

## Significance of C – Peptide in Type 2 Diabetics - A Study in the North Karnataka Population of India

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### Abstract

*Back ground:* Type II DM is a metabolic cum vascular disease and the burden of diabetes is its complications. It is imperative to address the basic biology of diabetes and not to simply treat the symptom complex.

*Aims and methodology:* 1. To estimate the c-peptide levels in elderly diabetics to assess the endogenous insulin secretor function. 2. To know the correlation between obesity and insulin secretion. 3. Modification of treatment in poorly controlled diabetes.

The cross sectional study was done in the diabetic outpatient clinic of a tertiary care hospital from Dec 2007 to May 2009. 75 type 2 diabetic patients were evaluated with their fasting plasma glucose, fasting c-peptide levels, HbA1c and BMI. Statistical analysis was done by chi square test and correlation. *Results:* The fasting c-peptide levels in the obese patients were increased compared to the non obese individuals, indicating insulin resistance. The fasting plasma glucose levels were elevated despite elevated c-peptide levels in the obese patients, proving the role of insulin resistance. The levels of HbA1c were increased more in obese patients indicating poor glycaemic due to insulin resistance. The fasting c-peptide levels decreased as the duration of diabetes increased. *Conclusion:* The fasting c-peptide levels are useful in type 2 diabetic patients with poor glycaemic control to assess the endogenous insulin reserve and to alter the modality of treatment. Very low c-peptide level indicates need for insulin treatment, and poor prognosis due to poor insulin reserve.

**Key words:** Type 2 DM, fasting c-peptide levels, HbA1c, insulin resistance.

### Introduction

Type II Diabetes mellitus results from combination of insulin resistance and inadequate secretion of insulin [1]. Nearly 90% fall in type II diabetes mellitus. Type II DM is a major health problem worldwide[2]. Its development can be prevented in many instances[3] and persons at risk can be identified with few common risk factors. A family history of diabetes, an increase in body mass index and impaired insulin secretion and action are important risk factors[4]. South Asians have a one in three lifetime risk for the development of diabetes, developing the condition ten years earlier than Europeans. India has the highest number of patients with known diabetes worldwide, with a prevalence of 11.6% in urban areas. One in three of 50 to 59 year old Indian is having diabetes. The only way to avoid is by early screening and effective management of people who are at risk of developing type II DM. For patients newly diagnosed with type II DM, early and aggressive intervention strategies that combine maximal glucose lowering efficacy along side potential cell preserving properties may provide an opportunity to delay or prevent progression of the disease [5]. The great interest in C-peptide is due to the limitations of the use of serum insulin as a measure of insulin secretion. After its secretion in to the portal vein, insulin passes through the liver where approximately 50% of the insulin delivered is extracted[6]. Peripheral insulin concentrations therefore reflect post hepatic insulin delivery rather than the actual secretory rates of insulin. Until the

development of C-peptide assays, evaluation of  $\beta$  cell function in insulin treated patients was impossible as the insulin assay is unable to discriminate between secreted and injected insulin. Further C-peptide determinations are disturbed to a lesser extent than insulin measurements by the presence of insulin binding antibodies. With the advent of newer drugs to overcome insulin resistance it has become all the more important to know about the pathophysiology of diabetes, whether endogenous insulin secretion is normal and to know about insulin resistance. Keeping this perspective in mind, this study was conducted to assess the endogenous Insulin secretory function in a randomised sample of patients with type II diabetes attending the Out patient clinic.

### Materials and Methods

*Selection of Cases :* A random sample of 75 patients, who attended the diabetic OP clinic were studied. Patients already taking oral hypoglycaemic agents were asked to stop the drugs for 3 days. The patients were asked to come in the fasting state. Venous blood samples were withdrawn in the fasting state, and fasting blood glucose levels, HbA1c and C-peptide levels were estimated.

*Inclusion Criteria:* a) Patients labelled as type 2 diabetics. *Exclusion Criteria:* Patients with Type 1 Diabetes. a) Patients with acute infections, renal failure, and pregnancy were excluded from the study.

