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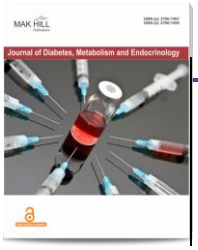

Research Article

Anatomical and Biochemical Alterations in Type 2 Diabetes Mellitus: Associations with Pancreatic Islet Dysfunction, Hepatic Metabolism, Insulin Resistance, Antidiabetic Pharmacotherapy and Clinical Outcomes.

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Abstract: ***Background:*** Type 2 diabetes mellitus is a progressive metabolic disorder characterized by insulin resistance, impaired pancreatic beta-cell function and disturbances in glucose and lipid metabolism. Beyond persistent hyperglycemia, T2DM is associated with structural and functional alterations involving pancreatic islets, hepatic tissue, adipose tissue, skeletal muscle and the cardiovascular system. Progressive beta-cell dysfunction, abnormal hepatic glucose production, ectopic lipid accumulation and chronic low-grade inflammation contribute to disease progression and the development of multisystem complications. Understanding the relationship between anatomical alterations and biochemical abnormalities may provide important insights into disease severity, treatment response and clinical outcomes. Objective: To evaluate anatomical and biochemical alterations in patients with T2DM and investigate their associations with pancreatic islet dysfunction, hepatic metabolic abnormalities, insulin resistance, antidiabetic pharmacotherapy and clinical outcomes. ***Methodology***: A proposed hospital-based cross-sectional study was designed involving 200 adult patients diagnosed with T2DM. Demographic characteristics, disease duration, anthropometric measurements, treatment history and clinical complications were assessed. Biochemical investigations included fasting blood glucose, glycated hemoglobin (HbA1c), fasting insulin, C-peptide, lipid profile, liver enzymes, renal function parameters and inflammatory markers. Insulin resistance was assessed using the homeostatic model assessment of insulin resistance (HOMA-IR). Pancreatic and hepatic anatomical findings were evaluated through clinically available imaging reports, including pancreatic morphology and hepatic steatosis. Associations between anatomical abnormalities, biochemical parameters, treatment patterns and clinical outcomes were assessed using appropriate statistical methods. ***Results***: Among 200 patients, 112 (56.0%) were male and 88 (44.0%) were female. The largest proportion belonged to the 51–60-year age group. Poor glycemic control (HbA1c ≥7%) was observed in 116 (58.0%) patients. Elevated HOMA-IR was identified in 128 (64.0%) patients, while reduced C-peptide levels were observed in 48 (24.0%). Hepatic steatosis was identified in 86 (43.0%) patients, and pancreatic structural abnormalities were documented in 54 (27.0%) patients. Patients with longer diabetes duration and poor glycemic control demonstrated a higher frequency of metabolic and clinical complications. Elevated triglycerides, increased liver enzymes and abnormal insulin resistance indices were associated with less favorable metabolic profiles. ***Conclusion***: T2DM involves interconnected anatomical and biochemical alterations affecting pancreatic endocrine function and hepatic metabolism. Insulin resistance, impaired beta-cell function, hepatic steatosis and dyslipidemia contribute to metabolic deterioration and increased clinical complications. Integrating biochemical evaluation, anatomical assessment and appropriate antidiabetic pharmacotherapy may improve disease monitoring and risk stratification.

Keywords: Type 2 diabetes mellitus; pancreatic islets; beta-cell dysfunction; hepatic steatosis; insulin resistance; HOMA-IR; C-peptide; HbA1c; antidiabetic pharmacotherapy; anatomical alterations.

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INTRODUCTION

Type 2 diabetes mellitus is a chronic metabolic disease characterized by persistent hyperglycemia resulting from a combination of peripheral insulin resistance, inadequate insulin secretion and progressive dysfunction of pancreatic beta cells. It represents a major public health challenge because of its increasing prevalence, long-term complications and substantial healthcare burden. The disease affects multiple organ systems and is associated with disturbances in carbohydrate, lipid and protein metabolism[1,2].Under normal physiological conditions, pancreatic beta cells respond to increased blood glucose concentrations by releasing insulin. Insulin facilitates glucose uptake in skeletal muscle and adipose tissue, suppresses hepatic glucose production and promotes glycogen synthesis. In individuals with T2DM, these regulatory

mechanisms become impaired. Peripheral tissues demonstrate reduced responsiveness to insulin, while pancreatic beta cells gradually lose their ability to compensate for increased metabolic demand.

The development of T2DM is therefore not simply a consequence of elevated blood glucose. It represents a complex pathophysiological process involving pancreatic endocrine dysfunction, hepatic metabolic abnormalities, altered adipose tissue activity, chronic inflammation and abnormalities in lipid handling[3].The progressive nature of the disease makes it particularly important to investigate both functional and structural changes in affected organs. Anatomical abnormalities may reflect long-standing metabolic disturbances, whereas biochemical abnormalities provide information regarding the severity of metabolic dysfunction and the effectiveness of treatment.

