

A STUDY OF CLINICAL, BIOCHEMICAL PROFILE AND COMPLICATIONS ASSOCIATED WITH LEAN TYPE 2 DIABETES MELLITUS

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Abstract

Background: Although obesity and higher waist circumference are predisposing factors for diabetes and complications, the lean type of diabetes mellitus with a BMI of <19 kg/m² is increasing in India. The current study evaluated lean type 2 diabetes mellitus for the clinical, biochemical parameters, and complications.

Methods: This cross-sectional observational study was conducted at the Diabetes Centre, KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi- India. A total of n=875 patients were identified with type 2 DM, out of which n=302 were lean diabetes mellitus (BMI<19 kg/m²) and n=573 were identified as non-lean Diabetes mellitus with BMI > 19 Kg/m².

Results: A positive family history of diabetes was noted in 21.85% of lean type 2 DM cases. The mean fasting blood sugar levels of lean type 2 DM was 182.96 ± 9.8 mg/dl versus non-lean DM cases with mean FBS 184.07 ± 11.3 mg/dl. The Post-prandial blood glucose in lean type 2 DM was 278.34 mg/dl compared to 250.85 mg/dl in non-lean type 2 DM cases. The incidence of macrovascular complications in 19.53 % of all cases and microvascular complications were in 7.28% of cases.

Conclusion: There is a considerable prevalence of lean type 2 DM in our population. These patients' clinical presentation and profile are likely to differ from expected or obese type 2 DM cases. It appears that lean type 2 DM cases suffer from severe hyperglycemia and complications.

Keywords: Lean type 2 Diabetes mellitus, hyperglycemia, microvascular complications, macrovascular complications

Introduction

Diabetes mellitus is the most common metabolic disorder prevalent across the world. It is characterized by an actual or absolute lack of insulin, leading to hyperglycemia and disturbance in carbohydrate, fat, and protein metabolism. [1] Epidemiological data in the past have revealed that the pattern and profile of diabetes mellitus in India are very different from other developing countries of Asia and the West. The developed countries have reported a prevalence of type 2

DM 60 – 80 % with obesity. [2] In India, 80% of diabetes mellitus is found in non-obese cases. [3] A prospective study conducted in association with the Indian Council of Medical Research (ICMR) found that 25% of cases of type 2 DM had body mass index (BMI) below 19 or were lean body weight individuals. Previously lean diabetics were grouped under the heading malnutrition-related diabetes mellitus (MRMD). However, over the years, studies have shown that neither malnutrition nor loss of weight was a factor in the prevalence of this metabolic state, and they are simply a subclass of type 2 DM. [4] Some studies have found that type 2 diabetes mellitus in lean patients has moderately severe basal hyperglycemia with levels of HbA1c higher than those of classical type 2 DM. [3,5] Patients with basal hyperglycemia in type 2 DM are due to increased hepatic glucose output. [6] The glucose entry into hepatocytes is not dependent on insulin, but glucose metabolism is subsequently affected. Insulin acts on specific genetic loci that coordinate the expression of several key enzymes of carbohydrate metabolism in hepatocytes. [7,8] The distinctive character of insulin kinetics in the liver with altered profile and the actions of key enzymes related to carbohydrate metabolism is responsible for type 2 DM. Hyperactive cytochrome system and non-suppressible glucokinase activity. [9] These peculiarities are also reflected in dyslipidemia, decreased HDL cholesterol, increased TG, and other markers of atherosclerosis, making them prone to developing microvascular disease. Das S et al. [10] found that lean types of diabetes had lower cholesterol, higher triglycerides, and normal HDL-C fewer other markers for atherosclerosis, making diabetes less prone to developing the macrovascular disease. Considering these facts, we decided to undertake a study to evaluate the clinical, biochemical profile, and complications found in lean type 2 diabetes mellitus.

Material and Methods

This cross-sectional observational study was conducted in the Diabetes Centre, KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi- 590 010, Karnataka, India. Institutional Ethical Committee permission was obtained for the study after duly following the protocol. Written consent was obtained from all the participants of the study. The nature of the study and possible outcomes were explained to the participants in their native language.

