complications. After discussing each of the criteria, a decision was taken to use what is normally followed in clinical practice, and the performa was approved. A standard performa for recording the complications was made and circulated to all the centers. Following criteria was followed to make the diagnosis of neuropathy, retinopathy, nephropathy, hypertension, dyslipidemia, ischemic heart disease (IHD) and obesity.

Retinopathy

Direct/indirect funduscopy was used to make the diagnosis and grading of retinopathy. Physician if trained or a Retinologist did the fundus examination after full dilatation of the pupil. All doubtful cases were referred for a second opinion before the performa was filled. Routine stereoscopic fundus photography was not done as it was not available across the country in all the centers.^[4]

Nephropathy

Nephropathy was diagnosed based on 24 h urine collection for proteinuria

(mg/24 h). A value of >300 mg/dl was taken as confirmed nephropathy. Twenty four hours collection was carried out by the treating physician taking care of the factors that interfere with proteinuria (like, uncontrolled hypertension, urinary infection etc.).^[5]

Neuropathy

Diagnosis of neuropathy was made on clinical grounds for senses of touch, pain, vibration and jerks ruling out all other non-diabetic causes for neuropathy. 128 Hz tuning fork for vibration perception and 10-g monofilament pressure sensation at the distal plantar aspect of both great toes and metatarsal joints were carried out along with assessment of ankle reflexes. Michigan neuropathy screening score was used in all cases. Combination of more than one test has > 87% sensitivity in detecting diabetic poly neuropathy.^[5,6]

Hypertension

Hypertension was defined as a value > 130/90 mm/Hg. BP was recorded twice, 10 min apart-both arms, standing and lying down. Known hypertensive patients were recorded separately. All baseline high values were retested over a period of 15 days for confirmation of hypertension (>130/90 mm/hg) to avoid the “White Coat Phenomenon.”^[4]

Dyslipidemia

For diagnosing dyslipidemia, whole lipid profile of the patient was tested in the fasting blood sample. Value over and above the goal of therapy (low density lipoprotein (LDL) > 100 mg/dl and total cholesterol > 200 mg/dl) was considered abnormal.^[4]

IHD

IHD diagnosis was made on the basis of treadmill test or coronary angiogram (if resting ECG showed changes) or chest pain relieved by nitrates in cases where patient complained of anginal pain.^[4]

Obesity

For anthropometry, BMI cut-off of 25 kg/m² for men and 23 kg/m² for women was used for making a diagnosis of obesity as recommended by various studies as Indians are having Asian-Indian Phenotype.^[7]

Data analysis

Data was collected from June 2006 till October 2011. Incomplete performas were excluded.

A total of 4600 completed performa's were included for analysis.

Quantitative variables were described as mean + 1SD unless otherwise indicated. Qualitative variables were described by percentages.

RESULTS

Our study is a specialized clinic-based survey rather than population based or epidemiological survey and reflects the prevalence of diabetic complications in the out-patient setting in the current health system of India. Doctors who contributed to this survey are Endocrinologist or Senior Diabetologists. The study recruited 4,600 patients with equal contribution from all the centers from June 2006 to October 2011. Of the total 4,600 newly diagnosed patients with T2D, majority were male (67%, N: 3,082) in comparison to female (33%, N: 1,518). The demographics are shown in Table 1.

The importance of age on the prevalence of newly diagnosed diabetes shows that the majority of the patients were from the age group 41-50 years (40%) as illustrated in Figure 1, which shows sex-specific estimates of diabetes prevalence by age.

The prevalence of diabetes specific micro vascular and IHD are shown in Table 2. In patients having diabetic retinopathy, majority (65.9%) were having non-proliferative diabetic retinopathy.

The prevalence of risk factors for macro vascular disease is shown below in Table 3.

Total number of patients	4,600
Male	67%
Female	33%
Positive family history	64%
Patients on medication for hypertension	14%
Patients on medication for dyslipidemia	8%
Obesity	26%

Complications	Male (%)	Female (%)	Overall (%)
Micro vascular			
Neuropathy	13	13.3	13.15
Retinopathy	5.8	6.4	6.1
Nephropathy	0.96	1.17	1.06
Macro vascular			
IHD	4	8	6

IHD: Ischemic heart disease

CV risk factors	Male %	Female %	Overall %
Obesity	25.5	26.5	26
Dyslipidaemia	23	31	27
Hypertension	19	27.6	23.3

DISCUSSION

T2D is an insidious illness with a long preclinical asymptomatic phase during which patients may be exposed to the ill-effects of asymptomatic hyperglycemia for many years before they are diagnosed. The present study reconfirms this and shows that a substantial proportion of patients with T2DM have evidence of diabetic tissue damage at the time of diagnosis of diabetes.

