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Ghrelin, Leptin, Insulin, Glucose, and Lipid Profile İnteractions in Type 2 Diabetic Patients: A Comparative Analysis

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Abstract

Background: Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disease characterized by impaired glucose homeostasis, insulin resistance, and progressive β-cell dysfunction, leading to significant multisystem complications and high global prevalence.

Objectives: This study was conducted to (I) measure and compare concentrations of ghrelin, leptin, and insulin in individuals with T2DM and non-diabetic controls; (II) analyze differences in metabolic profiles between the two groups; and (III) explore potential associations among insulin levels, BMI, and other hormonal and metabolic parameters assessed in the study.

Methods: A case-control study was conducted, comprising 80 individuals diagnosed with T2DM (cases) and 80 non-diabetic controls matched for age, sex, and body mass index (BMI). Clinical data were collected via standardized interviews, and venous blood samples were obtained to assess serum concentrations of ghrelin, leptin, insulin, glucose, lipid profile components, urea, and creatinine.

Results: Compared with the control group, participants with T2DM exhibited significantly higher insulin levels (28.8 ± 23.9 vs. 18.8 ± 13.5 µIU/ml; $P = 0.025$) and slightly elevated leptin concentrations (7.1 ± 2.7 vs. 5.9 ± 2.2 ng/ml; $P = 0.081$). Conversely, ghrelin concentrations were significantly lower among cases compared with controls (1189 ± 580 vs. 1531 ± 822 pg/ml; $P = 0.038$). Glucose (187.4 ± 74.1 vs. 98.3 ± 17.0 mg/dl; $P<0.001$) and triglyceride levels (212.5 ± 78.9 vs. 143.2 ± 50.4 mg/dl; $P<0.001$) were also markedly elevated in the cases group. Significant positive correlations were observed between insulin and both glucose ($P = 0.011$) and triglycerides ($P = 0.049$), whereas a weak, non-significant inverse correlation was identified between ghrelin and insulin levels (r = -0.213, $P = 0.057$).

Conclusion: Individuals with T2DM display distinct metabolic and hormonal alterations compared to non-diabetic controls, reflecting a complex endocrine interplay. The presence of both positive and inverse associations among insulin, leptin, and ghrelin highlights the multifaceted regulatory mechanisms underlying the pathophysiology of T2DM.

Keywords: Ghrelin, Insulin, Leptin, Lipid Profile, T2DM

1. Background

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder that has become increasingly prevalent worldwide, reaching levels indicative of a global epidemic.[1,2] It is characterized by abnormalities in carbohydrate, lipid, and protein metabolism, primarily resulting from insulin resistance, impaired insulin secretion, or a combination of both.[3,4] These metabolic disturbances arise from multi-factorial etiologies involving genetic susceptibility, environmental influences, and lifestyle-related risk factors. Among the major forms of diabetes, T2DM accounts for over 90% of all diagnosed cases, occurring far more frequently than type 1 diabetes mellitus or gestational diabetes.[5] Individuals with T2DM are predisposed to both acute and chronic complications, significantly increasing the risk of premature death.[6-8] The global burden of T2DM is further intensified by its high prevalence, gradual onset, and often delayed diagnosis, particularly in low-resource regions.[9] The disease is associated with microvascular complications, such as diabetic nephropathy, retinopathy, and neuropathy, as well as macrovascular complications, including coronary artery disease and cerebrovascular events.[10,11] Insulin resistance is a central pathophysiological feature in the development of T2DM and frequently precedes pancreatic β-cell dysfunction.[12]

Leptin, an adipocyte-derived peptide hormone, plays a crucial role in regulating energy homeostasis by suppressing neuropeptide Y activity in the hypothalamus, thereby reducing food intake and enhancing basal metabolic rate through increased lipid oxidation.[13,14] It

also acts as a growth-modulating factor in multiple tissues and interacts with several hormonal systems—including insulin, glucagon, growth hormone (GH), and glucocorticoids—to coordinate metabolic and endocrine functions.[15,16] Deficiency or dysregulation of leptin can result in hyperphagia, reduced energy expenditure, and altered insulin sensitivity, consequently disturbing glucose and lipid metabolism.[17] The relationship between leptin and T2DM remains controversial. Some studies report no significant association between circulating leptin concentrations and diabetes,[3,18] whereas others have demonstrated a positive correlation between leptin levels and the presence of diabetes.[19,20]

