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UTILITY OF FASTING C-PEPTIDE LEVELS IN THE CLASSIFICATION OF YOUNG DIABETES SUBJECTS WITH THE AGE OF ONSET OF DIABETES BETWEEN 15 TO 35 YEARS

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ABSTRACT

Background: Diabetes mellitus is a chronic metabolic disorder characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. It is a major cause of mortality and morbidity worldwide. Type 2 diabetes in youth has increased enormously in India and in addition the incidence of even type 1 diabetes is increasing in youth. So there are some patients who have mixed features. The objective of this study is to use fasting C-Peptide levels and classify diabetes in the young individuals from 15 to 35 years. **Methods:** The present study was conducted in the outpatient department of Karnataka Institute of Endocrinology and Research Bangalore, in 426 subjects with age of onset of diabetes between 15 to 35 years, over a period of 5 years. Informed consent was taken from all the subjects included in the study and the approval from hospital ethical committee was taken. Pregnant women with diabetes, subjects presenting with acute infections, septicaemia, patients with acute or chronic pancreatitis, and subjects with pancreatic carcinoma were excluded from the study. In this study C-Peptide levels were estimated by electro chemiluminescence immunoassay method. **Results:** 426 subjects with the age of onset of diabetes between 15 to 35 years were studied. 71.4% of the subjects are males. 55.4% were in the age of onset between 20 to 30 years. Duration of diabetes varied between new to 15 years. 54% of subjects had BMI from 18.5 to 24.9. Waist circumference was more than 80 cms in 78.2% of subjects. Study results show that 2.8% were type 1 diabetes, 11.5% could be either type 1 or type 2 diabetes and 85.7% were type 2 diabetes. Subgroup analysis showed that 5.5% type 1, 27.8% type 1 or type 2 and 66.7% type 2 diabetes were between 15 to 20 years. Similarly, between 20 to 35 years, 2.5% were type 1 diabetes, 10% could be either type 1 or type 2 diabetes and 87.5% were type 2 diabetes. **Conclusions:** C-peptide is secreted in equimolar amounts of insulin, so it can be used for estimation of residual insulin secretion in patients with diabetes. This C-peptide can be of great value in this era of precision medicine in classification of diabetes, with very low secretion in T1DM, high values in T2DM. C-peptide measurement is an inexpensive, widely available test that may assist the clinical management of diabetes, particularly in young and insulin-treated patients where there is uncertainty about diabetes subtype.

KEYWORDS: Fasting C-Peptide, type 1 diabetes, type 2 diabetes.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. It is a major cause of mortality and morbidity worldwide.[1] In recent times, diabetes in youth has been increasing worldwide and also in India. It has been observed that type 1 diabetes remains the most common cause of diabetes in youth but the incidence of type 2 diabetes has been increasing alarmingly. While, it is simple to differentiate between type 1 diabetes and type 2 diabetes, some patients may have indistinct features. Given the obesity epidemic, many youth with type 1 diabetes are either overweight or obese at diagnosis[2,3] making it difficult for clinicians to distinguish between type 1 and type 2 diabetes based on weight alone. Even though type 1 diabetes is characterized by a lack of insulin, some patients have significant residual beta-cell function. The progression rate of insulin deficiency, meaning the loss of beta-cell function, varies greatly among patients. Factors associated with significant residual beta-cell function include age at diagnosis, early diagnosis, and onset of DM after infection.[4] But, the classic criteria for distinguishing between two major types of diabetes (i.e., age at onset and weight) are also

becoming increasingly blurred and it is becoming absolutely necessary to develop better methods of diabetes classification in youth.

Measurement of C-peptide levels is currently believed to be the best method to evaluate endogenous insulin secretion and may assist in the clinical management of diabetes mellitus, especially in insulin-treated patients in whom the diabetes subtype is uncertain.[5] This is based on the understanding that both human insulin and c-peptide are synthesized as a single polypeptide chain known as proinsulin in the pancreatic islet by the beta cells. Proinsulin is cleaved proteolytically to form equimolar amounts of mature insulin and C-peptide and released in the portal vein. C peptide is a single peptide chain of 31 amino acids with molecular weight of 30200 g/mol. It is called as C-peptide because it connects the A and B chains of insulin in Proinsulin.[6] Modern ultrasensitive c-peptide assays are able to detect C-peptide values as low as 0.0015–0.0025 nmol/l.[7] In healthy individuals, the plasma concentration of C-peptide in the fasting state is 0.3–0.6 nmol/l (0.9 -1.8 ng/ml), with a postprandial increase to 1–3 nmol/l (3-9 ng/ml). (1 nmol/l = 3 ng/ml)[8] Higher levels are observed in overweight individuals. The majority of C-peptide is metabolized by the kidneys with 5–10% then excreted unchanged in the urine. This can make C-peptide measurement in individuals with chronic kidney disease inaccurate.

