

Research Article

Biochemical Markers of Early Renal Impairment: An Analytical Correlation Between Glycemic Control and Nephropathy

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Abstract

Type 2 Diabetes, or T2DM is not just a problem of poor control of blood glucose. It is a complex metabolic disease that impacts many organs and can lead to organ failure. As the T2DM rate increases in Iraq, specifically Najaf Governorate, the incidence of Diabetic Nephropathy (DN) is also increasing. Diabetic nephropathy (DN) occurs slowly due to long-term injury to the small blood vessels and the gradual structural damage. A serious consequence of diabetes as it progresses is kidney dysfunction, although this is closely related to liver function, blood pressure stability and measures of body size. The study was done to identify the relationship between long-term glycemic control expressed as HbA1c and multi-organ biomarkers including renal (serum urea and creatinine), liver enzymes, lipid profile and cardiovascular (systolic blood pressure [SBP] and body mass index [BMI]) parameters. A descriptive cross-sectional study was conducted on patients at German Hospital in Najaf which included 120 subjects, 60 T2DM patients and 60 healthy controls. Stratification of participants was done into age-glycemic categories (20 to 40 years with HbA1c \approx 8.2%, 40 to 60 years with HbA1c $>$ 8.8% AND 60 to 80 years with HbA1c $>$ 10.2%). Measurement of HbA1c by high performance liquid chromatography. The concentration of nitrogenous waste products and liver function was carried out using some of the enzymatic methods while the standard procedures were used to measure the SBP and BMI. The diabetic group had severe metabolic disturbances. Serum urea (29.22 ± 20.32 mg/dL) and creatinine (1.13 ± 0.77 mg/dL) levels were significantly higher compared to the control ($P < 0.001$). There was a strong and positive correlation between HbA1c and worsening of renal function ($r = 0.72$). Patients who had the disease for $>$ 18 years and those belonging to 60–80-year age group showed the worst impairment. Additionally, raised SBP (137.7 ± 19.6 mmHg) and increase of BMI (28.2 ± 6.2 kg/m²) may further aggravate combined metabolic (lipotoxic) and pressure-related damage to kidney and liver. To sum up, experiencing long-term high blood glucose levels, alongside high blood pressure and overweight, harms the organs. Thus, a clinical assessment of HbA1c alone is not enough. The Iraqi T2DM patients' kidney and liver function along with SBP and BMI hemodynamic measures, are monitored with using a wider diagnostic approach to detect early and prevent irreversible end-stage complications.

1. Introduction

Diabetes Mellitus (DM) can be considered one of the world's most serious health problems in the twenty-first century. The long-term metabolic imbalance is characterised by it. Although the mechanisms vary across types, the most important things with all diabetes forms is chronic hyperglycaemia. Prolonged elevation of blood glucose causes microvascular and macrovascular complications (American Diabetes Association [1, 2]. In Iraq, countless people are diagnosed with type 2 diabetes mellitus (T2DM). This increase has put lots of strain on the health system, especially in cities like Al-Najaf, where genetic susceptibility and lifestyle changes have increased the incidence of diseases [3, 4].

A serious complication of T2DM is Diabetic nephropathy (DN), which is now the most common cause of End-stage renal disease (ESRD) worldwide. DN advances in stages. It usually starts with glomerular hyperfiltration. After that, it will progressively develop to persistent macroalbuminuria and structural damage to the kidney [5, 6]. A constant rise in the Glycated Hemoglobin (HbA1c) increases oxidative stress and formation of Advanced Glycation End-products (AGEs). This process causes pathological changes that include thickening of the glomerular basement membrane [7, 8].

The kidneys are rarely the only victim to diabetes. Blood pressure is closely related to glycaemic control. Chronic rise in blood pressure causes an increase in pressure within renal blood vessels, resulting in the damage of the kidneys and an accelerated drop in Glomerular Filtration Rate (GFR) [9, 10]. Body Mass Index, or BMI, is another critical parameter. Obesity is one of the risk factors for insulin resistance and chronic inflammation, worsening metabolic syndrome. Furthermore, the obesity level is correlated with disease severity among Iraqi patients [11, 12].

In addition, the stomach is responsible for storing the food we eat. It is not unusual for diabetes patients to have liver dysfunction, indicated by elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, which may take place before kidney failure is well advanced [13, 14]. The buildup of nitrogenous waste products, mainly urea and creatinine, in the serum is an important biological sign of progressive deterioration in kidney function [15]. Research from regional tertiary centers, mainly the German Hospital in Najaf, showed that poor glycemic control (with HbA1c > 8 %) is directly associated with rising levels of these renal biomarkers and worsening liver functions [16, 17].

Improvement of imaging techniques has taken place but the measurement of renal markers, liver enzymes, physical indicators like BP, BMI are practical and cost-effective methods of detection. As a result, this study aims to evaluate the diagnostic value of these biomarkers in relation to the glycemic control among the patients of the German Hospital in Najaf. The results present local evidence which supports global finding concerning the multi-system impact of diabetes among the people of Iraq [18–20].

