Review Of Literature
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Low body weight type-2 DM is clinical subtype of type-2 DM and is characterized by low body weight i.e., BMI 18.5 Kg/m². They manifest with visible different presentation, morbidity & mortality pattern as well as biochemical profile when compared with classical patient of type-2 DM.

The onset of diabetes is insidious with varieties of somatic complaints and loss of general well being. All are not poor and some belong to upper middle class society. Leanness is an inherent characteristics of these individuals. Good metabolic control had little influence on their constitution, natural history or morbidity. These diabetics in due course, more often become insulin require as compared to classical type-2 DM patients\textsuperscript{17,18,19,20,21,22,23}. These clinical characteristics biochemical profile, hormonal status and other features has been assessed by different worker as.

1. Tripathi BB and Kar B.C\textsuperscript{14}

Tripathi and Kar in their premium publication on clinical type of diabetes in India way back in 1965, had reported that as high as 28 percent of adult onset diabetics were underweight. The said article had focussed on the relationship of malnutrition and presentation of diabetes, more so in the young with special emphasis on malnutrition related diabetes mellitus. Thus for past these adult onset diabetics were variously nomenclatured as under weight, under nourished, lean and even non obese by different authors.
However, the International workshop\textsuperscript{15,16} on type of diabetes peculiar to tropics gave these diabetics the defined nomenclature of low body weight as they were neither malnourished nor the loss of weight could be attributed to the prevalent metabolic state\textsuperscript{20}.

2. A.K. Baliareshinha and Siddarth Das\textsuperscript{13,23,24}

On the basis of their study as 380 patient of type-2 DM recruited consecutively, 91 (23\%) had BMI \leq 18.5 \text{ kg/m}^2 and fall over a period of two consecutive years.

They observed that more than 80\% of patient with LB type-2 DM were from the middle socio-economic class. In India middle class constitutes about 50\% of the population and these type of type-2 DM was probably the real representation of DM prevalent in such society.

Family history of DM could be ascertained in 16.5\% of such patients which is much higher than any form of malnutrition related diabetes mellitus of type-1 DM.

LB type-2 diabetics had much lower WHR and there was strong positive correlation between BMI and WHR suggesting that leanness as well as levels of central obesity were expression of a common underlying mechanism.

These LB type-2 diabetic patients presented with long standing Hyperglycemia without ketosis suggesting endogenous insulin reserve that prevent ketonebody production but are unable to prevent hepatic glucose suppression.

In these series PN was the commonest presenting feature followed by Tuberculosis, Skin or Fungal infection. On the other hand hypertension, CAD weir less common in comparison to obese or standard weight type-2 DM.
Glycemic status in majority of LB type-2 DM patient (80.5%) were controlled with OHA and only few (16%) required insulin or insulin & OHA both (4.5%). Initial response to OHA in majority of cases, indirectly denote that the LB type-2 DM patient had good β cell reserve and lack of insulin resistance. Both cholesterol & triglycerides were low or normal with a higher HDL values which could contribute to lower incidence of macro vascular disease in LB type-2 DM.

The basal IRI values in LB type-2 DM, despite more severe hyper glycemia was significantly lower than obese type-2 indicates that the LB patient are more insulinopenic or had decreased beta cell reserve.

The most significant finding of this study was that, although the basal, post glucose and post glucagon values of IRI were significantly lower in the LB type-2 DM there were no statistical difference in the corresponding C-peptide levels. Thus the β cell reserves of insulin and its response to secretagogues, both glucose and non-glucose, were identical in their two group which testified that they are classical type-2 diabetic patient. Yet gross disparity in the C-peptide versus IRI levels in the peripheral circulation requires explanation. The most plausible mechanism is inappropriate extraction of insulin by the liver in the LB compared to obese type-2 DM\textsuperscript{25}.

3. \textit{Anant Nigam}\textsuperscript{26}

This study was carried out at a diabetes center in North West India, the 1689 consecutively registered type-2 DM patient 167 (9.8%) of LB type-2. The majority of them had onset of disease at age of 30 yr as after had no ketone urea at diagnosis and did not need
insulin treatment at diagnosis. Of these 27% of LB type-2 DM patient were having central obesity as shown by increased WHR, suggested that central obesity is also probably a pointer that these patients are group of type-2 DM patients\textsuperscript{27}.