Potential uses of C-peptide are broad and include arriving at appropriate diagnosis, guiding therapy choices, and predicting morbidity in diabetes. Stimulated C-peptide sampling is a sensitive and specific test that can determine type and duration of diabetes. C-peptide is a useful indicator of beta cell function, allowing discrimination between insulin-sufficient and insulin-deficient individuals with diabetes. It is also hypothesised that a lower C-peptide, can most likely predict requirement for insulin. Lower C-peptide values have also been shown to correspond with increased incidence of microvascular complications. This suggests that C-peptide levels may be used as an essential diagnostic and monitoring tool in young persons with diabetes.

Despite of this, there is a lot of confusion regarding diagnosis of diabetes in young. Clinical features, BMI, waist circumference and measurement of fasting C-peptide levels will help in diagnosis and management of diabetes in young. This study was conducted to evaluate fasting C-peptide levels in young diabetics in the age group of 15 to 35 years and classify types of diabetes.

MATERIAL AND METHODS

An observational clinical study was conducted in 426 subjects with diabetes, with the age of onset of diabetes from 15 to 35 years with diabetes, presenting to the outpatient department of Karnataka Institute of Endocrinology and Research Bangalore over a period of 5 years. Informed consent was taken from all the subjects included in the study and the approval from hospital ethical committee was taken. Pregnant women with diabetes, subjects presenting with acute infections, septicaemia, patients with acute or chronic pancreatitis, and subjects with pancreatic carcinoma were excluded from the study.

Diagnosis of diabetes mellitus was made according to ADA criteria if: HBA1C>6.5% or, fasting plasma glucose greater than 126 mg/dl and in a patient with classic symptoms of hyperglycemia with plasma glucose ≥200mg/dl on more than one occasion. After taking informed consent of the patient, detailed history was taken. Complete general physical examination was done with due emphasis on anthropometry. BMI was calculated by dividing the weight in kilograms and the square of the height in meters.

A fasting and post prandial blood sample was taken for estimation of plasma glucose by Hexokinase method and serum lipids using a Hitachi C 311 autoanalyser (Roche Diagnostics, Mannheim, Germany). A1C was measured by the high-performance liquid chromatography method using the Bio-rad Variant 2 turbo analyser.

C-peptide was estimated by electro chemiluminescence immunoassay. The following values of fasting C-peptide levels given in table 1 were used to classify diabetes:

Fasting C peptide levels	Diagnosis
< 0.6 nanogram/ml	Type 1 Diabetes
0.6 to 1.5 nanogram/ml	Type 1 or Type 2 Diabetes
>1.5 nanograms/ml	Type 2 Diabetes

Statistical Methods: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data are made.

Assumptions: 1. Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, and Cases of the samples should be independent

The one-way analysis of variance (ANOVA) is employed to determine whether there are any statistically significant differences between the means of three or more independent (unrelated) groups. The one-way ANOVA compares the means between the groups you are interested in and determines whether any of those means are statistically significantly different from each other. Specifically, it tests the null hypothesis:

$$H_0: \mu_1 = \mu_2 = \mu_3 = \cdots = \mu_k$$

Where μ = group mean and k = number of groups. If, however, the one-way ANOVA returns a statistically significant result, we accept the alternative hypothesis

(H_A), which is that there are at least two group means that are statistically significantly different from each other.

Assumptions for ANOVA test

1. The dependent variable is normally distributed in each group that is being compared in the one-way ANOVA
2. There is homogeneity of variances. This means that the population variances in each group are equal.
3. Independence of observations.

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher Exact test used when cell samples are very small.

Significant figures

+ Suggestive significance (P value: 0.05<P<0.10)
* Moderately significant (P value:0.01<P ≤ 0.05)
** Strongly significant (P value: P≤0.01)

Statistical software: The Statistical software namely SPSS 22.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

RESULTS

426 Subjects in the age of onset of 15 to 35 years were studied. 71.4% of the subjects were males. 55.4% were in the age of onset between 20 to 30 years. Duration of diabetes varied between new to 15 years. 54% of subjects had BMI from 18.5 to 24.9. Waist circumference was more than 80 cms in 78.2% of subjects (Table 1- 8)

Table 1: Gender –frequency distribution of patients studied.

