

PREVALENCE OF PROINSULIN LEVEL AMONG CONTROLLED AND UNCONTROLLED TYPE 2 DIABETIC SUDANESE PATIENTS

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ABSTRACT

Background: Proinsulin concentrations are highly related to atherosclerosis and cardiovascular diseases in type 2 diabetes mellitus (type 2 DM). This study was carried out to assess serum level of proinsulin among type 2 Sudanese diabetic patients. **Materials and Methods:** 41 patients with type 2 DM (age mean \pm SD: 54.58 \pm 11.74 years) (9 Controlled diabetic patients (11.1%) and 32 uncontrolled (39.5%)); (20 males, 21 females) and 40 apparently healthy individuals serves as control group (age mean \pm SD: 46.30 \pm 15.72 years) (20 males, 20 females) were enrolled in this cross-sectional study which conducted in Khartoum state in the period between March to October 2018. Fasting venous blood was collected from each participant then circulating levels of fasting plasma glucose (FPG) and HbA1c were measured by fully automated chemistry analyzer (Cobas 311 Roche) and plasma proinsulin level was measured with highly sensitive two-site sandwich ELISA, then the statistical analysis was done by using SPSS computer program. **Results:** The proinsulin level was significantly increased in cases (mean \pm SD: 5.5 \pm 9.13 pmol/L) compared to control group (mean \pm SD: 1.95 \pm 1.78 pmol/L) (P.value = 0.018), no significant difference were found in the proinsulin level in males (mean \pm SD: 5.56 \pm 11.10 pmol/L) and females (mean \pm SD: 5.50 \pm 7.03 pmol/L) (P.value = 0.983). Proinsulin level was significantly increased in DM2 patients treated with insulin (6.96 \pm 10.53 pmol/L) compared to patients using tabs (mean \pm SD: 2.07 \pm 1.42 pmol/L) (P.value = 0.020), there was no significant difference between proinsulin level in controlled patients (mean \pm SD: 4.80 \pm 4.6 pmol/L) and uncontrolled patients (mean \pm SD: 5.73 \pm 10.08 pmol/L) (P.value = 0.79). There was a moderate positive correlation between HbA1c and FBS among patients ($r = 0.70$, $P = 0.00$), but no correlation were found between proinsulin level and FBS ($r = -0.169$, $P = 0.29$); proinsulin level and HbA1c ($r = 0.096$, $P = 0.55$); proinsulin level and duration of DM ($r = 0.020$, $P = 0.90$); and proinsulin level and age of patients ($r = -0.008$, $P = 0.96$). **Conclusions:** Proinsulin level is increased in type 2 DM and has no relation with control of DM and gender.

KEYWORDS: Proinsulin, CVD, Sudanese diabetics, Proinsulin and glycemc control.

INTRODUCTION

Type 2 diabetes mellitus is a significant risk factor for cardiovascular disease (CVD).^[1,2] Atherosclerosis is associated with type 2 insulin resistance, but the extent to which insulin resistance contributes to the risk of subsequent CVD has so far mostly been studied by using the plasma immunoreactive insulin (IRI) concentration as a diagnostic marker of insulin resistance or by the minimal model technique.^[3]

The plasma IRI concentration correlates only moderately to insulin sensitivity when measured with the gold standard euglycaemic insulin clamp technique.^[4] In addition, the role of IRI as a risk factor for CVD has been cast in doubt.^[5,6] Even if IRI is accepted as a marker for cardiovascular disease, it is weak compared with established risk markers.^[5,6] Also, the length of follow-up attenuates the strength of IRI as a risk marker.^[7] Further, the strength of various risk factors for CVD may change between middle-aged and elderly patients of DM2.^[8]

Proinsulin, in contrast to specific insulin, was recently shown to be a long-term predictor of CVD in middle-aged men in the UK and in Sweden.^[9,10] Also, in studies with a shorter follow-up, proinsulin predicts myocardial infarction and first-ever stroke.^[11,12]

Proinsulin concentrations are highly related to atherosclerosis and cardiovascular disease in DM type 2.^[13] A study reported Insulin resistance in patients with type 2 diabetes is associated with an increased risk of cardiovascular events.^[14] The high prevalence of large-vessel coronary heart disease (CHD) in diabetic patients is well recognized, but the magnitude of this problem is not always appreciated. Cardiovascular complications are now the leading causes of diabetes-related morbidity and mortality. The public health impact of cardiovascular disease (CVD) in patients with diabetes is already enormous and is increasing.^[14,15] To the best of our knowledge; no data were found concerning using proinsulin as a predictive biomarker for CVD risk among Sudanese diabetic type 2; that is why we attempt to do this study to assess the prevalence of proinsulin among Sudanese diabetics..

