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Article

Diabetes Patients Show Elevated Adipokines, Glucose, and Insulin Resistance Markers

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Abstract: This study evaluated adipokines and biochemical parameters in 70 children (44 males, 26 females, age 5-13 years, mean±SD 8.7±3.32 years) with type 1 diabetes mellitus (T1DM) and 30 healthy controls. Conducted at Azadi Teaching Hospital from December 2023 to February 2024, the study aimed to compare glucose, HbA1c, vitamin D, lactate dehydrogenase (LDH), adiponectin, and leptin levels between T1DM patients and healthy children. Results showed significant increases in glucose (321.93±89.15 vs. 85.21±9.46 mg/dL), HbA1c (12.04±1.83% vs. 5.01±0.31%), LDH (284.22±21.94 vs. 89.13±7.42 U/L), adiponectin (9.26±0.28 vs. 3.62±0.94 µg/mL), and leptin (21.84±2.62 vs. 4.48±0.62 ng/mL), and a significant decrease in vitamin D (13.93±4.93 vs. 28.72±6.08 ng/mL) in T1DM patients ($P<0.05$ for all). These findings highlight the importance of monitoring vitamin D and adipokine levels in children with T1DM, suggesting potential roles in disease management and complications prevention.

Keywords: Vit. D, T1DM, Leptin, Vitamin-D, Adiponectin.

1. Introduction

It is now known that type 1 diabetes mellitus (T1D) is an autoimmune illness caused by the immune system destroying the pancreatic cells that produce insulin, resulting in complete insulin insufficiency [1]. Insulin therapy is required for life in order to prevent diabetic ketoacidosis, which will lead to death ultimately. Type 1 diabetes, which accounts for 5–10% of all cases of the disease, is typically diagnosed in childhood but can also strike adults. Type 1 diabetes has a heavy cost; it can lead to long-term issues, a shorter life expectancy, a lower quality of life, and a substantial increase in medical expenses [2-4]. When the autoimmune death of the pancreatic beta cells severely impairs insulin production, type 1 diabetes mellitus (T1DM) results [5]. Usually, 80–90% of the beta cells are killed at the time of diagnosis. A different perspective was recently put up by Roep et al. [6], according to which aberrant β-cells are the primary cause of T1DM pathogenesis. Based on the outcomes of immunotherapy previously described in T1DM [7-8], they demonstrated [6] that β-cells with poor capacity for self-defense are susceptible to biosynthetic stress.

Researchers are looking for novel approaches to treating and preventing T1DM [9-10]. In order to prevent and reverse diabetes autoimmunity, Antigen vaccination (using oral insulin) and stem-cell-based replacement therapy are two areas of investigation in this field [11]. Adipose tissue secretes bioactive mediators called adipokines, which include resistin,

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adiponectin, and leptin [12]. They are involved in the inflammatory reactions and play a major function in controlling the metabolism of fats and carbohydrates [13].

The role of adipose tissue in the low-grade systemic inflammation linked to type 1 diabetes has received significantly less research than that of type 2. In fact, changes in circulating adipokine levels in type 1 diabetes suggest that adipose tissue plays a role in the pathophysiology of the disease [14]. Type 1 diabetes and vitamin D insufficiency have been linked in the past, and there is mounting evidence that low vitamin D concentration throughout pregnancy or during the early stages of life may raise the risk of the condition. This evidence is still ambiguous, albeit [15]. While some research [16, 17] revealed no correlation between serum vitamin D levels and insulin action parameters, other investigations have reported positive correlations. The current study therefore sought to evaluate several adipokines and biochemical parameters in patients with type I diabetes mellitus.

2. Materials and Methods

Subjects

70 patients (44 males and 26 females), age range (5-13) years (mean± SD) (8.7±3.32) years were enrolled in this study. All were consecutively admitted to the clinic at Azadi teaching hospital at December 2023 to February 2024. All patients had Type 1 Diabetes Mellitus (T1DM) as diagnosed by the physician. also, this study including 30 healthy volunteers as control group.

Blood collection

Five milliliters (ml) of venous blood were extracted, and the blood was extracted using disposable plastic syringes following a fifteen-minute centrifugation at 300 rpm. The separated sera were frozen at -20 OC before analysis.

