Connecting peptide (c-peptide) and the duration of diabetes mellitus amongst patients, at the Federal Medical Centre (FMC), Owerri, southeast, Nigeria

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Abstract

Objective: C-peptide is derived from proinsulin and it is secreted in equimolar concentration with insulin. Plasma C-peptide is more stable than insulin and it provides an indirect measure of insulin secretory reserve and beta cell function. To determine relationship between C-peptide and duration of diabetes mellitus, age, body mass index, systolic blood pressure and diastolic blood pressure.

Methods: This is a cross-sectional study of type 2 diabetes mellitus patients attending Endocrine Clinic. Information such as age, sex, height, weight, blood pressure and duration of diabetes were obtained. Blood samples were taken for fasting serum C-peptide. Data was analysed using SPSS version 16.

Results: Out of the 46 subjects recruited 23 (50%) were females and 23 (50%) were males. The mean age was 55.63 ± 14.7 years. Mean duration of diabetes for both sexes was 8 years with a range of 1 to 32 years. The mean BMI was 26.87 ± 5.00 kg/m^{2}for males and 30.09 ± 4.32 Kg/m^2 for females. The mean fasting serum C-peptide was 2.16 ± 1.41 ng/ml and there was no significant difference between males and females. There is statistically significant inverse correlation between C-peptide and duration of diabetes (r= -0.356, p= 0.015). Conversely there is a direct relationship between C-peptide and BMI (r=0.307, p=0.038).

Conclusion: Increasing duration of diabetes is associated with decreasing level of C-peptide and decreased beta cell secretory reserve.

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Connexion peptide (c-peptide) et la durée du diabète sucré chez les patients, au Centre médical fédéral (FMC), Owerri, au sud-est, au Nigeria

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Resume

Objectif: C-peptide est dérivé de la pro-insuline et il est sécrété à une concentration équimolaire avec l'insuline. Plasma peptide C est plus stable que l'insuline et elle fournit une mesure indirecte de la réserve de sécrétion d'insuline et la fonction des cellules bêta. Pour déterminer la relation entre C-peptide et la durée du diabète sucré, l'âge, indice de masse corporelle, la pression artérielle systolique et de la pression artérielle diastolique.

Méthodes: Ceci est une étude transversale des patients diabétiques de type 2 mellitus fréquentant Endocrine Clinic. Des informations telles que l'âge, le sexe, la taille, le poids, la tension artérielle et la durée du diabète ont été obtenus. Des échantillons de sang ont été prélevés pour sérique à jeun du C-peptide. Les données ont été analysées à l'aide du logiciel SPSS version 16.

Résultats: Sur les 46 sujets recrutés 23 (50%) étaient des femmes et 23 (50%) étaient des hommes. L'âge moyen était de 55,63 ± 14,7 années. la durée du diabète moyenne pour les deux sexes était de 8 ans avec une gamme de 1 à 32 ans. L'IMC moyen était de 26,87 ± 5,00 kg / m2for hommes et 30,09 ± 4,32 kg / m2 pour les femmes. Le sérum moyen jeûne C-peptide était de 2,16 ± 1,41 ng / ml et il n'y avait pas de différence significative entre les hommes et les femmes. Il existe statistiquement significative corrélation inverse entre le peptide C et la durée du diabète (r = -0,356, p = 0,015). A l'inverse, il existe une relation directe entre le C-peptide et l'IMC (r = 0,307, p = 0,038).

Conclusion: L'augmentation de la durée du diabète est associé à niveau de C-peptide diminuant et une diminution de la bêta réserve sécrétoire cellulaire.

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INTRODUCTION

Insulin is an essential hormone produced in the pancreas and is invaluable in carbohydrate metabolism. It also plays important roles in protein and lipid metabolism. Insulin is derived from a prohormone called proinsulin. C-peptide is derived from proinsulin in equimolar proportion with insulin. Proinsulin is derived from preproinsulin secreted by the beta cells of the endocrine pancreas (1, 2). Preproinsulin has 110 amino acids and proinsulin has 86 amino acids. Insulin has a double chain with 51 amino acids while C-peptide has 31 amino acids.

C-peptide derives its name because it connects the A and B chains of insulin in the pro-insulin molecule. While the liver clears a significant portion of insulin (50-60%) in a first pass; C-peptide does not undergo hepatic extraction and has constant peripheral clearance at various plasma glucose concentrations unlike insulin. It is excreted through the kidneys and its plasma half-life is about 30 minutes unlike plasma insulin with a half-life of 4 minutes. For these reasons plasma C-peptide levels may be more reliable than insulin in assessing beta-cell function (3).

