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Exploring the Association between Obesity, Inflammation, and Type II Diabetes: Insights from Body Mass Index Correlation and Immune Response Analysis

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Abstract

Diabetes mellitus (DM) is a group of physiological disorders characterized by a prolonged hyperglycemic state caused by insulin secretion and activity. Recently, several study positive correlations between the increase in BMI and T2D. Additionally, the immune system has contributed to the pathogenicity of T2D in obese individuals. The current study sought to investigate the correlation between obesity and inflammation in obese T2D and obese non-T2D individuals and also detected the role of increasing BMI in obese individuals and developing T2D. The finding involved 100 participants (50 obeseT2D and 50 obese without T2D). The serum of all participants underwent the following immunological and biochemistry tests, which include FBS, Insulin, IAA, ANA, BMI, and HOMA-IR. This study revealed that obese males develop T2D more than females (60.0%, 40.0% respectively) Moreover, Obese T2D and obese without T2D individuals were increased concentrations of IgG in serum levels with markers (ANA, HOMA-IR, and IL-6). While IgG levels in IAA serum were considerably greater in obese T2D individuals only. Furthermore, BMI has been positively associated with an increasing level of ANA, HOMA-IR, and IL-6 in both groups. This investigation unveiled a direct correlation between escalating BMI and the incidence of T2D. Additionally, it revealed the active impact of obesity on the immune response and its consequential contribution to the pathogenesis of T2D.

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Abbreviation

IDF: Diabetes federation of the world
CVD: Cardiovascular diabetes
BMI: Body mass index
T2D:Type2 diabetes
IAA: Insulin Autoantibodies
GADA: Glutamic acid decarboxylase antibodies
IA-2A: Insulinoma-associated antigen-2 autoantibodies
ZnT8A: Zinc transporter-8 autoantibodies.
FBS: Fasting Blood Sugar.
HOMA-IR: Homeostatic Model Assessment for Insulin Resistance

1. Introduction

Diabetes mellitus (DM) is defined as fasting or post-meal hyperglycemia. Furthermore, persistent hyperglycemia in diabetes is associated with damaged organs, dysfunction, and failure in organs and tissues such as the retina, kidneys, neurons, heart, and blood vessels [1]. According to the IDF, the worldwide incidence of diabetes mellitus was 366 million in 2011, with an increase to 552 million by 2030 [2]. Additionally, T2D is characterized by a dysfunction in insulin secretion which exacerbates in the context of insulin resistance [3]. Furthermore, environmental variables, including obesity and hereditary factors, contribute to the several pathophysiological diseases that cause poor glucose

homeostasis in T2D [4]. However, Obesity has been associated with T2D for decades, and the fundamental reason for this relationship is obesity's potential to induce insulin resistance [5]. However, Obesity is a significant risk factor for morbidity and mortality, contributing not only to CVD and diabetes, but also to various cancer and chronic diseases such as liver and kidney disease, sleep apnea, and depression [6]. Moreover, insulin resistance is a condition in the body where cells fail to properly respond to the usual influence of the insulin hormone [7]. Insulin resistance occurs when the body produces insulin, yet cells become less responsive to its effect, leading to ineffective utilization of glucose and subsequent hyperglycemia [8]. Moreover, Beta cells in the pancreas elevate insulin production, leading to hyperinsulinemia. This prompts further exploration into the notion that both insulin resistance and hyperglycemia played a play contributory role in obesity-induced pathogenesis [9-10]. Several studies have been undertaken on the relationship between inflammation and obesity; one definition of obesity is a state of persistent, mild inflammation [11,12]. Severe obesity intensifies acute pancreatic through unrestrained visceral fat disintegration, rich in unsaturated triglyceride. This triggers fatty acid release, impeding mitochondria complex function, causing tissue damage and worsening acute pancreatitis, which can increase the level of the IL-6 [13]. Moreover, numerous studies have revealed an association between inflammation, autoimmunity, and T2D association with obesity [14], this association between obesity and inflammation has prompted consideration of inflammatory conditions such as T2D and bowel disease [15,16]. The most popular strategies for detecting autoantibodies include immunomarkers such as IAA, GADA, IA-2A, and ZnT8A [17]. Finally, this study focused on the correlation between the increase in BMI and T2D. As well as the influence of obesity on the immune response and it is the role in T2D development.

