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A Clinical Profile of Lean Diabetic Patients with a Special Reference to Stimulated C-Peptide Levels.

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ABSTRACT

To find out the mode of presentation of lean patients with Diabetes Mellitus, to Study the clinical profile of lean diabetics with a special reference to stimulated C-Peptide Levels and to correlate the C-peptide levels to the complications of diabetes mellitus. This prospective study was done on 50 lean diabetic patients who were selected based on BMI.(<18.5 kg/m2.). Inclusion Criteria: Diabetic patients whose Body Mass Index (BMI) is <18.5 kg/m2. Patients from age group of 30-70 years. C-peptide is measured in all the patients by CLIA method (chemical linked immunosorbant assay), 2 hours after giving 100 grams of oral glucose (stimulated C-peptide levels). Exclusion Criteria: Diabetes patients with Body Mass Index >18.5 kg/m2, Patients with protein energy malnutrition from childhood, and Pregnant women, Patient suffering from any malignancies and Patients using long term steroid therapy (or) secondary cause of diabetes mellitus. The incidence of males affected were more than females Male : Female ratio (3:2), 36 (72%) of the patients are from middle socio economic status , 35 (70%) of patients had positive family history, 38 (76%) of patients were on OHAS, out of 50 patients, 43 (86%) patients had low c-peptide levels, and 7(14%) had normal c-peptide levels , 18 (36%) patients had Diabetic Retinopathy, 17 (34%) patients had Diabetic Nephropathy out of which 9 (18%) patients had micro albuminuria and 8 (16%) patients had macro albuminuria ,18 (36%) patients had Diabetic Neuropathy. In this study most of the lean diabetics (43/50) patients had a low C-peptide levels, poorly controlled diabetes mellitus and diabetic Complications. These patients eventually required insulin for their control of diabetes.

Keywords: c-peptide levels, lean diabetics, diabetic retinopathy, diabetic nephropathy, diabetic neuropathy.

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INTRODUCTION

Type 2 DM, previously nomenclature as Noninsulin Dependent Diabetes Mellitus (NIDDM),2is the most prevalent form of DM seen in India and constitutes more than 95% of the diabeticpopulation.3 Interestingly, almost 80% of our Type 2diabetic patients are non-obese whereas 60 to 80%of such diabetics in the West are obese [1]. The build and habitus, far from being overweight, is often 'lean' or low bodyweight, i.e. more than 20% below the ideal bodyweight for height and gender [2]. In a prospective study, sponsored by the Indian Council of Medical Research (ICMR), we observed that about one fourth of our Type 2 DM patients had a body mass index (BMI) below 19, or in other words were low bodyweight/lean. Analysis of data from the 9 centres spread over India, which included three metropolises viz. Delhi, Calcutta (Kolkata), Madras (Chennai), indicated that the prevalence of Type 2 DM-Lean varied from 11 to 25%. This characteristic persisted even at the end of the study period of five years (1985-90). Therefore leanness was the inherent characteristic and not related to the diabetic state [3].

C-peptide is used to monitor insulin production and to help determine the cause of hypoglycaemia. Any insulin that the body does make will be reflected in the C-peptide levels. Therefore, the C-peptide test can be used to monitor beta-cell activity and capability over time and to determine when to begin insulin treatment. C-peptide measurement is a useful alternative to testing endogenous insulin production.

Aims and Objectives

- 50 lean patients of BMI less than 18.5kg/m^2 were included in this study.
- To find out the mode of presentation of lean patients with Diabetes Mellitus.
- To Study the clinical profile of lean diabetics with a special reference to stimulated C-Peptide Levels.
- To correlate the C-peptide levels to the complications of diabetes mellitus.

MATERIALS AND METHODS

This prospective study was done on 50 lean diabetic patients who were selected based on BMI.(<18.5 kg/m2.)

Inclusion Criteria

Diabetic patients whose Body Mass Index (BMI) is <18.5 kg/m2. Patients from age group of 30-70 years. C-peptide is measured in all the patients by CLIA method (chemical linked immunosorbant assay), 2 hours after giving 100 grams of oral glucose (stimulated C-peptide levels).