Ghrelin is a peptide hormone predominantly produced by endocrine cells of the gastric mucosa, particularly the X/A-like (type 1) cells, with smaller amounts secreted by pancreatic epsilon cells.[21] It acts on hypothalamic centers to stimulate appetite and promote adiposity.[22] Ghrelin also enhances the secretion of GH from the anterior pituitary by binding to growth hormone secretagogue receptors (GHSR), which are distributed in adipose tissue, myocardium, and hypothalamic regions.[23] Beyond its orexigenic properties, ghrelin influences neuroendocrine signaling pathways involved in energy regulation and neural communication.[24] Experimental studies have demonstrated that ghrelin modulates glucose-insulin homeostasis, adipocyte differentiation, and inflammatory responses.[25] Reduced circulating ghrelin levels have been observed in individuals with insulin resistance and metabolic syndrome.[26,27]

2. Objectives

This study was conducted to: (I) measure and compare concentrations of ghrelin, leptin, and insulin in individuals with T2DM and non-diabetic controls; (II) analyze differences in metabolic profiles between the two groups; and (III) explore potential associations among insulin levels, BMI, and other hormonal and metabolic parameters assessed in the study.

3. Methods

3.1. Study Population

This case-control study included 80 individuals with T2DM as cases and 80 non-diabetic individuals as controls. The groups were matched for age, sex, and BMI. Cases were previously diagnosed according to the World Health Organization (WHO) diagnostic criteria for diabetes and were recruited from multiple public healthcare centers across the Gaza Strip.[28] The cases comprised both newly diagnosed and previously diagnosed patients. The control group consisted of apparently healthy individuals from the general population residing in the same governorates.

The sample size was determined using the standard formula for case-control studies. Calculations were performed with EPI-INFO software (version 3.5.1), assuming a 95% confidence level, 80% statistical power, a baseline proportion of 50% (as a conservative estimate), and an expected odds ratio exceeding 2. Under a 1:1 case-to-control ratio, the required sample size was estimated at 74 participants per group. To compensate for potential non-response, the sample size was increased to include 80 cases and 80 controls.

3.2. Inclusion and Exclusion Criteria

Based on clinical documentation, individuals diagnosed with type 1 diabetes mellitus, other specific forms of diabetes, or any endocrine disorders were excluded from the study. Additional exclusion criteria included pregnancy, lactation, current use of corticosteroid therapy, and abnormal thyroid function profiles. Eligible participants were Palestinian adults aged between 40 and 60 years.

3.3. Questionnaire Interviews and Patient Records

Face-to-face interviews were conducted by the principal investigator with both case and control participants. The questionnaire was derived from the standardized diabetic clinic forms issued by the Palestinian Ministry of Health and supplemented with items from previously published studies,[29,30] with minor modifications to suit the study objectives. Most items utilized a dichotomous (yes/no) response format.[31] Prior to administration, the questionnaire was validated and pilot-tested on ten individuals who were subsequently excluded from the main analysis. The survey encompassed sociodemographic variables, including age, educational level, employment status, family history of diabetes, and frequency of daily meals. Clinical data were obtained from patient medical records and included disease duration and the presence of diabetes-related complications such as retinopathy, cardiovascular disease (CVD), and neuropathy.

3.4. Samples Collection and Biochemical Analysis

After an overnight fasting period, 9 ml of venous blood was drawn from each participant by a certified medical laboratory technologist using a plain vacutainer tube free of anticoagulants, adhering strictly to standardized biosafety and quality assurance procedures. From this sample, 3 ml was transferred into a polypropylene tube containing 15 µl of protease inhibitor to prevent ghrelin degradation, while the remaining 6 ml was placed into a separate plastic tube. Both specimens were allowed to stand undisturbed at room temperature for approximately 20 minutes before centrifugation at 4000 rpm for 10 minutes to separate the serum.