The venous blood samples were withdrawn at the out patient department where the patients attended for follow up. The blood samples were taken in the fasting state. The patient's treatment was modified according to their fasting c-peptide level in their next visit. They were followed up with FBS level, for assessing glycaemic status after modification of the treatment. CLIA was used in this study to estimate the fasting c-peptide level. The c-peptide CLIA is a solid phase two-site immunoassay. Blood was collected using standard venipuncture without any anticoagulant, and the serum separated. Affinity separation method was used in this study. Blood samples collected with anticoagulant were used.

BMI was calculated by dividing the Weight in Kg and the square of the Height in meters.

$$\text{BMI} = \text{Wt in kgs} / \text{Ht in m}^2.$$

**Results:**

Table 1: Age wise distribution of the study subject

Age	Number of Patients	Percentage
30-39	10	13
40-49	26	35
50-59	32	43
60-69	7	9
	75	100

Table-1 shows that out of 75 patients with type 2 diabetes mellitus in the present study, a maximum of 32 (43%) patients were between the age groups of 50-59 years, followed by 26 (35 %) patients in the age group of 40-49 years. 10 (13%) patients out of 75 study patients were in the age group of 30-39 years.

7(9%) were in the age group of 60-69 years. Mean age group in present study was  $49.2 \pm 7.239$

Table 2: Sex wise distribution of the study subjects

Sex	Number of patients	Percentage
Male	33	44
Female	42	56
	75	100

The Table-2 shows that out of 75 patients of type 2 diabetes, 42 (56%) patients were females, while 33 (44%) were males. The male: female ratio in the present study with type 2 diabetes mellitus was 1.28:1.

Table 3: Distribution of study subjects based on Duration of diabetes

Duration	Number of patients	Percentage
< 5yrs	62	83
$\geq$ 5yrs	13	17
	75	100

The Table-3 shows the duration of diabetes in our study population of 75 patients. In this present study, the number of type 2 diabetic patients with duration < 5 years was 62(83%), while that with > 5 years duration was 13(17%).

Table 4: Presence of Family History in type 2 diabetes

Family history	Number of patients	Percentage
Present	48	64
Absent	27	36
	75	100

Table 4 shows that out of 75 patients with type 2 diabetes in our study, the numbers of type 2 diabetic patients with positive family history for diabetes was 48 (64%) and those with negative family history was 27(36%) patients.

Table 5: Distribution of type 2 diabetics based on BMI

BMI	Number of patients	Percentage
<25	46	61
≥25	29	39
	75	100

Table 5 shows that out of 75 patients with type 2 diabetes in the present study, 46 (61%) patients were non-obese and 28 (39%) were obese individuals. Those with Body mass Index of  $\geq 25$  were considered obese and those with BMI of  $< 25$  are considered non-obese. The mean BMI of the study was  $23.792 \pm 3.439$ .

Table 6: Fasting c-peptide levels in type 2 diabetics

Fasting CP	Number of patients	Percentage
<0.1	2	3
0.1-0.5	2	3
0.6-0.9	19	25
1-2	39	52
≥2	13	17
	75	100

The Table 6 shows the levels of fasting c-peptide in the present study. Out of 75 patients, 39 (52%) patients had fasting c-peptide levels between 1 – 2 ng/ml, 19(25.4%) patients had fasting c-peptide levels between 0.6-0.9 ng/ml and 13 (17.3%) patients had  $> 2$  ng/ml. Only 4 (5.3%) patients had  $< 0.6$  ng/ml. The mean fasting c-peptide level of the study was  $1.315 \pm 0.811$ .

Table 7: HbA1c levels in type 2 diabetics

Hb A1c	Number of patients	Percentage
7.5-9.0	28	37
>9	47	63
	75	100

In the present study of 75 patients with type 2 diabetes, the number of patients with HbA1c levels between 7.5-9.0 were 28(37%) and those with levels > 9 were 47(63%). So the number of patients was more in the group with HbA1c levels > 9.0. The mean HbA1c level of the study was 9.585±0.939.