Measurements

- Glucose: Blood sugar testing was performed according to the manufacturer's procedures (BioLabo, France) and using a spectrophotometer.
- HbA1c: Using quantitative reflectometry and immunoassay technologies, the Multicare analyzer (SD BIOSENSOR, Korea) was able to detect HbA1c in the serum of T1DM patients.
- Lactate Dehydrogenase: Blood sugar testing was performed according to the manufacturer's procedures (SUNLONG, China) and using a spectrophotometer
- Vitamin D: The Vit. D ELISA Kit (SUNLONG, China) assays VD R levels in human serum, plasma, or other biological fluid using Sandwich-ELISA, an ELISA technique.
- Adiponectin: Adiponectin was measured using ELISA kits from United States Biological Company (My biosource, USA).
- Leptin: using the Leptin (sandwich) Enzyme Immunoassay Kit to measure serum leptin levels. The sole intended application for this assay is in vitro diagnostics. The sandwich principle serves as the foundation for this solid phase enzyme-linked immunosorbent test (ELISA).

Statistical analysis

Each date of data was sorted, and the total was expressed as a percentage and a number. Any two selected groups' mean values were compared using the student t-test to see how significant the difference was; a P-value of less than 0.05 was considered statistically significant. The Pearson correlation coefficient (R) test is used to characterize the relationship between the different parameters under investigation; a statistically significant result is defined as P<0.05 [18].

3. Results and Discussion Glucose and HbA1c

Table (1) show the levels of glucose and HbA1c in T1DM patients and healthy subjects, where glucose levels in serum of T1DM patients (321.93 ± 89.15) demonstrated significant (P <0.05) increase in compared with healthy children (85.21± 9.46), as shown in figure (1). the levels of HbA1c demonstrated significant (P <0.05) increase in T1DM patients (12.04 ± 1.83) compared with healthy children (5.01 ± 0.31), as shown in figure (2).

Table 1. the levels of glucose and HbA1c in both groups

Parameter \ Groups	Control (30)	Patients (70)	P-Value
Glucose (mg/dl)	85.21± 9.46	321.93 ± 89.15*	0.001
HbA1c (%)	5.01 ± 0.31	12.04 ± 1.83*	0.001