4. Mohan et al\textsuperscript{10,12,28}

This study was conducted in a sub set of low body weight type-2 DM for presence of GADA and ICA. GADA were present in 10% of low body weight patient compared to a frequency of 5% in normal weight and 4% in obese type-2 diabetics. The frequency of ICA was 0% in low body weight 13% in normal weight and 7% in obese diabetics respectively. This data suggest that islets antibody were not more frequent in low body weight type-2 DM compared to diabetics with higher BMI.

5. Ram Chandran et al\textsuperscript{29,30}

They had revealed that GADA have low positivity and lower sensitivity with regard to prediction for insulin requirement in Indian type-2 diabetics. The prevalence of autoantibodies in type-2 DM was low so also its predictability to determine insulin requiring state in such diabetics was statistically of no consequence.

6. K. Kanan and A.J Arirratham\textsuperscript{11,31,32}

In this study peak C-peptide response measured in the small groups of type-2 and type-1 subjects revealed typical finding which are the basis of categorization of LB type-2 subject as distinct entity.

LB type-2 diabetics did not have much insulin resistance but C-peptide output was the least of the three categories but much higher than type-1 diabetes.
They finally concluded that the absence of any strong family tendency and a strong male preponderance of cases make it possible that LB type-2 DM is in same way different from the other subjects with type-2 disease. The low incidence of hypertension and severe dyslipidemia can also be explained by low BMI and absence of hyperinsulinemia in these diabetics ECG and clinical of LHD is low at 12%.

The absence of evidence for any degree of insulin resistance in these diabetics conveys a message that biguanides and/or other insulin sensitizers are not going to have much therapeutic advantage in them. It is unlikely that chronic infective condition like tuberculosis might have contributed to the loss of weight as the incidence of tuberculosis is lower than what is seen in other type-2 diabetics.

7. Alok Patnaik, Sidhartha Das & B.K. Patniak\textsuperscript{33}

Current knowledge reveals that HGU is usually normal in type-2 diabetics while HGO is high due to hepatic insulin resistance [lead to repression of key hepatic glycolytic enzymes and depression of glucogenic enzymes] and less of futile cycles of carbohydrate metabolism taking place with in the hepatocytes\textsuperscript{34,35} Leading to decreased trapping of insulin by liver causing excess liberation of insulin into systemic circulation leading to hyper insulinemia\textsuperscript{36}

LB type-2 diabetic have moderately severe to severe basal hyperglycemia. According to Das there was a negative correlation between FBG and BMI which negated the likely possibility of insulin resistance in the peripheral tissue and hence glucose handling of the liver by LB type diabetics demands special attention. But low circulating levels of insulin is an universal observation\textsuperscript{37}. This indicate
that hyperactive metabolic state observed in the liver of these diabetics having low body weight is probably an inherent characteristic in them which is responsible for excess utilization of insulin during it first pass. There is probably excess extraction of insulin in the portohepatic circulation leading to lower levels of circulating insulin. This may be due to excessive futile cycle of carbohydrate metabolism in the liver.

The LB type-2 diabetics had the highest FBG vis a vis highest circulating levels of glucokinase suggests excess of futile cycles of carbohydrate metabolism in liver especially inter conversion of glucose to glucose phosphate and again back to glucose. The reconverted glucose is liberated into the circulation causing excess rise of hepatic glucose output.

