Fasting C-peptide Levels as Predictor Marker for Type1 Diabetes Mellitus among Diabetic Children at Khartoum State.

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Abstract:
Background: Diabetes Mellitus (DM) is a major health problem worldwide. It can lead to life-threatening complication. So C-peptide (Cp) serves as a surrogate of pancreatic beta-cell reserve which can predict complication.

Objectives: To evaluate the clinical significance of basal Cp as a predictor of type 1 diabetes (T1D) and investigate the association of serum C-peptide level and BMI, HbA1c, age, age of onset and duration of disease in children with diabetes mellitus.

Methods: It was a descriptive cross sectional study conducted at Mohammed Elamin Hamid Pediatric Hospital during the period from November to April 2018. In this study 40 blood samples were collected and analyzed colorimetrically using ELISA technique, 40 samples (18 boys and 22 girls) from children with diabetes mellitus conducted in it. Statistical analysis: all the data was analyzed using (SPSS) version 21. The results were expressed as Mean±SD and percentage. One sample t-test and personal correlation test used to correlate between C-peptide and age, age of onset, duration of disease, HbA1c and BMI at p-value of < 0.05 considered as significant.

Results: It demonstrated that C-peptide was significantly decreased in diabetic patients compared to the mean of normal value (0.45±0.52, 1.55), (p value = 0.001), While HbA1C was significantly increased in diabetic patients compared to the mean of normal value (10.1± 2.5, 5.25). Also we found that C-peptide was weakly negative insignificant correlated with age, age of onset and HbA1C (R = -0.016, -0.016 and -0.046 respectively), (p value = 0.9, 0.9 and 0.7 respectively), while weakly positive insignificant correlated with BMI (R = 0.021), (p value = 0.8).

Conclusion: The study has concluded that the children with diabetes mellitus have significant decrease in C-peptide level and significant increase in HbA1c level in both male and female, compared to the reference value.

Keywords: Type1 Diabetes Mellitus, C-and glycemic control, C-peptides, BMI.

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INTRODUCTION:

Diabetes Mellitus (DM) is a major health problem worldwide (Jawad A.A. Al-Lawati, 2017). In 2017, approximately 5 million deaths worldwide were attributable to diabetes. Patients may experience acute life-threatening hyperglycemic episodes; As the disease progresses, and patients are at increased risk for the development of specific complications that cause considerable morbidity through microvascular complications as well as premature mortality is predominantly driven by macrovascular complications. The destruction of beta cells leads to insulin deficiency and abnormalities in carbohydrate, fat, and protein metabolism. Retention of cell function in patients with type 1 diabetes is known to result in improved glycemic control and reduced hypoglycemia, retinopathy, and nephropathy, (R.Goldenberg and Z. Punthakee, 2013). Diagnostic approaches for diabetes to prevent the complications which are related to diabetes are very important to diagnose diabetes at an early stage (Ali A et al, 2017). Until recently, the laboratory diagnosis of diabetes has been based on the presence of elevated fasting plasma glucose (126 mg/dl) or 2 h postprandial plasma glucose levels greater than 200 mg/dL (Janaka Karalliedde and Luigi Gnudi, 2016). There are several parameters which can serve as a diagnostic marker to diabetes. Some of the diagnostic markers, which can be utilized for the types of diabetes are, when a patient is suffering from blood sugar, HbA1c, c-peptide, autoantibodies, glycated albumin and glycated protein (Ali A, et al., 2017). C-peptide is a useful tool in the classification of diabetes. It can
help differentiate T1DM, T2DM, and MODY. C-peptide is associated with duration of disease as well as age of diagnosis. Whilst C-peptide is useful in classifying diabetes it must always be interpreted in clinical context of disease duration, comorbidities, and family history (Limei Wang et al, 2012).

Materials and Methods:

The study comprised a total of 40 children who were, previously, diagnosed with diabetes on the basis of clinical signs and symptoms of diabetes mellitus, and who were under exogenous insulin treatment. Their ages ranged between 7-18 years old and were classified into three groups according to duration: (30 patients) were 0-5 years of duration, (10 patients) were from 6-10 years duration with diabetes and two group according. Subjects who were suffering from chronic kidney disease, liver disease and obese children were excluded from the study. Informed consent was taken from the patients and subjects who participated in the present study, after the agreement of general managers of hospitals and private centers. Ethical committee approval has also been obtained from Omdurman Islamic university, Khartoum State, Ministry of Health Research Department and from Mohammed El-amin Hamid Pediatric Hospital. In all the children, fasting serum C-peptide and glycated hemoglobin were estimated. The serum C-peptide was estimated by immune-enzymometric assay and blood glycated hemoglobin by fluorescence immunoassay.
Statistical data:
All the data were expressed in Mean and Standard deviation. For the statistical significance, One sample T test was performed using SPSS software.