Gender	No. of Patients	%
Female	122	28.6
Male	304	71.4
Total	426	100.0

Table 2: Age at onset of diabetes (Years)-frequency distribution of patients studied.

Age at onset of diabetes (YEARS)	No. of Patients	%
<20	33	7.7
20-30	236	55.4
31-35	157	36.9
Total	426	100.0

Mean ± SD: 28.14±5.02

Table 3: Duration of DM in years-frequency distribution of patients studied.

Duration	No. of Patients	%
New Diagnosis	71	16.7
0-2 Yrs	165	38.7
2-5 Yrs	109	25.6
5-10 Yrs	62	14.6
10-15 Yrs	13	3.1
16-20 Yrs	6	1.4
Total	426	100.0

Table 4: BMI (kg/m2)-Frequency Distribution of Patients Studied.

BMI(kg/m2)	No. of Patients	%
<18.5	26	6.1
18.5-24.9	230	54.0
25.0-29.9	156	36.6
>30.0	14	3.3
Total	426	100.0

Table 5: Waist Circumference (cm)-Frequency Distribution of Patients Studied.

Waist circumference (cm)	No. of Patients	%
<70	13	3.1
70-80	80	18.8
>80	333	78.2
Total	426	100.0

Table 6: Comparison of Clinical Variables According to Duration of DM of Patients Studied.

Variables	Duration of DM						Total
	New Diagnosis	0-2 Yrs	2-5 Yrs	5-10 Yrs	10-15 Yrs	16-20 Yrs	
Gender							
Female	20 (28.2%)	42 (25.5%)	29 (26.6%)	22 (35.5%)	8 (61.5%)	1 (16.7%)	122 (28.6%)
Male	51 (71.8%)	123 (74.5%)	80 (73.4%)	40 (64.5%)	5 (38.5%)	5 (83.3%)	304 (71.4%)
Age at onset of diabetes (Years)							
<20	8 (11.3%)	7 (4.2%)	7 (6.4%)	6 (9.7%)	2 (15.4%)	3 (50%)	33 (7.7%)
20-30	36 (50.7%)	85 (51.5%)	57 (52.3%)	45 (72.6%)	10 (76.9%)	3 (50%)	236 (55.4%)
31-40	27 (38%)	73 (44.2%)	45 (41.3%)	11 (17.7%)	1 (7.7%)	0 (0%)	157 (36.9%)
BMI							
<18.5	3 (4.2%)	12 (7.3%)	10 (9.2%)	1 (1.6%)	0 (0%)	0 (0%)	26 (6.1%)
18.5-24.9	40 (56.3%)	82 (49.7%)	59 (54.1%)	39 (62.9%)	6 (46.2%)	4 (66.7%)	230 (54%)
25.0-29.9	27 (38%)	64 (38.8%)	37 (33.9%)	21 (33.9%)	6 (46.2%)	1 (16.7%)	156 (36.6%)
>30.0	1 (1.4%)	7 (4.2%)	3 (2.8%)	1 (1.6%)	1 (7.7%)	1 (16.7%)	14 (3.3%)
Total	71 (100%)	165 (100%)	109 (100%)	62 (100%)	13 (100%)	6 (100%)	426 (100%)

Table 7: Fasting C-peptide frequency distribution in relation to duration of DM of patients studied.

Fasting C-peptide	Duration of DM						Total
	New Diagnosis	0-2 Yrs	2-5 Yrs	5-10 Yrs	10-15 Yrs	16-20 Yrs	
<0.6 nanogram/ml	0 (0%)	5 (3%)	5 (4.6%)	1 (1.6%)	0 (0%)	1(16.7%)	12 (2.8%)
0.6 to 1.5 nanogram/ml	3 (4.2%)	14 (8.5%)	20 (18.3%)	9 (14.5%)	3 (23.1%)	0 (0%)	49 (11.5%)
>1.5 nanogram/ml	68 (95.8%)	146 (88.5%)	84 (77.1%)	52 (83.9%)	10 (76.9%)	5 (83.3%)	365 (85.7%)
Total	71 (100%)	165 (100%)	109 (100%)	62 (100%)	13 (100%)	6 (100%)	426 (100%)

Table 8: Comparison of study variables in relation to Duration of DM of patients studied.