8. UK PDS\textsuperscript{38,39}

In UKPDS cohort of 3672 patient 10% newly diagnosed NIDDM patient were positive for ICA and 6% for GADA. The frequency of ICA and GADA were higher in those with an younger age at onset. Most importantly ICA or GADA positive patient require insulin earlier and more frequently than patient negative for antibodies. In UKPDS report among patient less than 35 years of age at onset with GADA or ICA positively lead to an insulin requirement in 84% and 94% of NIDDM individuals by 6 yrs. Thus GADA may be a better predictor of insulin requirement than other clinical (low BMI) or biochemical (C-peptide levels) parameters.
9. Tuomi et al\textsuperscript{40,41}

On the basis of study in Finland reported that 9.3% of the type-2 DM patients were positive for GADA. In contrast to GADA the frequency of IA-2 antibodies directed against the antigen tyrosin phosphates are in frequent in type-2 diabetics. They detected IA-2 antibodies in only 17% of GADA positive individuals and in 0.5% of those in whom GADA was absent.


They evaluated 72 North Indian type-2 DM patient and reported a prevalence of 25% for GADA which was similar to prevalence in type-1 DM patient. While only 4% of type-2 diabetes mellitus were tyrosine phophatase (IA-2) positive Vs 22% of type-1 DM. Thus IA-2 antibodies are likely to be better discriminator of type-1 & type-2 DM.

In visible absence of ICA in low body weight type-2 diabetics with fairly preserved C-peptide level and reserve suggest that they are immunologically classical type-2 diabetics and not slowly evolving type-1 DM\textsuperscript{43}

11. Irivin et al\textsuperscript{44,45}

According to them GADA may be a better predictor of insulin requirement in type-2 DM patient than other clinical low BMI or biochemical C-peptide level parameters. Patient having secondary failure to OHA were likely to be positive for GADA or ICA\textsuperscript{46}

12. Siddartha Das and Baruna Mishra\textsuperscript{48}

They took 146 newly diagnosed and untreated cases of type-2 DM without any other major illness and were recruited for the evaluation of dietary habit and its impact on metabolic profile. Detailed dietary counseling was done. The LB were asked to
increase intake by more than 350 Kcal/day while obese were asked to cut down their intake by 900 Kcal/day. During follow up marginal improvement in mean BMI was observed in low body weight subjects.

From the dietary and nutrition point of view the best balanced were the standard weight subject. The alteration and influences of dietary components in the over weight diabetics was similar to most of the international data with negative influence of carbohydrate diet on blood glucose. In LB type-2 group an inherent defect for carbohydrate handling was obvious. Both over weight and low body weight type-2 diabetics probably represent the two end of the U shaped curve with regards to the metabolism and blood glucose levels\textsuperscript{49}.

13. S. Banerjee and U.K. Pal\textsuperscript{11,32,47}.

They selected 75 cases of type-2 DM (25 cases of lean 25 cases of non obese and 25 cases of obese) after exclusion hepatic endocrine cardiorespiratory and other systemic diseases.

This study revealed a male predominance (3:2) amongst LB type-2 DM. The mean age of presentation was in mid forties and most were presented with usual symptoms. The prevalence of family history was much higher. These LB type-2 DM were not restricted to a poor socioeconomic status but were more from rural areas as compared to non obese and obese subject FBG in the LB type-2 was not statistically different from either non obese or obese type-2. The fasting C-peptide levels were lower than those in other two groups of diabetics, which suggest that level of fasting hyper insulinemia. But the rise in the plasma level of C-peptide was much more brisk than the latter group, following diet intake near normal C-peptide levels vis
a vis basal hyperglycemia is an important characteristic of LB type-2 diabetics. Probably serve as a marker for the low circulating levels of insulin with fairly preserved β cell reserve. Therapeutically a large number of LB subjects respond well to oral hyper glycemic agent.

14. G.R.Sridhar, S.Veena, K.Madhu\textsuperscript{50,51}

In this study characterized the clinical profile of a group of LB type-2 and evaluated the quality of life well being and psychological adjustment to diabetes. They conducted similar clinical profile to other study but LB type-2 DM had a higher prevalence of sleep disturbance than other group. Finally they scored lower on quality of life well being psychological adjustment to diabetes scales compared to non lean type-2 diabetics. Thus the common phenotype runs through in patients with LB type-2 DM who have a poor quality of life than their peer’s. They therefore need appropriate evaluation and extra attention for better management.


In their study they observed that mortality amongst hospitalized patient with non insulin dependent diabetics mellitus (NIDDM) was 20%. Major causes of mortality are cardio vascular accident, Ischemic heart diseases & infections.