Exclusion Criteria

Diabetes patients with Body Mass Index >18.5 kg/m2. Patients with protein energy malnutrition from childhood. Pregnant women, Patient suffering from any malignancies and Patients using long term steroid therapy (or) secondary cause of diabetes mellitus.

ANALYSIS OF RESULTS

Table-1: Sexwise Distribution

Variables	Numbers	Percentage (%)
Male	30	60
Female	20	40

In my study, 30 patients (60%) were males and 20 patients (40%) were females

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Graph 1: Sexwise Distribution

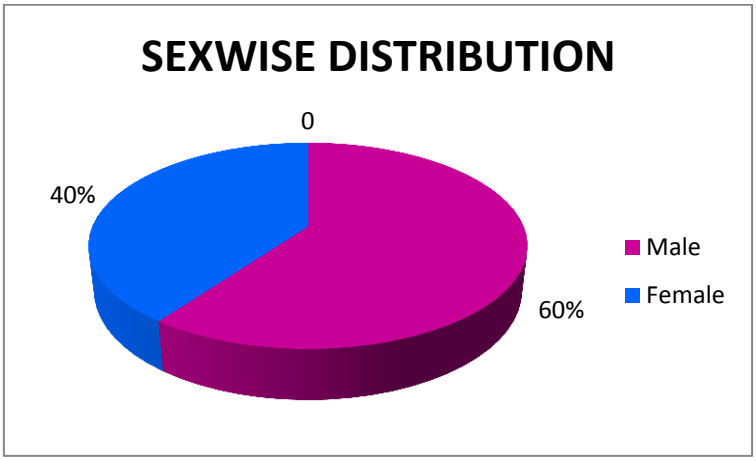

Table 2: Socio Economical Status

Variables	Numbers	Percentage (%)
Poor	14	28
Middle	36	72

Out of 50 patients, 36 (72%) patients belong to middle socioeconomic status and 14 (28%) patients belong to lower socioeconomic status.

Graph 2: Socio Economical Status

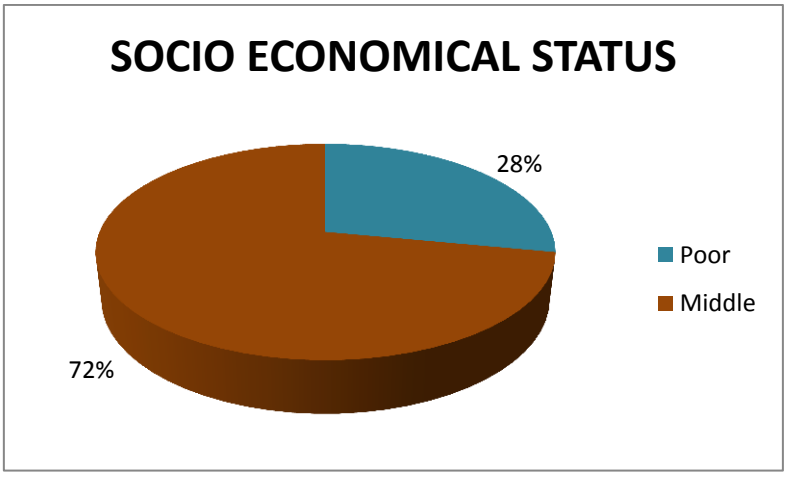

Table 3: Family History

Variables	Numbers	Percentage (%)
Present	35	70
Absent	15	30

Out of 50 patients, 35 patients (70%) had family history of diabetes mellitus.