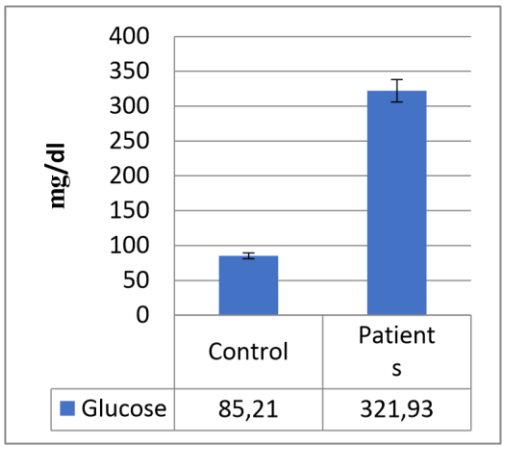

Figure 2. Glucose levels in patients and control

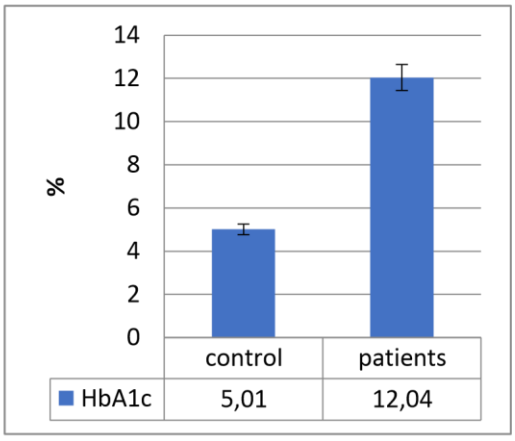

Figure 1. HbA1c levels in patients and control

Calculating the HbA1c and glucose levels is regarded as a significant biochemical test that is frequently used to screen for diabetes mellitus and track its progression [19]. The current findings showed that every patient included in the study had an elevation above typical standard values. The American Diabetes Association (ADA) recommends that levels less than 6.5% be used as a diagnostic indication for diabetes mellitus [20]. The fact that type 1 diabetes (T1DM) develops due to beta cell loss rather than insulin resistance, as in classic type 2 diabetes-mellitus, has been connected to the difficulties in achieving glycemic control in T1DM patients [21]. HbA1c levels in T1DM patients were measured in parallel studies. For example, one study found that children with diabetes had HbA1c levels above 7.8% [22]. Another study found that HbA1c levels were higher than 9.4% in newly diagnosed T1DM patients before beginning insulin treatment [23], and a third study found that HbA1c levels were higher than 10% [24].

Glucose and HbA1c

Table (2) show the levels of vit. D and LDH in T1DM patients and healthy subjects, where vit. D concentration in serum of T1DM patients (13.93± 4.93) demonstrated significant (P <0.05) reduced compared with healthy children (28.72 ± 6.08), as shown in figure (3). the levels of LDH demonstrated significant (P <0.05) increase in T1DM patients (284.22 ± 21.94) compared with healthy children (89.13 ± 7.42), as shown in figure (4).

Table 2. The concentrations of vit. D and LDH in both groups

Parameter \ Groups	Control (30)	Patients (70)	P-Value
Vit. D (ng/ml)	28.72 ± 6.08	13.93± 4.93*	0.001
LDH (U/L)	89.13 ± 7.42	284.22 ± 21.94*	0.001

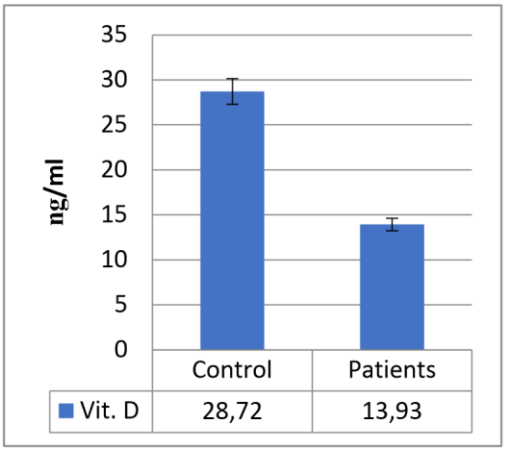

Figure 3. Glucose levels in patients and control

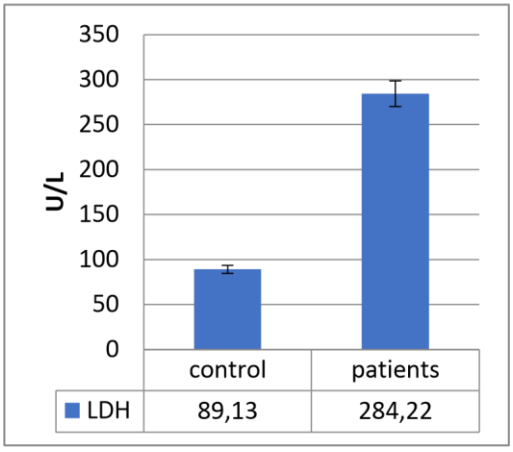

Figure 4. Glucose levels in patients and control

It is hypothesised that the low level of vitamin D at the time of diagnosis plays a harmful effect in immune-mediated β-cell death, which initiates the onset of clinical diabetes [25–26]. Vitamin D levels were found to be lower in the diabetes patients during the current investigation as compared to the control group. The findings are consistent with those of previous researchers who discovered that 25(OH) vitamin D levels in newly diagnosed T1DM patients were lower than in healthy controls (P<0.01) [27-28]. Studies have revealed that vitamin D supplementation lowers the risk of acquiring T1DM and that there is a correlation between the severity and frequency of T1DM and vitamin D insufficiency. [29– 30] In addition, some researchers came to the conclusion that vitamin D deficiency was quite variable in children and adolescents with T1DM, ranging from 15% to 90% [31-32]. The reasons for the variations in frequency could be linked to the definition of vitamin D insufficiency. This heterogeneity may be influenced by genetic predisposition, dietary consumption, dark skin tone, sun avoidance behavior, latitude, and geographic environment [33]. Conversely, Hongyan Yang et al. found that elevated LDH was a DM risk factor [34]. Additionally, our research validated the link between LDH and T1DM.

