The impact of Serum Amylin on Body mass index in Children with type1 Diabetes Mellitus newly diagnosis

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KEYWORDS
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ABSTRACT
Background: Pancreatic β cells' inability to synthesize insulin is the defining feature of type 1 diabetes mellitus (T1DM), an endocrine illness. This action involves the peptide hormone amylin, which is co-secreted with insulin and plays a key role in controlling glucose homeostasis and appetite. It also influences body weight, calorie intake, stomach emptying, glucagon release suppression, and satiety.
Subjects, Material, and Method: This study included 120 pediatric individuals aged between(2-14) years. They were divided into four groups. Group one contains 40 lean patients with T1DM, with a BMI≥85 percentile, and group two contains 40 underweight patients with (T1DM) with a BMI≥5 percentile. The Group contains 40 healthy pediatrics and ages matched with the patients subdivided into (group three, lean control with a BMI less than 85 percentile. The group numbered 22, and four groups, underweight control with BMI≥5 percentile, consisted of 18 pediatric underweight healthy as controls. They were analyzed for fasting serum glucose, amylin, and HbA1c.
Results: The levels of Amylin in the control group(lean and underweight) were higher than in the patients with diabetes mellitus(lean and underweight). Also, fast blood glucose(FBG) was found in the Lean DM group. Similarly, the Underweight DM group was higher than those observed in the Lean Control and Underweight Control groups. For HbA1c%, the Lean DM group. The Underweight DM group exhibited a higher mean HbA1c%. In contrast, the Lean Control and Underweight Control groups had significantly lower mean HbA1c% values.
Conclusion: The control group had higher Amylin levels, a potential biomarker for metabolic status in children with T1DM, and could inform therapeutic strategies to optimize glycemic control and body weight management. In comparison, the patient group had higher FBG values. The Lean DM group had higher HbA1c% values, while the Underweight DM group had slightly higher values. Both control groups had significantly lower HbA1c% values.

1. Introduction

Type 1 diabetes mellitus (T1DM) is characterized by a chronic metabolic disease caused by an autoimmune disease attack and leads to defects in insulin-producing β-cells of the pancreas in genetically susceptible people. (1) in children who had T1DM, Symptoms include thirst, polyuria, vision disorders, and weight loss. In some cases, the complications of diabetes are ketoacidosis and hyperosmolar, which may lead to coma. But most symptoms are not severe, which over time may harm or even destroy various organs, resulting in permanent ailments like blindness, amputation, stroke, and finally death. (2) Before the illness showed symptoms, children with T1DM were bigger than their healthy counterparts. The body of research indicates that a higher Body Mass Index (BMI) is linked to an increased risk of developing Type 1 Diabetes (T1DM). (3). The pancreatic peptide hormone amylin is co-stored and elevated with insulin in response to dietary intake. In addition to impacting glucose management by postprandial reduction of nutrient-mediated glucagon secretion and delayed stomach emptying, it stimulates receptors in the hypothalamus and hindbrain to promote satiation. (4). Amylin has acute effects on body weight as a satiety signal connected with the homeostatic effects of an adiposity signal, indicating a significant function for Amylin in body mass regulation. (5).

Aim: The present study aims to examine the link between weight (represented by body mass index) and some metabolic hormones (Amylin) in newly diagnosed children with type 1 diabetes mellitus to shed light on the weight control mechanism in such patients.

2. Subjects, Material, and Method:

This case-control study included 120 pediatric T1DM newly diagnosed aged between (2 and 14) years at Welfare

Teaching Hospital_ Baghdad Medical City and in addition to the central teaching hospital of Pediatric in Alkarkh district from the first of February to the end of May 2024. Every individual provided their informed consent. The University of Baghdad Ethics Committee, the Department of Biochemistry, and the College of Medicine approved the study. The participants were classified into the following groups: the first group consisted of 40 pediatric with lean T1DM, and the second group consisted of 40 pediatric underweight T1DM. The Third group numbered 22 pediatric lean healthy as controls. The fourth group consists of 18 pediatric underweight healthy as controls.

Exclusion criteria:

1) Type 2 diabetes mellitus.

2) Patients on nutritional supplements.