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Graph 3: Family History

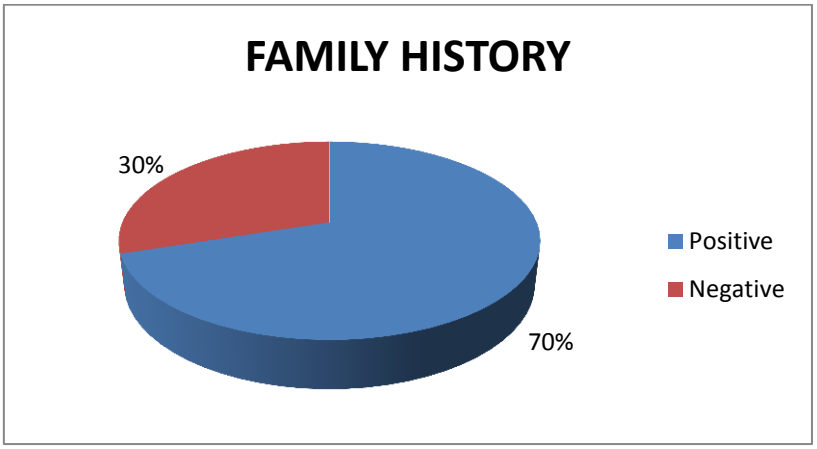

Table 4: Drug History

Variables	Numbers	Percentage (%)
None	3	6
OHA	38	76
Insulin	5	10
Both	4	8

In my study, 38 (76%) patients were on oral hypoglycemic agents, 5 (10%) patients were on insulin and 4 (8%) patients were on both insulin and oral hypoglycemic agents.

Graph 4: Drug History

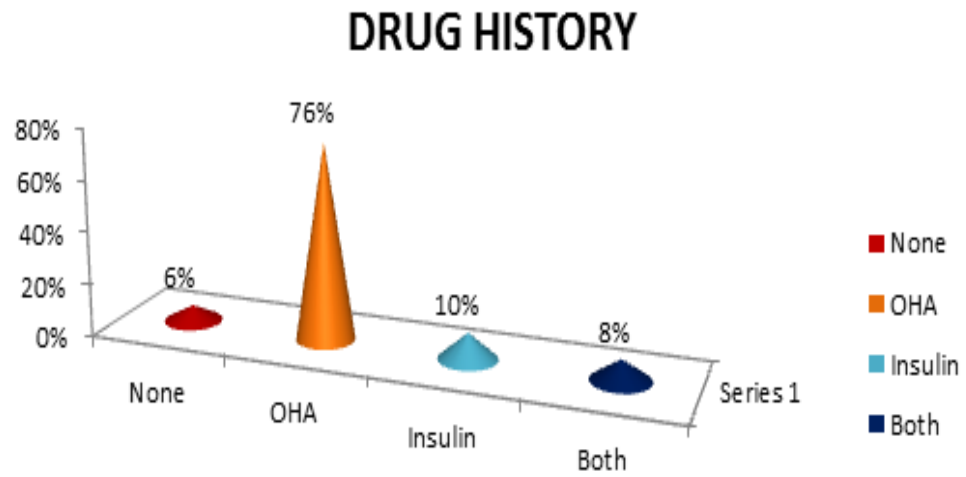

Table 5: C-Peptide

Variables	Numbers	Percentage (%)
Low	43	86
Normal	7	14

Out of 50 patients, 43 (86%) patients had low c-peptide levels, and 7(14%) had normal c-peptide levels.

