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Research Article

Biochemical and Physiological Assessment of Inflammation, Insulin Resistance, and Cardiovascular Risk among Patients with Type 2 Diabetes Mellitus

Sadia Majeed[1], Bushra Samoon[2], Farooq Ahmad Malik[3], Aneeqa Shahid[4], Sajjad Ghani[5], Tariq Hussain[6*]

[1]Senior Demonstrator, Department of Biochemistry, DG Khan Medical College, Dera Ghazi Khan, Pakistan.
[2]Demonstrator, Department of Physiology, Sheikh Zayed Medical College, Rahim Yar Khan, Pakistan.
[3]Associate Professor, Department of Biochemistry, DG Khan Medical College, Dera Ghazi Khan, Pakistan.
[4]Assistant Professor, Department of Biochemistry, Aziz Fatima Medical and Dental College, Faisalabad, Pakistan.
[5]Assistant Professor, Department of Biochemistry, Aziz Fatima Medical and Dental College, Faisalabad, Pakistan.
[6*]Associate Professor, Bakhtawar Amin Medical and Dental College, Multan, Pakistan.
Corresponding Author: Tariq Hussain
Email: Tariq_h600@yahoo.com
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ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic condition that is associated with insulin resistance, chronic hyperglycemia, and systemic inflammation. These abnormalities account for much of the cardiovascular morbidity and mortality and early identification of metabolic and inflammatory abnormalities are key to good disease management.

Objective: To evaluate biochemical markers of inflammatory, insulin resistance and physiological cardiovascular risk factors in Type 2 Diabetes Mellitus patients and healthy controls.

Methods: This comparative cross-sectional study was conducted at Sheikh Zayed Medical College and Hospital, Rahim Yar Khan, Pakistan, and Aziz Fatima Medical and Dental College, Faisalabad, Pakistan, from March 2024 to March 2025. One hundred and thirty individuals were recruited, of whom ninety were patients with T2DM, and forty healthy controls. Anthropometric measurements, blood pressure, fasting blood glucose, HbA1c, fasting insulin, lipid profile, high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) were assessed. HOMA-IR (Homeostatic Model Assessment for Insulin Resistance) was used for the estimation of insulin resistance.

Results: Patients with T2DM exhibited significantly higher body mass index, waist circumference, systolic and diastolic blood pressure, fasting glucose, HbA1c, fasting insulin, and HOMA-IR values compared with controls ($p<0.001$). Inflammatory biomarkers including hs-CRP, IL-6, and TNF-α were markedly elevated among diabetic patients. Significant dyslipidemia was observed, characterized by increased total cholesterol, triglycerides, LDL cholesterol, and reduced HDL cholesterol. HOMA-IR had strong positive relationships with inflammatory markers and cardiovascular risk indicators.

Conclusion: Type 2 Diabetes Mellitus (DM) has been linked to significant inflammation, insulin resistance and cardiovascular risk. Biochemical and physiological evaluation could help to identify risk at an early stage and to optimize the prevention of cardiovascular complications.

Keywords: Type 2 Diabetes Mellitus, Insulin Resistance, Inflammation, Cardiovascular Risk, HOMA-IR, Hs-CRP.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the most prevalent chronic metabolic disorders worldwide and represents a major public health challenge due to its rapidly increasing incidence and associated complications[1]. T2DM is a condition of persistent hyperglycemia due to insulin resistance and progressive pancreatic β-cell dysfunction and is a problem faced by millions of people in both developed and developing countries[2]. According to the International Diabetes Federation, the cost of diabetes globally is still increasing at an alarming rate, with low- and middle-income nations having a large share of the disease burden. The prevalence of diabetes is rising at an alarming rate in Pakistan, especially as a result of urbanization, sedentary lifestyle,

dietary shifts, obesity and population aging. With the increasing prevalence of T2DM has come significant clinical, social and economic consequences, and the need to better understand the underlying mechanisms of disease progression and complications[3].