The pancreas is central to endocrine and exocrine regulation, and its endocrine component, the islets of Langerhans, contains beta cells that secrete insulin, alpha cells that secrete glucagon, delta cells that secrete somatostatin. In type 2 diabetes mellitus, the islets undergo reduced beta-cell mass, impaired insulin-secretory capacity, abnormal architecture, cellular stress, and increased apoptosis[4-6]. Chronic exposure to elevated glucose and fatty acids causes glucotoxicity and lipotoxicity, impairing mitochondrial activity, calcium signaling, and insulin synthesis and secretion while accumulation of islet amyloid polypeptide or amylin, oxidative damage, endoplasmic reticulum stress further contribute to beta-cell injury. Insulin secretion normally involves glucose metabolism, increased ATP/ADP ratio, closure of ATP-sensitive potassium channels, membrane depolarization, calcium influx and exocytosis of insulin granules, but in T2DM there is reduced glucose-stimulated and first-phase insulin secretion, impaired responsiveness, mitochondrial dysfunction and reduced survival. C-peptide, released in equimolar amounts with insulin during proinsulin cleavage and not substantially extracted by the liver on first pass, provides an indirect assessment of endogenous insulin secretion, with reduced levels indicating diminished secretory reserve in advanced disease and elevated levels reflecting compensatory hypersecretion in earlier stages. However, pancreatic imaging cannot directly establish beta-cell mass or amyloid deposition, which require histopathological examination.

The liver plays an essential role in glucose regulation, lipid metabolism, glycogen storage, and insulin clearance. Normally, insulin suppresses hepatic gluconeogenesis and glycogenolysis while promoting glycogen synthesis, but in T2DM hepatic insulin resistance impairs this suppression, so the liver continues to release glucose despite hyperinsulinemia and contributes substantially to fasting hyperglycemia. Hepatic insulin resistance is also associated with increased lipogenesis, impaired fatty acid oxidation, and triglyceride accumulation in hepatocytes, leading to metabolic dysfunction-associated steatotic liver disease, formerly termed NAFLD, along with altered glycogen storage, increased oxidative and inflammatory stress, and impaired metabolic regulation. Hepatic steatosis is closely associated with obesity, insulin resistance, dyslipidemia, and poor glycemic control[7,8]. Liver enzymes ALT and AST may be elevated, but normal levels do not exclude steatosis or advanced disease.

Insulin resistance is a central mechanism in T2DM, defined as reduced biological response of insulin-sensitive tissues to insulin, involving skeletal muscle, liver and adipose tissue. In skeletal muscle, reduced insulin-mediated glucose uptake impairs postprandial glucose disposal; in the liver, resistance prevents adequate suppression of glucose output; and in adipose tissue, reduced suppression of lipolysis increases circulating free fatty acids, promoting hepatic lipid accumulation, ectopic fat deposition and further resistance[9]. Biochemical disturbances reflected these processes, including fasting glucose, HbA1c, fasting insulin, C-peptide, triglycerides, HDL ,LDL cholesterol, ALT, AST, GGT, creatinine/eGFR, urinary albumin-to-creatinine ratio, and CRP. Dyslipidemia in T2DM typically involves increased triglycerides, reduced HDL and abnormal LDL particle composition contributing to atherosclerosis while chronic hyperglycemia promotes advanced glycation end products that cause oxidative stress, endothelial dysfunction, vascular inflammation and tissue damage.

Pharmacological treatment aims to improve glycemic control, preserve beta-cell function reduce insulin resistance, prevent cardiovascular and renal complications with different agents acting through distinct mechanisms. Metformin primarily reduces hepatic glucose production and improves insulin sensitivity, sulfonylureas stimulate insulin secretion via closure of ATP-sensitive potassium channels, DPP-4 inhibitors increase incretin activity and improve glucose-dependent insulin secretion, GLP-1 receptor agonists improve glucose-dependent insulin secretion, reduce glucagon, slow gastric emptying, and often produce weight loss, SGLT2 inhibitors increase urinary glucose excretion with cardiovascular and renal benefits, and insulin therapy provides exogenous insulin particularly in advanced beta-cell dysfunction or severe hyperglycemia[10,11].

Treatment evaluation therefore consider not only HbA1c but also weight, lipids, liver and renal function, and cardiovascular outcomes. Long-standing T2DM is associated with microvascular complications including retinopathy, nephropathy, and neuropathy, macrovascular complications including coronary artery disease, myocardial infarction, ischemic stroke, and peripheral arterial disease, and other manifestations such as diabetic foot disease, impaired wound healing, recurrent infections, and MASLD, influenced by diabetes duration, glycemic control, hypertension, dyslipidemia, obesity, smoking, and renal function. An integrated assessment of anatomical and biochemical abnormalities may therefore help identify individuals at increased risk of complications.

By combining pancreatic and hepatic imaging findings with biochemical markers, insulin resistance indices, pharmacological treatment patterns and clinical complications, the study aims to provide a broader understanding of the metabolic and anatomical characteristics of T2DM.