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Graph 5: C-Peptide

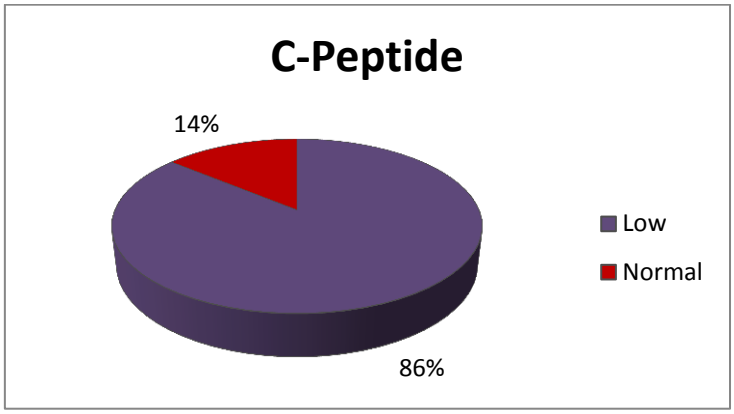

Table 6: Diabetic Retinopathy

Variables	Numbers	Percentage (%)
Present	18	36
Absent	32	64

In my study, 18 (36%) patients had diabetic retinopathy

Graph 6: Diabetic Retinopathy

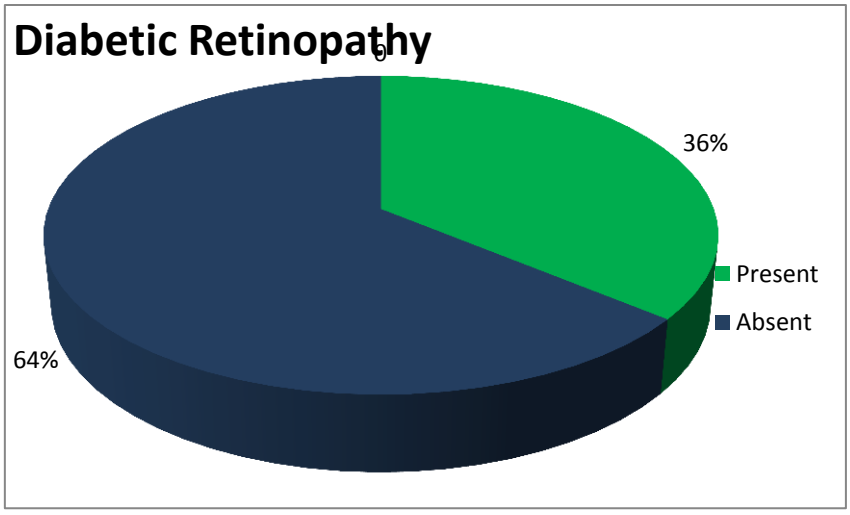

Table 7: Diabetic Nephropathy

Variables	Numbers	Percentage (%)
Micro albuminuria	9	18
Macro albuminuria	8	16
Absent	33	66

Out of 50 patients, 17 (34%) patients had diabetic nephropathy, out of which 9 (18%) patients had micro albuminuria and 8 (16%) patients had macro albuminuria.

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Graph 7: Diabetic Nephropathy

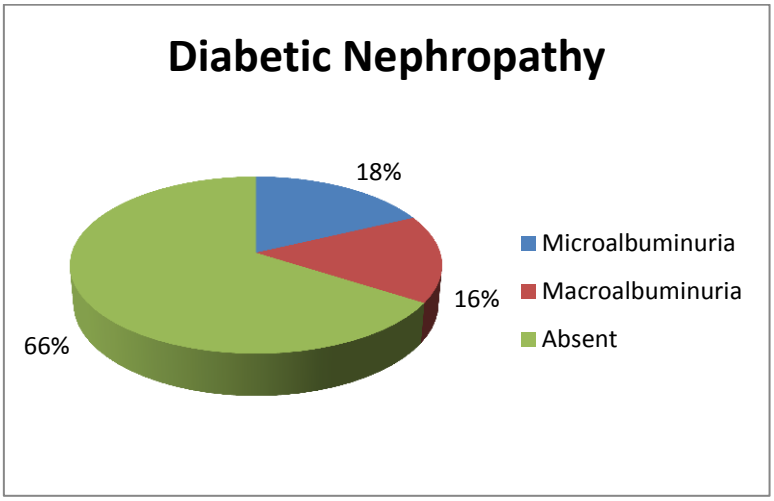
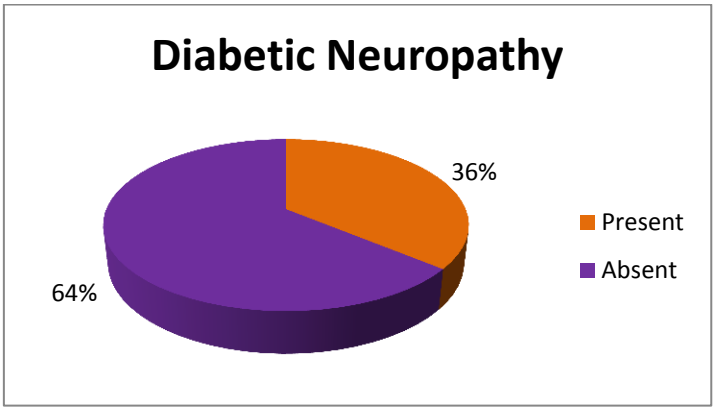