Insulin resistance is now known to be the primary pathophysiological abnormality of T2DM and is an important factor in both metabolic and cardiovascular abnormalities[4]. Insulin normally promotes the uptake of glucose in skeletal muscle, adipose tissue and inhibits glucose production in liver. In insulin resistant people, target tissues are less responsive to insulin, which results in poor use of glucose and the development of hyperinsulinism[5]. Over time, this continued insulin resistance puts more and more of a strain on the pancreatic β-cells, causing them to become exhausted and lead to chronic hyperglycemia. In addition to the metabolic changes in glucose metabolism, insulin resistance is associated with a wide range of metabolic abnormalities such as dyslipidaemias, hypertension, endothelial dysfunction and vascular inflammation that lead to cardiovascular diseases[6].

In recent years, there has been a growing focus on the association of chronic low-grade inflammation with the pathogenesis of T2DM[7]. There is increasing evidence that T2DM is not just a metabolic disorder, but also an inflammatory disorder with ongoing innate immune activation. The accumulation of excess adipose tissue is an active endocrine organ that can produce a large number of inflammatory mediators called adipokines and cytokines, especially visceral fat. Such inflammatory molecules include tumour necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) and other pro-inflammatory molecules, which affect the activity of insulin signalling pathways and lead to metabolic dysfunction. Chronic inflammation participates in the development and establishment of insulin resistance by several molecular pathways such as disturbances in insulin receptor signaling, activation of stress-related kinases and increase in oxidative stress[8].

High-sensitivity C-reactive protein (hs-CRP), IL-6, and TNF-α are inflammatory biomarkers which have become important markers of systemic inflammation and cardiometabolic risk in the context of T2DM[9]. Since high levels of hs-CRP are linked to insulin resistance, endothelial dysfunction and future cardiovascular events. In the same way, IL-6 stimulates the synthesis of acute-phase reactants in the liver and helps in chronic inflammatory reactions and TNF-α interferes directly with insulin receptor signaling by inhibiting insulin receptor substrate activity[10]. Many studies have shown that the levels of these inflammatory mediators are associated with poor glycemic control, obesity, vascular dysfunction and adverse cardiovascular outcomes in patients with T2DM[11].

Despite all the advances made in the care of people with T2DM, cardiovascular disease continues to be the primary cause of death and morbidity in this patient population, and is responsible for a significant number of diabetes related deaths globaly[12]. Diabetics are at a much higher risk of coronary artery disease, cerebrovascular disease, peripheral arterial disease, heart failure and other vascular complications than non-diabetics. Hyperglycemia is not the only reason for the higher cardiovascular risk in T2DM. Rather, it is a result of a complicated interplay of insulin resistance, systemic inflammation, oxidative stress, dyslipidaemia, endothelial dysfunction and hypertension. These pathological processes are mutually linked and help in the initiation of atherosclerosis and in vascular damage prior to the onset of cardiovascular disease[13,14].

Endothelial dysfunction is regarded as an early event in diabetic vascular disease. Excessive generation of reactive oxygen species (ROS) that leads to oxidative stress and decreased nitric oxide (NO) bioavailability is associated with hyperglycemia and insulin resistance[15]. This results in abnormal vascular reactivity, increased vascular permeability, greater adherence of leukocytes and activation of pro-thrombotic pathways. The pathological conditions are chronic and induce formation of atherosclerotic plaques and predispose to cardiovascular events. Thus, detecting early biochemical and physiological abnormalities that are linked with endothelial dysfunction is crucial to avoiding cardiovascular complications among patients with diabetes[16].

Another significant risk factor for cardiovascular disease in T2DM is dyslipidaemia. Diabetic dyslipidaemia usually involves raised triglycerides, raised small dense low-density lipoprotein cholesterol (LDL-C) and lowered high-density lipoprotein cholesterol (HDL-C)[17]. These lipid abnormalities promote the development of atherosclerotic plaques and have a major effect on the progression of cardiovascular disease. Also, insulin resistance contributes to lipid metabolism disturbances by

enhancing the production of very-low-density lipoprotein (VLDL) by the liver and decreasing the clearance of lipids from the bloodstream. People with T2DM are at a high-risk cardiovascular profile especially when combined with dyslipidaemia and hyperglycaemia, and with inflammation[18].

