



## GLYCEMIC CONTROL AND ITS RELATION TO MICROVASCULAR COMPLICATIONS IN NEWLY DETECTED DIABETES MELLITUS

### KEYWORDS

Type 2 Diabetes mellitus (T2DM), Microvascular Complications, Proteinuria, Glycemic control.

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**ABSTRACT** Diabetes is one of the largest global health emergencies of 21st century. Each year more and more people live with this condition, which results in life changing complications. Type 2 Diabetes mellitus (T2DM) is characterized by an asymptomatic phase between the actual onset of diabetic hyperglycemia and clinical diagnosis. This asymptomatic phase is estimated to last at least 4-7 years and consequently 30-50% patients may remain undiagnosed. Long-standing untreated hyperglycemia is responsible for high prevalence of Microvascular Complications (MC) in newly diagnosed T2DM patients. Presence of MC at the time of T2DM diagnosis are showing increasing trends in India. Present study is aimed at studying the prevalence of MC of T2DM patients at the time of diagnosis in relationship to glycemic control.

### INTRODUCTION

Over 415 million people worldwide, or 8.8% of adults aged 20-79, are estimated to have diabetes<sup>1</sup>. About 75% live in low and middle income countries. If these trends continue, by 2040 some 642 million people, or one adult in ten, will have diabetes. India had 69.2 million people living with diabetes (8.7%) as per the 2015 data<sup>1</sup>. Of these, it remained undiagnosed in more than 36 million people.<sup>1</sup> Diabetes as a single disease affects nearly all organ systems of the body. Chronic complications of diabetes develop from the cumulative effects of altered metabolic milieu and the resultant tissue toxicity. Diabetic kidney disease is leading cause of end stage renal disease and diabetic eye disease is commonest cause of blindness in people below 65 years.<sup>2</sup>

Type 2 Diabetes mellitus (T2DM) is characterized by an asymptomatic phase between the actual onset of diabetic hyperglycemia and clinical diagnosis. The onset of T2DM is usually subtle and many years may elapse before diagnosis. This asymptomatic phase is estimated to last at least 4-7 years and consequently 30-50% patients may remain undiagnosed.<sup>3</sup> Long-standing untreated hyperglycemia is responsible for high prevalence of Microvascular Complications (MC) in newly diagnosed T2DM patients.<sup>3</sup> Presence of MC at the time of T2DM diagnosis are showing increasing trends in India. It is apparent that evidence on prevalence of T2DM related complications is essential for the adjustment of policies and practices in diabetic care management. Present study is aimed at studying the prevalence of MC in T2DM patients at the time of diagnosis in a tertiary care hospital in India.

### MATERIAL AND METHODS

#### SOURCE OF POPULATION:

This is a hospital based cross-sectional study carried out at Dr.Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinnoutapalli, tertiary care, teaching hospital in South India. 400 newly detected type 2 diabetes patients, those attending medical outpatient department were included in this study. These patients presented with various complaints, few with classical symptoms of diabetes and few with symptoms of diabetes related complications and others with inter-current illnesses.

#### Inclusion criteria

Newly detected type 2 diabetes mellitus patients.

#### Exclusion criteria

Type 1 diabetes mellitus, Gestational diabetes mellitus, Type 2 diabetes patients already on treatment, Diabetics with a co-morbid illness such as CHF, stroke, chronic liver disease, and chronic kidney disease were excluded from the study.

#### METHODOLOGY

All 400 members that participated in the study were enquired for the presence of symptoms of diabetes related long term complications, with the help of predesigned proforma that contained symptom questionnaire validated in previous studies.

Diabetes was diagnosed according to American Diabetic Association criteria.

**Overweight** is defined as BMI  $\geq 25$  and obesity as BMI  $\geq 30$  kg/m<sup>2</sup>.

**Hypertension** was defined as blood pressure  $\geq 140/90$  mmHg 5 ml of blood was collected in eight hour fasting state for fasting plasma glucose, Lipid profile and HbA1c.

#### ASSESSMENT FOR COMPLICATIONS:

**Retinopathy:** Fundus(F) examination was performed after dilating with tropicamide eye drops. Optic fundi were examined by consultant ophthalmologist, and graded according to International Classification of Diabetic Retinopathy.

**Nephropathy:** Albuminuria was assessed with MICRAL test. (Immunological visual testing strips for semi quantitative determination of microalbuminuria).

MICRAL test(MT): A ratio of albumin (mcg/L) to creatinine (mg/L) of less than 30 is normal; a ratio of 30-300 signifies microalbuminuria and values above 300 are considered as macroalbuminuria.

**Neuropathy:** assessed with modified Neuropathy Disability Score (NDS).

### RESULTS

#### TABLE 1: DISTRIBUTION OF PATIENTS AS PER AGE CATEGORIES

Age	Number	Percent
31-40	60	15%
41-50	132	33%

51-60	96	24%
61-70	96	24%
71-80	16	4%
Total	400	100

Total numbers of patients were 400 and 40-50 year age group was the largest in the study(33%)

**Out of 400 patients 212 are males and 188 are females.**

**Table 2: Demographic and clinical characters of study subjects**

Patient characteristics	Frequency	Percentage (%)
Age(mean + SD)	55.5+ 24.5	
Sex male	212	53
female	188	47
Smoking	96	24
Alcohol	92	23
Hypertension	148	37
Obesity	28	7
Hypercholesterolemia	76	19
Hypertriglyceridemia	88	22
HbA1C (6.5-7.5)	284	71
HbA1C (>7.5)	116	29
<b>Neuropathy</b>	60	15
<b>Nephropathy</b>	44	11
<b>Retinopathy</b>	28	7

Out of 400 study population 100 patients had atleast one microvascular complication. The prevalence of diabetic neuropathy, nephropathy and retinopathy was 60, 44 and 28 respectively.

