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PREVALENCE OF MICROVASCULAR COMPLICATIONS IN YOUNG ONSET INDIAN TYPE 2 DIABETES SUBJECTS LESS THAN 40 YEARS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: The aim of this study was to determine the prevalence of microvascular complications in young Indian type 2 diabetic subjects less than 40 years attending a tertiary diabetic institute. **Research Design and Methods:** Type 2 diabetic subjects 100 in number were randomly selected from patients attending Karnataka institute of endocrinology and research over one year. Microalbuminuria was estimated by immunoturbidometric assay and diagnosed if albumin excretion was between 30 and 299 µg/mg of creatinine, and overt nephropathy was diagnosed if albumin excretion was ≥300 µg/mg of creatinine. Diabetic retinopathy was assessed by vitreo retinal specialist using stereoscopic retinal colour photography, neuropathy by monofilament and biothesimeter tests. **Results:** 100 persons with diabetes aged less than 40 years were randomly selected. There were 54 males and 46 females. 81% had their waist circumference between 80 to 110 cms. BMI of 79% was between 18.5 to <30 kg/sqmt. Mean BMI was 26.35 **±4.38**. Mean HBA1c was 9.65 **±2.29.** 44% had low HDL, 79% high LDL and 59% had high triglyceride levels. Prevalence of Retinopathy was 21% and 22% had nephropathy and neuropathy. 4% had all the three microvascular complications. **Conclusions:** Prevalence of Retinopathy was 21%, out of which 17% had mild NPDR, 2 % had moderate NPDR and 2 % had severe NPDR. Prevalence of Neuropathy was 22 %. Prevalence of Nephropathy was 22 %, out of which 4% had macroalbuminuria.4% of subjects had all 3 microvascular complications.

KEYWORDS: Type 2 diabetes, nephropathy, retinopathy, microalbuminuria.

INTRODUCTION

The prevalence of type 2 diabetes mellitus (T2DM) in India is increasing exponentially. There has also been an increase in the number of young adults with T2DM. Patients diagnosed to have T2DM under the age of 40 years are designated to have Young onset Diabetes (YOD).[1]

In Asian Indians, diagnosis of diabetes occurs at younger ages and lower body mass index (BMI).[2] Patients with YOD often have inadequate glycemic control and multiple cardiovascular (CV) risk factors. This contributes to an increase in micro and macrovascular complications over time.[1,3,4,5]

Asian Indians are known to develop T2DM at a younger age and at a lower BMI.[2] Data from CINDI indicates that 46%, i.e., almost half of the patients with type 2 diabetes are diagnosed under the age of 40 years in India.[6] Estimates of prevalence across Asia from the JADE Program report that 20%, i.e. nearly one in every five clinic patients have YOD.[1]

Diabetes and its complications are one of the leading causes of death and disability worldwide. The global diabetes prevalence in 20–79 year olds in 2021 was estimated to be 10.5% (536.6 million people), rising to 12.2% (783.2 million) in 2045 as per IDF atlas 2021. As per Indian Council of Medical Research – India Diabetes (ICMR INDIAB) study published in 2023, in India there are 101 million people with diabetes 136 million with prediabetes.

Type 2 diabetes mellitus is the most common form of diabetes, representing about 95% of all diabetes cases worldwide. Many patients present with complications at the time of diagnosis and within the first ten years from diagnosis.

Microvascular and macrovascular complications are the major cause of morbidity and mortality in people with diabetes. Microvascular complications of type 2 diabetes include retinopathy, nephropathy and neuropathy. The glycemic control in young type 2 diabetes persons is not good and they develop both micro and macrovascular

complications quite early in the course of diabetes. So we have decided to study the prevalence of microvascular complications in diabetes persons less than 40 years.

RESEARCH DESIGN AND METHODS

Young Type 2 diabetic subjects less than 40 years 100 in number were randomly selected from patients attending Karnataka institute of endocrinology and research over 12 months. Informed consent was taken from all the subjects.

Clinical and biochemical studies

Measurements of weight, height, and waist circumference were obtained using standardized techniques. The BMI was calculated using the following formula: weight (kg)/height (m^2). Blood pressure was recorded in the sitting position in the right arm. Two readings were taken 5 min apart, and the mean of the two was taken as the final blood pressure reading.

A fasting blood sample was taken for estimation of plasma glucose and serum lipids using a Hitachi 912 autoanalyser (Roche Diagnostics, Mannheim, Germany). A1C was measured by the high-performance liquid chromatography method using the Variant machine (Bio-Rad, Hercules, California).