Table 8: Fasting blood sugar(FBS) levels in the study population

FBS	Number of patients	Percentage
<200	19	25
200-250	42	56
≥ 250	14	19
	75	100

Table 8 shows that out of 75 patients in the present study with type 2 diabetes, 42(56%) patients had fasting plasma glucose level between 200-250 mg/dl, 19(25%) patients had < 200 mg/dl and 14(19%) patients had ≥ 250 mg/dl. So the study shows that majority of the patients (42) patients had fasting plasma glucose levels between 200-250 mg/dl. The mean plasma glucose level of the study was 222.92±29.11.

Table 9: BMI and fasting c-peptide levels

BMI	FASTING C-PEPTIDE					Total
	<0.1	0.1-0.6	0.6-1.0	1.0-2.0	> 2.0	
< 25	2	2	17	24	1	46
≥ 25	0	0	2	15	12	29
	2	2	19	39	13	75

Pooled  $\chi^2 = 24.485$  P=0.000

The table 9 shows that out of 75 patients with type 2 diabetes, the number of patients with BMI ≥ 25 was 29(39%). Out of these 29 patients, 15(51.8%) patients had fasting c-peptide level between 1.0-2.0 ng/ml, 12(41.3%) patients had fasting c-

peptide levels > 2 ng/ml. Out of the 29 patients, 27 had adequate or higher fasting c-peptide level. Only 2(6.9%) patients had levels < 0.6 ng/ml.

It also shows that out of 46 non obese patients, the c-peptide level was between 0.6-1.0 ng/ml in 17(36.9%) patients, 1-2 ng/ml in 24(52.2%) patients and > 2 ng/ml in 1(2.2%) patient. The fasting c-peptide level of < 0.6 ng/ml was seen in 4(8.7%) patients, indicating poor insulin reserve. Table 9 shows that as the BMI value of the patient increases, the fasting c-peptide level also increases. The number of patients with fasting c-peptide levels > 2 ng/ml was 13 and was seen mainly in the obese (12) patients as compared to non-obese.

Similarly low levels of fasting c-peptide < 0.6 ng/ml was seen in 4 patients of the non-obese group. This indicated that there was very low insulin production.

The table 9 shows that the BMI values and the levels of fasting c-peptide (p=0.000) were highly associated. The correlation was found to be moderately positive (r=0.558) (p=0.000), indicating that as the BMI increases the fasting c-peptide levels increases, though not in a linear fashion.

The mean fasting c-peptide levels of the non-obese in the present study is 0.825±0.512, while that of the obese is 1.886±0.657. Thus the level of fasting c-peptide is highly associated with BMI (t=6.41, p=0.000).

Table 10: BMI and FBS

BMI	FBS			Total	Test value P value
	<200	200-250	≥250		
<25	19	25	2	46	X <sup>2</sup> =25.103 P=0.000
≥25	0	17	12	29	
	19	42	14	75	

Table 10 shows that in the study population of 75 patients, 46 patients were non obese and their fasting plasma glucose value was, 200-250 mg/dl for 25 patients, < 200 mg/dl for 19 patients, and ≥ 250 for only 2 patients. So majority had their fasting plasma glucose values < 250 mg/dl. In the obese group of 29 patients, all of them had fasting blood glucose value above 200 mg/dl. 17 patients had value between 200-250 mg/dl and 12 patients had value above 250 mg/dl.

Thus above observations suggest that there was strong association between the fasting blood sugar levels and BMI (p=0.000). The correlation between FBS and BMI was moderately positive(r=0.547) (p=0.000).

Table 11: Fasting c-peptide and FBS

Fasting cp	FBS			Total	Test value P value
	<200	200-250	≥250		
<0.1	0	2	0	2	χ <sup>2</sup> =19.78 p=0.05
0.1-0.6	0	2	0	2	
0.6-1.0	6	12	1	19	
1-2	13	21	5	39	
≥2	0	5	8	13	
	19	42	14	75	

Table 11 shows that out of 75 patients, those with fasting c-peptide level <0.6ng/ml, were having fasting blood glucose level between 200-250 mg/dl. Out of 58 patients with fasting c-peptide levels between 0.6 – 2.0 ng/ml, 33 patients had fasting blood glucose level between 200-250 mg/dl, 6 patients had ≥ 250 mg/dl. Only 19 patients had fasting blood glucose levels < 200 mg/dl.