One ml aliquot of the ghrelin-stabilized serum was then placed into a new vial, and 10 µl of 5 N hydrochloric acid was added for stabilization. These samples were stored at –20 ± 5 °C until analysis of serum ghrelin concentrations. Serum obtained without a protease

inhibitor was likewise stored at –20 ± 5 °C for subsequent measurement of insulin and leptin levels. Serum insulin, leptin, and ghrelin concentrations were determined using the Monobind Insulin ELISA (MAPS), competitive enzyme immunoassay, and enzyme immunoassay methods, respectively. The residual serum was used for biochemical evaluation of fasting glucose, total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), urea BUN, and creatinine. Insulin resistance was estimated using the homeostasis model assessment index (HOMA-IR), calculated as: HOMA-IR = [fasting glucose (mg/dl) × fasting insulin (μIU/ml)] / 405.[32]

3.5. Statistical Analysis

The data were analyzed using IBM SPSS Statistics for Windows, version 22.0 (SPSS Inc., Chicago, IL, USA). The normality of data distribution was assessed through skewness analysis and Z-value testing. Comparisons of quantitative variables between study groups were performed using the Mann–Whitney U test. Spearman's rank correlation coefficient was applied to determine associations among the evaluated parameters. Statistical significance was defined as a *P*-value less than 0.05. The relative difference between two values was calculated according to the following equation:

$$\text{Percent difference} = \frac{|V_1 - V_2|}{(V_1 + V_2)/2} \times 100$$

This equation quantifies the absolute variation between two measurements as a percentage of their mean.

4. Results

4.1. Sociodemographic and Clinical Profiles of Cases and Controls

As shown in Table 1, there were no statistically significant differences between cases and controls in terms of age (P = 0.326), BMI (P = 0.245), educational level (P = 0.109), and employment status (P = 0.204). However, individuals with diabetes exhibited a significantly higher prevalence of a positive family history of diabetes and a greater frequency of daily meals (P = 0.007 and P<0.001, respectively). Table 2 summarizes the distribution of participants with diabetes according to disease duration and routine blood glucose monitoring practices. Among the diabetic cohort, 40 individuals (50.0%) had been diagnosed within the preceding five years, 14 (17.5%) had a disease duration of 5–10 years, and 26 (32.5%) had been living with the condition for more than ten years. A large proportion of cases (82.5%) reported regular self-monitoring of blood glucose levels, with over half (60.6%) performing these assessments on a monthly basis.

Table 1. Sociodemographic and Clinical Profiles of Cases versus Controls (n = 160)

Characteristics	Cases (n = 80)	Controls (n = 80)	*P*-value
Age (year)	51.3 ± 7.0	49.8 ± 6.5	0.326
BMI (kg/m²)	28.5 ± 4.1	27.6 ± 3.4	0.245
Education			
University	12 (15.0)	22 (27.5)	
Secondary	26 (32.5)	28 (35.0)	0.109
Preparatory	20 (25.0)	18 (22.5)	
Primary	22 (27.5)	12 (15.0)	
Employment			
Yes	40 (50.0)	48 (60.0)	0.204
No	40 (50.0)	32 (40.0)	
Family history of diabetes			
Yes	44 (55.0)	27 (33.8)	0.007
No	36 (45.0)	53 (66.3)	
Meal frequency/day			
One	0 (0.0)	4 (5.0)	
Two	16 (20.0)	40 (50.0)	< 0.001
Three	50 (62.5)	32 (40.0)	
Four and more	14 (17.5)	4 (5.0)	

n: Number; BMI: Body mass index; Values are number (%) except age and BMI where values are expressed ss means ± standard deviation. *P*<0.05: Significant, *P*>0.05: non-significant.