16. Siddartha Das, E.A.Sotaniemi, A.K. Baliarsinha and A.Rautia\textsuperscript{53,54,55}

They interpreted that, the LB Type 2 diabetics seen in India not only have hyperactive hepatic metabolic state but such metabolic process is inherent to them and not influenced by other co-existence factors. The hyperactive hepatic metabolic state is very likely
responsible for excess extraction / trapping of insulin during its first pass which consequently leads to low circulating insulin levels. This reasonably explains the insulin-C peptide disparity observed in LB Type 2 diabetics. Such metabolic activities causes excess of futile cycles which not only dissipate energy, utilize insulin but causes raised FBG levels.


Glycosylated haemoglobin (HbA_{1c}) is formed by the addition of a molecule of glucose to the N-terminal valine of one or both beta chains of adult haemoglobin by a spontaneous and non-enzymatic reaction. Apart from diabetes, HbA_{1c} is altered in many physiological and pathological states like pregnancy, iron deficiency anaemia, haemochromatosis and renal failure.

In renal failure, shortened life span of erythrocytes is well known and low levels of HbA_{1c} are expected^{1}. On the other hand a raised HbA_{1c} is possible because there occurs a disordered carbohydrate metabolism in renal failure. While a majority of workers have noted increased levels of HbA_{1c} in chronic renal failure (CRF), the rise being more pronounced in diabetic nephropathy, some demonstrated decreased levels.

They concluded that glycosylation of haemoglobin is influenced by glycemic status as well as shortened life span of erythrocytes in renal failure. Thus decreased HbA_{1c} is possible in both diabetic and non-diabetic renal failure. One must be cautious in interpreting the glycosylated haemoglobin values as an indicator of diabetic long term control in the presence of renal failure.
18. K.C. Samal, Sidhartha Das, C.R. Parija, B.B. Tripathy\textsuperscript{60,61,62}

They concluded that C-peptide has no biological activity. In the serum of normal subjects C-peptide is much higher than proinsulin and its intermediates. Proinsulin reacts less well than C-peptide with C-peptide antiserum. Direct assay of total serum CPR in normal subjects represents mainly C-peptide level. Hence it is justified to presume that the value of CPR is very close to C-peptide level, particularly in insulin deficient diabetics in whom the proinsulin level in circulation is negligible. Further we selected patients who were not on insulin therapy, thus excluding the possibility of any interference by exogenous proinsulin.

As anticipated, plasma levels of glucose were remarkably higher following oral glucose than mixed meal and values of IRI both basal as well as in response to glycemic stimuli, were low in both group of patients. Inspite of this there was no significant difference in the IRI level following glucose are mixed meal in either group of patients suggesting poor insulinogenic reserve. The mean CPR level observed in the present study are lower than those reported from the west, both at basal and one hour after oral glucose. This is consistent with our previous observation of low insulin level in the local population. Result of this study indicates that residual B cell function, although adequate to maintain near normal basal CPR level in freshly detected case of FCPD, appear to be grossly insufficient to raise hormone production appropriately in response to glycemic stimuli. It was further observed that although the difference between the rise of IRI following mixed meal and oral glucose was not statistically
significant in normal controls the difference in the corresponding CPR values was highly significant (P < 0.01). This suggests that CPR is a better indicator of B cell performance than plasma insulin, passively due to insignificant trapping of C-peptide level in the liver. In freshly detected case of IDDM on the other hand lower level of CPR suggest that B cell function compromised even in the basal state. Yet, definite rise in C-peptide value following both oral glucose and mixed meal indicate presence of certain quantum of residual β cell activity. It is well known that most of these patients ultimately develop complete loss of β cell function in course of time. The remarkably lower incidence of ketosis in FCPD as compared to IDDM may be an account of better residual β cell function as indicated by higher CPR level at basal state and in response to glucose challenge. However, the relatively lower difference in the peripheral IRI levels of these two groups of diabetics can be explained by the well known fact that a larger proportion of insulin (70-90%) is trapped by the liver in diabetics.