Physiological measurements like body mass index, waist circumference, and blood pressure give more insight into the cardiometabolic risk in diabetic patients[19]. Insulin resistance and chronic inflammatory state have been linked to obesity, especially central obesity. Visceral adiposity increases inflammatory cytokines and free fatty acid production, which exacerbates insulin sensitivity and also causes vascular dysfunction. Likewise, hypertension is also often associated with T2DM and significantly raises the risk of cardiovascular events. Obesity, hypertension, dyslipidaemia and hyperglycaemia collectively represent a clustering of metabolic abnormalities which greatly increase cardiovascular risk[20].

Although numerous studies have independently investigated inflammation, insulin resistance, and cardiovascular risk in diabetic populations, comprehensive evaluation of these interconnected factors within a single clinical framework remains limited, particularly in developing countries such as Pakistan[10-13]. The knowledge of the correlation between inflammatory biomarkers and insulin resistance indices with the physiological cardiovascular parameters could allow an earlier recognition of high risk patients and better management of the disease and prevention of complications. This integrated assessment is especially applicable in healthcare environments with limited resources in which diabetes burden is rapidly rising and cardiovascular complications are a leading cause of disability and premature death[15,17].

Therefore, the present study was designed to evaluate biochemical markers of inflammation, indices of insulin resistance, and physiological cardiovascular risk factors among patients with Type 2 Diabetes Mellitus. These parameters will be compared with the respective parameters in healthy individuals to gain a holistic insight into the metabolic and cardiovascular changes in patients with T2DM and to find the potential markers that can help in risk stratification and management of diabetic patients[18].

MATERIALS AND METHODS

Study Design and Setting

This comparative cross-sectional study was conducted to evaluate biochemical markers of inflammation, insulin resistance, and physiological indicators of cardiovascular risk among patients with Type 2 Diabetes Mellitus (T2DM). The study was carried out at Sheikh Zayed Medical College and Hospital, Rahim Yar Khan, Pakistan, and Aziz Fatima Medical and Dental College, Faisalabad, Pakistan, over a period of one year from March 2024 to March 2025. The study was designed to compare diabetic patients with healthy controls to examine the correlation between the metabolic dysfunction and inflammatory status and cardiovascular risk factors.

Study Population

A total of 130 participants were enrolled using a non-probability consecutive sampling technique. A total of 90 patients with Type 2 Diabetes Mellitus and 40 apparently healthy controls of the same age and sex were studied. The participants were obtained from the outpatient diabetic clinics and medical wards of participating institutions. Both male and female subjects between 30 and 70 years of age were included. The inclusion criteria for the patients in the study were: History of Type 2 Diabetes Mellitus for more than one year as per the American Diabetes Association criteria and they were on regular medical treatment. Apparently healthy individuals with normal blood glucose levels and without any known diabetes mellitus, cardiovascular disease, endocrine or chronic inflammatory diseases were included as the control group.

Patients with Type 1 Diabetes Mellitus, gestational diabetes, chronic kidney disease, chronic liver disease, autoimmune disease, malignancy, acute or chronic infection, congestive heart failure, recent myocardial infarction, recent cerebrovascular accidents and patients using corticosteroid or immunosuppressive drugs were excluded from the study. The women who were pregnant and those who didn't want to do the study were also not included.

Ethical Considerations

Ethical Review Committees of Sheikh Zayed Medical College and Hospital, Rahim Yar Khan and Aziz Fatima Medical and Dental College, Faisalabad approved the study protocol. All the procedures were performed in accordance with the ethical principles outlined in the declaration of Helsinki. Prior to enrollment, all participants were given a comprehensive description of the

goals and procedures of the study and written informed consent was sought. The confidentiality and anonymity of all participants was preserved throughout the process of the research.

Clinical, Physiological, and Anthropometric Assessment

A structured proforma was used for detailed demographic and clinical information. Age, sex, duration of diabetes, history of medications used, smoking and family history of diabetes were documented. Anthropometric measurements were done using standard technique. Weight was measured using a calibrated digital weighing scale, participants wore light clothing and no footwear. A wall mounted stadiometer was used to measure the height and Body mass Index (BMI) was calculated as body weight in kg divided by height in m2. Central obesity was evaluated by measuring waist circumference (WC) at the midpoint between the lower rib margin and the iliac crest with a non-elastic measuring tape.