Table 2. Duration of Diabetes and Regular Blood Glucose Level among Case Group (n = 80)

Item	Number	Percentage
Duration of diabetes (Year)		
< 5	40	50.0
5 – 10	14	17.5
> 10	26	32.5
Regular blood glucose testing		
Yes	66	82.5
No	14	17.5
If yes		
Daily	4	6.1
Weekly	22	33.3
Monthly	40	60.6

Table 3. The Main Self-Reported Complications in Cases (n = 80) Compared to Controls (n = 80)

Complication	Cases n (%)	Controls n (%)	*P*-value
Retinopathy			
Yes	36 (45.0)	18 (22.5)	0.003
No	44 (55.0)	62 (78.5)	
CVD			
Yes	12 (15.0)	2 (2.5)	0.012
No	68 (85.0)	78 (97.5)	
Neuropathy			
Yes	34 (42.5)	16 (20.0)	0.002
No	46 (58.5)	64 (80.0)	

n: Number, CVD: Cardiovascular disease, *P*<0.05: Significant, *P*>0.05: non-significant.

Table 3 presents the most frequently observed complications within the diabetic cohort. The incidences of retinopathy, CVD, and neuropathy were significantly higher among cases compared to the control group (P = 0.003, P = 0.012, and P = 0.002, respectively). As shown in Table 4, a positive correlation was identified between disease duration and the prevalence of self-reported complications. This time-dependent relationship reached statistical significance for both retinopathy and neuropathy (P<0.001 and P = 0.036, respectively).

4.2. Insulin, Leptin, and Ghrelin Concentrations within the Study Population

As shown in Table 5, serum insulin and leptin concentrations were elevated in the case group compared with the control group (28.8 ± 23.9 µIU/ml and 7.1 ± 2.7 ng/ml vs. 18.8 ± 13.5 µIU/ml and 5.9 ± 2.2 ng/ml), corresponding to increases of 42.0% and 18.5%, respectively. The rise in serum insulin levels was statistically significant (P = 0.025), whereas the increase in leptin concentration did not reach statistical significance (P = 0.081). Conversely, serum ghrelin levels were significantly reduced in the case group compared to controls (1189 ± 580 pg/ml vs. 1531 ± 822 pg/ml), representing a 25.1% decrease (P = 0.038).

4.3. Glucose, Lipid Profile, and Non-Protein Nitrogenous Components in the Study Population

As shown in Table 6, the case group demonstrated a statistically significant increase in serum glucose and triglyceride concentrations compared with the control group. Serum glucose levels were substantially elevated (187.4 ± 74.1 vs. 98.3 ± 17.0 mg/dl; percent change: 62.4%; P<0.001), as were triglyceride levels (212.5 ± 78.9 vs. 143.2 ± 50.4 mg/dl; percent change: 39.0%; P<0.001). Furthermore, the homeostasis model assessment of insulin resistance (HOMA-IR) index was significantly higher in the case group than in the control group (13.3 ± 2.9 vs. 4.6 ± 0.8; P<0.001). In contrast, there were no statistically significant differences between the two groups regarding total cholesterol (P = 0.180), LDL-C (P = 0.625), HDL-C (P = 0.459), urea (P = 0.059), or serum creatinine (P = 0.119).

Table 4. Self-Reported Complications among Cases Group in Relation to Duration of the Disease (n = 80)

Complication	Duration of diabetes			*P*-value
	< 5 n = 40 n (%)	5-10 n = 14 n (%)	> 10 n = 26 n (%)	
Retinopathy (n = 36)	10 (25.0)	5 (35.7)	21 (80.7)	< 0.001
CVD (n = 12)	4 (10.0)	3 (21.4)	5 (19.2)	0.425*
Neuropathy (n = 34)	11 (27.5)	6 (42.9)	17 (65.4)	0.036

CVD: Cardiovascular diseases, n.: Number. *P*<0.05: Significant, *P*>0.05: non-significant.

Table 5. Insulin, Leptin, and Ghrelin Concentrations within the Study Cohort (n = 160)

Hormone	Casas (n = 80)	Controls (n = 80)	% difference	*P*-value
Insulin (µIU/ml)	28.8 ± 23.9	18.8 ± 13.5	42.0	0.025
Range (min - max)	4.9-103.4	2.9-61.1		
Leptin (ng/ml)	7.1 ± 2.7	5.9 ± 2.2	18.5	0.081
Range (min - max)	5.1-13.3	3.8-10.4		
Ghrelin (pg/ml)	1189 ± 580	1531 ± 822	25.1	0.038
Range (min - max)	692-3850	833-6244		

n: Number, %: percentage, min: minimum, max: maximum, all values are presented as mean ± SD. *P*<0.05: Significant, *P*>0.05: non-significant.