The table also shows that those with fasting c-peptide levels > 2ng/ml, instead of having lower FBS levels had elevated FBS level above 200mg/dl. 8 patients out of the 13 had ≥250 mg/dl of FBS. The observations suggest that fasting c-peptide levels and FBS were moderately associated (p=0.05). They were moderately positively correlated (r=0.532) (p=0.000).The positive correlation indicates that as the fasting c-peptide level increases, the FBS level also increases, but not in a linear fashion.

Table 12 a: Duration of diabetes and fasting c-peptide

Duration Yrs	Fasting c-Peptide					TOTAL
	<0.1	0.1-0.6	0.6-1.0	1.0-2.0	≥2	
<5	1	0	15	33	13	62
≥5	1	2	4	6	0	13
	2	2	19	39	13	75

χ<sup>2</sup> = 14.041    p=0.01

Table 12a shows us that out of the 62 patients studied with duration < 5 years, 33 had fasting CP level between 1.0-2.0 ng/ml while 13 had fasting CP level > 2.0 ng/ml. only 1 patient had fasting CP level <0.6 ng/ml.

In the group of 13 patients with duration  $\geq 5$  years, 3 patients had fasting CP level  $<0.6$  ng/ml, while 10 patients had fasting CP level between 0.6-1.0 ng/ml. None of the patients in this group had fasting CP level  $> 2.0$  ng/ml.

Thus the observation of the above table indicate that there is an association between duration of diabetes and fasting c-peptide level ( $p=0.01$ ). The association was moderately negatively correlated ( $r = -0.258$ ) ( $p=0.025$ ), as p value is significant. Hence as the duration of diabetes increases, the fasting c-peptide level decreases, but not in a linear fashion.

Table 12 b: Comparison of fasting c-peptide based on duration

Duration of DM	No. of Patients	c-peptide Mean $\pm$ S.D	Test applied
$< 5$ years	62	1.442 $\pm$ 0.807	Z=3.23
$\geq 5$ years	13	0.878 $\pm$ 0.510	P=0.003

The above table compares the mean fasting c-peptide level of patients with duration  $< 5$  years and those with duration  $\geq 5$  years by Z test, which shows that they are associated and it is highly significant ( $p=0.003$ ). The Mean  $\pm$  S.D of fasting c-peptide level is lesser in the group with duration of DM  $\geq 5$  years (0.878 $\pm$ 0.510).

Table 13: BMI and HbA1c

BMI	HbA1c		Total	Test value
	7.5-9.0	$>9.0$		
$<25$	25	21	46	$\chi^2 = 14.721$
$\geq 25$	3	26	29	P = 0.000
	28	47	75	

The above table shows that out of 75 study patients, 46 patients have BMI  $< 25$ . Of these 46 patients, 25 have HbA1c levels in the range of 7.5-9.0, while 21 have HbA1c levels  $> 9.0$ . In the obese group of 29 patients, 26 patients have elevated HbA1c level of  $> 9.0$ , while only 3 have levels  $< 9.0$ . The observations of the above table suggest that there is significant association between the levels of HbA1c and BMI ( $p=0.008$ ). The association is moderately positively correlated ( $r=0.303$ ).



## Discussion

In our present study population of 75 patients labelled as type 2 DM, 42 (56%) patients were females and 33 (44%) patients were males. The age group of the study patients range from 30-60 years. The age group with maximum number of patients was 50-60 years. The mean age of the study group is  $49.2 \pm 7.239$ . Khatib et al [7] in their study in Wardha, showed that most of the diabetes were in the age group of 50 – 60 years. In our study also the age group with most patients is 50 -60 years. The number of patients, with duration of diabetes < 5 years was 83% and with duration of diabetes > 5 years was 17%. The number of patients was less in the longer duration group as they got excluded due to presence of infection or nephropathy. Based on BMI, 29 of the 75 studied patients were having a BMI of  $25 \text{ kg/m}^2$  or more, considered obese as per American Diabetic Association, Clinical Practice Recommendation 2002[8]. From this study, we infer that 39% of study population with type II DM were obese. This strengthens the view that obesity is one of the important factors in development of type II DM. Obesity is almost considered as the forerunner of type II DM. The number of non obese patients was 61%.