Results:
Our result demonstrated that C-peptide was significantly decreased in diabetic patients compared to the mean of normal value (0.45±0.52, 1.55), (p value = 0.001), While HbA1C significantly increased in diabetic patients compared to the mean of normal value (10.1± 2.5, 5.25). Also we found that C-peptide was weakly negative and insignificantly correlated with age, age of onset and HbA1C (R = -0.016, -0.016 and -0.046 respectively), of (p value = 0.9, 0.9 and 0.7 respectively), while weakly positive insignificantly correlated with BMI (R = 0.021), (p value = 0.8). The disease was more common in patients with history of DM (55%) compared to those with no family history of DM (45%). Also the results revealed that frequency of disease in male was 45% and in females 55% which indicates predominance of disease in female more than male. Among children of study there was 55% of them with normal weight and 40% underweight, while 5% of them appeared over weight. The frequency of disease in patients with age up to 10 years was 22% and 78% in patients with more than 10 years of age.
**Figure 1:** frequency of disease among gender.

The figure revealed that frequency of disease in male 45% and female 55% which indicates predominance of disease in female more than male.
The figure shows the frequency of disease in patients with up to 10 years of age 22% and 78% in patients with age more than 10 years.
Figure 3: Frequency of disease in family history of DM. It was obvious that disease was more common in patients with history of DM (55%) in contrast to those with no family history of DM (45%).
Figure 4: BMI frequency among children. The figure shows that among children of study there are 55% of them with normal weight and 40% underweight, while 5% of them appeared over weight.
Table 1: Comparison of HbA1C and C-peptide with mean of normal value (result expressed as Mean ±SD). Our result demonstrated that HbA1C was significantly increased in diabetic patients compared to the mean of normal value (10.1± 2.5, 5.25), (p value = 0.000), while C-peptide was significantly decreased in diabetic patients compared to the mean of normal value (0.45±0.52, 1.55), (p value = 0.001).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ±SD</th>
<th>Mean of normal value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1C %</td>
<td>10.1± 2.5</td>
<td>5.25</td>
<td>0.000</td>
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<tr>
<td>C-peptide ng/ml</td>
<td>0.45±0.52</td>
<td>1.55</td>
<td>0.001</td>
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Table 2: Shows the correlation of C-peptide with age, age of onset, duration of Disease, BMI and HbA1C. The study revealed that C-peptide was weakly negative insignificantly correlated with age, age of onset and HbA1C (R = -.016, -.016 and -.046 respectively), of (p value = 0.9, 0.9 and 0.7 respectively), while weakly positive insignificant correlated with BMI (R = 0.021), (p value = 0.8).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>R and P value</th>
<th>Age</th>
<th>duration</th>
<th>age of onset</th>
<th>BMI</th>
<th>HbA1C</th>
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<tr>
<td>C peptide</td>
<td>R value</td>
<td>.016</td>
<td>.056</td>
<td>.016</td>
<td>.021</td>
<td>-.046</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.9</td>
<td>0.7</td>
<td>0.9</td>
<td>0.8</td>
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Discussion:

Type 1 diabetes results from an immune mediated destruction of pancreatic beta cells that begins long before, and is believed to continue long after, the clinical diagnosis of type 1 diabetes (Palmer JP 2009). So measurement of C-peptide is a well-accepted method for the quantification of endogenous insulin secretion, beta cell function (Jones AG and Hattersley AT 2013; Kulkarni CM and Patil S 2016) also to differentiate between type 1 diabetic patients and MODY being misdiagnosed as type 1 diabetes. (Maria Thunander et al., 2012); especially in children. This study showed that C-peptide level was significantly decrease in diabetic children compared to the mean of normal value (0.45+0.52, 1.55), (p value =0.001) that was agreed with studies were done by Emma Leighton, Landin-Olsson M, Jung Won Hwang and Kuhtreiber (Landin-Olsson M et al., 1990; Kuhtreiber et al., 2015; Emma Leighton et al., 2017; Jung Won Hwang et al., 2017). While the HbA1c level was significantly increased in diabetic children compared to the mean of normal value (10.1+2.5, 5.25), (p value =0.000) in this study. According to new ADA criteria for diagnosis of diabetes, a study done by Aljabri KS and Bokhari SA 2013 in Saudi Arabia. (Aljabri KS and Bokhari SA2013).

C-peptide was insignificant correlated with Age, Age of onset, HbA1c and BMI, this study opposite to study done by Lauria, who found significant correlation when the C-peptide level decrease (Lauria et al., 2015), this disagree due to; low sample size used in our study, difference in classification groups according to duration, age group

Conclusions:
From the results of this study it was inferred that: the level of fasting c-peptide is decrease in the type 1 diabetes mellitus and poor glycemic control in those patient. There is no correlation between level of c-peptide and age, age of onset, glycocylated hemoglobin and body mass index.

REFERENCES.


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17- M. Landin-Olsson t, K. O. Nilsson 2, A. Lernmark 1, 3 and G. Sundkvist 1 (1990) Islet cell antibodies and fasting C-peptide predict insulin requirement