In our study Chronic complications in newly diagnosed patients with Type 2 Diabetes Mellitus in India

CINDI, many patients were from a younger age 31-40 years (35%) and almost equal (40%) population was from the age group 41-50 years, which confirms similar finding of other studies showing that in developing countries the majority of patients with diabetes are in the age range of 45-64 years, whereas age group is higher (>65 years) in the developed countries.^[1,8]

Younger age of onset implies that these subjects develop diabetes in the most productive years of their life and have a greater chance of developing complications. Both environmental and genetic factors might explain the younger onset of age along with high prevalence of diabetes in the Indian population.^[2]

The Indian patients also had a more sedentary life-style and a higher prevalence of family history of known diabetes than the other groups. Ramachandran *et al.*, observed similar findings in their study of parental influence on the spectrum of T2D in the offspring among Indians. Familial clustering of T2D is well-known and is high in Indians, which was also observed in our study with more than half of the patients (64%) having positive diabetes family history for first degree relatives.^[9,10]

While the relatively low rate of diabetic retinopathy (6%) in CINDI is similar to some of the studies from South

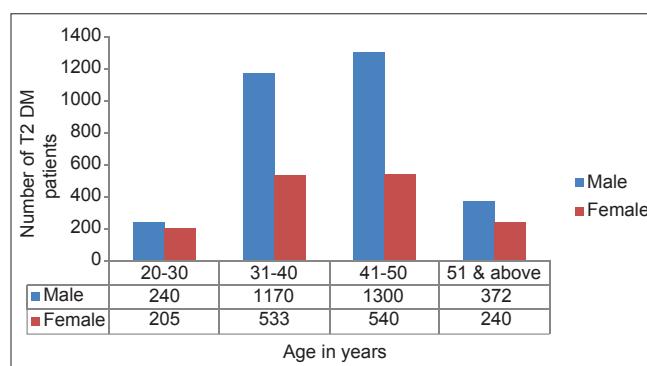


Figure 1: Age distribution in CINDI

India (7.3%) and abroad that include Denmark (5%), where they suggested that the low prevalence is due to the Danish health system, which is free of charge and results in early diagnosis of diabetic patients. the results for diabetic retinopathy are in contrast to findings of other studies showing higher prevalence in Romania (14.37%) and Taiwan (25.5%).^[11-14] the prevalence of diabetic retinopathy in newly diagnosed patients among various studies, Chennai Urban Rural Epidemiology Study (CURES) (5.1%) and United Kingdom Prospective Diabetes Study (UKPDS) (35%) is shown below in Figure 2.^[15,16]

Although, it is difficult to identify the reasons for such variation in prevalence rates among various populations, race, age, method of detecting diabetic retinopathy, health-care facilities, and other risk factors could have contributed to the differences. as mentioned in one of the study from India, inherent ethnic difference in the Indians in relation to the susceptibility to diabetic retinopathy may be one aspect and another reason may be the type of diet which although rich in carbohydrates includes more vegetables, less fat and perhaps more antioxidants and anti-inflammatory agents like curcumin.^[17]

Overall prevalence of nephropathy in CINDI is only 1.02%, which is comparable to other studies from India CURES, which showed overt nephropathy in 0.8% but low in comparison to UKPDS which showed 7% as shown below in Figure 3.^[18,19] Unlike CURES, CINDI did not include diabetic retinopathy in defining nephropathy. However, all patients with nephropathy had retinopathy including proliferative retinopathy. It is possible that micro-albuminuria may have been transient considering glycemic control may have modulated the albumin excretion. This question would be addressed in future longitudinal studies

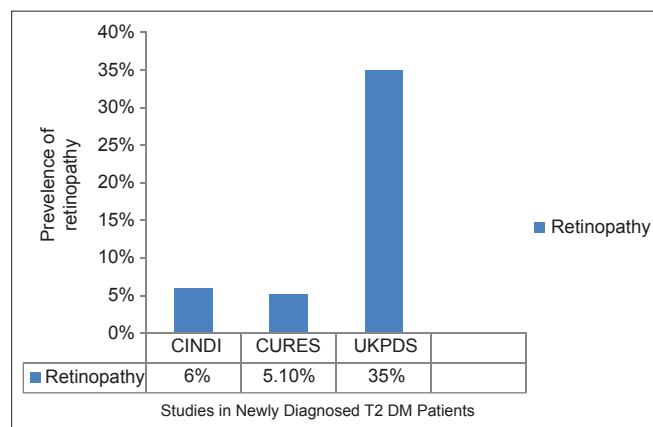


Figure 2: Prevalence of retinopathy in newly diagnosed Type 2 diabetes mellitus patients

In CINDI prevalence of peripheral neuropathy is 13.15%, which is again comparatively low in comparison to other studies from Sri Lanka (25.2%) and Amsterdam (48.3%).^[20,21]

Literature search for articles on the prevalence of neuropathy in newly diagnosed T2DM in India (<3 months duration) for comparison are very few. Karmakar *et al.* have shown 9% prevalence at diagnosis and Rani *et al.* have also reported 13% in established cases of retinopathy having neuropathy.^[22,23] Explanation for a lower rate of diabetic neuropathy among Indians may be due to better skin micro-vascularization compared to Europeans despite having similar risk factors.^[24]

Whether this low rate for micro vascular complications found in CINDI and other studies from India in comparison to western studies like UKPDS is due to increased screening/earlier detection of diabetes, or a change in risk factors is unclear. Furthermore, the observed differences may be due to the difference in the study designs, methodologies and possibly ethnic differences among various populations.