*Insulin Reserve:* The endogenous insulin secretory function of patients in our study population was assessed by measuring C-peptide levels. C-peptide assays is a useful marker of endogenous insulin secretion because it is secreted along with insulin in equimolar concentrations and unlike insulin, the hepatic extraction of C-peptide is negligible.

In our study, 71 patients had adequate insulin reserve. Only 4 patients had poor insulin reserve. Fasting C-peptide level < 0.6 ng/ml was considered as an indicator of poor insulin reserve. Hence C-peptide is a useful guide in initiating therapy to prevent complications. The number of patients in the fasting CP range of 0.6-2.0 ng/ml was 58 (77%). The mean fasting CP level is  $1.315 \pm 0.811$ . The HbA1c level indicates the glycaemic control over the duration of 2-3 months. The HbA1c level of > 9.0 in 63% of patients, indicates poor glycaemic control, in spite of being on treatment. The FBS level of 56% of patients was between 200-250 mg/dl. The mean HbA1c level of this study is  $9.585 \pm 0.939$ . The mean FBS level of this study is  $222.92 \pm 29.11$ .

*Obesity and Insulin Secretion:* In our study, the mean fasting C-peptide level of the obese was 1.89ng/ml whereas that of the non obese was 0.83ng/ml. We observe from the table 9 that the fasting C-peptide levels were higher in the obese patients than in the non obese patients ( $\chi^2=24.485$ ,  $p=0.000$ ). They were moderately positively correlated, although not linear. Hence this study suggests that obese patients are hyperinsulinemic. C. Snehalatha, A. Ramachandran et al [9] conducted a study which analysed the insulin secretion in Asian Indians. That study also observed lesser insulin levels in non obese compared to obese. Also noted by Andrea Tura et al[10] in which they measured insulin and C-peptide levels during a three hour oral glucose tolerance test. A positive correlation between BMI and basal serum c-peptide levels was also observed by S.W. Park et al[11]. According to Banerji et al, Asian Indians have an unexpectedly high percentage of body fat relative to BMI and muscle mass; this is associated with a proportionate increase in visceral fat. They are markedly insulin resistant and hyperinsulinemic. In their study the majority (66%) of

non obese men were insulin resistant. A mean BMI of  $24.5 \pm 2.5 \text{ kg/m}^2$  was associated with an unusually high percentage of body fat [12].

*FBS Levels and Fasting C-Peptide Levels:* The relationship between fasting c-peptide level and the parallel fasting blood sugar level was analyzed. In our study, the number of patients with fasting c-peptide  $>1 \text{ ng/ml}$  was 52, out of which 39 patients had FBS  $> 200 \text{ mg/dl}$ . We observed from table 11 that the increase in fasting c-peptide levels were associated with increased plasma glucose due to insulin resistance and this was proved significant in our study by  $\chi^2$  value of 19.782 and p value of 0.05. A positive correlation exists in our study with r value of 0.532. From table 10 we inferred that obese patients had elevated c-peptide levels. So majority of patients with elevated FBS and fasting c-peptide were obese. Our study infers that obese are more insulin resistant than non obese. N Clare, Jones O et al [13] in their study observed that basal plasma glucose, insulin and c-peptide concentrations are higher in obese than non obese patients. Relimpio F et al studied [14] relationship between c-peptide/blood sugar ratios in orally treated well controlled diabetics. In well controlled NIDDM patients not receiving exogenous insulin, both c-peptide levels and the c-peptide/blood sugar ratio have statistically significant relationships with clinical/biochemical variables presenting a well known association with insulin resistance.

*Obesity and Fasting Plasma Glucose Levels:* In our study, patients with fasting plasma glucose levels  $> 250 \text{ mg/dl}$  were mostly obese. The elevated levels of FBS was common in obese than non obese. From table 10, we observed that there was a significant association between FBS and BMI as  $\chi^2$  test value was 25.103 and p value 0.000. This indirectly indicates that the insulin resistance plays an important role in causing elevated FBS level despite elevated c-peptide levels in the obese patients. This increase in plasma glucose values is associated further rapid worsening of diabetic complications.