Objective

- To investigate anatomical and biochemical alterations in patients with type 2 diabetes mellitus a
- To determine their associations with pancreatic islet dysfunction, hepatic metabolic abnormalities, insulin resistance, antidiabetic pharmacotherapy and clinical outcomes.
- To assess demographic, anthropometric and clinical characteristics of patients diagnosed with T2DM.
- To evaluate pancreatic structural abnormalities and their possible relationship with impaired insulin secretion.
- To investigate hepatic anatomical alterations, particularly hepatic steatosis, and their association with glycemic control and lipid abnormalities.
- To assess biochemical alterations, including fasting blood glucose, HbA1c, fasting insulin, C-peptide and lipid profile.
- To determine insulin resistance using HOMA-IR and investigate its relationship with obesity, diabetes duration and glycemic status.
- To assess antidiabetic pharmacotherapy patterns and their association with metabolic and biochemical outcomes.
- To investigate the prevalence of diabetic complications, including cardiovascular disease, nephropathy, neuropathy and retinopathy.

MATERIALS AND METHODS

This hospital-based analytical cross-sectional study was conducted over 12 months in the Departments of Medicine and Endocrinology of Abbasi Shaheed hospital. A total of 200 patients diagnosed with type 2 diabetes mellitus were included to evaluate demographic, biochemical, and clinical associations. Data were collected using a structured proforma covering demographic characteristics, diabetes duration, family history, comorbidities, medication history, anthropometric measurements, laboratory findings, imaging reports, documented diabetic complications. Assessment was divided into five components: demographic and anthropometric evaluation, pancreatic anatomical and functional assessment, hepatic anatomical and biochemical assessment, evaluation of insulin resistance and metabolic abnormalities, and antidiabetic pharmacotherapy and clinical outcomes

Demographic and anthropometric assessment included age, sex, duration of diabetes, family history, and lifestyle characteristics, along with weight, height, body mass index calculated as weight in kg divided by height in m^2, waist circumference, and blood pressure, with BMI categories classified according to the study protocol and lower thresholds considered for an Asian population. Pancreatic assessment reviewed available abdominal ultrasonography, for size ,morphology, echogenicity, atrophy, fatty infiltration but routine imaging cannot reliably quantify beta-cell mass or identify microscopic islet amyloid deposition, so endocrine function was evaluated biochemically using fasting insulin and C-peptide interpreted in relation to concurrent glucose, renal function, treatment status, and categorized as relatively preserved or reduced endogenous insulin secretion using laboratory-specific reference intervals. Hepatic assessment was performed through abdominal ultrasonography for normal echotexture, mild, moderate, or severe steatosis, hepatomegaly, and other abnormalities, together with ALT, AST, alkaline phosphatase, GGT, total bilirubin, serum albumin. Steatosis was evaluated in relation to BMI, HbA1c, triglycerides, HOMA-IR and diabetes duration

Biochemical investigations were performed on blood samples collected after an overnight fast of approximately 8-12 hours, including glycemic parameters such as fasting glucose, HbA1c, fasting insulin, and C-peptide, lipid profile including total cholesterol, triglycerides, HDL, LDL cholesterol, hepatic parameters, renal parameters including creatinine, urea, eGFR, and urinary albumin-to-creatinine ratio and CRP where available. Insulin resistance was estimated using HOMA-IR, calculated as fasting glucose in mg/dL multiplied by fasting insulin in μU/mL divided by 405, with a value above 2.5 used as an operational threshold for elevated resistance.

Antidiabetic pharmacotherapy was reviewed for metformin monotherapy, metformin-based combination therapy, DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists, sulfonylureas, thiazolidinediones, insulin therapy, combination injectable therapy, and its relationship with HbA1c, fasting glucose, BMI, liver enzymes, lipids, renal function. They were investigated along with treatment duration, adherence, adverse effects, with differences interpreted as associations rather than proof of efficacy because of the cross-sectional design. Clinical outcomes included documented retinopathy, nephropathy, peripheral neuropathy, coronary artery disease, previous myocardial infarction, stroke, peripheral vascular disease, diabetic foot disease, hypertension, and recurrent infections, evaluated in relation to diabetes duration, glycemic control, HOMA-IR, hepatic steatosis, and biochemical abnormalities.

Inclusion criteria

- Adults aged 18 years or above.

- Patients diagnosed with T2DM according to established diagnostic criteria.
- Patients with a documented history of diabetes for at least six months.
- Patients receiving lifestyle modification, oral antidiabetic medication, injectable therapy or insulin.
- Patients willing to participate and provide informed consent.
- Patients with available clinical and laboratory records.

Exclusion criteria

- Patients diagnosed with type 1 diabetes mellitus.
- Gestational diabetes.
- Secondary diabetes due to pancreatic disease, endocrine disorders or medication exposure.
- Acute pancreatitis or pancreatic malignancy.
- Advanced hepatic disease unrelated to metabolic dysfunction.
- Active malignancy or severe systemic illness.
- Recent major surgery or acute metabolic emergencies.
- Patients with incomplete essential clinical or biochemical information.