**Table 3 : Relationship between HbA1C and diabetic complications**

	Category	HbA1c				Total		P-value
		6.5-7.5		>7.5		number	%	
		number	%	number	%			
F	Negative	268	97.1	104	83.9	372	93	0.03
	Positive	8	2.9	20	16.1	28	7	
NDS	<6	260	94.2	80	64.5	340	85	<0.000
	> 6	16	5.8	44	35.5	60	15	1
MT	Negative	272	98.6	84	67.7	89	89	<0.000
	Positive	4	1.4	40	32.3	11	11	1
Total		276	100	124	100	100	100	

**DISCUSSION**

Diabetes mellitus a chronic disease affecting many individuals in India, has increased over the past two decades and expected to continue in epidemic proportions. This increase has been attributed to the rapid economic, demographic and nutritional transition experienced in India. Diabetes is a significant public health issue with many types of adverse outcomes and disability. T2DM 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<sup>4</sup>.

The present study re-confirms 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 many patients were in the age group of 40-50 years (33%), which is similar to 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.<sup>5</sup> 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, because the duration of exposure to hyperglycemia and diabetes is increased.

Both environmental and genetic factors might explain the younger onset of age along with high prevalence of diabetes in the Indian population.<sup>6</sup> The Indian patients also had a more sedentary life style and a higher prevalence of family history of known diabetes than the other groups.

**Table 4: Comparison of prevalence of microvascular complications with previous studies**

	Neuropathy	Nephropathy	Retinopathy
<b>Present study</b>	<b>15%</b>	<b>11%</b>	<b>7%</b>
Sosale et al <sup>7</sup>	13.5%	1.06%	6%
RP Agrawal et al <sup>8</sup>	30.1%	32.5%	28.9%
UKPDS <sup>9,10</sup>		7%	35%
CURES <sup>11,12</sup>		27.4%	5.1%

**Diabetic Neuropathy**

Prevalence of peripheral neuropathy is 15%, which is comparable to the study of Sosale et al<sup>7</sup> of 13.15%. Explanation for a lower rate of diabetic neuropathy among Indians may be due to better skin microvascularization compared to Europeans despite having similar risk factors.<sup>13</sup>

**Nephropathy**

The prevalence of nephropathy is 11%, which is high when compared to other studies from India Sosale et al<sup>7</sup> (1.06%) and UKPDS<sup>9</sup> (7%) respectively.

The prevalence of nephropathy in present study is low when compared to other studies CURES<sup>11</sup> (27.4%) RP Agrawal et al<sup>8</sup> (32.5%).

Unlike, present study did not include diabetic retinopathy in defining nephropathy. The prevalence of nephropathy is quite low in Sosale et al study because the study included only those with overt proteinuria (>300mg/24hours).

The large differences observed in the prevalence of nephropathy among different studies could be attributed to the differences in study design and methodologies adopted for defining the disease. Many of the studies were clinic based, and this could have introduced a referral bias<sup>12</sup>.

**Diabetic retinopathy**

While the relatively low rate of diabetic retinopathy (7%) in this study is similar to CURES(5.1%),<sup>12</sup> Sosale et al (6%)<sup>7</sup>, from India

The results for diabetic retinopathy are in contrast to findings of other studies showing higher prevalence in RP Agrawal et al (28.9%)<sup>8</sup>, United Kingdom Prospective Diabetes Study (UKPDS) (35%).<sup>10</sup>

**Relationship of Glycemic control to complications**

The importance of glucose as a factor in the progression of diabetic complications, as initially suggested from epidemiologic and preclinical studies, was clearly demonstrated in the Diabetes Control and Complications Trial (DCCT) study in patients with T1DM.<sup>14</sup> In both the primary and secondary prevention aim of the study, any decrease in HbA1c was strongly associated with a reduction in the risk of development of diabetic complications.

In the present study there is a strong relationship between glycemic control and the prevalence of MC, with neuropath, nephropathy and retinopathy being 5.8%, 1.4%, 2.9% among HbA1C between 6.5-7.5% compared to 35.5%, 32.3%, and 16.1% among HbA1C > 7.5% respectively.

**LIMITATIONS OF OUR STUDY**

The major limitation of the study was that it was conducted in small population that may not represent entire population. The study was conducted from those population attending the hospital and thus

may reflect high prevalence of complications observed in this study. The gold standard fundus photography was unavailable to evaluate retinopathy.

#### CONCLUSION:

Microvascular complications are a major cause of morbidity and mortality in T2DM. The prevalence of the long term MC of type 2 diabetes was as high as 25% at the time of diagnosis because of long phase of asymptomatic hyperglycemia. Complications correlate with the degree of hyperglycemia. Assessment for these complications must be done at the time of diagnosis in all patients. Once complications develop, in addition to strict control of hyperglycemia, steps have to be taken to prevent or retard further progression of these complications. Education of high risk group regarding diabetes and its complications by electronic and print media is required so that they seek medical consultation at the earliest. We need to screen our population for diabetes at a younger age to prevent and in treatment of microvascular complications.

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