Estimation of microalbuminuria

Microalbumin concentration was measured in a fasting urine sample using a immunoturbidometric assay (Hitachi 902 autoanalyser; Roche Diagnostics).

Retinopathy

The ocular fundi were photographed using four-field stereo color retinal photography (Zeiss FF 450 plus camera). Photographs were graded by an ophthalmologist (R.M.). The minimum criterion for diagnosis of diabetic retinopathy was the presence of at least one definite microaneurysm in any field photographed. Photographs were assessed and assigned a retinopathy level, and the final diagnosis for each patient was determined from the grading of the worse eye according to the Early Treatment Diabetic Retinopathy Study criteria for severity of an individual eye.[9]

DEFINITIONS

Hypertension

Subjects with self-reported hypertension and those who had a systolic blood pressure of ≥140 mmHg and/or diastolic blood pressure of ≥90 mmHg[10] were considered to have hypertension.

Microalbuminuria

Microalbuminuria was diagnosed if the albumin excretion was between 30 and 299 µg/mg of creatinine.[3] Overt nephropathy was diagnosed if albumin excretion was ≥300 µg/mg of creatinine in the presence of diabetic retinopathy.

International classification of diabetic retinopathy

Diabetic Retinopathy	Findings Observable on Dilated Ophthalmoscopy
No apparent DR	No abnormalities
Mild nonproliferative DR	Microaneurysms only
Moderate nonproliferative DR	Microaneurysms and other signs (e.g., dot and blot hemorrhages, hard exudates, cotton wool spots), But less than severe non proliferative DR
Severe nonproliferative DR	Moderate nonproliferative DR with any of the following: Intraretinal hemorrhages (≥20 in each quadrant) Definite venous beading (in 2 quadrants) Intraretinal microvascular abnormalities (in 1 quadrant); No signs of proliferative retinopathy
Proliferative DR	Severe nonproliferative DR and 1 or more of the following: Neovascularization Vitreous/preretinal hemorrhage

Statistical Methods: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, **Assumptions: 1.**Dependentvariables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance. A t-test is a statistical test that is used to

compare the means of two groups. It is often used in hypothesis testing to determine whether a process or treatment actually has an effect on the population of interest, or whether two groups are different from one another with the null hypothesis (H_0) is that the true difference between these group means is zero and the alternate hypothesis (H_a) is that the true difference is different from zero.

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher exact test used when cell samples are very small.

Significant figures
+ Suggestive significance (P value: 0.05<P<0.10)
* Moderately significant (P value:0.01<P ≤ 0.05)
** Strongly significant (P value : P≤0.01)

Statistical software: The Statistical software namely SPSS 22.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

RESULTS
In this observational study 100 persons with diabetes aged less than 40 years were randomly selected. There were 54 males and 46 females. 81% had their waist circumference between 80 to 110 cms. BMI of 79% was between 18.5 to <30 kg/sqmt. Mean BMI was 26.35 **±4.38.** Mean HBA1c was 9.65 **±2.29.**
Prevalence of Retinopathy was 21%, out of which 17% had mild NPDR, 2 % had moderate NPDR, 2% had severe NPDR.
Prevalence of Neuropathy was 22 %.
Prevalence of Nephropathy was 22 %, out of which 4% had Urine macroalbuminuria.
4% of subjects had all 3 complications.
44% had low HDL, 79% high LDL and 59% had high triglyceride levels.

Table 1: Gender-frequency distribution of patients studied.

Gender	No. of Patients	%
Female	46	46.0
Male	54	54.0
Total	100	100.0

Table 2: Age in Years-frequency distribution of patients studied.

Age in Years	Gender		Total
	Female	Male	
<30	8(17.4%)	8(14.8%)	16(16%)
31-40	38(82.6%)	46(83.2%)	84(84%)
Total	46(100%)	54(100%)	100(100%)

Table 3: Waist circumference-frequency distribution of patients studied .

Waist circumference	Gender		Total
	Female	Male	
<80	9(19.6%)	4(7.4%)	13(13%)
80-110	34(73.9%)	47(87%)	81(81%)
>110	3(6.5%)	3(5.6%)	6(6%)
Total	46(100%)	54(100%)	100(100%)

Table 4: BMI(kg/m2)-Frequency Distribution of Patients Studied.