Ethical considerations

Ethical approval was to be obtained from the institutional review board or ethics review committee before initiation of the study. Written informed consent was obtained from participants.

STATISTICAL ANALYSIS

Data were entered and analyzed using IBM Statistical Package for the Social Sciences (SPSS), version 22.Continuous variables, including age, BMI, diabetes duration, fasting blood glucose, HbA1c, fasting insulin, C-peptide, HOMA-IR, liver enzymes and lipid profile parameters were summarized as mean ± standard deviation when normally distributed. Categorical variables, including sex, pancreatic imaging abnormalities, hepatic steatosis, medication categories and diabetic complications, were presented as frequencies and percentages.

Independent-sample t-tests were used to compare normally distributed continuous variables between two groups. One-way analysis of variance (ANOVA) was used for comparisons involving more than two groups

Binary logistic regression analysis was used to identify independent predictors of hepatic steatosis, pancreatic imaging abnormalities and poor glycemic control. Potential explanatory variables included age, sex, diabetes duration, BMI, HbA1c, HOMA-IR, triglycerides and antidiabetic treatment. Adjusted odds ratios (ORs) with 95% confidence intervals .A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 200 patients diagnosed with T2DM were considered for the proposed analysis. The findings demonstrated the possible relationships between pancreatic and hepatic abnormalities, biochemical disturbances, insulin resistance, pharmacotherapy and clinical complications.

Table 1. Demographic and baseline clinical characteristics of the study population (n = 200)

Variables	Frequency (n)	Percentage (%)
Age groups (years)		
18–40	20	10.0
41–50	35	17.5
51–60	65	32.5
61–70	55	27.5
Above 70	25	12.5
Diabetes duration		
Less than 5 years	50	25.0
5–10 years	75	37.5
More than 10 years	75	37.5
Comorbidities		
Hypertension	118	59.0
Dyslipidemia	104	52.0
Chronic kidney disease	32	16.0
Cardiovascular disease	38	19.0

The study population comprised 200 patients, including 112 (56.0%) males and 88 (44.0%) females. The largest age category was 51–60 years, representing 65 (32.5%) participants, followed by 61–70 years, comprising 55 (27.5%) participants.Diabetes duration was more than 10 years in 75 (37.5%) patients, indicating a substantial proportion with long-

standing disease. Hypertension was the most frequently observed comorbidity, affecting 118 (59.0%) participants, followed by dyslipidemia in 104 (52.0%).

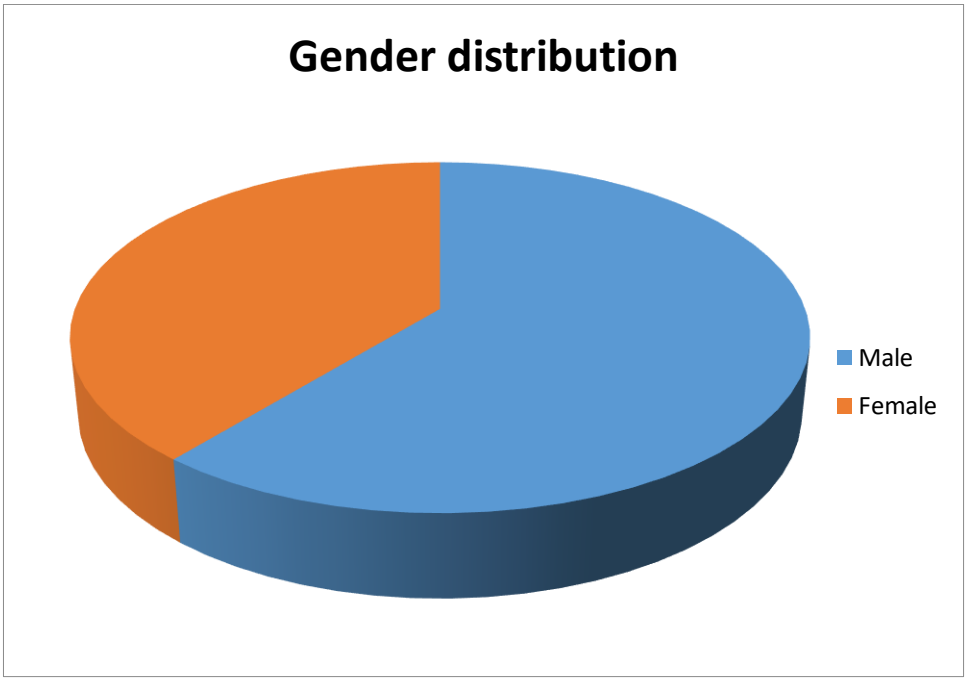

Figure 1 showed the gender wise distribution of the participants

These characteristics are important because increasing age, longer diabetes duration, hypertension and dyslipidemia may contribute to progressive metabolic dysfunction and the development of diabetic complications.