3) Patients with complications of Type 1 diabetes such as neuropathy, retinopathy, or nephropathy.

4) Thyroid disease and celiac disease.

Blood samples:

Five milliliters of the peripheral blood sample was obtained from the patient, Two ml was taken in an EDTA (Ethylenediaminetetraacetic acid) anticoagulant tube to measure the HbA1c test, and the remaining Three ml was placed in a gel tube. The blood samples allowed clotting for 15-30 minutes and were separated by centrifugation for 10 minutes at 3000 rpm to obtain serum. This is subdivided into two tubes. The separated serum samples were stored in aliquots at -20 °C until the time of measurements of glucose and Amylin.

Measurement of Biochemical Parameters:

The following biomarkers were measured in the blood: Glucose measured by spectrophotometer and HbA1c on the Cobas c 111 system, and serum Amylin was determined using an enzyme-linked immunosorbent assay (ELISA)and anthropometric measurements, including body mass index (BMI)

3. Result:

The Age for the lean control and underweight group was a mean, respectively, Age of (9.73± 0.80) years, (9.39± 0.62) years. The underweight DM group showed a n age had a lower mean age of 8.03± 0.58years. And a mean age of 9.33±0.31 years for lean DM. P= 0.108 indicates that the age distribution was not statistically significant. There is a statistically significant variation in weight between the groups (P< 0.0001). The mean weight of the underweight and lean control groups is (34.55±2.67) kg. (28.72± 2.11)

The weights of the underweight and lean T1DM groups were, respectively, (24.54± 1.75 kg and (37.28± 1.47) kg. .. P=0.05 indicates that height was not statistically significant. Table 1-1 shows that the groups' mean heights were very constant, with the lean and underweight control group measuring (133.23± 4.45) and (137.33± 4.12) cm, respectively, and the lean and underweight T1DM group measuring (135.15± 2.10) and (125.97± 3.98) cm, respectively.

In the present study, the differences in BMI among the groups were significant (P< 0.001) in Table 1-2. The lean and underweight control groups had mean percentile scores of (70.82± 2.23). They were shown to be significantly different from the underweight control group, the underweight DM group, and the lean DM group. The mean percentile score for the lean DM group was 85.67± 1.53, distinguishing it meaningfully from the underweight, underweight DM, and lean control groups. The underweight control group had a mean percentile score significantly different from the lean control and DM groups. The underweight DM group had a mean percentile score of 19.15± 3.68and was significantly different from the lean control and lean DM groups. In the present study, HbA1c%, the Lean DM group had a mean value of (11.40± 0.25). The Underweight DM group exhibited a slightly higher mean HbA1c% (11.77± 0.32). In contrast, the Lean Control and Underweight Control groups had significantly lower mean HbA1c% values of (5.16±0.04) and (5.16± 0.05), respectively. The Lean DM group had a mean FBG of 214.33 ± 14.93 mg/dL. Similarly, the Underweight DM group had a mean FBG of 213.35 ±18.92 mg/dL. These values are considerably higher than those observed in the Lean Control and Underweight Control groups, with mean FBS levels of 86.63 ±1.70 mg/dL and 86.99 ± 1.64, respectively. Amylin levels in the control group(lean and underweight) with a mean of(202.68± 44.34)(354.88± 90.00) pg/ml respectively. The patient's diabetes mellitus(lean and underweight) with means respectively (27.27± 2.46)(31.38± 2.44) pg/ml. The differences in Amylin levels were highly significant (P< 0.000001)

Table (1-1) Mean (±SEM) values of Age, Weight, control, and diabetes mellitus:

	Age		
	Control n=40	Patient n=80	PValues
Lean	9.73± 0.80	9.33± 0.31	
Underweight	9.39± 0.62	8.03± 0.58	P=0.108
Weigh			
Lean	34.55± 2.67	37.28± 1.47	
Underweight	28.72± 2.11	24.54± 1.75	P<0.0001
Height			
Lean	133.23± 4.45	135.15± 2.10	
Underweight	137.33± 4.12	125.97± 3.98	P=0.04

Table (1-2) Mean (±SEM) values of Body mass index of control and diabetes mellitus patients.