4.4. Association of Insulin Concentrations with Glucose, Triglyceride, Ghrelin, and Leptin Levels in the Study Cohort

As shown in Table 7, insulin levels exhibited a statistically significant positive correlation with both glucose and triglyceride concentrations (r = 0.286, P = 0.011; r = 0.224, P = 0.049, respectively). Conversely, the association between insulin and leptin was positive but did not attain statistical significance (r = 0.187, P = 0.098). An inverse, non-significant correlation was also observed between insulin and ghrelin concentrations (r = -0.213, P = 0.057).

4.5. Association of BMI with Glucose, Insulin, Leptin, Triglycerides, and Ghrelin in the Study Cohort

As presented in Table 8, a statistically significant positive correlation was identified between triglyceride levels and BMI (r = 0.228, P = 0.044). Positive but non-significant correlations were observed between BMI and insulin (r = 0.183, P = 0.104), leptin (r = 0.207, P = 0.063), and glucose levels (r = 0.082, P = 0.39). In contrast, ghrelin exhibited a non-significant negative correlation with BMI (r = -0.149, P = 0.192).

Table 6. Glucose, Lipid Profile, and Non-Protein Nitrogenous Components in the Study Cohort (n = 160)

Parameter (mg/dl)	Cases (n = 80)	Controls (n = 80)	% difference	*P*-value
Glucose Range (min - max)	187.4 ± 74.1 82 – 365	98.3 ± 17.0 70 – 158	62.4	< 0.001
Cholesterol Range (min - max)	195.2 ± 44.6 121 – 304	183.5 ± 31.5 127 – 256	6.2	0.180
Triglycerides Range (min - max)	212.5 ± 78.9 90 - 406	143.2 ± 50.4 42 – 239	39.0	< 0.001
LDL-C Range (min - max)	115.4 ± 45.5 40 - 227	111.3 ± 26.7 63 – 118	3.6	0.625
HDL-C Range (min - max)	41.0 ± 7.9 29 - 68	42.2 ± 6.4 32 – 63	2.9	0.459
Urea Range (min - max)	33.5 ± 11.0 15 - 65	28.3 ± 13.3 10 – 60	16.8	0.058
Creatinine Range (min - max)	0.81 ± 0.20 0.5 - 1.3	0.89 ± 0.24 0.5 - 1.6	9.4	0.119

n: Number, LDL-C: Low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol, No.: Number, SD: Standard deviation, *min*: minimum, *max*: maximum, all values are expressed as mean ± SD, P<0.05: Significant, P>0.05: non-significant.

Table 7. Association of Insulin Concentrations with Glucose, Triglyceride, Ghrelin, and Leptin Levels in the Study Cohort

Variable	Insulin (µlU/ml)	
	r	*P*-value
Glucose (mg/dl)	0.286	0.011
Triglycerides (mg/dl)	0.224	0.049
Ghrelin (pg/ml)	-0.213	0.057
Leptin (ng/ml)	0.187	0.098

Spearman's test is used. r: correlation coefficient. P<0.05: Significant, P>0.05: non-significant.

Table 8. Association of BMI with Glucose, Insulin, Leptin, Triglycerides, and Ghrelin in the Study Cohort

Variable	BMI (kg/m²)	
	r	*P*-value
Glucose (mg/dl)	0.82	0.39
Insulin (µlU/ml)	0.183	0.104
Leptin (ng/ml)	0.207	0.063
Triglycerides (mg/dl)	0.228	0.044
Ghrelin (pg/ml)	-0.149	0.192

Spearman's test is used. r: correlation coefficient. P<0.05: Significant, P>0.05: non-significant.