Table 2. Anthropometric and glycemic characteristics of patients with T2DM

Parameter	
Age (years)	56.8 ± 10.2
BMI (kg/m^2)	28.9 ± 4.6
Waist circumference (cm)	98.4 ± 11.2
Systolic blood pressure (mmHg)	134.6 ± 15.8
Diastolic blood pressure (mmHg)	82.3 ± 9.6
Diabetes duration (years)	8.2 ± 5.7
Fasting blood glucose (mg/dL)	158.6 ± 42.3
HbA1c (%)	7.8 ± 1.3
Fasting insulin (µU/mL)	14.8 ± 7.2
C-peptide (ng/mL)	2.1 ± 1.0
HOMA-IR	5.8 ± 3.1

The mean BMI was 28.9 ± 4.6 kg/m^2, suggesting a considerable burden of excess body weight. The mean fasting blood glucose was 158.6 ± 42.3 mg/dL, while the mean HbA1c was 7.8 ± 1.3%.The mean fasting insulin concentration of 14.8 ± 7.2 µU/mL and HOMA-IR of 5.8 ± 3.1 suggested substantial estimated insulin resistance in the population.The mean C-peptide concentration was 2.1 ± 1.0 ng/mL, indicating considerable variation in endogenous insulin secretion.
These findings showed the coexistence of hyperglycemia, peripheral insulin resistance and variable pancreatic secretory function in T2DM.

Table 3. Glycemic control among study participants (n = 200)

Glycemic status	HbA1c	Frequency (n)	Percentage (%)
Controlled glycemia	Below 7.0%	84	42.0
Poor glycemic control	7.0% or above	116	58.0
Total		200	100.0

Poor glycemic control was observed in 116 (58.0%) participants, whereas 84 (42.0%) patients demonstrated HbA1c levels below 7%.The relatively high proportion of patients with HbA1c of 7% or above suggests inadequate glycemic control in a considerable proportion of the study population.Persistent hyperglycemia may contribute to pancreatic beta-cell stress, increased oxidative stress, abnormal hepatic glucose metabolism and progression of vascular complications.
The findings also emphasized the importance of considering treatment adherence, duration of diabetes, insulin resistance and progressive beta-cell dysfunction when evaluating glycemic control.

Table 4. Distribution of pancreatic anatomical abnormalities on available imaging (n = 200)

Pancreatic imaging findings	Frequency (n)	Percentage (%)
Normal pancreatic morphology	146	73.0
Pancreatic atrophy	22	11.0
Increased pancreatic echogenicity/fatty infiltration	18	9.0
Pancreatic calcification	6	3.0
Other structural abnormalities	8	4.0
Total	200	100.0

Normal pancreatic morphology was documented in 146 (73.0%) participants, whereas 54 (27.0%) demonstrated at least one reported structural abnormality. Pancreatic atrophy was the most frequently documented abnormality, occurring in 22 (11.0%) patients, followed by increased pancreatic echogenicity or fatty infiltration in 18 (9.0%).These findings suggested that structural pancreatic abnormalities may be present in a subset of patients with T2DM.

Table 5. Hepatic anatomical findings on abdominal ultrasonography (n = 200)

Hepatic findings	Frequency (n)	Percentage (%)
Normal liver morphology	114	57.0
Mild hepatic steatosis	45	22.5
Moderate hepatic steatosis	29	14.5
Severe hepatic steatosis	12	6.0
Total	200	100.0

Hepatic steatosis was identified in 86 (43.0%) participants. Mild steatosis was observed in 45 (22.5%), moderate steatosis in 29 (14.5%) and severe steatosis in 12 (6.0%) patients.The findings showed a substantial burden of hepatic fat accumulation among patients with T2DM.

Hepatic steatosis reflect the interaction of insulin resistance, increased free fatty acid delivery to the liver, increased de novo lipogenesis and impaired hepatic lipid oxidation.The relationship between hepatic steatosis and metabolic dysfunction is particularly relevant because the presence of T2DM increases the risk of progressive steatotic liver disease and adverse hepatic outcomes.

Table 6. Biochemical profile of the study population

Biochemical parameter	Mean ± SD
Fasting blood glucose (mg/dL)	158.6 ± 42.3
HbA1c (%)	7.8 ± 1.3
Fasting insulin (µU/mL)	14.8 ± 7.2
C-peptide (ng/mL)	2.1 ± 1.0
HOMA-IR	5.8 ± 3.1
Total cholesterol (mg/dL)	192.4 ± 38.6
Triglycerides (mg/dL)	178.5 ± 65.2
HDL cholesterol (mg/dL)	39.8 ± 9.4
LDL cholesterol (mg/dL)	116.2 ± 31.5
ALT (U/L)	38.6 ± 19.4
AST (U/L)	32.4 ± 14.8
GGT (U/L)	42.8 ± 24.6
Serum creatinine (mg/dL)	1.08 ± 0.42
eGFR (mL/min/1.73 m^2)	79.6 ± 21.3

The biochemical profile demonstrated abnormalities involving glucose regulation, lipid metabolism and hepatic enzyme concentrations.The mean triglyceride concentration was 178.5 ± 65.2 mg/dL, while mean HDL cholesterol was 39.8 ± 9.4 mg/dL. These findings illustrate an atherogenic lipid profile frequently associated with insulin resistance.