2. Materials and Methods

2.1. Subjects and Samples

This study included 100 participants suffering from obesity (50 obese with T2D and 50 obese without T2D) aged between 35 and 55 years old, and they were from both genders. All of the subjects were registered in the Baghdad-specialized hospital from January to May 2023. The diagnosis of T2D is made based on the recommendations of a specialized Consultant. Five ml of venous blood was obtained from each individual in a fasting condition and then rotated at (6000 rpm) for 3 min to obtain serum. Next, the serum was used for the tests of the current study. The approval for this study was granted by the committee of scientific research ethics at the Departments of Science, College of Basic Education, Wasit University, with number 5545 on 10/2/2023.

2.2. Estimation of serum level of biochemical parameters

Serum levels of insulin and fasting blood sugar in the study subjects were measured using the electrochemiluminescence immunoassay method by Coba's machine. The kits were performed by (Roche Diagnostics, D-68305 Mannheim. 2020). Then, the HOMA-IR was calculated

2.3. Estimation of serum level of immunological parameters

Chemiluminescence immunoassay method (MX3) by Maglumi Diagnostics was used to measure the serum level of IL-6, IAA, and ANA. A specialized kit was performed by (Shenzhen Genius Electronics Co., Ltd. China 2019).

2.4. Statistical Analysis

The results of this funding are evaluated using SPSS Statistics 27 (New York 10504-1722, USA). The threshold for statistically significant was established at (P=0.05). For data analysis, statistical tests such as the independent t-test and percentage were applied. Body mass index BMI was calculated by the following:

https://www.calculator.net/bmi-calculator.html.
The HOMA-IR was calculated by:
https://thebloodcode.com/homa-ir-calculator/

3. Results and Discussion

The current study involved 100 participants afflicted by obesity, split evenly between those with, and without T2D. We reported that obese males were higher than females, a percentage of males (60%), while females were (40%) as shown in Figure 1. According to Table 1, obese patients with T2D had significantly higher serum concentrations of

insulin autoantibodies (IAA) than obese patients without T2D (P<0.006). Additionally, serum levels of all ANA, IL-6, and HOMA-IR were non-significant differences between the two compared groups; however, these results were not statistically significant. The findings in Table 2 showed a significant positive connection between BMI and all of the FBS (r = 012, P = 0.001), HOMA-IR (r = 068, P = 0.009), IAA (r = 0.55, P = 0.003), ANA (r = 0.68, P = 0.009), and IL-6 (r = 0.44, P = 0.002) among obese individuals with T2D. These findings suggest that all the examined parameters in the group of obese - T2D patients and without – T2D raised as their BMI increased.

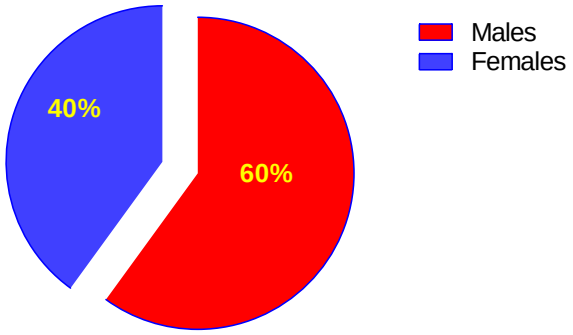

Figure 1. Distribution of participant according to sex.