BMI(kg/m2)	Gender		Total
	Female	Male	
<18.5	1(2.2%)	1(1.9%)	2(2%)
18.5-24.9	20(43.5%)	19(35.2%)	39(39%)
25.0-29.9	19(41.3%)	21(38.9%)	40(40%)
>30.0	6(13%)	13(24.1%)	19(19%)
Total	46(100%)	54(100%)	100(100%)

Table 5: Duration in years-frequency distribution of patients studied.

Duration	Gender		Total
	Female	Male	
<2 Years	15(32.6%)	17(31.5%)	32(32%)
>2 Years	31(67.4%)	37(68.5%)	68(68%)
Total	46(100%)	54(100%)	100(100%)

Table 6: Comparison of Baseline clinical variables in males and females.

Variables	Gender		Total	P Value
	Female	Male		
AGE IN YEARS	34.46±5.14	35.3±5.17	34.91±5.15	0.419
HEIGHT	163.59±8.13	165.81±10.16	164.79±9.3	0.236
WEIGHT	69.11±12.59	73.45±13.28	71.45±13.08	0.098+
WAIST CIRCUMFERENCE	90.35±10.98	92.19±10.3	91.34±10.6	0.390
BMI	25.88±4.49	26.76±4.27	26.35±4.38	0.320

Table 7: Comparison of Clinical variables in males and females studied,

Variables	Gender		Total	P Value
	Female	Male		
SBP	129.57±16.32	126.22±13.12	127.76±14.7	0.259
DBP	82.17±6.64	83.15±7.97	82.7±7.37	0.513
FBS	202.63±75.08	196.76±77.59	199.46±76.12	0.703
PPBS	297.11±105.98	308.81±101.06	303.43±102.99	0.574
HBAIC	9.66±2.39	9.65±2.22	9.65±2.29	0.982

Table 8: LIPIDS -frequency distribution of patients studied.

Variables	Gender		Total
	Female	Male	
TC			
• <160	11(23.9%)	16(29.6%)	27(27%)
• >160	35(76.1%)	38(70.4%)	73(73%)
HDL			
• <35	18(39.1%)	26(48.1%)	44(44%)
• 35-65	28(60.9%)	28(51.9%)	56(56%)
• >65	0(0%)	0(0%)	0(0%)
LDL			
• <100	9(19.6%)	12(22.2%)	21(21%)
• 100-129	17(37%)	24(44.4%)	41(41%)
• 130-159	14(30.4%)	12(22.2%)	26(26%)
• >160	6(13%)	6(11.1%)	12(12%)
TG			
• <150	18(39.1%)	23(42.6%)	41(41%)
• 150-199	11(23.9%)	11(20.4%)	22(22%)
• 200-499	15(32.6%)	17(31.5%)	32(32%)
• >500	2(4.3%)	3(5.6%)	5(5%)
Total	46(100%)	54(100%)	100(100%)

Table 9: Urine Albuminuria-Frequency Distribution of Patients Studied.

U.ALBUNURIA	Gender		Total
	Female	Male	
<30	36(78.3%)	42(77.8%)	78(78%)
>30	10(21.7%)	12(22.2%)	22(22%)
Total	46(100%)	54(100%)	100(100%)
Mean ± SD	37.08±72.88	27.6±40.67	31.96±57.64

P=0.415, Not Significant, Student t Test

Table 10: Prevalence of Retinopathy and Neuropathy of young Type 2Diabetes persons studied.

Variables	Gender		Total
	Female	Male	
RETINOPATHY			
NO	36(78.3%)	43(79.6%)	79(79%)
YES	10(21.7%)	11(20.4%)	21(21%)
• MILD NPDR	9(19.6%)	8(14.8%)	17(17%)
• MODERATE NPDR	0(0%)	2(3.7%)	2(2%)
• SEVERE NPDR	1(2.2%)	1(1.9%)	2(2%)
NEUROPATHY			
NO	39(84.8%)	39(72.2%)	78(78%)
YES	7(15.2%)	15(27.8%)	22(22%)
DPN	7(15.2%)	15(27.8%)	22(22%)
Total	46(100%)	54(100%)	100(100%)

DISCUSSION

This study revealed high prevalence of micro vascular complications in the young persons with diabetes. The implications of the study findings are: burden of micro vascular complications is quite high in our young type 2 diabetes population, hence need for regular screening to prevent further progression. Among the microvascular complications 22% had peripheral neuropathy and nephropathy, 21% had retinopathy.