The mean ALT and AST concentrations were 38.6 ± 19.4 U/L and 32.4 ± 14.8 U/L, respectively.These findings may reflect hepatic metabolic stress in a subset of participants, although liver enzyme concentrations alone cannot establish the presence or severity of hepatic steatosis or fibrosis.The mean eGFR was 79.6 ± 21.3 mL/min/1.73 m^2, indicating variation in renal function across the study population.

Table 7. Association between pancreatic anatomical findings and C-peptide levels

Pancreatic findings	Preserved C-peptide, n (%)	Reduced C-peptide, n (%)	Total
Normal pancreatic morphology	124 (84.9)	22 (15.1)	146
Pancreatic abnormalities	28 (51.9)	26 (48.1)	54
Total	152 (76.0)	48 (24.0)	200

Among 146 patients with normal pancreatic morphology, 22 (15.1%) demonstrated reduced C-peptide levels. In contrast, reduced C-peptide was observed in 26 (48.1%) of the 54 patients with pancreatic imaging abnormalities.This pattern suggested a possible association between pancreatic structural abnormalities and reduced endogenous insulin secretion.

Table 8. Association between hepatic steatosis and glycemic status

Hepatic ultrasound findings	HbA1c below 7%, n (%)	HbA1c ≥7%, n (%)	Total
Normal liver	62 (54.4)	52 (45.6)	114
Mild steatosis	15 (33.3)	30 (66.7)	45
Moderate steatosis	5 (17.2)	24 (82.8)	29
Severe steatosis	2 (16.7)	10 (83.3)	12
Total	84 (42.0)	116 (58.0)	200

The proportion of poor glycemic control increased across the hepatic steatosis categories. Among patients with normal hepatic morphology, 52 (45.6%) had HbA1c levels of 7% or above. This proportion increased to 66.7% among patients with mild steatosis and 82.8% among those with moderate steatosis. Among patients with severe steatosis, 10 (83.3%) demonstrated poor glycemic control.

This distribution suggests a potential relationship between hepatic fat accumulation and inadequate glycemic regulation.The underlying mechanisms may involve hepatic insulin resistance, increased endogenous glucose production, altered lipid metabolism and systemic metabolic inflammation.

Table 9. Relationship between insulin resistance and selected metabolic characteristics

Metabolic characteristic	Elevated HOMA-IR, n (%)	Normal HOMA-IR, n (%)
BMI ≥25 kg/m^2	94 (73.4)	38 (52.8)
Hypertriglyceridemia	82 (64.1)	28 (38.9)
Low HDL cholesterol	78 (60.9)	26 (36.1)
Hepatic steatosis	69 (53.9)	17 (23.6)
Poor glycemic control	84 (65.6)	32 (44.4)
Hypertension	84 (65.6)	34 (47.2)

Each row represents a separate clinical characteristic and percentages are calculated within the respective HOMA-IR group. Elevated HOMA-IR was observed in 128 (64.0%) participants, while 72 (36.0%) had values below the selected operational threshold.

Patients with elevated HOMA-IR demonstrated a higher proportion of excess body weight, hypertriglyceridemia, low HDL cholesterol and hepatic steatosis.Hepatic steatosis was observed in 69 (53.9%) patients with elevated HOMA-IR compared with 17 (23.6%) patients with normal HOMA-IR.Similarly, poor glycemic control was more frequent among patients with elevated HOMA-IR.

These findings showed the close relationship between insulin resistance, obesity, abnormal lipid metabolism and hepatic fat accumulation.

Table 10. Distribution of antidiabetic pharmacotherapy among patients with T2DM

Antidiabetic treatment	Frequency (n)	Percentage (%)
Metformin-based therapy	68	34.0
Metformin + DPP-4 inhibitor	36	18.0
Metformin + sulfonylurea	28	14.0
SGLT2 inhibitor-containing therapy	24	12.0
GLP-1 receptor agonist-containing therapy	8	4.0
Insulin-based therapy	28	14.0
Other combination therapy	8	4.0
Total	200	100.0

Metformin-based treatment was the most frequently reported pharmacological approach, accounting for 68 (34.0%) patients. Combination therapy with metformin and a DPP-4 inhibitor was observed in 36 (18.0%) participants, whereas 28 (14.0%) were receiving metformin and a sulfonylurea.SGLT2 inhibitor-containing treatment was documented in 24 (12.0%) patients, while 28 (14.0%) were receiving insulin-based therapy.