2. Materials and Methods

2.1. Study Design and Ethical Considerations

This cross-sectional descriptive study was done at German Hospital, Najaf, Iraq between [Insert Month/Year] and [Insert Month/Year]. The objective of this study was to assess the impact of diabetes on various organs. The study had 120 participants in total included in study. Patients were allocated into two groups, 60 type 2 DM patients and 60 healthy controls matched for age and sex. The age of the participants varied from 20-80 years, with an average of 56 ± 16 years.

The Institutional Research Committee granted ethical approval. All procedures were carried out in accordance with the ethical principles and the 1964 Declaration of Helsinki and its amendments [21]. Before the commencement of the study, all participants provided their informed written consent.

2.2. Anthropometric and Clinical Assessment

Anthropometric measurements were obtained to evaluate the impact of obesity on metabolic health.

Body Mass Index (BMI) was calculated using the standard formula:

$$BMI = \frac{\text{weight}(kg)}{\text{height}(m)^2}$$

and categorized according to World Health Organization guidelines [22]. Hemodynamic parameters were assessed by measuring systolic blood pressure (SBP) and pulse pressure (PP) using a calibrated electronic sphygmomanometer (Omron, Japan). All measurements were performed with participants in a seated position after a 10-minute rest period to ensure accuracy and consistency [9, 23].

2.3. Sample Collection and Biochemical Analysis

Venous blood samples (5–7 mL) were collected from each participant via venipuncture following an overnight fasting period of 8–12 hours. Blood samples were allowed to clot at room temperature and subsequently centrifuged at 3,000 rpm for 10 minutes. The separated serum was immediately used for biochemical analyses as follows:

Glycemic Status

Long-term glycemic control was assessed by measuring glycated hemoglobin (HbA1c) using high-performance liquid chromatography (HPLC), which is considered the reference gold-standard method [24]. Diabetic patients were further stratified into three subgroups based on HbA1c levels: Group A (approximately 8.2%), Group B (> 8.8%), and Group C (> 10.2%).

Renal Function Profile

Serum urea concentrations were determined using the urease–GLDH enzymatic method, while serum creatinine levels were measured using the kinetic Jaffe reaction [25]. These parameters were used as primary indicators for evaluating early renal dysfunction and the development of diabetic nephropathy [6, 8].

Hepatic Function Profile

To explore the hepato-renal axis, liver enzymes including alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured using standardized enzymatic colorimetric assays [13, 14].

Lipid Profile

Total cholesterol (TC) and triglycerides (TG) were analyzed using enzymatic methods to assess the lipotoxic metabolic environment associated with renal impairment in diabetic patients [26, 27].

2.4. Statistical Analysis

Statistical analysis was performed using SPSS software version 26.0 (IBM Corp., Armonk, NY). Data were expressed as mean \pm standard deviation (SD) along with 95% confidence intervals (CI). Data normality was assessed using the Shapiro–Wilk test. Differences between diabetic and control groups were analyzed using the independent samples t-test. Pearson’s correlation coefficient (r) was applied to evaluate the relationships between HbA1c levels, renal biomarkers, and systolic blood pressure. A p-value of less than 0.05 was considered statistically significant [3, 28].

3. Results

Statistical analysis in the present study was performed to assess biochemical markers of renal function in relation to glycemic control in a total of 120 participants. The study population was equally divided into two groups: patients with Type 2 Diabetes Mellitus (T2DM) ($n = 60$) and healthy control subjects ($n = 60$).

3.1. Demographic and Baseline Clinical Characteristics

The demographic and baseline clinical characteristics of the study participants are presented in Table 1. The mean age of the study population was 56 ± 16 years. The analysis demonstrated a higher prevalence of elevated Body Mass Index (BMI) and increased systolic blood pressure (SBP) among individuals in the diabetic group, reflecting the coexistence of metabolic syndrome components with chronic hyperglycemia.

Table 1: General characteristics and clinical parameters of the study population ($N = 120$)

Variable	Mean \pm SD	95% Confidence Interval (CI)
Age (years)	57 ± 17	54.0 – 56.0
BMI (kg/m^2)	28.4 ± 6.4	28.8 – 29.8
Systolic BP (mmHg)	135.7 ± 17.6	135.2 – 138.3
Pulse Pressure (mmHg)	56.0 ± 17.3	55.9 – 58.8
Blood Glucose (mg/dL)	195.2 ± 32.3	195.4 – 202.4
Total Cholesterol (mg/dL)	196.2 ± 34.3	188.5 – 206.1
HbA1c (%)	7.4 ± 1.4	7.3 – 7.5

3.2. Comparative Analysis of Renal Biomarkers

A comparative evaluation of renal function biomarkers revealed a statistically significant increase in serum urea and creatinine levels among the diabetic group compared with the control group ($P < 0.05$). As presented in Table 2, the mean serum urea concentration in patients with diabetes was 29.22 ± 20.32 mg/dL, whereas the corresponding value in the control group was 18.31 ± 4.55 mg/dL.