Variables	Duration						Total	P Value
	New Diagnosis	0-2 Yrs	2-5 Yrs	5-10 Yrs	10-15 Yrs	16-20 Yrs		
Age at onset of diabetes (years)	27.83±5.39	29.05±4.76	28.69±4.78	26.76±4.58	23.54±4.67	21.67±5.32	28.15±5.02	<0.001**
BMI	24.04±3.06	24.39±3.64	23.74±3.53	24.15±2.75	24.98±2.64	24.93±2.78	24.16±3.36	0.608
Waist circumference	85.23±12.07	86.87±8.79	86.43±8.73	86.17±6.63	87.23±9.12	92.33±12.08	86.47±9.19	0.521
SBP (MmHg)	122.35±13.66	126.82±17.23	123.62±14.09	126.31±12.87	129.62±16.04	123.83±8.4	125.23±15.21	0.221
DBP (MmHg)	77.28±10.05	84.03±51.21	78.63±9.39	79.92±7.47	83.31±9.48	76.67±6.77	80.8±32.71	0.683
FPG	202.93±81.93	180.25±70.63	196.65±70.79	181.9±70.18	156.85±58.87	227.33±67.02	188.42±72.79	0.051+
PPG	308.9±116.84	262.84±108.33	292.75±114.02	295.66±106.82	263.85±100.47	316.17±81.59	283.73±111.47	0.037*
Hba1c	12.64±10.18	9±2.31	9.42±2.5	9.9±2.32	8.9±1.77	9.15±2.32	9.85±4.83	<0.001**
Fasting C-peptide	2.85±1.22	2.89±1.48	2.72±1.71	2.48±1.2	2.23±0.61	2.21±1.25	2.75±1.45	0.256
Sr creatinine	0.76±0.11	0.78±0.13	0.78±0.15	0.78±0.12	0.82±0.25	0.8±0.15	0.78±0.13	0.847

12 (2.8%) persons with C-peptide < 0.6 nanogram/ml were diagnosed as type 1 diabetes. 49 (11.5%) persons with C-peptide 0.6 to 1.5 nanogram/ml could be either type 1 or type 2 diabetes. 365 (85.7%) persons with C-peptide more than 1.5 nanogram/ml were diagnosed as type 2 diabetes. BMI and waist circumference were lower in diabetes subjects with lower c peptide levels. (Table 9 & 10)

Table 9: Fasting C-peptide-frequency distribution of patients studied.

Fasting C-peptide	Diagnosis	No. of Patients	%
<0.6 nanogram/ml	Type 1 Diabetes	12	2.8
0.6 to 1.5 nanogram/ml	Type 1 or Type 2 Diabetes	49	11.5
>1.5 nanogram/ml	Type 2 Diabetes	365	85.7
Total		426	100.0

Table 10: Comparison of study variables in relation to Fasting C-peptide of patients studied.

Variables	Fasting C-peptide			Total	P Value
	<0.6 nanogram/ml	0.6 to 1.5 nanogram/ml	>1.5 nanogram/ml		
Age At Onset Of Diabetes (Years)	25.75±6.12	24.96±5.71	28.65±4.71	28.15±5.02	<0.001**
BMI	19.94±2.47	21.44±3.82	24.66±3.04	24.16±3.36	<0.001**
Waist Circumference	77.82±4.61	80.08±9.59	87.61±8.75	86.47±9.19	<0.001**
SBP (MmHg)	115.58±15.65	117.55±12.46	126.57±15.15	125.23±15.21	<0.001**
DBP (MmHg)	73.83±9.4	86.82±93.17	80.22±9.74	80.8±32.71	0.315
FPG	179.67±98.5	182.92±74.81	189.44±71.75	188.42±72.79	0.770
PPG	390±150.71	288.94±114.64	279.54±108.14	283.73±111.47	0.003**
Hba1c	10.61±2.73	10±3.08	9.8±5.07	9.85±4.83	0.827
Fasting C-Peptide	0.27±0.24	1.15±0.23	3.04±1.34	2.75±1.45	<0.001**
Sr Creatinine	0.78±0.13	0.74±0.13	0.78±0.14	0.78±0.13	0.106

Overall, there were 36 persons (8.5%) with the age of onset of diabetes from 15 to 20 years and 390 persons (91.5%) with the age of onset of diabetes from >20 to 35 years (Table 11 &12).