Physiological assessment was done to determine SBP and DBP with a standard mercury sphygmomanometer. The participants were given at least ten minutes of rest prior to measurements being taken. BP was measured three times, 5 minutes apart, and the mean of three measurements was taken for analysis. These physiological measurements allowed to assess the risk of cardiovascular disease and cardiometabolic profile of the studied subjects.

Biochemical Analysis

Venous blood samples were taken from all participants under aseptic conditions after an overnight fast of 10–12 hours. The blood samples were collected from each subject and approximately 8 mls of the blood was taken and processed for biochemical investigations. Fasting blood glucose was determined by the glucose oxidase-peroxidase method and glycated hemoglobin (HbA1c) was determined by high performance liquid chromatography. Serum insulin levels were obtained at fasting by commercially available enzyme linked immunosorbent assay (ELISA) kits as per the manufacturer's instructions.

The serum lipid profile data were obtained by measuring serum total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) using automated clinical chemistry analyzers and standard enzymatic methods. All laboratory testing was done with quality control procedures to assure accuracy and reliability of results.

Systemic inflammation was assessed by measuring serum concentration of high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) using commercially available sandwich ELISA kits. Each biochemical assay was conducted following manufacturer's instructions, with assays performed in duplicate to reduce analytical variability.

Evaluation of Insulin Resistance and cardiovascular risk

Insulin resistance was calculated as Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) from the fasting glucose and fasting insulin levels. Peripheral insulin sensitivity was measured using HOMA-IR, which is a measure of insulin resistance; a higher value indicates greater insulin resistance. Cardiovascular risk factors were evaluated by measuring blood pressure parameters, anthropometric indices, lipid profile abnormalities and inflammatory parameters. Furthermore, the lipid-derived cardiovascular risk markers such as Total Cholesterol to HDL-C ratio, LDL-C to HDL-C ratio were also calculated to estimate the atherogenic risk. Cardiovascular risk factors such as high levels of inflammatory markers, dyslipidaemia, obesity, hyper tension and insulin resistance were regarded as significant players among diabetic individuals.

Statistical Analysis

Collected data were entered and analyzed by using the Statistical Package for Social Sciences (SPSS) version 26.0. Data on continuous variables were reported as mean ± standard deviation (S.D.) while categorical variables were reported as frequencies and percentages. Before statistical analysis, distribution of quantitative variables was evaluated. Independent sample t-tests were also used to compare continuous variables, and chi-square tests were used to compare categorical variables, between diabetic and healthy controls. Pearson correlation analysis was carried out to assess the association between inflammatory biomarkers, IR indices and cardiovascular risk parameters. Statistically significant differences were defined as a p value < 0.05 with 95% confidence interval for all statistical tests.

RESULTS

A total of 130 participants were enrolled in the study, including 90 patients diagnosed with

Type 2 Diabetes Mellitus (T2DM) and 40 healthy controls. The mean age of diabetic patients was 54.8 ± 9.1 years, while the mean age of controls was 52.6 ± 8.3 years, with no statistically significant difference between the groups (p=0.211). The sex distribution was also similar with males being 54.4% in the diabetic group and 52.5% in the control group. However, significant differences were observed in anthropometric and physiological parameters. The BMI, WC, SBP and DBP were significantly higher in patients with T2DM, than healthy controls (p<0.001 for all). The mean BMI was 30.8 ± 4.3 kg/m² in the diabetic group and 25.4 ± 3.1 kg/m² in the control group, and the mean waist circumference was 104.7 ± 10.2 cm in the diabetic group and 88.9 ± 7.8 cm in the control group. Similarly, mean systolic blood pressure was 144.6 ± 15.9 mmHg in the diabetic group compared with 121.8 ± 10.7 mmHg in controls, whereas mean diastolic blood pressure was 89.4 ± 9.8 mmHg and 76.5 ± 6.9 mmHg, respectively. These findings show that diabetics had much higher rates of obesity, central adiposity and hypertension, and that they were burdened with the disease and had a higher cardiovascular risk as demonstrated in table 1.