MATERIALS AND METHODS

A cross-sectional study conducted in Khartoum state during the period from March to October 2018, a total of 81 participants were included in this study; 41 of them were type 2 diabetic patients who admitted to El-Amel Hospital, Khartoum 2 center for diabetics (9 (11.1%) controlled diabetic patients and 32 (39.5%) uncontrolled) and 40 of them were apparently healthy individuals serve as a control group. The age mean \pm SD was: 54.58 \pm 11.74 years and 46.30 \pm 15.72 years in patients and controls respectively. Patients with CVD, CHD, hypertension, obesity and any other disorders that may affect the level of proinsulin were excluded from the study.

Ethical considerations

This study was approved by scientific committee of Clinical Chemistry Department of Faculty of medical Laboratory Science, Al-Neelain University. An informed consent was obtained from participants who accepted to participate in this study. Information concerning previous diseases and current pharmacological treatment was collected from clinical records and a demographic data was collected by a questionnaire.

Sampling

about 5 ml of venous fasting blood samples were collected from patients and controls under aseptic

conditions; About 2.5 ml of whole blood were collected in EDTA, and the remained 2.5 ml were collected in plain containers, the samples were then centrifuged in 3000 rpm for 5 minutes to obtain serum which used for immediate estimation of blood fasting sugar (FBS) and proinsulin; and plasma was used for estimation of HbA1c.

METHODS

The practical work was conducted at research laboratory of College of Medical Laboratory Sciences, Sudan University of Sciences and Technology in accordance with good clinical practice guidelines. FBS was measured by hexokinase method in cobas 311 (Glucose HK Gen.3, Catalog Number: 04404483190), HbA1c was measured by heamolysate preparation in cobas 311, and Proinsulin was measured by ELISA Kit (ab213977).

Quality Control

Accuracy and precision of all results were assured by running of normal and pathological control sera.

STATISTICAL ANALYSIS

Student's unpaired t-test was used for comparison of quantitative variables and chi-square test was used for comparison of proportions. Pearson's correlation coefficients and multiple regression analysis were also performed to study the relation between study variables and study parameters. A significance level of 5% was chosen for all the tests (p value = 0.05 considered significant). Statistical analyses were performed with SPSS version 16.

RESULTS

In comparison with the controls, type 2 diabetic patients had significantly increased mean serum proinsulin (Table: 1). There was no significant difference in proinsulin level in males when compared to females patients (Table: 2). Proinsulin level showed a significant increase in DM2 patients used insulin than patients used tablets (Table: 3).

There was no significant difference between proinsulin level in controlled patients and uncontrolled patients (Table: 4). There was moderate positive correlation between HbA1c and FBS (P.V=0.00, r=0.70), but no correlation was found between proinsulin level and HbA1c, FBS, duration of DM and age of patients (r=-0.169, P.V=0.29) (r=0.096, P.V=0.55), (r=0.020, P.V=0.90) and (r=-0.008, P.V=0.96) respectively (Figures: 1, 2, 3 and 4).

Table. 1: Comparison of means of serum Proinsulin level in type 2 diabetes mellitus compared to control group.

	Group	N	Mean	Std. Deviation	P.value
Proinsulin (pmol/L)	Case	41	5.5334	9.13089	0.018
	Control	40	1.9528	1.78871	

P- value \leq 0.05 considered significant

Table. 2: Comparison of means of serum Proinsulin level in cases (male and female).

	Sex	N	Mean	Std. Deviation	P. Value
Proinsulin (pmol/L)	Male	20	5.5660	11.10695	0.983
	Female	21	5.5024	7.03903	

P- value ≤ 0.05 considered significant

Table. 3: Comparison of means of serum Proinsulin level in DM2 patients used insulin and DM2 patients used tablets.

	Drug	N	Mean	Std. Deviation	P.value
Proinsulin (pmol/L)	Tab	29	6.9645	10.53871	0.020
	Insulin	12	2.0750	1.42068	

P- value ≤ 0.05 considered significant

Table. 4: Comparisons of means of serum Proinsulin level in controlled and un controlled patients.

Variable	Controlled patients (n=9) Mean \pm SD	Uncontrolled patients (n=32) Mean \pm SD	P- value
Proinsulin (pmol/L)	4.8078 \pm 4.69040	5.7375 \pm 10.08488	0.791

P- value ≤ 0.05 consider significant

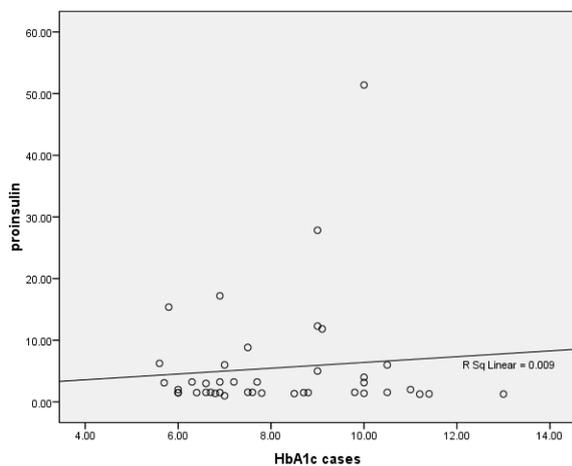


Figure. (1): Correlation between proinsulin level and HbA1c(r=-0.169, P.V=0.29).