Prevalence of hypertension was comparable to that found in the Asian population subset of UKPDS, but lower in comparison to other ethnic groups as shown below in Figure 4.^[25]

This is an interesting finding when compared to the known high-risk for cardiovascular disease of the Asian population.

Another important finding emerging is that the prevalence of hypertension is higher for female in comparison to male across all the studies including CINDI and UKPDS subgroups as shown in Figure 4. This combined with higher prevalence of diabetic dyslipidemia in female (31%) in comparison to male (23%) seen in CINDI might account for high-risk of coronary artery disease in female in line

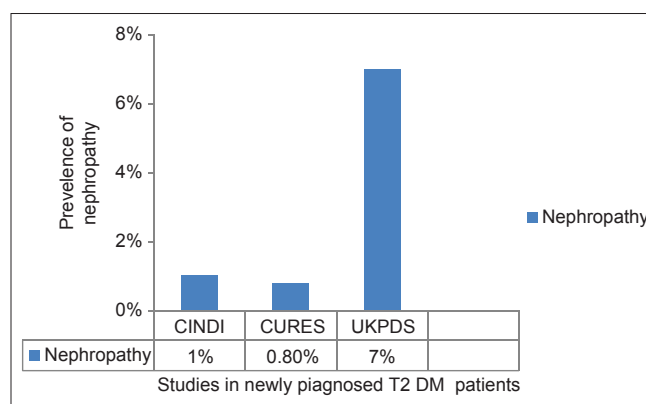


Figure 3: Prevalence of nephropathy in newly diagnosed Type 2 diabetes mellitus patients

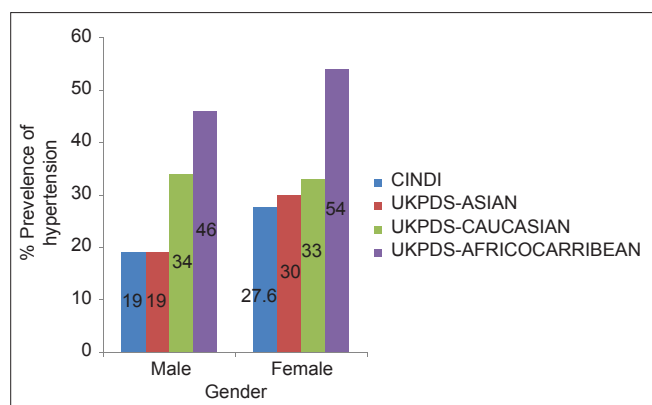


Figure 4: Prevalence of hypertension in newly diagnosed Type 2 diabetics

with latest International diabetes federation data, which shows higher all-cause mortality in female than a male who were having diabetes. To add more to cardiovascular burden, in CINDI, all lipid parameters were more disturbed in female as compared to male [Table 3].^[26]

CINDI data has not compared glycemic parameters with chronic complications as the glycosylated hemoglobin estimations were not carried out in a centralized lab, the values may not all be comparable, although each individual center followed good laboratory practice methods.

Limitations of the study

CINDI data was collected from specialized diabetes centers across the country where Endocrinologists or Diabetologists see the cases. This is a clinic based survey and not an epidemiological study. Prevalence of complications may change in a population based epidemiological study.

Methodology used to diagnose various complications was based on ‘practice pattern’ rather than methods used as ‘gold standards.’ Specificity and sensitivity for diagnosing Neuropathy may slightly change based on methods used.

Mismatch between the number of patients (male vs. female) is just a coincidence as more number of male patients attended the specialized clinics with duration of diabetes < 3 months when the data was being collected. Being an office and hospital based study the gender difference of subjects who presented did not match the population prevalence of diabetes.

CONCLUSION

CINDI reconfirms that screening for both micro vascular and macro vascular complications along with assessment of CV Cardiovascular risk factors must be done at diagnosis in all patients with T2DM. Prevalence of complications may appear low compared to the available western data but is

quite high considering the population at risk at the time of diagnosis of T2D in India. This is probably because of the insidious onset of diabetes and asymptomatic nature of the disease before symptoms develop. Lack of awareness can also be a contributing factor in a developing country like India. Furthermore, once complications develop, treating hyperglycemia alone usually does not suffice and complications from diabetes can be prevented only up to a certain point, beyond, which these will progress.

Although in CINDI, the prevalence of micro vascular complications appears to be low, if one were to extrapolate these results to all of India, the number would still be quite staggering. Furthermore, the number of subjects with diabetes is expected to increase to > 100 million by 2030, which could translate into a heavy economic burden and compromise the quality of life.

This underlines for the high importance of screening of all newly diagnosed T2D patients not only for early detection of micro vascular and macro vascular complications, but also to prevent or retard the progression of complications by aggressive management.

Beyond screening, education of our high risk population regarding diabetes related complications must be started to encourage earlier medical consultation. Medical stakeholders must be encouraged to formulate new guidelines as to how aggressive physicians should be in diagnosing and managing diabetes in Indian population.

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