Table 1. Demographic, Anthropometric, and Physiological Characteristics of Study Participants

Variable	T2DM (n=90)	Controls (n=40)	p-value
Age (years)	54.8 ± 9.1	52.6 ± 8.3	0.211
Male, n (%)	49 (54.4)	21 (52.5)	0.841
Female, n (%)	41 (45.6)	19 (47.5)	0.841
Body Mass Index (kg/m²)	30.8 ± 4.3	25.4 ± 3.1	<0.001
Waist Circumference (cm)	104.7 ± 10.2	88.9 ± 7.8	<0.001
Systolic Blood Pressure (mmHg)	144.6 ± 15.9	121.8 ± 10.7	<0.001
Diastolic Blood Pressure (mmHg)	89.4 ± 9.8	76.5 ± 6.9	<0.001

Patients with T2DM had significant biochemical abnormalities. There was a significant increase in fasting blood glucose and HbA1c in the diabetic population, suggesting poor glycemic control. The mean fasting blood glucose level was 181.6 ± 46.2 mg/dL in diabetic patients compared with 91.7 ± 10.9 mg/dL among controls (p<0.001), while HbA1c values were 8.7 ± 1.5% and 5.2 ± 0.4%, respectively (p<0.001). Fasting insulin concentrations were also significantly higher in diabetic patients (20.4 ± 6.8 µIU/mL) than in controls (8.5 ± 2.2 µIU/mL), resulting in substantially elevated HOMA-IR values (8.9 ± 3.4 vs. 2.1 ± 0.8, p<0.001). In addition, there were significant increases for inflammatory biomarkers among the people with diabetes. Levels of mean hs-CRP, IL-6 and TNF-α were significantly elevated in T2DM group than healthy controls, suggesting that chronic systemic inflammation exists in the T2DM group. These findings suggest that insulin resistance and inflammation coexist and may contribute synergistically to disease progression and cardiovascular complications in diabetic patients as shown in table 2.

Table 2. Glycemic Status, Insulin Resistance, and Inflammatory Biomarkers

Parameter	T2DM (n=90)	Controls (n=40)	p-value
Fasting Blood Glucose (mg/dL)	181.6 ± 46.2	91.7 ± 10.9	<0.001
HbA1c (%)	8.7 ± 1.5	5.2 ± 0.4	<0.001
Fasting Insulin (µIU/mL)	20.4 ± 6.8	8.5 ± 2.2	<0.001
HOMA-IR	8.9 ± 3.4	2.1 ± 0.8	<0.001
hs-CRP (mg/L)	6.8 ± 2.7	1.8 ± 0.7	<0.001
IL-6 (pg/mL)	10.2 ± 3.8	3.3 ± 1.0	<0.001
TNF-α (pg/mL)	16.9 ± 5.5	6.0 ± 1.9	<0.001

This was also reflected in the significantly more atherogenic cardiovascular risk profile of diabetic patients in the analysis of lipid profile parameters. Significant differences existed in total cholesterol, triglycerides and LDL cholesterol levels between the T2DM group and controls (p<0.001 for all comparisons). Mean total cholesterol was 218.3 ± 37.5 mg/dL among diabetic patients compared with 176.8 ± 28.7 mg/dL in controls, while triglyceride levels were 223.6 ± 70.2 mg/dL and 128.5 ± 38.9 mg/dL, respectively. Likewise, the amount of LDL cholesterol was also significantly higher in the diabetic patients (141.7 ± 30.9 mg/dL) than in controls (101.4 ± 24.6 mg/dL). Contrarily, the diabetic group had significantly

reduced HDL (37.9 ± 7.9mg/dl) levels compared to the healthy group (50.2 ± 7.4mg/dl). Cardiovascular risk indices showed similar trends, with both Total Cholesterol/HDL ratio and LDL/HDL ratio being significantly elevated in diabetic patients. These results suggest that the atherosclerotic cardiovascular disease risk profile is significantly elevated in people with T2DM and that there is a strong correlation between dyslipidaemia and diabetic cardiovascular outcomes as well as indicated in table 3