Plasma C-peptide was previously considered an inactive peptide but recent study suggests that it is an active peptide involved in glucose transport and stimulation of microvascular blood flow (4).

Measurement of plasma C-peptide has attained increased significance following the findings from Diabetes Control and Complication Trial (DCCT) which demonstrated that higher C-peptide is associated with decreased incidence of diabetic retinopathy and nephropathy in subjects living with diabetes (5). Another study has shown that serum C-peptide is an independent risk factor for cardiovascular disease, cancer and total mortality (6).

In a study of elderly diabetics in India, fasting C-peptide was increased in obese subjects when compared to non-obese individuals indicating insulin resistance (7). It also showed decreasing levels of C-peptide with increasing duration of diabetes. In Nigeria Oli et al demonstrated that type 2 diabetic subject with poor glycemic control had lower fasting and post-glucagon stimulation C-peptide (8). In another study in Northern Nigeria, type 2 diabetes subjects were found to have lower beta cell reserve using C-peptide (9).

At the time of diagnosis of type 2 diabetes mellitus, about 50% of beta cell function has been lost, and this deteriorates by about 4% yearly. In normal non-diabetic population from the age of 40 years, the rate of beta cell decline is 1%. The causes of beta cell dysfunction are multifactorial and include genetic, obesity, hyperglycaemia, dyslipidaemia, and hormonal (10, 11). Serum C-peptide is used in distinguishing type 1 from type 2 diabetes and evaluation of hypoglycaemia. Persistence of C-peptide is an important feature of maturity onset diabetes of the young (MODY). It helps to identify these patients as they are commonly misdiagnosed as type 1 diabetes.

The normal fasting reference value in Federal Medical Centre, Owerri is 0.7 – 1.9ng/ml (234-635 pmol/l). The objective of this study is to evaluate the relationship between serum C-peptide with duration of diabetes, body mass index, systolic and diastolic blood pressures.

MATERIALS AND METHODS

A cross sectional study of subjects with type 2 diabetes mellitus attending the Endocrine Medical Out-Patient Clinic of FMC Owerri, between June 2013 and May. Subjects were recruited by systematic random sampling of patients living with diabetes. Age and duration of diabetes was assessed from the records. Height was measured to the nearest 0.5 cm using a stadiometer. Weight was measured to the nearest 0.5kg using a weighing scale. Body mass index was calculated by body weight divided by the square of height. Blood pressure was measured using Accoson mercury sphygmomanometer to determine the brachial systolic and diastolic blood pressures.

Venous blood after 10-12hours overnight fast, were collected into plain specimen containers. The samples were left to stand for about 20mins for clot retraction, after which they were spun at 3000rmp for 5mins and serum were collected for C-peptide assay. Serum C-peptide level was analyzed with Accubind C-peptide enzyme linked immunosorbent assay kit (MonobindInc, Lake forest, CA USA) Data was analysed using the statistical package for social science (SPSS) version 16. Continuous variables will be expressed as mean ± standard deviation and categorical variables will be expressed as frequency table and chart. The relationship between C-peptide and duration of diabetes, blood pressures and body mass index was determined using Pearson correlation coefficient. Test of significance was set at p-value ≤ 0.05

RESULTS

A total of 46 subjects were included in the analysis, 23 (50%) males and 23 (50%) females. Males and female subjects were similar with respect to mean age, duration of diabetes, systolic blood pressure, diastolic blood pressure and fasting C-peptide. Mean body mass index was significantly higher in female subjects at p=0.024. Subjects who had diabetes for less than one year had the highest value of fasting C-peptide 3.63 ng/mL while the lowest level 0.5 ng/mL was seen in those with diabetes lasting more than 31 years. 21.7% of the subjects had C-peptide less than 0.9 ng/mL and 23.9% had C-peptide greater than 3.0 ng/mL. There was a moderate positive correlation between body mass index and C-peptide (r=370, p=0.011) and a moderate negative correlation between duration of diabetes and C-peptide (r= -366, p=0.012).

DISCUSSION

C-peptide levels was higher in subjects whose duration of diabetes was less than one year and there was a progressive decline as the duration of diabetes increases (figure 1). There was also moderate negative correlation between fasting C-peptide and duration of diabetes (r= -366, p=0.012). This findings is similar to other studies (12, 13), which described progressive beta cell decline as the hallmark of type 2 diabetes mellitus. This however, contrast with the study by Young et al (14) who did not find any statistical significant decline of C-peptise with increasing duration of diabetes. The findings of slightly higher C-peptide in the group of subjects with duration of diabetes 16-20 years may be due to other factors. These factors include hyperglycemia, increased adiposity, genetic factors, type of anti-diabetic medications and renal failure (15). There was no significant correlation between C-peptide and the age of the subjects. This may be due to variable onset of diabetes among the subjects.

