

Clinical and biochemical profile of lean type 2 diabetes mellitus

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ABSTRACT

Background: Type 2 diabetes mellitus is the most prevalent form of diabetes worldwide. In western countries majority of the cases are obese. The scenario may be different in certain parts of India. Various studies have reported a high prevalence of lean type 2 diabetes mellitus with a body mass index < 19 kg/m². **Materials and Methods:** We evaluated 100 cases of lean type 2 diabetes mellitus (62 males and 38 females). **Results and Conclusion:** The mean duration of diabetes was 51.7 months (range 5-180 months). The glycemic control was poor according to standard guidelines. The majority of them showed response to oral hypoglycemic agents. Secondary failure to oral hypoglycemic agents was seen in 27 patients. The prevalence of microvascular complications was much higher than macrovascular complications. Neuropathy was the commonest complication seen in 70%, followed by retinopathy in 25%. Only 12 patients had hypertension, one had coronary artery disease and two had cerebrovascular accident. Lipid profile was not significantly deranged in our patients.

Key words: Lean type diabetes mellitus, macrovascular, microvascular

INTRODUCTION

Type 2 diabetes mellitus is the most prevalent form of diabetes seen worldwide. Epidemiological data over the past decades have shown that the pattern and profile of type 2 diabetes mellitus are very different in India compared to the West.^[1] In Europe and America majority of type 2 diabetes are obese. In 1965 Tripathy and Kar highlighted that 27% of elderly diabetics were lean.^[2] Following that various studies in India have reported a prevalence of low body weight/lean (Body mass index, BMI < 19 kg/m²) type 2 diabetes mellitus ranging from 1.6% to 26%.^[3-7] The clinical and biochemical profile of these patients are different from classic type 2 diabetes mellitus.^[5,6,8,9] These patients are neither related clinically or pathophysiologically

to latent autoimmune diabetes of adults (LADA). Markers of autoimmune destruction of β -cells are absent in the vast majority of these patients.^[5,10,11] Homeostatic model assessments by Das *et al.*, suggest that they are typical cases of type 2 diabetes and the low body weight does not reflect poor beta cell function or loss of body weight due to long-standing uncontrolled diabetes.^[11] However, more recent study by Bera *et al.*, suggested poor β -cell function in such patients.^[12]

With this background, we studied the clinical and biochemical profile of lean type 2 diabetic patients in Manipur, as there is no published data from our part of the country.

Aims and objectives

To study the clinical and biochemical profile of lean type 2 diabetes mellitus.

MATERIALS AND METHODS

Cross-sectional study carried out in the Diabetes Clinic, Department of Medicine, Regional Institute of Medical Sciences Hospital, Imphal, Manipur. One hundred cases

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of lean type 2 diabetes mellitus were evaluated.

Inclusion criteria

All patients with type 2 diabetes mellitus irrespective of age, sex with BMI less than 19. Diagnosis of diabetes mellitus was based on American Diabetes Association (ADA) criteria.

Exclusion criteria

Type 2 diabetes mellitus with BMI more than 19.

Any seriously ill patient whose sensorium and higher functions are altered.

Patients suffering from acute myocardial infarction, renal failure, liver disease, critical illness, tuberculosis, carcinoma and any severe infection.

Methods

A detailed history of clinical information including the age, sex and intercurrent illness was taken. Anthropometric parameters – height, weight, waist and hip circumference were recorded and clinical examination performed to detect diabetic complications.

Glycemic status was assessed using fasting and two hours postprandial blood glucose (BG) and HbA1c (glycosylated haemoglobin). HbA1c level was estimated by Fast Ion Exchange Resin separation method using REF 10657 kit from Human Wiesbaden, Germany. Lipid profile was assessed for each patient. Urinary microalbumin was examined using dipstick. Nephropathy was diagnosed on basis of persistent proteinuria in the absence of urinary tract infection. Fundus examination was done by expert ophthalmologist. Neuropathy was diagnosed on the basis of subjective symptoms, objective evidence of absence of ankle jerk, glove stocking type of anesthesia or monofilament testing. Patients were considered to have ischemic heart disease based on electrocardiogram (ECG).