	BMI Percentile		
	Control n=40	Patient n=80	PValues
Lean	70.82± 2.23	85.67± 1.53	
Underweight	21.44± 4.14	19.15± 3.68	P<0.001

Table (1-3) Mean (±SEM) values of Glycated Hemoglobin and glucose of control and diabetes mellitus patients:

			HBA1C%
	Control n=40	Patient n=80	Values
Lean	5.16± 0.04	11.40± 0.25	
Underweight	5.16± 0.05	11.80± 0.32	P<0.0001
Glucose mg/dl			
Lean	86.63± 1.70	214.33± 14.93	
Underweight	86.99±1.64	213.35± 18.92	P<0.0001
AMYLIN pg/ml			
Lean	202.68± 44.34	27.27± 2.46	
Underweight	354.88± 90.00	31.38± 2.44	P<0.0001

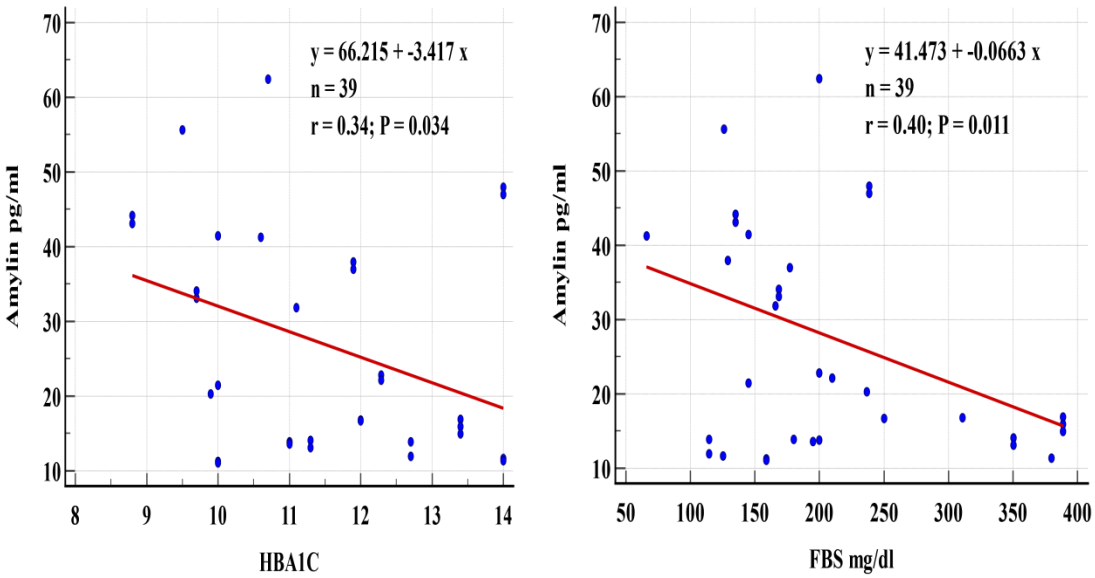

Figure 1 shows the correlation between amylin and glucose. Figure 2 shows the correlation between amylin and HbA1C in lean DM.

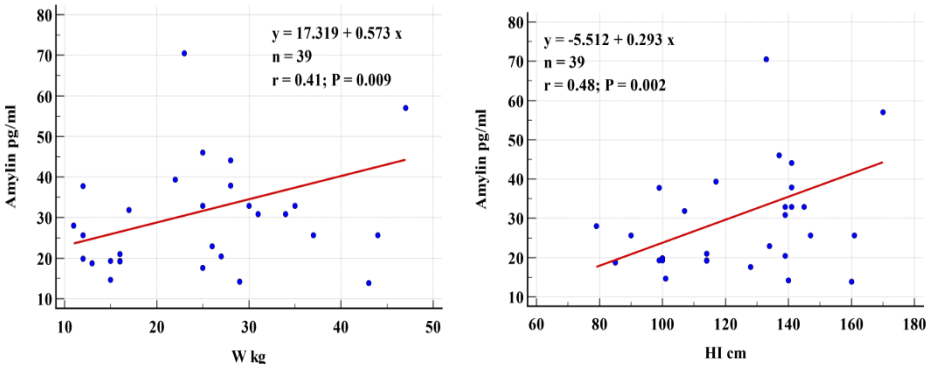

Figure 3 shows the correlation between amylin and high. Figure 4 shows the correlation between amylin and weight in underweight DM.