Inclusion criteria

1. Cases of type 2 diabetes mellitus new and old
2. type 2 diabetes mellitus in males and females.
3. Aged 30 years and above

Exclusion criteria

1. History of chronic illnesses that could affect Bodyweights like chronic liver and chronic kidney disease
2. Thyroid abnormalities
3. Those who have significantly lost weight in the recent past (3 months)
4. With other diseases such as cancers and metastasis.
5. HIV positive cases

A total of n=875 patients were identified with type 2 DM, out of which n=302 were lean diabetes mellitus (BMI<19 kg/m²) and n=573 were identified as non-lean Diabetes mellitus with BMI > 19 Kg/m². A detailed history was obtained from each patient, including the age of onset of diabetes mellitus, duration of diabetes mellitus, family history of the same, dietary pattern, presenting symptoms, and complaints at the time of diagnosis. A complete general examination was performed to identify any existing complications which may be present. Biochemical investigations were done for blood glucose (both fasting and post-prandial),

HbA1c, Thyroid-stimulating Hormone (TSH) serum urea, creatinine, and urinary microalbumin, lipid profile. The measurement of body height in meters and weight of the person in Kg was done, and BMI was calculated using the Quetelet Index where BMI is Kg/m². All the patients with BMI < 19 Kg/m² were classified as lean type 2 DM. Waist hip Ratio (W/H Ratio) ‘Waist Circumference’ is measured at the midpoint between the costal margin and anterior superior iliac spine. The hip measurement is taken as the maximum diameter at the greater trochanter. Blood pressure was measured with a standard sphygmomanometer in a sitting position after resting for 5 minutes. An average of three readings was considered the blood pressure of the patient and recorded. Ophthalmoscopy was done to diagnose diabetic retinopathy. Neuropathy was diagnosed based on subjective symptoms and objective evidence in loss of ankle jerk, glove, and stocking-type anesthesia. Nephropathy was diagnosed based on the blood urea, creatinine, and urinary microalbumin values. All the available data was uploaded on an MS Excel spreadsheet and analyzed by SPSS version 21 in Windows format for descriptive statistics. (Monotonous)

Results

During the conduction of this study n=875, diabetic cases were found, out of which n=302 were <19 kg/m² identified as lean type 2 DM. The minimum age of the patient in males was 32 years, and the maximum age was 73 years. The Mean age was 52.20±12.40 years (table 1). In females, the minimum age was 34 years, and the maximum age was 74 years. The mean age was 54.87±12.45 years. The mean fasting blood sugar levels of lean type 2 DM were 182.96 ± 9.8, comparable to non-lean DM cases with a mean FBS of 184.07 ± 11.3. However, the post-prandial blood glucose levels were significantly higher in lean type 2 DM cases depicted in Table 1. Based on the age for lean type 2 DM males out of n=212 cases, n=25(11.79%) were between 30 - 40 years age group, and n=80 (37.73%) were between 41 – 50 years. N=72(33.96%) cases were found in the age group 51 – 60 years, n=31(14.62%) were between the age group 61 – 70 years, and > 70-year n=11(5.18%) cases were seen. For lean type, 2 DM female patients out of n=90 cases, the age group division revealed n=9 cases between 30 and 40 years. N=15 between the age group 41 – 50 years n=38 between 51 – 60 years and n=21 cases between 61 – 70 years and n= 7 cases above 70 years of age were included in the study.

Table 1: Characteristics of the patients evaluated.

<i>Diabetics</i>	<i>Mean Age (yrs)</i>	<i>Sex (n)</i>		<i>Mean Values ± SD</i>			
		<i>M</i>	<i>F</i>	<i>FBS (mg %)</i>	<i>PPBS (mg %)</i>	<i>SBP (mmHg)</i>	<i>DBP (mmHg)</i>
<i>Lean DM</i>	54.18 ± 5.5	212	90	182.96 ± 9.8	278.34 ± 25.4	129.35 ± 6.6	78.38 ± 3.2
<i>Non-lean DM</i>	54.36 ± 4.5	418	155	184.07 ± 11.3	250.85 ± 20.3	131 ± 8.7	81.98 ± 2.9

A comparison of lean type 2 DM between male and female cases revealed that the difference in weight was statistically significant, p <0.05. The average waist circumference in males was more significant than in females, indicating greater abdominal fat deposition in males. The p values were significant. Similarly, the waist-hip ratio comparison revealed the mean values of males were 0.99 while that of females was 0.90, which was also found to be significant (Table 2).

Table 2: Anthropometric features of Lean diabetic patients

Variable	Male (mean ± SD)	Female (mean ± SD)	p-value
Age (yrs)	52.20±10.40	54.87±12.45	0.225
Height (cm)	170.5±30.81	158.35±25.27	0.0555
Weight (kg)	63.19±8.78	50.51±7.26	0.001*
Waist circumference (cm)	87.05±7.73	82.30±7.39	0.51
Hip circumference (cm)	90.10±6.10	94.31±5.13	0.054
Waist-hip ratio	0.99±0.10	0.90± 0.73	0.01*
BMI (kg/m ²)	18.89 ± 2.89	17.55 ± 2.87	0.7785

* Significant

The record of the Family history of lean type 2 DM in males revealed that out of n=212 cases, n=45(21.22%) had a family history of diabetes mellitus. In females, out of n=90 cases, n=21(23.33%) had a positive family history of diabetes. The overall family history of diabetes in both groups was 21.85%. The biochemical parameters of lean diabetes between males and females are given in Table 3. Out of all the parameters, serum triglycerides were significantly higher in males with p values <0.05. The serum HDL-C was found to be lower in males as compared to females.