RESULTS

In this study 100 cases of lean diabetic patients were evaluated from August 2008 to 2010. Among the patients 62 (62%) were males and 38 (38%) were females. The age of patients ranged from 32 to 75 years with a mean of 53 years.

Clinical profiles

In the present study, the mean age of the patient was 53 years (range 32-75 years). The mean duration of diabetes mellitus is 51.7 months (range 5-180 months). The mean height of patients was 158.2 cm \pm 9.5 and weight was 46.9 kg \pm 5.6 with BMI of 18.7 kg/m² \pm 0.2. The mean

waist and hip circumferences was 75.1cm \pm 5.1 and 79.5 cm \pm 5.7, respectively, with waist-hip ratio of 0.9 \pm 0.2, the systolic and diastolic blood pressure are 127.6 \pm 14.2 and 80.5 \pm 10.4. The clinical parameters according to sex distribution are shown in Table 1.

In the present study secondary OHA (oral hypoglycemic agent) failure was seen in 27 patients (27%) (20 males and 7 females).

Biochemical parameters

The mean fasting blood glucose in the present study was 132.5 \pm 68.2 mg% and postprandial was 193.9 \pm 100.1 mg%. The mean HbA1c was 7.7 \pm 2.2%. Total cholesterol was 188.5 \pm 25.8 mg%, triglyceride 146.0 \pm 32.2 mg%, low density lipoprotein (LDL) 106.5 \pm 25.5 mg%, high density lipoprotein (HDL) 49.8 \pm 7.1 mg% and very low density lipoprotein (VLDL) 32.1 \pm 7.0 mg% as shown in Table 2. There was no significant difference in biochemical parameters between the male and the female lean diabetic patients.

Diabetics with OHA failure had higher blood glucose (fasting BG-192.8 \pm 89.6 vs 119.2 \pm 40.4; postprandial BG-291.6 \pm 127.5 vs 157.8 \pm 54.6; $P=0.00$), higher HbA1c (9.9 \pm 2.9 vs 6.9 \pm 1.2; $P=0.00$) and total cholesterol level (202.4 \pm 33.0 vs 183.3 \pm 20.3; $P=0.001$) than the diabetics without OHA failure significantly. However, there was no significant difference in other parameters between the patients with and without OHA failure.

Diabetic complications

It was found that the prevalence of peripheral neuropathy (70%) and retinopathy (25%) is higher among the lean diabetic patients as compared to macrovascular complications. When data of both micro and macrovascular complications were clubbed together in the present study, it was found that 73% of the patients suffers from either micro or macrovascular complications or both. Among

Table 1: Clinical parameters in male and female lean diabetic patients

Parameters	Female (Mean \pm SD) n=62	Male (Mean \pm SD) n=38	P value
Height (cm)	150.18 \pm 5.98	163.13 \pm 7.75	0.00
Weight (kg)	42.26 \pm 3.31	49.76 \pm 4.83	0.00
BMI (kg/m ²)	18.69 \pm 0.18	16.68 \pm 0.27	0.78
Waist circumference (cm)	71.66 \pm 3.39	77.16 \pm 4.92	0.00
Hip circumference (cm)	76.32 \pm 5.00	81.40 \pm 5.17	0.00
Waist-hip ratio	0.89 \pm 0.31	0.94 \pm 0.03	0.16
Systolic BP	127.27 \pm 11.95	127.97 \pm 15.49	0.79
Diastolic BP	78.11 \pm 11.20	81.98 \pm 9.68	0.07
Duration of diabetes (months)	46.00	51.15	0.39

Comparison by independent *t* test, BMI: Body mass Index, BP: Blood pressure

Table 2: Biochemical parameters of lean diabetic patients

Parameters	Mean	SD
Fasting BG (mg%)	132.51	68.21
Postprandial BG (mg%)	193.95	100.02
HbA1c%	7.75	2.25
Total cholesterol (mg%)	188.46	25.67
Triglyceride (mg%)	145.96	32.16
LDL (mg%)	106.52	25.46
HDL (mg%)	49.77	7.09
VLDL (mg%)	32.08	7.03

BG: Blood glucose, HbA1c: Glycosylated hemoglobin, LDL: Low density lipoprotein, HDL: High density lipoprotein; VLDL: Very low density lipoprotein

the 100 patients, 12 patients (12%) had hypertension one (1%) had coronary artery disease and two patients (2%) had cerebrovascular accident. And 8 patients presented with foot or systemic infections.