These findings demonstrated the use of different therapeutic approaches depending on glycemic status, diabetes duration and clinical characteristics.The relatively high proportion of patients with poor glycemic control highlights the importance of treatment individualization, medication adherence and regular reassessment of therapeutic effectiveness.

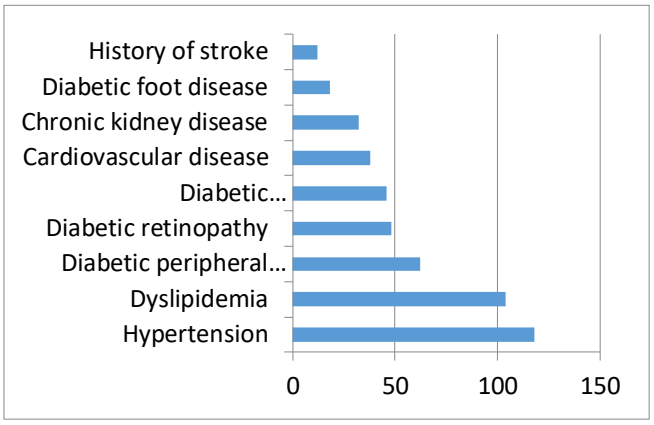

Figure 2 Distribution of diabetic complications and associated clinical conditions

Hypertension and dyslipidemia were the most frequent associated conditions, occurring in 118 (59.0%) and 104 (52.0%) patients, respectively.Peripheral neuropathy was identified in 62 (31.0%) participants, followed by diabetic retinopathy in 48 (24.0%) and diabetic nephropathy or albuminuria in 46 (23.0%).Cardiovascular disease was documented in 38 (19.0%) patients.

A higher frequency of diabetic complications was observed among patients with diabetes duration exceeding 10 years. Peripheral neuropathy was documented in 37 (49.3%) patients with long-standing diabetes compared with 25 (20.0%) patients with diabetes duration below 10 years.Similarly, diabetic retinopathy was more frequent in the longer-duration group (38.7% versus 15.2%).These findings demonstrate the potential relationship between prolonged metabolic exposure and progressive microvascular and macrovascular complications.

Table 11. Multivariable logistic regression analysis for hepatic steatosis

Variables	Adjusted OR	95% CI	p-value
BMI ≥25 kg/m^2	2.31	1.24–4.31	0.008
Elevated HOMA-IR	2.76	1.45–5.24	0.002
Triglycerides ≥150 mg/dL	1.94	1.08–3.48	0.026
HbA1c ≥7%	1.82	1.01–3.28	0.046
Diabetes duration >10 years	1.41	0.78–2.56	0.250
Male sex	1.18	0.66–2.12	0.570

The regression analysis identified elevated HOMA-IR as an important factor associated with hepatic steatosis (adjusted OR 2.76, 95% CI 1.45–5.24).BMI of 25 kg/m^2 or above was also associated with higher odds of hepatic steatosis (adjusted OR 2.31, 95% CI 1.24–4.31).Hypertriglyceridemia and HbA1c of 7% or above demonstrated additional associations. These findings suggested that insulin resistance, excess body weight and abnormal lipid metabolism may be important contributors to hepatic steatosis in T2DM.

DISCUSSION

The present study examined the relationship between anatomical and biochemical alterations in patients with type 2 diabetes mellitus, focusing on pancreatic islet dysfunction, hepatic metabolic abnormalities, insulin resistance, antidiabetic pharmacotherapy and clinical complications. The findings demonstrated several interconnected abnormalities, including poor glycemic control, elevated HOMA-IR, variable C-peptide concentrations, pancreatic structural changes, hepatic steatosis and dyslipidemia. More than half of the population had HbA1c of 7% or above, elevated HOMA-IR was observed in nearly two-thirds, and hepatic steatosis was documented in 43% of participants[12,13]. These results showed that T2DM is not an isolated disorder of glucose metabolism, but a complex multisystem disease involving pancreatic endocrine dysfunction, hepatic lipid accumulation, peripheral insulin resistance, and vascular injury.

One major aspect of the study was the evaluation of pancreatic structural abnormalities and their association with endogenous insulin secretion. Pancreatic imaging abnormalities were found in 27% of patients, including atrophy, increased echogenicity and reduced C-peptide concentrations observed in 24% of patients, were more frequent in those with pancreatic abnormalities. Diabetes duration was negatively related to C-peptide suggesting progressive loss of insulin-secretory reserve.

A study suggested that beta-cell apoptosis, progressive beta-cell failure and inadequate compensation for insulin resistance underlie the development of T2DM. However, imaging findings alone cannot establish islet amyloid deposition, microscopic beta-cell destruction or fibrosis[14-16].