Table 11.

Fasting C peptide levels	Diagnosis	Number of persons	Percentage
< 0.6 nanogram/ml	Type 1 Diabetes	2	5.5
0.6 to 1.5 nanogram/ml	Type 1 Or Type 2 Diabetes	10	27.8
>1.5 nanograms/ml	Type 2 Diabetes	24	66.7

Table 12.

Fasting C peptide levels	Diagnosis	Number of persons	Percentage
< 0.6 nanogram/ml	Type 1 Diabetes	10	2.5
0.6 to 1.5 nanogram/ml	Type 1 or Type 2 Diabetes	39	10
>1.5 nanograms/ml	Type 2 Diabetes	341	87.5

DISCUSSION

Diabetes mellitus (DM) is a multisystem disease with multifactorial etiopathology, diverse clinical manifestations and varied clinical outcomes. It is not a single disease entity, but a heterogeneous group of diseases characterized by hyperglycemia induced by variable combination of insulin resistance and deficiency. Depending on the predominant pathophysiological component, diabetes is classified as type 1 diabetes (T1DM), type 2 diabetes (T2DM), gestational diabetes (GDM) and other specified types of diabetes. Of these, major forms of DM are T1DM and T2DM. T1DM is insulin-deficiency diabetes caused by autoimmune or idiopathic pancreatic ß-cell destruction. T2DM is insulin-resistant diabetes that is caused predominantly by insulin resistance and a relative insulin deficiency. Type 1 diabetes is common in children but now type 1 diabetes is seen in all age groups. Similarly, type 2 diabetes is being diagnosed at younger age. Accurate classification of diabetes is essential for precise pharmacological therapy. The treatment option of either oral anti diabetic medication or insulin therapy depends on the type of DM.

DM classification depends on age, clinical symptoms, presence of ketonuria, obesity, family history, evidence of autoimmune disease, and serum C-peptide level. The patients with younger age of onset, significant symptomatology, presence of ketoacidosis, and suspected autoimmune disease tend to be classified as T1DM. On the other hand, patients who are obese, have a family history of T2DM, have few or no diabetic symptoms or have signs of insulin resistance tend to be classified as T2DM. However, it is difficult to classify DM in some cases, even though there are significant differences in each type (9, 10). In such scenarios, C-peptide can work as a marker for endogenous insulin secretion and also a diagnostic tool. C-peptide also gives valuable information on why patients are more or less stable/ in their blood glucose and more or less easy to treat.

Unfortunately, there is limited research on the utility of C-peptide in classifying diabetes. Evidence-based guidelines have not focused on classifying diabetes accurately on the basis of C-peptide. C-peptide is rarely used clinically to classify type of diabetes even though it is self evident that it is important to estimate the pancreatic beta cell function.

In a study done with nation-wide cohort, the Better Diabetes Diagnosis study, a random, non-fasting serum sample was done at diagnosis. 56% of the patients had a C-peptide value >0.2 nmol/L. Children classified as T2DM had the highest mean C-peptide (1.83 + 1.23 nmol/L) followed by MODY (1.04 ± 0.71 nmol/L) and T1Dm (0.28 ± 0.25 nmol/L). Predictive value of C-peptide >1.0 nmol/L for the classification of either T2DM or MODY was 0.46. Serum C-peptide < 0.2 nmol/L in a random sample at diagnosis was found to be a strong support for the diagnosis of T1DM. At the other end of the C-peptide spectrum, a value ≥ 1.0 nmol/L was suggestive of another type of diabetes, most often T2DM. The authors concluded that a random C-peptide taken at diagnosis may help to classify diabetes (4). But, the Swedish study used random C-peptide levels instead of fasting C-peptide levels. Fasting C-peptide level correlate well with late postprandial serum C-peptide level, but overnight fast is preferred for purposes of standardization and more routinely used.