Comparison of clinical and biochemical parameters between those with complications and without complications is shown in Table 3.

Neuropathy

In the present study 70 patients (70%) were suffering from peripheral neuropathy. And the prevalence of neuropathy was found to be higher in the older patients (54.3 ± 9.4 vs 49.5 ± 11.0 ; $P=0.03$), with lesser body weight (45.8 ± 5.2 vs 49.4 ± 5.8 ; $P=0.003$), shorter (156.4 ± 8.8 vs 162.4 ± 9.9 ; $P=0.003$) and narrower waist circumference (74.3 ± 5.2 vs 77.0 ± 4.4 ; $P=0.02$). There was no statistically significant difference in other parameters between those with neuropathy and those without neuropathy.

Retinopathy

Retinopathy was seen in 25 cases (25%). The prevalence was found to be higher in older age group (56.3 ± 8.9 vs 51.7 ± 10.2 ; $P=0.05$), higher blood glucose level [(fasting blood glucose - 270.7 ± 103.2 vs 115.9 ± 40.7 ; $P=0.00$; postprandial blood glucose - 270.7 ± 152.2 vs 168.4 ± 56.8 ; $P=0.00$), and higher HbA1c (9.3 ± 3.3 vs 7.2 ± 1.4 ; $P=0.00$)]. Retinopathy was also seen more in patients who are taller, heavier, with broader waist circumference, higher blood pressure and longer duration of diabetes but the findings were not significant statistically.

Nephropathy

Thirteen patients (13%) were suffering from nephropathy. The prevalence of nephropathy was found to be higher in taller (163.8 ± 11.1 vs 157.4 ± 9.0 ; $P=0.02$) patients with higher waist (78.0 ± 6.6 vs 74.6 ± 4.8 ; $P=0.03$) and hip circumference (82.8 ± 5.6 vs 79.0 ± 5.5 ; $P=0.02$), higher blood glucose level [(fasting blood glucose - 235.3 ± 99.5 vs 117.1 ± 46.2 ; $P=0.00$; postprandial blood glucose - $333.5 \pm$

Table 3: Comparison of parameters between lean diabetic patients with and without complications

Parameters	Without complications	With complications	P value
Age	46.85±11.34	54.32±9.24	0.003
BMI (kg/m ²)	18.69±0.30	18.68±0.22	0.09
Waist-hip ratio	0.943±0.03	0.917±0.22	0.60
Systolic BP	127.4±13.09	127.75±14.52	0.92
Diastolic BP	81.05±9.61	80.38±10.61	0.80
Fasting BG (mg%)	105.80±16.07	139.19±74.45	0.05
PP BG (mg%)	148.45±27.32	05.32±108.17	0.02
HbA1c	6.72±0.56	8.01±2.44	0.02
TC (mg%)	180.75±18.48	190.39±26.92	0.13
TG (mg%)	140.15±34.71	147.41±31.55	0.37
LDL (mg%)	98.05±21.02	108.51±26.11	0.11
HDL (mg%)	52.25±5.02	49.15±7.42	0.08
VLDL (mg%)	31.89±4.63	32.12±7.50	0.90

Comparison by independent t test, BMI: Body mass index, BP: Blood pressure, BG: Blood glucose, HbA1c: Glycosylated haemoglobin, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein

128.7 vs 173.1 ± 76.3 ; $P=0.00$), high HbA1c (11.4 ± 2.9 vs 7.2 ± 1.5 ; $P=0.00$), higher total cholesterol (211.5 ± 38.1 vs 185.0 ± 21.5 ; $P=0.00$) and triglyceride (178.3 ± 50.9 vs 141.1 ± 25.4 ; $P=0.00$) and lower high density lipoprotein level (42.8 ± 9.6 vs 50.8 ± 6.0 ; $P=0.00$). The findings with the other parameters were not significant.