5. Discussion

5.1. Sociodemographic and Clinical Profiles of Cases versus Controls

Diabetes mellitus (DM) constitutes a major global metabolic disorder, with projections indicating a substantial increase in prevalence over the coming decades. For example, recent data estimate a worldwide prevalence of approximately 10.5% (536.6 million adults aged 20–79 years) in 2021, rising to an estimated 12.2% (783.2 million) by 2045.[33] While these global figures are well established, region-specific epidemiological information, such as for the Gaza Strip, is notably limited.[30,34] In this geographic context, few studies have investigated circulating levels of adipokines among individuals with T2DM. To date, only two published investigations have measured serum leptin concentrations in T2DM patients in that region. [20,35] Conversely, the role of the orexigenic peptide ghrelin in T2DM pathophysiology has not been assessed in these prior studies. Accordingly, the present study represents the first effort to assess the inter-relationships among ghrelin, leptin, and insulin concentrations in a cohort of T2DM patients living in the Gaza Strip.

In the present study, the mean age was 51.7 ± 7.0 years, consistent with observations from previous reports that the onset of T2DM commonly occurs after the fourth decade of life.[36] A family history of diabetes emerged as a significant correlate of disease presence, aligning with established evidence that hereditary predisposition significantly contributes to T2DM risk.[37] Moreover, individuals in the case group reported a significantly higher frequency of consuming three or more meals (or more than four meals) per day compared with control participants. This finding corroborates earlier research suggesting that persons with T2DM may experience altered eating patterns—potentially reflecting increased appetite or compensatory meal frequency associated with dietary restriction or glycaemic variability.[38] It underscores

the importance for clinicians and dieticians to factor in meal frequency and eating behavior when designing nutritional management plans for T2DM patients.

Approximately half of the individuals with diabetes had a disease duration of less than five years, suggesting that many participants were in the early stages of T2DM. This finding supports the understanding that T2DM often progresses insidiously, with an extended asymptomatic or subclinical period preceding clinical recognition and formal diagnosis. During this latent period, micro- and macrovascular damage may already begin to accrue.[39] In this study, diabetic cases had a significantly higher prevalence of documented complications (e.g., retinopathy, neuropathy, cardiovascular disease) compared to controls. Despite guidelines recommending routine glycaemic monitoring,[40] over half of the participants reported performing self-monitoring of blood glucose only on a monthly basis—consistent with findings from comparable settings where monitoring frequency is suboptimal.[41] Taken together, these observations point to a substantial educational gap: targeted interventions are needed to enhance patients' engagement in regular glucose self-monitoring, thereby enabling earlier detection of dysglycaemia and prompt therapeutic adjustment. Furthermore, the three most commonly reported complications in our cohort were diabetic retinopathy, peripheral neuropathy, and cardiovascular disorders; the prevalence of each increased with longer duration of the disease—supporting the well-recognized association between longer T2DM duration and complication risk.[42,43]

5.2. Insulin, Leptin, and Ghrelin Concentrations within the Study Cohort

In the present study, individuals in the case cohort exhibited significantly elevated fasting insulin and leptin concentrations compared to control groups, while circulating ghrelin levels were markedly lower in the case group. These findings are consistent with a growing body of evidence demonstrating altered endocrine profiles in IR and diabetic states.[44-47] Hyperleptinaemia has been implicated in the pathophysiology of IR, as elevated leptin may signal adipose-tissue expansion and contribute to impaired insulin-mediated glucose disposal, thereby facilitating hyperglycaemia in affected individuals. Concurrently, the observed reduction in ghrelin among cases aligns with reports of lower active ghrelin concentrations in those with impaired glucose regulation.[24,48] Furthermore, correlation analysis in this study revealed both positive and negative associations among insulin, leptin, and ghrelin levels in the diabetic group. This interplay suggests a complex hormonal crosstalk in the diabetic milieu: for instance, short-term insulin infusion in humans has been shown to suppress circulating ghrelin levels, supporting the notion that hyperinsulinaemia may negatively regulate ghrelin secretion.[49,50] Although the mechanistic pathways underlying long-term hyperinsulinaemia or IR on ghrelin regulation remain incompletely defined, the findings of this study reinforce the hypothesis that dysregulated interactions among these three hormones may contribute to metabolic perturbations, including altered appetite regulation and glucose homeostasis, in individuals with T2DM.[51]