In a large population-based cohort of 1180 adults with newly diagnosed diabetes in Kronoberg County, mean fasting C-peptide level was 0.73 ± 0.5 (range 0.13–1.80) nmol/l. C-peptide level increased with age also within each BMI group. The highest area under the curve (AUC) in the ROC analysis was found for C-peptide, followed by age and BMI. The authors concluded that at diagnosis of diabetes, C-peptide was superior to age and BMI in discriminating between autoimmune and non-autoimmune diabetes.[11]

Iqbal et al in a systematic review and meta-analysis of 12 studies reflective of almost 9000 participants found that the plasma C-peptide level is strongly associated with DM and accurately predicts the diagnosis and classification of the major subtypes of diabetes. Lower concentrations of plasma C-peptide or its lower cutoffs are highly discriminative in diagnosing T1D from T2D and are one of the major findings of this systematic review and meta-analysis. The C-peptide level was the primary outcome measure among all included studies, being crucial in DM classification. However, fewer studies had used additional clinical characteristics/criteria such as the age at diagnosis, BMI, GADA, anti-islet autoantibody status, and a family history of T2D along with the C-peptide levels to diagnose the T1D and T2D statuses of patients with diabetes. C-peptide levels in both scenarios affirm its critical role in routine clinical practices. Moreover, it not only is a quantitative measure to assess insulin secretion and the beta-cell function in the body but also helps clinicians with the diagnoses and discrimination of patients with T1D from those with T2D, especially in cases with active honeymoon period or those difficult to diagnose. Furthermore, a more resourceful plan could be initiated that ultimately will develop a healthier and better clinical care management system through the evaluation of the plasma C-peptide levels while keeping the potential to improve patient outcomes. In addition, the C-peptide laboratory measures/indices will direct the appropriate allocation of health care resources.[12]

Superiority of C-Peptide over Clinical Characteristics in Diagnosing the Diabetes Subtype -Nowadays, it has become arduous to classify diabetes in adults at its presentation. These difficulties are also increasingly reported among adolescents and elderly patients, where autoimmune diabetes incidences are as high as in the younger age groups. In such conditions, age, BMI, ketoacidosis, and other symptoms based classification may acquire a better or additional tool in accurately classifying the 2 major subtypes of diabetes. Indeed, simple clinical judgment would not work alone. Therefore, as evidenced in this analysis, C-peptide levels emerged as a superior discriminator than other clinical predictors such as age and BMI in patients with positive results for GADA and/or Islet cell antibody.[12]

Our study results showed that 2.8% were type 1 diabetes, 11.5% could be either type 1 or type 2 diabetes and 87.5% were type 2 diabetes, in the age of onset 15 to 35 years. Subgroup analysis showed that 5.5% were type 1 diabetes, 27.8% were type 1 or type 2 diabetes and 66.7% were type 2 diabetes in the age group of 15 to 20 years. Similarly in those persons between 20 to 35 years, 2.5% were type 1 diabetes, 10% were either type 1 or type 2 diabetes and 87.5% were type 2 diabetes. In the second group where there is difficulty in diagnosing type1 or type 2 diabetes age, BMI, family history of diabetes, history of ketoacidosis, GAD antibody or other islet antibody status along with stimulated C-peptide levels should be considered to make accurate diagnosis of type of diabetes.

Accurate classification of diabetes type is crucial in its management in this era of precision medicine. C-peptide not only classifies the diabetes types but is also crucial in devising criteria to ensure its better management. C-peptide very low concentration value in plasma discriminates T1D from T2D. Plasma C-peptide could form evidence-based guidelines in diabetes classification.

Clinical relevance – This study if of importance for the practicing clinical diabetologist/endocrinologist. The use of C-peptide measurement can often be very helpful in clinical practice to differentiate the various types of diabetes or the necessity for insulin therapy; data surrounding how to best interpret the values can potentially benefit many providers and patients.

Our Recommendations

On the basis of our study findings, we recommend fasting C-peptide measurement in subjects with young onset diabetes for appropriate classification and treatment. In diabetes subjects with c-peptide values between 0.6 to 1.5 nano gram/ml where diagnosis is either type 1 or type 2 diabetes stimulated c-peptide along with other clinical features should be used to make a precise diagnosis.

CONCLUSIONS

C-peptide is secreted in equimolar amounts of insulin, so it can be used for estimation of residual insulin secretion in patients with diabetes. The fasting C-peptide can be of great value in this era of precision medicine in classification of diabetes, with very low secretion in T1DM, high values in T2DM. C-peptide measurement is an inexpensive, widely available test that may assist the clinical management of diabetes, particularly in young and insulin-treated patients where there is uncertainty about diabetes subtype.

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Abbreviations

DM-Diabetes mellitus.
T1DM –Type 1 diabetes mellitus
T2DM-Type 2 diabetes mellitus.
BMI-Body mass index.
ADA-American diabetes association.
GAD-Glutamic acid decarboxylase.

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