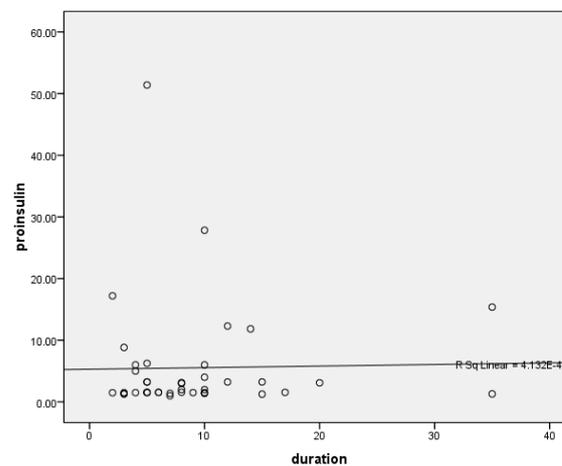


Figure 3: Correlation between proinsulin level and duration of disease (r=0.020 P.V=0.90)

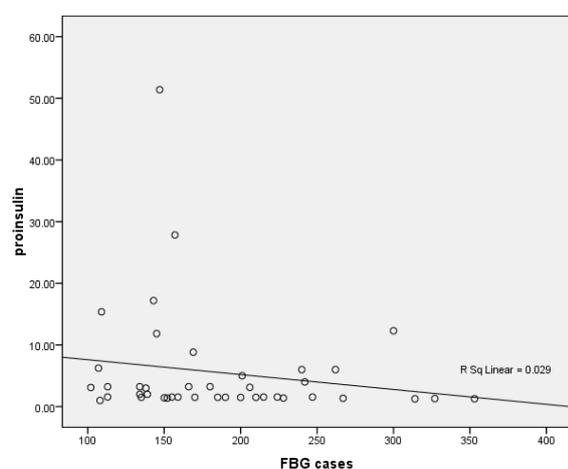


Figure 2: Correlation between proinsulin level and FBGS (r=0.096, P.V=0.55)

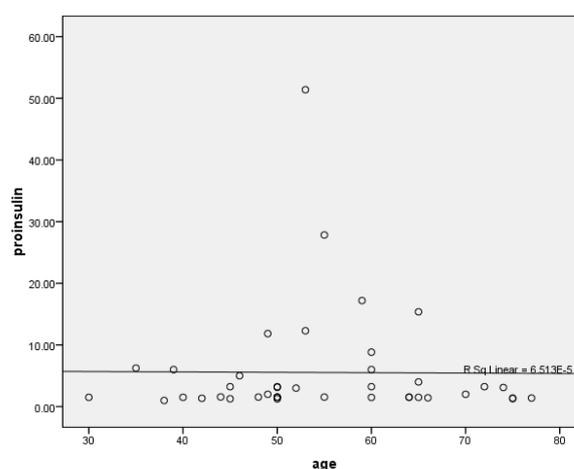


Figure 4: Correlation between proinsulin level and age of patients (r=-0.008, P.V=0.96)

DISCUSSION

Proinsulin concentrations are highly related to atherosclerosis and cardiovascular disease in DM type 2^[13]. Results of this study showed that, the level of proinsulin in type 2 DM was significantly increased compared to control group (P- value =0. 018); This result agreed with study done by Beckman *et al.*, which found significant increased in proinsulin in type 2 DM.^[14] Elevated level of proinsulin lead to cardiovascular risk by stimulating plasminogen activator inhibitor-1 secretion and blocking fibrinolysis^[15,16]. Also this result agreed with another study result which found cardiovascular risk factors clustering with endogenous hyperinsulinaemia predict death from coronary heart disease in patients with Type 2 diabetes.^[17] But this result disagreed with study done by Andreas Pfützner and Thomas Forst, which found insignificant difference in proinsulin level in diabetic patients type 2 compared to control group.^[14]

The current study results revealed no significant difference in proinsulin level in males compared to females patients; this result is in agreement with result of study carried out by Lindahl *et al.*, which found no significant difference between proinsulin level and sex.^[12]

In this study proinsulin level increased in diabetic patients type 2 treated by insulin than diabetic patients type 2 treated by tablets; this result agreed with previous study result which found a significant increase in proinsulin level in diabetic patients type 2 treated by insulin.^[17]

The results of the current study showed a positive correlation between proinsulin level and glycated hemoglobin (HbA1c) which found to be agreed with result done by many authors.^[18]

On the other hand; there was no correlation between proinsulin level with duration of diabetes mellitus, which agreed with study done by Pfützner *et al.*, who reported that about intact proinsulin is confirmed as a highly specific indicator for insulin resistance in a large cross-sectional study design.^[19]

CONCLUSION

Sudanese diabetic patients had increased level of proinsulin which might increase the risk of CVD.

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