*Duration of DM and Insulin Secretion:* Mean fasting c-peptide level of patients with duration of DM  $< 5$  years was  $1.442 \pm 0.807$  whereas that of patient with duration  $> 5$  years was  $0.878 \pm 0.510$ . The comparison of the fasting c-peptide value with duration by Z test was found to be significant as Z value was 3.23 and p value was 0.003. This indicates that  $\beta$  cell function deteriorates with time. So duration of diabetes was one important confounding factor in worsening glycaemic control.

Christian Weyer et al [15] observed Indians with impaired glucose tolerance over 6 years. At the end of study period they developed overt Diabetes.  $\beta$  cell secretory dysfunction increases with duration, is supported by our study. In our study, from table 14 the  $\chi^2$  value for comparing fasting c-peptide with duration of diabetes was 14.04 with p value 0.01. The r value was  $-0.258$  with p value of 0.025. This indicated moderately negative correlation and p value was significant. From this we infer that as the duration of DM increases, the insulin secretion decreases. The UKPDS and the Belfast study [16] used homeostasis model assessment of cell function to analyse insulin secretion in patients with newly diagnosed type 2 DM.

Both studies showed that  $\beta$  cell function decreased during the 5-10 years after diagnosis of diabetes and this decrease was associated with deterioration in glycaemic control. Saad et al[17] also reported that fasting and 2 hour post-glucose challenge insulin concentration in Pima Indians decreased during the first 5-7 years after diagnosis of diabetes. Niskanen et al[18] reported that the cumulative incidence of insulin deficiency, defined as plasma c-peptide concentration of  $<0.7$  nmol/lit after intravenous injection of 1 mg of glucagon, increased from 3% at five years after diagnosis of diabetes to 7% at 10 years after diagnosis. The duration of diabetes had no significant association with obesity and HbA1c levels as seen from the tables 12 and 13 respectively. There was neither positive nor negative correlation as the r values were -0.082 and -0.051, with p values 0.483 and 0.664 respectively.

*Obesity and HbA1c:* The number of patients in the present study with BMI  $>25$  having HbA1c level  $>9.0$  was 26, whereas those with HbA1c  $<9$  was only 3. Thus from the table 15 we observed that HbA1c levels was significantly associated with BMI as the  $\chi^2$  value was 14.721 with p value of 0.000. The r value was 0.303 which indicates moderately positive correlation.

*Family History:* The number of patients who had positive family history was 64%. This observation supports the guidelines of ADA, which suggests early screening of subjects with first degree relatives having Diabetes. Though the number of patients in this study was small, 56% was females. D Shobha Malini et al [19] in their study on working women in Orissa, found 58% positive family history.

*Treatment Based on C-Peptide Levels:* Gary TC Ko et al [20] reported that patients with low c-peptide levels who received insulin had the best clinical outcomes. Patients with normal to high c-peptide who received insulin had worst outcomes. This study examined the effects of interactions between c-peptide levels and antidiabetic treatments on clinical outcomes after a 9 year follow up of patients with type 2 diabetes.

Despite interventions with effective oral glucose lowering agents, most patients with type 2 diabetes will experience a gradual loss of glycaemic control. The mechanisms responsible for loss of  $\beta$  cell function are likely to be multifactorial, but may involve toxicity because of elevated blood glucose and / or lipid levels, increased secretory demand because of insulin resistance, amyloid deposition and altered levels of cytokines. Preservation of  $\beta$  cell function has the potential to reduce or stabilise the progression of type 2 diabetes. There is a growing body of animal / preclinical evidence for improved and preserved  $\beta$  cell function with current glucose lowering agents, such as the thiazolidinediones, metformin and the glucagon like peptide analogue, Exenatide [21].

In our study, the number of patients with fasting c-peptide level  $>1.0$  ng/ml was 59, out of the 75 studied patients. All patients were treated with only dietary modifications and oral hypoglycaemic agents. Few of those in this group, who were on insulin, were tapered and glycaemic control achieved using oral drugs, dietary modifications and exercises only.