DISCUSSION

In the present study of 100 lean type 2 diabetic patients, there were 62 males and 38 females. The mean age of the patient was 53 years and the mean duration of diabetes ranged was 52 months. The mean age of our patients is older than that of Das *et al.*,^[8] who reported a mean age of 48 years and Sinharoy *et al.*,^[9] reported a mean age of 47 years. However, the study Mukhyaparna *et al.*,^[6] reported higher mean age of 60 years.

The glycemc profile of our cases is much better than reported by various authors.^[5,6,8,9] These may be because most of our patients are from the vicinity of our hospital and are on regular follow-up.

A high prevalence of microvascular complications [peripheral neuropathy (70%), retinopathy (25%) and nephropathy (13%)] was observed in our patients. Mohan *et al.*,^[5] in their study, also found a higher prevalence of microvascular complications among lean type 2 diabetic patients, compared to diabetics with ideal body weight or obese diabetic patients. The prevalence of complications they found was neuropathy (male-44.6%, female-38.6%) retinopathy (male-37.3%, female-33.3%) and nephropathy (male-4.7%, female-4.4%). Mukhyaparna *et al.*,^[6] reported 35%, 6.6% and 27% prevalence of neuropathy, nephropathy and retinopathy, respectively. Sinharoy *et al.*,^[9] reported the

prevalence of neuropathy to be 32%, nephropathy 28% and retinopathy 28%.

Patients with diabetic complications were more aged and had significantly higher blood glucose levels compared to patients without complications in our study. Prevalence of microvascular complications among lean type 2 diabetics are related to duration of diabetes and glycemic control.^{16,91} In the study by Singh *et al.*,¹¹³ patients with diabetic retinopathy had significantly higher prevalence of microalbuminuria but fasting glucose and duration of diabetes were not significantly different from those without retinopathy. Low prevalence of macrovascular complications and hypertension as seen in our study had been reported by various authors. The probable reason for low incidence of ischemic heart disease and hypertension is less obesity in these patients.¹⁶¹

Secondary OHA failure was observed in 27% of the patients. In the study by Mohan *et al.*,¹⁵¹ nearly 47% of male and 53% of female lean type 2 diabetes were successfully treated with diet and OHAs even after a mean duration of 9 years of diabetes. Serum insulin level is lower in lean type 2 diabetics than in obese type 2 diabetics but there was no significant difference in c-peptide level which may be due to excess extraction of insulin by the liver.¹⁸¹

In the present study it was observed that the lipid profile was not much deranged. Das *et al.*,¹⁸¹ revealed the conspicuous absence of hyperlipidemia in their patients. HDL levels were high among lean diabetic patients. High HDL has been postulated to be due excess hepatic lipase activity.¹⁴⁴ Ikeda *et al.*,¹¹⁵¹ showed no major difference irrespective of glycemic status in lean type 2 diabetics (BMI < 25 kg/m²). Mukhyaprana *et al.*,¹⁶¹ also showed normal lipid profile in their patients. Whereas, study by Sinharoy *et al.*,⁹¹ showed elevated TG in lean type 2 diabetics compared to normal weight and obese type 2 diabetics. LDL was also elevated although lower than the other two groups.

CONCLUSIONS

The lean type 2 diabetes mellitus is a distinct clinical entity. The clinical presentation and profile of associated complications is different in lean patients of type 2 diabetes, as compared to obese or non-lean diabetics. The prevalence of microvascular complications is much higher than macrovascular complications. The prevalence of peripheral neuropathy is highest, followed by retinopathy and nephropathy. Patients who are more aged or have poor glycemic control are more likely to develop diabetic complications. Lean type 2 diabetics can usually achieve glycemic control with OHAs, but secondary OHA failure is observed in 27% of the patients.

Limitations of the study

The number of patients in our study is small. We did not evaluate for autonomic neuropathy, and also we did not subject our patients to echocardiography or stress test in the absence of clinical suspicion of ischemic heart disease. This may have led to underreporting of neuropathy and coronary artery disease.

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