4. Discussion:

In the present study, age was a control group that closely matched the patients, and no significant differences in age were found. This finding is consistent with the results obtained by Marcovecchio et al.(6). Additionally, a statistically significant ($P < 0.0001$) weight difference was found in the current study between the groups with underweight healthy and underweight DM, as well as lean healthy and lean healthy.

A decrease in total body and muscular weight characterizes the first week of type 1 diabetes in children. This occurs due to the body's inability to generate insulin, which cells need to convert glucose into energy. Therefore, there is a decrease in ATP generation and a breakdown of protein and fat. (Keşim et al., 2024)(7)

Conversely, the variation in height among the four groups was not statistically significant. This result aligns with a previous study by Polkowska et al. (2016), which indicated that children with newly diagnosed diabetes had significantly lower body weight but did not differ considerably in height(8)

Also, another study done by Shaikh et al. (2024) that did not agree with a present study on T1DM patients found significant differences in height (9). The current study found the percentile scores of body mass index in (the lean healthy and lean DM) groups are significantly higher compared to (the underweight healthy and underweight DM groups), a finding similar to the previous study by De Keukelaere et al. (2018)(10)as shown in table 1-2.

Additionally, in this investigation, lean and underweight diabetic patients had serum HbA1c levels that were considerably greater than those of lean and underweight healthy people. In a similar vein, the lean and underweight diabetic persons had considerably higher serum glucose levels than the lean and underweight healthy individuals. These results are in line with Ashiqur Rahman et al.'s earlier investigation from 2023. who showed that the loss of glycemic control was responsible for the significantly raised HbA1c readings. A good indicator of chronic glucose sensitivity is HbA1c. (11) The study's findings also support a different study by Ochocińska et al. that discovered newly diagnosed individuals had the greatest blood glucose and HbA1C values(12). The current study shows that serum Amylin levels in the healthy group were significantly higher than in patients with diabetes mellitus. This result agrees with previous research by Mabilleau et al., 2024, who found Plasma Amylin levels of the children with T1DM were significantly lower than those of healthy controls (13). Also, the study's results agree with a previous study by Mathiesen et al., which found that patients with type 1 diabetes have lower serum Amylin concentrations (5). Beta cells in the pancreas generate amylin, which is secreted alongside insulin. Thus, amylin secretion is either absent or inadequate in T1DM. While those with early-stage diabetes mellitus or glucose intolerance typically have higher Amylin levels after hyperinsulinemia (14), another study did not agree while showing the Amylin in T1DM higher than healthy control subjects (12). Amylin and insulin are secreted in a 20:1 molar ratio upon adding glucose. Thus, there is a decrease in amylin synthesis in people with type 1 diabetes mellitus (T1DM). (5) in the present study, Figure 1 shows that Amylin has negative correlations with FBG and HbA1c in lean DM, suggesting different regulatory mechanisms in diabetic conditions. Figures 3 and 4 show a positive correlation between amylin, height, weight, and Age in underweight DM. Notably, the correlation coefficients were positive for anthropometric measures and Amylin, which agrees with the previous study by Hammel et al.,2011 (15). T. Lutz suggests that the area of postrema (AP), distinguished by an open blood-brain barrier, controls the impact of amylin on the homeostatic regulation of eating. This facilitates the identification of the caudal hindbrain neurotransmitters necessary for controlling

the function of amylin. Amylin directly stimulates the central nervous system, which regulates its effects on metabolism. However, the brain's amylin receptor (AMY) is activated by mature amylin in its soluble monomeric form. This has a good impact on weight reduction and the prevention of diabetes in addition to the hormonal effects on glucose metabolism (inhibition of glucagon release, modification of stomach emptying, nutrient intake, and induction of satiation).(16)

5. Conclusion:

It was found that amylin levels were reduced in patients with type 1 diabetes mellitus (T1DM) compared to healthy pediatric subjects. A negative correlation between fasting glucose and HbA1c was found in Lean DM subjects, a positive correlation was found in weight and height in underweight DM subjects, and there was no correlation between Amylin and healthy groups.

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