Table 3: Biochemical parameters of lean diabetic patients

Parameters	Male (mean ± SD)	Female (mean ± SD)	p-value
FBS (mg %)	180.82±55.60	191.15±60.2	0.309
PPBS (mg %)	255.54±97.49	267.586±110.63	0.219
HbA1c (mg %)	10.88 ± 2.26	9.25 ±1.86	0.373
Cholesterol (mg %)	183.42±30.35	194.24 ±45.19	0.139
Triglycerides (mg %)	195.17±85.17	181.42 ±75.11	0.0246*
LDL (mg %)	114.32 ±75.69	119.88 ± 41.82	0.4320
HDL (mg %)	38.54 ± 13.83	46.35±13.65	0.010*

* Significant

A critical analysis of complications of type 2 DM in lean males and females (table 4) found the rates of complication in males were 28.77% and in females 33.33%. A detailed analysis revealed that out of n=61 complications in male cases, n=31(50.81%) were suffering from diabetes of duration > 10 years and n=17(27.86%) were with diabetes mellitus of duration 5 – 10 years, and n=13(21.31%) were with diabetes of duration less than five years. Similarly, in females out of n=30 cases, n=14(46.66%) cases with diabetes mellitus of duration > 10 years n=9(30%) cases with a duration of 5 – 10 years, and n=7(23.33%) cases with diabetes mellitus of duration less than five years.

Table 4: complications of Type 2 DM-Lean subjects in male and female

Complication	Male (%)	Female (%)
Coronary Artery Disease	11(5.18)	5 (5.55)
hypertension	25(11.79)	15(16.67)
Peripheral vascular disease	2 (0.94)	1 (1.11)
Peripheral Neuropathy	8 (3.77)	4 (4.44)

Nephropathy	3 (1.41)	1 (1.11)
Retinopathy	4 (1.88)	2 (2.22)
Diabetic Foot	5 (2.35)	1 (1.11)
Tuberculosis	3(1.41)	1(1.11)
Total	61 (28.77)	30 (33.33)

In this study, out of a total of n=212 male cases, n=25(11.79%) cases were suffering from hypertension, n=6(2.83%) cases were detected with hypothyroidism, n=3(1.41%) cases were diagnosed with Tuberculosis. In the female cases, hypertension was detected in n=15(16.67%) cases; hypothyroidism was in n=3(3.33%) cases tuberculosis was diagnosed in n=1(1.11%). The comparison of parameters between the cases with complications and those without complications is depicted in Table 5. Out of all the parameters, the duration of diabetes was an essential predictor of complication with p values of 0.01. The Fasting blood sugar levels were found to be significantly higher in the patients with complications, and HbA1c levels were also found to be higher in the cases with complications.

Table 5: Comparison of parameters between lean diabetic patients with and without complications

Parameters	Lean Diabetics with complications (n=91)	Lean Diabetics without complications (n=211)	P-value
Duration (years)	10.5 ± 1.5	3.8 ± 2.5	0.01*
BMI (Kg/m ²)	20.84±1.65	20.35±2.03	0.37
Waist-hip ratio	0.93±0.12	0.91±0.15	0.29
Systolic BP	130.33±17.42	126.72±16.35	0.11
Diastolic BP	78.16±8.75	78.37±7.58	0.83
Fasting BG (mg %)	181.92 ± 28.58	165.21± 30.72	0.02*
PPBG (mg %)	282.40 ±65.65	259.47 ± 75.35	0.25
HbA1c	10.47± 2.96	8.08 ± 2.81	0.041*
LDL (mg %)	110.26±50.13	111.88±33.93	0.83
HDL (mg %)	43.66±20.23	41.44±11.91	0.47
TSH (mIU/L)	2.24±2.54	2.08±1.78	0.72