Table 8: Diabetic Neuropathy

Variables	Numbers	Percentage (%)
Present	18	36
Absent	32	64

In my study, 18 (36%) patients had diabetic neuropathy.

Graph 8: Diabetic Neuropathy



DISCUSSION

Profile of A Lean Diabetes Mellitus

In India large number of Diabetes are thin (BMI < 18.5). They manifest with different presentation, morbidity & mortality patterns as well as biochemical & hormonal profile. Lean DM is probably resulting from under nutrition and its adverse effects on β-cell function.

Some postulate that uncared poorly controlled diabetic state is the causes of leanness' is obviated by the fact that they continue to be lean even after years of good metabolic control. Incidence of lean diabetes was observed to be 11 to 25 percent in all diabetics.

Though initially for some years they may respond to oral sulphonylureas. These diabetics in due course more often become insulin requiring as compared to classical NIDDM. They may respond well to combination of sulphonylurea and insulin.

Clinical Presentation

Adult lean diabetic patients present with symptoms and signs suggestive of long standing hyperglycaemia. Peripheral neuropathy was the commonest presenting features in the lean, while hypertension and CAD were conspicuously absent in lean NIDDM.

Hormonal Changes in Lean diabetics

Circulating levels of insulin (IRI) have been found to be lower in Type 2 DM-Lean, whether fasting or post prandial, and in all studies as compared to classic Type 2 DM. Persistence of lower insulin levels had provoked many investigators to designate these diabetics as late onset IDDM/ Type 1 DM or the adult form of MRDM. But after years, these lean subjects do have substantial levels of insulin in circulation which are similar to levels seen in healthy controls in a fasted state [4, 5, 7, 9, 12, 13].

It is a well-known fact that in Type 2 DM the beta-cells and their secretory apparatus become refractory to the changing blood glucose levels owing to glucotoxicity, while retaining their responsiveness to other stimuli like non-CHO diet, amino acids, glucagon and catecholamines [23] . Even by eating a non-CHO diet or a mixed meal, which act as insulin secretagogues, one can evaluate the beta-cell reserve for insulin in different types of diabetics [24,25]. This was studied in Type 2 DM-Lean along with patients suffering from MRDM and healthy controls for comparison. They were fed with oral glucose and a diet containing low (R&C) and high arginine (S) levels. The increment in insulin glucose index following these dietary challenges (isocaloric) was highest with S in controls as well as Type 2 DM-Lean but least in MRDM [13]. This not only testified to the presence of significant insulin reserve in Lean but also differentiated Type 2 DM Lean from both MRDM and Type I DM.