Adiponectin and Leptin

Table (3) show the concentrations of some adipokines in T1DM patients and healthy subjects, where Adiponectin concentration in serum of T1DM patients demonstrated significant (P <0.05) increase in (9.26± 0.28) compared with healthy children (3.62 ± 0.94), as shown in figure (5). the concentration of Leptin demonstrated significant (P <0.05) increase in T1DM patients (21.84 ± 2.62) compared with healthy children (4.48 ± 0.62), as shown in figure (6).

Table 3. The concentrations of Adiponectin and Leptin in both groups

Parameter \ Groups	Control (30)	Patients (70)	P-Value
Adiponectin (µg/ml)	3.62 ± 0.94	9.26± 0.28*	0.001
Leptin (ng/ml)	4.48 ± 0.62	21.84 ± 2.62*	0.001

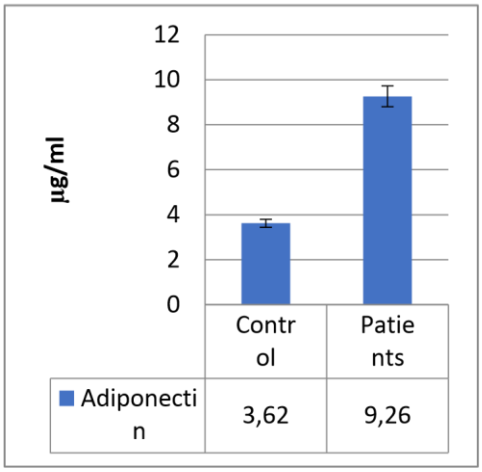

Figure 5. Adiponectin levels in patients and control.

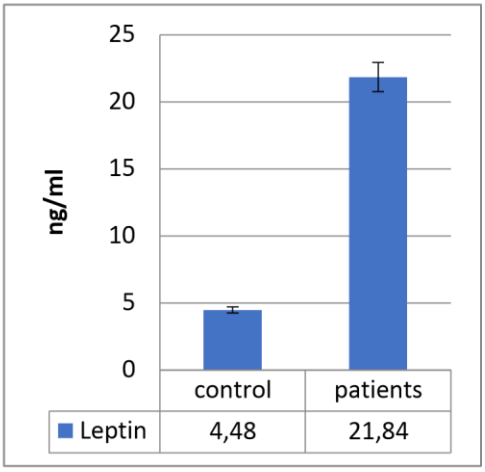

Figure 6. Leptin levels in patients and control.

Lower levels of adiponectin and leptin are associated with type 2 diabetes and obesity. They also modulate the action of insulin, enhancing peripheral insulin sensitivity in an inverse relationship to insulin resistance [35]. The current investigation shown that T1D children had considerably higher serum levels of leptin and adiponectin than healthy controls; this finding may be explained by the patients' higher body fat percentage. According to a different theory, long-term insulin therapy raises leptin levels by directly affecting adipocytes [36]. Insulin, fat mass, gender, activity, and the location of adipose tissue all influence serum adiponectin and leptin concentrations [35, 37]. Lo et al. [38], however, did not discover that insulin affected the level of leptin in the blood in kids with diabetes. Divergent outcomes in this domain could potentially stem from variations in the dosage and length of insulin therapy, caloric consumption, and metabolic regulation within the pediatric population. A prior study showed that children with type 1 diabetes had greater levels of total serum adiponectin than healthy controls [37]. Although the exact cause of T1D's vascular problems is unknown, chronic, low-grade inflammation may play a role [37-38]. In this investigation, we discovered that T1D patients with nephropathy and neuropathy had significantly higher serum levels of adiponectin and leptin than those without. Adiponectin and leptin total levels were found to

be higher in type 1 diabetic individuals with microvascular problems compared to those without [35, 39].

4. Conclusion

Compared to children without diabetes, diabetic children are more likely to experience severe Vitamin-D deficiencies and elevated levels of adipokines. Based on our findings, we advise measuring vitamin D and adipokines in children with type 1 diabetes.

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