* Significant

Discussion

In this study, n=302 were <19 kg/m² included as lean type 2 DM there were n=212 males and n=90 females. The mean age of the patients was 54.18 ± 5.5 years. The mean duration of diabetes was 50 months. The mean age of patients reported by Mukhyaprana et al. [11] was 60 years. In a similar study, Das S et al. [3] reported 48 years, and Sinharoy et al. [12] found the mean age of the patients of 47 years. In this study, the mean age of non-lean diabetes mellitus was 54.36 ± 4.5 years. Therefore, no significant difference was found between the lean and non-lean based on age. A study in the US with 18000 cohorts of type 2 diabetes found that 13% belonged to ideal body weight BMI (17 – 25 Kg/m²). However, there was no difference between lean and non-lean at the age of diagnosis, which was 43 ± 13 years. They also reported male preponderance among the lean diabetic group, which is like the results of this study. They also found that Ethnic Asians had a fivefold higher prevalence of the lean type of diabetes than other ethnic groups. [13] This study noted positive family history in patients with lean type 2

DM in 45.07% of cases. The results were in concordance with the study of Mukhyaparana et al.,^[14] They reported a positive family history in 45% of cases of lean diabetes mellitus. Gohel et al.^[13] reported a low incidence of positive family history with 20%. SIMILAR STUDY, S M Shavana et al. [16] reported a meager positive family history of 9.6% in lean type 2 DM. The mean fasting blood glucose levels in males was 182.82 ± 55.60 mg/dl and in females was 191.15 ± 60.2 mg/dl. The Post-prandial blood glucose levels were 255.84 ± 97.49 mg/dl and 267.96 ± 110.63 mg/dl for males and females, respectively, and the HbA1c values were $10.88 \pm 2.26\%$ and $9.25 \pm 1.86\%$ for males and females. PD Barma et al.,^[15] in a study of lean type 2 Diabetes Mellitus in Manipur, found lower mean fasting blood glucose of 132.5 ± 68.2 mg% and post-prandial 193.9 ± 100.1 mg%. The mean HbA1c was $7.7 \pm 2.2\%$. Shrivastav M et al.,^[16] in Western Uttar Pradesh found that in lean type 2 DM, the mean fasting blood glucose levels were 226.5 mg/dl, mean post-prandial blood glucose 282.5 mg/dl, and HbA1c values of 9.15%, respectively. The observation of fasting blood glucose levels in lean body type 2 DM was comparable to non-lean type 2 DM (Table 1). However, the post-prandial glucose levels were higher in lean type 2 DM than in non-lean type 2 DM. These observations are similar to the observations of S Das et al.^[17] These observations suggest lower insulin secretion in fasting and post-prandial states in lean type 2 DM. The daily regulation of insulin may be defective. Coleman NJ et al.^[13] have reported rapid beta-cell failure in lean type 2 DM instead of insulin resistance. This was confirmed because lean patients had a higher prevalence and early initiation of insulin use. The hyperglycemia in lean type 2 DM is due to impaired pancreatic insulin secretion.^[18, 19] This is due to decreasing beta-cell mass, demonstrated in autopsies of such cases.^[20, 21] Apart from the above, the Chicago study [13] found that the lean group had a higher prevalence of smoking, alcoholism, and pancreatitis. Chronic alcohol consumption leads to beta-cell apoptosis or beta-cell dysfunction.^[22] Because these unhealthy habits are often found in males, there is a greater prevalence of lean type 2 DM in males than in females. In this study, the mean total cholesterol was comparable between males and females. The triglyceride levels were higher in both males and females. The difference was also statistically significant. GP Chandra et al.^[23] found lean type 2 DM cases with low mean total cholesterol and higher triglyceride results agreeing with the current study. Significantly raised triglycerides in lean type 2 DM is an important observation consistent with the results of other similar studies.^[24, 25] Our study found macrovascular complications in 19.53% of all cases and microvascular complications in 7.28% of cases (table 4). Mohan et al.^[26] found a higher prevalence of microvascular complications among lean type 2 DM than non-lean type 2 Diabetic patients. Our study revealed a linear relationship in cohorts with complications and the duration of diabetes. Studies have found the prevalence of microvascular complications in lean type 2 DM based on duration and glycemic controls.^[11, 12] Singh et al.,^[27] have reported a higher prevalence of microalbuminuria in cases with diabetic retinopathy.

Conclusion

There is a considerable prevalence of lean type 2 DM in our population. These patients' clinical presentation and profile are likely to differ from expected or obese type 2 DM cases. It appears that lean type 2 DM cases suffer from more severe hyperglycemia and poor metabolic control. The increased levels of triglycerides and decreased HDL-C are some of the essential features. They are more likely to suffer from macrovascular and microvascular complications. Therefore, the appropriate therapy is required to maintain euglycemia in lean diabetics also to prevent microvascular complications.

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