Diabetic PN (DPN) is a well-known micro-vascular complication of T2DM attributed to chronic hyperglycemia and is defined as the presence of peripheral nerve dysfunction in diabetics after exclusion of other causes.[7] Clinically, diabetic neuropathy is a destructive disease of the peripheral nerve leading to symptoms of pain or paraesthesia or problems arising from neurological deficit. Distal Symmetrical Polyneuropathy (DSP) is one of the most common complications occurring in type 2 diabetes.[8]

DPN is considered as one of the commonest causes of foot complications like amputation and difficulty in ambulation. DPN is also the most common cause of non traumatic amputation.

Incidence of DPN in diabetes is up to 50%. Complications of Peripheral Neuropathy include severe pain, loss of ambulation, and increased risk of foot ulceration and amputation.[9] Various studies conducted in United States of America have reported the incidence of neuropathic pain syndromes in American population with diabetes to be around 70%.[10] In an observational study in patients with type 2 diabetes it was found painful symptoms had an occurrence of 26% in patients without neuropathy and 60% of patients with severe neuropathy.[11]

Studies have shown the prevalence of peripheral neuropathy in South India to range from 10.5% to 60.4%. The prevalence was higher in urban areas when compared to rural area.[12-14] The prevalence of peripheral neuropathy in young type 2 diabetes in our study is 22% and all young type 2 diabetes subjects had distal symmetrical neuropathy.

In this study prevalence of Retinopathy was 21%, our results are consistent with the previous studies by Raman *et al*. (18.1%), Rema *et al*. (17.6%), Namperumalsamy *et al*. (10.6%), Narendran *et al*. (26.2%) and Dandona *et al*. (22.58%), and so on.[15,16,17]

A recent meta-analysis concluded that among eight studies published in India, 14.8% of persons with known diabetes aged ≥30 years and 18.1% of those aged ≥50 years had diabetic retinopathy.[18]

The Sankara Nethralaya-Diabetic Retinopathy Epidemiology and Molecular Genetic Study-Phase 1 (SNDREAMS-1) reported 18 % (95% CI: 16.0–20.1) prevalence of DR in an urban population with DM and SNDREAMS-3 reported 10.0% prevalence for the rural population aged >40 years.[19,20]

On applying multiple regression analysis for diabetic retinopathy, a positive association was observed for age of patients, duration of diabetes, blood pressure, HBAIC.

Diabetic nephropathy is the leading cause of end-stage renal disease world-wide. A study done in rural India reported that the prevalence of diabetic nephropathy was 13.6%..[21]

In a study done by Ranjit et al prevalence of microalbuminuria and overt nephropathy was computed in relation to duration of diabetes and A1C. There was an increase in the prevalence of microalbuminuria with the increase in duration of diabetes. There was a significant increase in the prevalence of overt nephropathy with the increase in duration of diabetes. Prevalence of both microalbuminuria (A1C <7.0%: 14.5%, 7.0–8.9%: 22.6%, 9–10.9%: 35.1%, and >10.9%: 43.4%, and overt nephropathy (A1C <7.0%: 0.2%, 7.0–8.9%: 1.1%, 9–10.9%: 3.5%, and >10.9%: 5.5%) increased with the increase in A1C levels (*P* for trend <0.001).[22]

In a study prevalence of microalbuminuria and associated risk factors in young Indian type 2 diabetes subjects attending a tertiary diabetes care institute by R.Anil kumar, microalbuminuria was present in 23.3% and macroalbuminuria in 4.6% of young diabetes subjects. Systolic BP, HBA1c, BMI and duration of diabetes are correlated with microalbuminuria.[23] The prevalence of nephropathy is similar in this study with 22% and 4% having macroalbuminuria.

Nephropathy was assessed by urine albuminuria/creatinine ratio and eGFR (CKD EPI calculator) which requires age, gender, serum creatinine value of patients. Using this simple method yearly once screening of patients for nephropathy is highly recommended to diagnose early and prevent further progression of the disease.

CONCLUSIONS

Prevalence of Retinopathy was 21%, out of which 17% had mild NPDR, 2 % had moderate NPDR and 2% had severe NPDR. Prevalence of Neuropathy was 22%. Prevalence of Nephropathy was 22 %, out of which 4% had macroalbuminuria.4% of subjects had all 3 microvascular complications.

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Abbreviations

T2DM-Type 2 diabetes mellitus.
TIDM-Type 1 diabetes mellitus.
MA-Microalbuminuria.
BMI-Body mass index.
HBA1C-Glycosylated haemoglobin
GFR-Glomerular filteration rate.
BP-Blood pressure.
DPN-Diabetic peripheral neuropathy.
DSN-Distal symmetrical neuropathy.
CKD-Chronic kidney disease.
NPDR-Non proliferative diabetic retinopathy.

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