Hepatic steatosis is an important finding with a higher proportion of poor glycemic control among patients with moderate and severe steatosis. This is consistent with the established association between T2DM, hepatic insulin resistance and

metabolic dysfunction-associated steatotic liver disease. In insulin-resistant states, insulin fails to adequately suppress hepatic glucose production, while increased fatty acid delivery and enhanced de novo lipogenesis promote triglyceride accumulation in hepatocytes. The ADA Standards of Care highlight the substantial burden of MASLD in T2DM and the risk of progressive steatohepatitis and fibrosis, and emphasize weight reduction, metabolic risk assessment, and appropriate pharmacological management. Liver enzymes ALT, AST, and GGT provide useful information but have limitations, as steatosis may occur with normal enzymes and elevated enzymes may result from other causes, so they should be combined with clinical evaluation, ultrasound, and noninvasive fibrosis risk assessment[17,18].

Insulin resistance was another central component, with a mean HOMA-IR of 5.8 ± 3.1 and elevated insulin resistance in 64% of participants. Patients with elevated HOMA-IR had higher frequencies of excess body weight, hypertriglyceridemia, low HDL cholesterol, and hepatic steatosis, consistent with the relationship between obesity, adipose tissue dysfunction, and peripheral insulin resistance. At the molecular level, impaired insulin receptor signaling reduces glucose uptake in skeletal muscle and impairs suppression of hepatic glucose production, while adipose dysfunction increases lipolysis and circulating free fatty acids[19,20]. The biochemical findings also showed characteristic diabetic dyslipidemia, with mean triglycerides of 178.5 ± 65.2 mg/dL and mean HDL cholesterol of 39.8 ± 9.4 mg/dL, a pattern driven by increased hepatic VLDL production and associated with formation of small, dense LDL particles and increased cardiovascular risk[21,22].

The study also examined antidiabetic pharmacotherapy and complications. Metformin-based treatment was most frequent, followed by DPP-4 inhibitor combinations, sulfonylurea combinations, SGLT2 inhibitor-containing therapy, and insulin-based treatment, each targeting distinct mechanisms: metformin reduces hepatic glucose production, DPP-4 inhibitors enhance incretin activity, SGLT2 inhibitors promote urinary glucose excretion with cardiovascular and renal benefits, GLP-1 receptor agonists improve glucose-dependent insulin secretion and support weight reduction, and insulin is important in substantial endogenous deficiency. These patterns should be interpreted descriptively, as the cross-sectional design cannot establish treatment superiority[23-25]. A higher frequency of neuropathy, retinopathy, and nephropathy was observed with diabetes duration exceeding 10 years, consistent with prolonged hyperglycemia promoting oxidative stress, advanced glycation end-product formation, endothelial dysfunction, and microvascular injury. The most important contribution of the study was therefore its integrated assessment: pancreatic changes reflect structural abnormality, C-peptide and fasting insulin reflect endocrine function, hepatic steatosis reflects lipid accumulation, and ALT, AST, triglycerides, and HOMA-IR provide complementary metabolic information for comprehensive evaluation of T2DM.

STRENGTHS OF THE STUDY

1. Integrated anatomical and biochemical assessment: It evaluates pancreatic and hepatic structural findings alongside biochemical indicators of metabolic dysfunction.
2. Assessment of pancreatic endocrine function: Inclusion of fasting insulin and C-peptide provides additional information regarding endogenous insulin secretion.
3. Evaluation of insulin resistance: HOMA-IR allows an indirect assessment of insulin resistance and its relationship with obesity, dyslipidemia and hepatic steatosis.
4. Hepatic metabolic evaluation: Assessment of hepatic steatosis and liver enzymes provides information about the relationship between diabetes and metabolic dysfunction-associated steatotic liver disease.
5. Pharmacological assessment: Different antidiabetic medication categories are considered to explore their relationship with metabolic and biochemical parameters.
6. Clinical relevance: The inclusion of microvascular and macrovascular complications provides a broader understanding of the clinical burden of T2DM.
7. Potential clinical application: The integrated approach may help identify patients requiring more comprehensive metabolic and organ-specific assessment.

CONCLUSION

The study highlighted the importance of evaluating anatomical and biochemical alterations together to understand the underlying mechanisms of disease progression. Pancreatic endocrine dysfunction contributes to inadequate insulin secretion, while hepatic insulin resistance and fat accumulation further aggravate metabolic disturbances. The coexistence of elevated glucose concentrations, abnormal lipid profiles, increased insulin resistance and hepatic steatosis demonstrated the interconnected nature of these pathological processes.The assessment of C-peptide, fasting insulin, HOMA-IR, HbA1c, lipid parameters and liver enzymes may provide complementary information regarding metabolic status and pancreatic endocrine function. Radiological assessment can additionally identify clinically relevant pancreatic and hepatic structural abnormalities.

Antidiabetic pharmacotherapy remains essential for improving glycemic control and reducing long-term complications. Treatment should be individualized according to metabolic status, residual insulin secretion, body weight, cardiovascular risk, renal function and associated hepatic abnormalities.Overall, an integrated anatomical, biochemical and clinical assessment may improve understanding of T2DM pathophysiology and support comprehensive disease monitoring, early

identification of complications and appropriate therapeutic decision-making.

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