The patients with fasting c-peptide levels  $<1.0$  ng/ml were treated either with oral drugs alone or combination of insulin and oral drugs. This was found to vary with age of the patient, duration of diabetes as well BMI.

According to Tetsuya Motomiya[22], the results of their study showed that more than 90% patients with fasting c-peptide 1.4 ng/ml or higher, were either in a dietary treatment or oral hypoglycaemic agents treatment group and blood glucose control was achieved without insulin therapy. Hence c-peptide is useful in the selection of initial therapeutic modality for type 2 diabetic patients. Munishi et al [23] in their study showed that glycaemic control improved significantly in patients with a simplified regimen and patients reported fewer hypoglycaemic episodes. G. Biesenbach et al [24] in their study showed that insulin requirement was higher in the low c-peptide group, though the body weight increases with the rising c-peptide levels. This quotient was only a potent predictor for insulin requirement in patients with low and normal c-peptide level. A ratio of c-peptide/NBG < 0.01 was found in all patients with low and nearly all subjects with normal c-peptide. The ratio c-peptide/FBS < 0.01 had a predictive potency only in patients with low and normal c-peptide (< 2.0 ng/ml).

### Summary

In the present study, 75 cases of type II DM who were not on treatment for at least 3 days or newly diagnosed, were evaluated. The patient's fasting venous blood samples were analysed for plasma glucose levels and c-peptide levels. The HbA1c levels were also determined. The findings of the study can be summarised as follows:

- Out of the 75 cases studied, the number of female patients was 42 (56%) and the number of male patients was 33 (44%).
- The age group of distribution of the study patients was from 30-70 years, with 43% in the 50-60 age group.
- The number of patients with diabetes having obesity was 39%, while non-obese was 61%.
- The fasting c-peptide level in the obese patients was increased compared to the non obese individuals, indicating insulin resistance. The mean fasting c-peptide level in obese patients was  $1.886 \pm 0.657$ , while in non-obese was  $0.825 \pm 0.512$ .
- The fasting plasma glucose level was also elevated despite elevated c-peptide levels in the obese patients, proving the role of insulin resistance.
- The level of HbA1c was also more in obese patients indicating poor glycaemic control due to insulin resistance.
- There was a minority of patients with low c-peptide levels, not influenced by obesity and duration of diabetes, requiring insulin treatment. The fasting c-peptide levels < 0.6 ng/ml indicated low c-peptide levels and hence very low insulin production.
- The significance of c-peptide level in obese individuals was to assess the endogenous insulin reserve and to alter the treatment modality based on it.
- Those patients with adequate insulin reserve, with c-peptide level > 1.0 ng/ml required diet and exercise modalities of treatment to improve insulin sensitivity in addition to oral hypoglycaemic drugs.

- Those patients with poor insulin reserve in the form of low c-peptide levels required insulin therapy. The poorer insulin reserve is seen in obese patients too, as the  $\beta$  cell dysfunction worsens with duration of diabetes.
- Few patients who were obese with poor glycaemic control and thought to be candidates for insulin treatment, had normal c-peptide levels and were treated with oral drugs and life style modifications only.

### Conclusions

1. Nearly 94% had adequate insulin reserve of  $>0.6$  ng/ml. The obese patients had higher c-peptide levels compared to the non obese patients and the levels of HbA1c were more elevated in the obese patients than non obese, indicating insulin resistance.
2. The insulin reserve decreased with the duration of diabetes as seen by the decrease in the levels of fasting c-peptide levels. This indicates that  $\beta$  cell dysfunction increases with the duration of diabetes.
3. There is no significant association between the duration of diabetes and HbA1c levels as well as with obesity.
4. Minority of patients had low c-peptide levels and were started on insulin therapy. The obese patients with adequate insulin reserve, required dietary and exercise management along with oral hypoglycaemic drugs to improve the level of insulin sensitivity to receptors.

In conclusion, this study suggests;

- Routine c-peptide testing in patients with poor glycaemic control to decide treatment modalities;
- Early screening of subjects with positive family history and
- To create awareness about lifestyle modifications and education to prevent obesity.

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