5.3. Lipid Profile, and Non-Protein Nitrogenous Components in the Study Cohort

In the present investigation, triglyceride levels were found to be markedly elevated in the case group compared with controls, whereas concentrations of total cholesterol, LDL-C, HDL-C, urea, and creatinine did not exhibit statistically significant differences between groups. Among individuals with T2DM, hypertriglyceridaemia is a well-documented phenomenon in the literature.[52,53] For example, the review by Björnstad et al. describes the characteristic lipid perturbation in insulin-resistant states—including elevated triglycerides, diminished HDL-C, and increased apolipoprotein B-containing lipoproteins—as a hallmark of adipose tissue dysfunction.[54]

Mechanistically, this dyslipidaemic profile is often attributed to enhanced lipolysis in adipocytes driven by insulin resistance. Normally, insulin suppresses hormone-sensitive lipase activity, thereby restraining the release of free fatty acids (FFA) from adipose stores; however, in insulin-resistant states, this suppression is impaired, leading to increased FFA flux to the liver. Once delivered to the liver, excess FFAs are re-esterified and packaged into triglycerides, phospholipids, and cholesterol ester moieties, which are subsequently secreted in VLDL particles into the systemic circulation. This pathway contributes to elevated serum triglyceride concentrations and altered lipoprotein composition.[55]

Our data further demonstrated a significant positive correlation between insulin levels and triglyceride concentrations, reinforcing the link between hyperinsulinaemia (as a marker of insulin resistance) and dyslipidaemia. This finding is compatible with recent observations that triglyceride levels are directly associated with measures of insulin resistance in both diabetic and non-diabetic populations.[56,57] However, this study has several limitations, including a relatively small sample size, restricted hormonal assessment, and incomplete documentation of dietary and lifestyle factors.

6. Conclusion

The present study demonstrated a significantly higher prevalence of T2DM among individuals with a positive family history, emphasizing the critical role of genetic and hereditary factors in the disease's pathogenesis. Patient-reported outcomes revealed a higher frequency of

diabetic complications in individuals with T2DM compared with healthy controls, with complication rates showing a clear association with disease duration. Serum analyses indicated significantly elevated concentrations of insulin, leptin, glucose, and triglycerides in the diabetic cohort, accompanied by markedly reduced ghrelin levels. Moreover, insulin levels exhibited strong positive correlations with leptin, glucose, and triglyceride concentrations, and a negative correlation with ghrelin. These findings underscore the intricate interrelationship between metabolic and hormonal dysregulation in T2DM, highlighting the potential clinical utility of these biomarkers for early detection, risk stratification, and targeted management of metabolic complications.

Research Highlights

What Is Already Known?

In Type 2 diabetes, insulin resistance disrupts glucose and lipid metabolism, causing dyslipidemia. Ghrelin levels decrease and leptin levels increase with resistance, both affecting appetite and energy balance. These hormonal imbalances worsen insulin sensitivity and lipid abnormalities, creating a cycle that exacerbates metabolic dysfunction and disease progression.

What Does This Study Add?

Individuals with a family history of T2DM showed a higher prevalence and more complications linked to disease duration. Compared to controls, T2DM patients had elevated levels of insulin, leptin, glucose, and triglycerides, but lower levels of ghrelin. Insulin correlated positively with leptin, glucose, and triglycerides, and negatively with ghrelin levels.

Author Contributions

MMY and FMS came up with the experimental design, while FMS handled all the actual experiments and collected the samples. MMY and MML worked together to interpret the results and shape the overall research plan. MMY also supervised the whole project, providing guidance and managing the coordination. MML wrote the first draft of the paper, created the figures, and took the lead in reviewing and polishing the article. All authors approved the final version for publication.

Conflict of Interest Disclosures

All authors declared that they have no conflict of interest.

Ethical Approval

The research received ethical approval from the Palestinian Health Research Council on 5 September 2011 (Reference Code: PHRC/HC/09/11). The approval process conformed to the ethical principles outlined in the Declaration of Helsinki and was documented through formal authorization by both the institutional ethics review committee and the Palestinian Ministry of Health. Furthermore, written informed consent was voluntarily obtained from all participants prior to their enrollment in the study.

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