Obesity which is a key risk factor for diabetes mellitus contributes significantly to development of insulin resistance. In this study the mean body mass index was 28.40±4.9 kg/m^2. Females had significantly higher body mass index than males (p=0.024). Obesity is increasing in most populations (16, 17, 18) and this has contributed to increasing prevalence of diabetes. Physical inactivity, food high in saturated fat and simple sugar has contributed tremendously to the global rise in the incidence and prevalence of obesity (19). Higher insulin values in obesity signify an attempt by the body to overcome insulin resistance associated with obesity. Hyperinsulinemia, a consequence of obesity in diabetes contributes to vascular endothelial damage.

Our study did not find any statistically significant relationship between serum C-peptide and blood pressures (systolic and diastolic blood pressures) this however contrast with the study by Every et al who reported that a higher serum C-peptide levels were associated with higher blood pressures (21).

CONCLUSION

The low beta cell reserve in some subjects living with diabetes mellitus and the progressive decline of beta cell function with increasing duration of diabetes necessitate the need for early initiation of appropriate treatment to reduce the rate of beta cell exhaustion. This will also help improve glycemic control and reduce onset of complications.

Routine assessment of beta cell function using C-peptide at diagnosis should be considered in the management of diabetes. This will help in choosing appropriate antidiabetic medications.

Obesity remains a major problem among subjects with type 2 diabetes. There is the need to emphasize on lifestyle modifications which may include medical nutrition therapy and physical exercise with the aim of achieving good body mass index.

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Conflict of interest: No conflict of ineterst declared

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Table 1. Characteristics of male and female subjects

	Male	Female
n	23	23
Age (years)	58.30 ± 16.21	53.00 ± 12.96
Duration of diabetes(years)	8.00 ± 7.72	8.04 ± 6.72
Systolic blood pressure(mmHg)	136.52 ± 19.45	130.00 ± 16.52
Diastolic blood pressure(mmHg)	84.35 ± 11.61	83.48 ± 12.20
Body mass index(kg/m ^{2})	26.87 ± 5.00	30.09 ± 4. 32
Fasting C-peptide(ng/mL)	1.91 ± 1.18	2.40 ± 1.60

Table 2. Correlation table between age, duration of diabetes, body mass index, systolic blood pressure, diastolic blood pressure and serum fasting C-peptide.

		Age (years)	Duration of diabetes (years)	BMI (kg/m²)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Fasting C-peptide (ng/ml)
Age (years)	Pearson correlation p-value N	1 46	0.363 0.013 46	-0.274 0.065 46	0.311 0.036 46	-0.076 0.618 46	0.027 0.861 46
Duration of diabetes (years)	Pearson correlation p-value N	0.363 0.013 46	1 46	-0.301 0.042 46	0.059 0.695 46	-0.161 0.285 46	-0.366 0.012 46
BMI (kg/m²)	Pearson correlation p-value N	-0.274 0.065 46	-0.301 0.042 46	1 46	0.043 0.775 46	0.230 0.123 46	0.370 0.011 46
Systolic blood pressure (mmHg)	Pearson correlation p-value N	0.311 0.036 46	0.059 0.695 46	0.043 0.775 46	1 46	0.612 0.000 46	0.160 0.289 46
Diastolic blood pressure (mmHg)	Pearson correlation p-value N	-0.076 0.618 46	-0.161 0.285 46	0.230 0.123 46	0.612 0.000 46	1 46	0.232 0.121 46
Fasting C-peptide (ng/ml)	Pearson correlation p-value N	0.027 0.861 46	-0.366 0.012 46	0.370 0.011 46	0.160 0.289 46	0.232 0.121 46	1 46

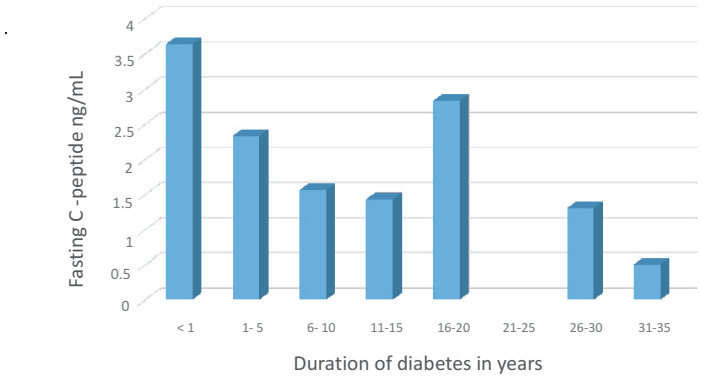

Figure 1. Bar chart of duration of diabetes and fasting C-peptide.