Table 3. Lipid Profile and Cardiovascular Risk Indicators

Parameter	T2DM (n=90)	Controls (n=40)	p-value
Total Cholesterol (mg/dL)	218.3 ± 37.5	176.8 ± 28.7	<0.001
Triglycerides (mg/dL)	223.6 ± 70.2	128.5 ± 38.9	<0.001
LDL Cholesterol (mg/dL)	141.7 ± 30.9	101.4 ± 24.6	<0.001
HDL Cholesterol (mg/dL)	37.9 ± 7.9	50.2 ± 7.4	<0.001
Total Cholesterol/HDL Ratio	5.8 ± 1.3	3.5 ± 0.7	<0.001
LDL/HDL Ratio	3.8 ± 0.9	2.0 ± 0.5	<0.001

Correlation analysis was also done among the diabetic patients to delve more into the relation between metabolic dysfunction and inflammation. HOMA-IR demonstrated a strong positive correlation with hs-CRP ($r=0.61$, $p<0.001$), IL-6 ($r=0.57$, $p<0.001$), and TNF-α ($r=0.53$, $p<0.001$), indicating that worsening insulin resistance was associated with increasing systemic inflammation. Significant positive correlations were also observed between HOMA-IR and body mass index ($r=0.49$, $p<0.001$), waist circumference ($r=0.51$, $p<0.001$), systolic blood pressure ($r=0.42$, $p<0.001$), and LDL cholesterol ($r=0.46$, $p<0.001$). Conversely, HDL cholesterol demonstrated a significant negative correlation with HOMA-IR ($r=-0.39$, $p<0.001$). The findings in this study justify that there is a correlation between obesity, inflammation, insulin resistance, dyslipidemia and cardiovascular risk in patients with Type 2 Diabetes Mellitus as demonstrated in table 4.

Table 4. Correlation of HOMA-IR with Inflammatory and Cardiovascular Risk Parameters in T2DM Patients

Variable	Correlation Coefficient (r)	p-value
hs-CRP	0.61	<0.001
IL-6	0.57	<0.001
TNF-α	0.53	<0.001
Body Mass Index	0.49	<0.001
Waist Circumference	0.51	<0.001
Systolic Blood Pressure	0.42	<0.001
LDL Cholesterol	0.46	<0.001
HDL Cholesterol	-0.39	<0.001

Overall, the results demonstrate that patients with Type 2 Diabetes Mellitus exhibit significantly greater

Insulin resistance, systemic inflammation, obesity, hypertension, dyslipidemia, and cardiovascular risk compared with healthy individuals. The significant correlations between inflammatory markers and HOMA-IR clearly underscore the significance of chronic inflammatory process in the pathogenesis of insulin resistance and cardiovascular disease in diabetic patients. The results highlight the importance of the use of biochemical and physiological assessment for early detection of high-risk individuals and holistic management of Type 2 Diabetes Mellitus.

DISCUSSION

In the present study, biochemical and physiological parameters of inflammation, insulin resistance and cardiovascular risk were assessed in patients with Type 2 Diabetes Mellitus (T2DM) and appreciable metabolic, inflammatory and cardiovascular abnormalities were found in T2DM patients when compared to control individuals. These results show that T2DM is not only a glucose metabolism disorder, but a systemic disease with chronic inflammation, insulin resistance, obesity, dyslipidemia and increased cardiovascular risk[1-3].

The study found that the diabetic group had fasting blood glucose values, HbA1c, fasting insulin and HOMA-IR which were significantly

greater[4]. These findings are indicative of inadequate glycaemic control and significant insulin resistance which are key components of the pathogenesis of T2DM. Chronic insulin resistance results in a decreased uptake of glucose by peripheral tissues and elevated production of glucose by the liver, causing hyperglycemia. The higher HOMA-IR levels found in the diabetic group reflect a significant reduction in insulin sensitivity and are consistent with other studies showing insulin resistance is highly associated with metabolic dysfunction and the progression of cardiovascular diseases[5,6].

In addition, inflammatory markers (hs-CRP, IL-6, and TNF-α) were significantly elevated in patients with T2DM. The results are in line with the increasing evidence of T2DM as a chronic state of low-grade inflammation[7]. As adipose tissue expands, especially visceral fat, pro-inflammatory cytokines are secreted which disrupt the insulin signalling pathways and lead to insulin resistance. The high levels of hs-CRP seen in the current study may reflect the activation of systemic inflammatory pathways and have been linked to endothelial dysfunction and cardiovascular risk. Likewise, IL-6 and TNF-α have been shown to affect insulin receptor signaling, as well as cause vascular inflammation, which can lead to metabolic worsening and to vascular complications[8,9].