Earlier studies had established that high basal levels of growth hormone (hGH) and its paradoxical rise following glucose challenge are a reasonable marker for MRDM. The same was tested in both Lean and obese Type DM and the levels of hGH were found to be at low normal values in the fasted state with hardly any change after oral glucose [22]. This not only differentiated Type 2-Lean DM from MRDM but also distinguished it as not to be influenced by chronic malnutrition as proposed to be the modulator for Malnutrition Modulated Type 1 Diabetes Mellitus (MMDM).[22] Further, in order to probe the beta-cell function and reserve in subjects with Type 2 DM, both Lean and Obese, cases were so selected that their mean age was in the mid-forties and the mean duration of diabetes more than four years. Hypoglycaemic drugs were stopped for one week before the tests. The lean Type 2 diabetics had much higher FBG levels than obese patients on withdrawal of drugs. They were subjected to insulin-secretagogues such as oral glucose and intravenous glucagon on different occasions. The response to glucagon was much higher than that for oral glucose in both groups, yet the IRI levels were persistently lower in the Type 2 DM-Lean at all stages . On the contrary the C-peptide levels were surprisingly similar , suggesting a good beta-cell reserve in the Lean with probably excess extraction of insulin in the porto-hepatic circulation leading to lower levels of circulating insulin. Studies on insulin and C-peptide levels in Type 2 Lean diabetics both at fasted and post-stimulation states, also yielded similar results at other centers when compared with classic Type 2 DM.[9, 12, 29] Studies done on C-peptide levels at different places in India ,have revealed good beta-cell reserve in Type 2 DM-Lean on par with other Type 2 DM which happens to be complementary to earlier reports.[9, 22] This finding corroborated well with our concomitant observation that Type 2 DM-Lean patients have hyperactive futile cycles of CHO metabolism in the liver , an excess of glucokinase activity which could be responsible for excess insulin utilization in the liver. Disparity between circulating levels of insulin and C-peptide, more so in the post-stimulated state, can be reasonably considered as a marker for Type 2 DM-Lean.

Serum insulin levels are lower both during fasting and fed state compared to obese and normal weight DM. C-peptide response to glucose was there. Lean DM also show low normal values of growth hormone at basal state.

C - Peptide

The connecting peptide, or C-peptide, is a short 31-amino-acid protein that connects insulin's A-chain to its B-chain in the proinsulin molecule[25]. C-peptide has been found to be a bioactive peptide in its own right,

with effects on micro vascular blood flow and tissue health. C peptide also has been reported to have anti-inflammatory effects as well as aid repair of smooth muscle cells.

USES

- Newly diagnosed diabetes patients often get their C-peptide levels measured as a means of distinguishing type 1 diabetes and type 2 diabetes.
- Differential diagnosis of hypoglycaemia. Insulin intake vs. hypoglycaemic medication OD, where it will be decreased in the former (endogenous synthesis shut off) and increased in the latter.
- C-peptide is also used for determining the possibility of gastrinomas associated with Multiple Endocrine Neoplasm syndromes (MEN 1).
- C-peptide levels are checked in women with Polycystic Ovarian Syndrome (PCOS) to determine degree of insulin resistance.

INTERPRATATION OF C PEPTIDE LEVELS

Low test result values

- Low levels of c-peptide and high blood glucose levels could be an indicator of type 1 diabetes.
- Low levels of both c-peptide and blood glucose could indicate liver disease, a severe infection or Addison's disease.

High test result values

- High levels of c-peptide with a low level of blood glucose could be an indication of insulin resistance, either type 2 diabetes or Cushing's syndrome.
- High levels of c-peptide but low blood glucose levels may be a result of insulinoma (a tumour of the pancreas) unless glucose lowering medication has influenced the result.

CONCLUSION

- The prospective study titled clinical profile of lean diabetics with special reference to stimulated C-peptide levels was conducted
- The incidence of males affected were more than females. Male: Female ratio (3:2)
- Most 36 (72%) of the patients are from middle socio economic status.
- Most 35 (70%) of patients had positive family history.
- Most 38 (76%) of patients were on OHAS.
- Out of 50 patients, 43 (86%) patients had low c-peptide levels, and 7(14%) had normal c-peptide levels
- 18 (36%) patients had diabetic retinopathy
- Out of 50 patients, 17 (34%) patients had diabetic nephropathy, out of which 9 (18%) patients had micro albuminuria and 8 (16%) patients had macro albuminuria
- 18 (36%) patients had diabetic neuropathy.

In this study most of the lean diabetics (43/50) patients had a low C-peptide levels, poorly controlled diabetes mellitus and diabetic complications. These patients eventually required insulin for their control of diabetes.

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