In this study conducted in Baghdad province, it was observed that 60% of obese males and 40% of obese females developed T2D. In disagreement with our study, Al-Badri et al. found that Iraqi females suffer T2D more than males and reach (66%, and 34%), respectively [18]. According to prevalence rates, it was shown that women were more likely than men to have T2D, with percentages of 58.0% and 42.0%, respectively. This result is consistent with research carried out in Iran, Saudi Arabia [19], and Basra in 2020 [20]. However, it is different from another study done in Saudi Arabia [21]. We suggested that racial differences and the distribution of gender within society may be responsible for the difference in T2D prevalence between genders. In the serum of the two groups under comparison, there was an increased level of IgG antibodies at ANA, furthermore, HOMA-IR, IL-6, and FBS were evaluated for them. Whereas, IAA showed an increase in obese T2D individuals only as shown in Table 1. These outcomes agreed with Janahi et al., who mentioned the individuals with diabetic peripheral neuropathy had considerably more antinuclear antibodies in their blood serum (p< 0.001) compared to the control groups, it was reported that the likelihood of having positive ANA results in the neuritis group was 50 times greater compared to the control groups [22]. Conversely, the level of ANA was 58.6±2.6AU/ml in males and 22.5±3.9 AU/ml in women; a constructive correlation between ANA, according to studies based on gender. In addition, HOMA-IR and IL-6 levels were heightened in patients comparable to healthy controls [23]. We suggested the increase in HOMA-IR is associated with an increase of in BMI in obese individuals causing leading to inflammation in the beta-cells of the pancreas and also a negative influence on cells and it coincides with an increase in IL-6, and other autoantibodies leading to causing T2D. Our result is similar to that of Amelia et al., who mentioned that People with T2D have reduced beta-cells as compared to those who are not diabetic and have a similar BMI. It appears that there is a threshold at which blood glucose gets raised if the beta-cells mass is as much as 1.1% [24]. However, T2D associated with obesity is a condition marked by dysfunction of pancreatic beta cells and insulin resistance [25]. Although a hypothesis of the involvement of beta-cell mass in the development of type 2 diabetes associated with obesity has recently gained popularity, further research is still needed [26]. The present study shows that increasing BMI and FBS concentrations are associated with obese individuals. In concurrence with our outcome, Šimonienė *et al.* mentioned that people Patients with late analytical type 2 diabetes are also presumably to be overweight than non-diabetic patients [27]. Obesity also has a role in the etiology of T2D [28]. Obesity is uncommon among those with T1D, and individuals afflicted with T1D tend to be younger [29]. According to our results in Table 2, we investigated the connection between immune response and weight in individuals with T2D. Also, we discovered a positive correlation between IL6 response and BMI. Zheng et al. have noted that T2D patients exhibited significantly higher levels of IL6 and TNF in their serum compared to control [30]. This discovery corroborates what we saw. While interleukin-1 receptor antagonists and intercellular adhesion molecule-1 were connected to the development of DSPN, Herder et al. reported that TNF-1 and IL-6 were indicative of episode DSPN [31].

Table 1. Levels of Immunological and Biochemical in obese-T2D and obese-without T2D individuals.

Parameters	Obese with T2D (n=50)	Obese without T2D (n=50)	P -Value
	Mean ± SE		
BMI Kg/m2	50.33 ±2.29	48.50 ±10.63	0.82^{ns}
F.B.S (mg/dl)	197.50 ±11.09	120.76 ±1.59	0.01*
Antinuclear Antibody (ANA)(IgG) (AU/dl)	55.5±6.4	50.9±5.3	0.789^{ns}
Insulin Autoantibodies (IAA)(IgG)(AU/dl)	100.3±15.6	12.6±1.3	0.006**
Interleukin -6 (pg/ml)	55.2±4.2	50.6±3.6	0.641^{ns}
HOMA – IR	53.±9.6	50.5 ±6.6	0.623^{ns}
Significant value at ≤ 0.05, NS; non -significant, SE; standard error. t-test was analyzed the data. *Significant, ** high significant.			

Table 2. Correlation coefficient between BMI, and other immunological parameters in Obese-T2D and Obese- without T2D individuals.

Parameters	Correlation coefficient- r Obese with T2D Patients	P-value
BMI & F.B. S	0.42	0.001**
BMI & HOMA – IR	0.68	0.009**
BMI & IAA	0.55	0.003**
BMI & ANA	0.68	0.009**
BMI & IL-6	0.44	0.002**

4. Conclusions

In conclusion, the current study's findings show that IL-6, ANA, and HOMA-IR are higher in the two compared groups. Likewise, IAA was reported as highly significant in both comparers' groups. All parameters measured in this study showed a positive correlation with disease activity. As the results show, BMI correlates positively with all biochemical and immunological parameters. These findings suggest that increasing weight triggers the humeral immune response and causes an inflammatory disease. We hope to use other markers to complete the modularity study.

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Conflicts of Interest: Authors declare no conflict of interest.

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