Diabetic patients had higher values of BMI, Waist circumference, SBP and DBP than the controls, which were significant[10]. These data underscore the strong link between obesity, hypertension and diabetes. Central obesity is acknowledged as one of the key factors in insulin resistance, and it is known to be associated with greater release of inflammatory mediators and free fatty acids from the visceral adipose tissue (VAT). In addition, hypertension is often accompanied by diabetes and significantly speeds up the development of cardiovascular disease. In this study, obesity, hypertension and insulin resistance co-existed, which is a common combination of cardiometabolic risk factors seen in patients with T2DM[11].

Many lipid metabolism abnormalities were also found in patients with diabetes. The levels of total cholesterol (TC), triglycerides (TG), LDL cholesterol and the atherogenic lipid ratios were significantly high while the level of HDL cholesterol was significantly low[12]. This diabetic dyslipidemia is well established and is a very important factor in the development of atherosclerosis. High triglycerides, high LDL cholesterol, and low HDL cholesterol are involved in the development of plaques, in the damage to the vessels and in the decrease in reverse cholesterol transport and vascular protection. The marked higher ratios of Total Cholesterol/HDL and LDL/HDL in the present study further highlights that the diabetic patients are at a higher cardiovascular risk[13].

A major advantage of this research is that it shows that insulin resistance is significantly correlated with inflammatory markers[14]. HOMA-IR was highly positively correlated with hs-CRP, IL-6 and TNF-α, suggesting that as insulin sensitivity decreases, so does systemic inflammation. The same positive correlations were found between HOMA-IR and obesity indices, blood pressure, and LDL cholesterol, as well as the inverse correlation between HDL cholesterol. These findings help to reinforce the idea that inflammation, insulin resistance, obesity, dyslipidaemia and cardiovascular dysfunction are not discrete abnormalities, but linked processes. These associations indicate that chronic inflammation might be a significant part of the mechanisms that underlie the association between metabolic dysfunction and cardiovascular disease in patients with T2DM[15].

The results of this study have clinical implications. Regular monitoring of inflammatory markers, insulin sensitivity scores and cardiovascular risk indices could help to detect diabetic patients susceptible to poor cardiovascular events early. Thus, the comprehensive management strategies based on glycemic control, weight reduction, blood pressure management, lipid optimization, and inflammation reduction can offer significant benefits in preventing long-term diabetic complications and improving patient outcomes[16, 17].

The study has some limitations. The cross-sectional design prevents conclusions about relationships and causality between inflammation, insulin resistance and cardiovascular risk[18]. Further, the study was performed in two institutes and might not be wholly representative of the entire diabetic population in Pakistan. Larger sample size and multicenter studies in the longitudinal direction are warranted to explore these associations in more depth and to assess their prognosis[19, 20].

CONCLUSION

Type 2 Diabetes Mellitus patients have significantly higher systemic inflammation, insulin resistance, obesity, hypertension and dyslipidemia than healthy people. The rise in

levels of hs-CRP, IL-6 and TNF-α, in combination with the increase in HOMA-IR values, support a strong association between chronic inflammation and decreased insulin sensitivity. In addition, the unfavourable lipid profile and high cardiovascular risk indices indicate the significant cardiovascular burden in T2DM. The strong associations found between inflammatory markers, insulin resistance, and cardiovascular risk factors indicate that inflammation, insulin sensitivity, and cardiovascular risk factors work together to help create disease. Therefore, a thorough biochemical and physiological evaluation could be a useful tool for early risk stratification and individualized care of diabetic patients to decrease cardiovascular complications and enhance long-term clinical consequences.

Authors' Contributions

Sm: Conceptualization, data collection, biochemical analysis, manuscript writing.
Bs: Study supervision, physiological assessment, data interpretation.
Fam: Study design, methodology development, critical manuscript review.
As: Data acquisition, statistical analysis, literature review.
Sg: Laboratory investigations, quality control, manuscript editing.
Th: Project administration, final review, correspondence, and approval of the manuscript.

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Conflict of Interest

The authors declare no conflict of interest.

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