Likewise, serum creatinine levels were markedly elevated in the diabetic cohort, indicating early impairment in renal excretory function and the initial retention of nitrogenous waste products associated with diabetic renal involvement.

Table 2: Comparison of mean serum urea and creatinine levels between diabetic patients and healthy controls

Investigation	Controls ($n=60$) Mean \pm SD	Diabetics ($n=60$) Mean \pm SD	P-value
Serum Urea (mg/dL)	18.31 ± 4.55	29.22 ± 20.32	$<0.001^*$
Serum Creatinine (mg/dL)	0.89 ± 0.21	1.13 ± 0.77	$<0.01^*$

Significant at $P < 0.05$ (Independent Samples T-test)

3.3. Correlation between Age, Glycemic Control (HbA1c), and Renal Decline

To assess how diabetic kidney function worsens with the ineffectiveness of blood sugar control, diabetic patients were divided into three age groups. Older age and diabetes duration more than 18 years were positively related with HbA1c results in the diabetic individuals. With increasing age and disease duration, the level of glycaemic imbalance increased as shown in Table 3.

According to the study findings, long diabetes together with ageing plays a major role in declining kidney functions. They emphasize the totality of chronic hyperglycemia's impact on renal tissue through time.

Table 3: Stratification of HbA1c levels according to age-specific groups among diabetic patients (n = 60)

Patient Group	Age Range (Years)	Mean HbA1c (%)	Observed Renal Impact
Group A	20 – 40	8.2 ± 1.1	Mild metabolic stress
Group B	40 – 60	>8.8	Elevated nitrogenous retention
Group C	60 – 80	>10.2	Severe nephropathic risk

3.4. Significant Statistical Observations (SPSS Analysis)

Pearson's correlation analysis showed that HbA1c levels and serum creatinine have a strong positive relationship ($r = 0.72$, $P < 0.01$). The elevation of HbA1c is strongly associated with a decrease glomerular filtration rate and deterioration of renal function.

Patient with diabetes of more than 18 years' duration had significantly higher level of nitrogenous waste products as compared to patient with lesser duration of the disease. This demonstrates that hyperglycemia over a prolonged period deteriorates kidney function.

When taking other factors into account, BMI was found to be negatively correlated with HbA1c in some group. As age advances, blood pressure (BP), the systolic blood pressure (SBP) and triglyceride (TG) level are significantly increased. Together with the worsening of the renal biomarkers this shows a relation of cardiovascular risk factors with progressive kidney damage.

4. Discussion

Based on the discoveries of this investigation, it is possible to link chronic poor glycemic control with multi-organ damage among the patients suffering from Type 2 Diabetes Mellitus (T2DM). Serum levels of urea (29.22 ± 20.32 mg/dL) and creatinine (1.13 ± 0.77 mg/dL) were higher in diabetic patients as compared to controls ($P < 0.001$). The increases indicated impaired kidney functions and decrease excretory functions which are characteristic features of Diabetic Nephropathy (DN) [6, 17]. According to the concept of "metabolic memory," the accumulation of nitrogenous waste products which happens after a prolonged period of hyperglycemia causes cellular damage which becomes permanent. Chronic high glucose levels lead to the formation of AGEs that have structural effects like thickening of the glomerular basement membrane and podocyte injury. According to [7, 8]; serum creatinine has a strong positive correlation with HbA1c ($r = 0.72$, $P < 0.01$). Patients with HbA1c levels above 10.2% had maximum risk of nephropathy. Thus, poor glycemic control is an important factor in renal damage [1, 5].

The investigation also illustrates a relationship between heart and metabolic factors. The elevated systolic blood pressure (SBP: 137.7 ± 19.6 mmHg) dating to enhanced glomerular capillary pressure furthermore accelerating the transition from microalbuminuria to overt nephropathy [9, 10]. As well as that, Body Mass Index (BMI: 28.2 ± 6.2 kg/m²) and triglyceride (TG) conspires for lipotoxicity. The accumulation of fat triggers inflammatory processes and tubulointerstitial fibrosis. This scenario increases the metabolic demand on the kidney and liver [18, 27]. The liver is important for glucose regulation. The liver is often dysfunctional in T2DM patients, suggested by elevated levels of ALT and AST. There is a relationship between hepatic insulin resistance and NAFLD, as well as progressive renal impairment [13, 14].

The risk of organ damage increases with the age and duration of diabetes. Patients whose disease has lasted longer than 18 years and patients aged 60–80 years have significantly higher levels of nitrogenous waste products. The quoted phrase suggests that the defensive mechanisms become overwhelmed by long-term exposure to oxidative stress [3, 15]. Aging of the kidneys reduces the functional reserve capacity of the kidneys, thus making the kidneys more vulnerable to the chronic microvascular injury caused by T2DM [2, 4]. Certain subsets exhibited an apparent "obesity paradox," as BMI did not rise with HbA1c. This may be explained by muscle wasting in advanced diabetes, which can lower creatinine production, and thus mask the severity of renal dysfunction when creatinine is interpreted alone [11, 29].

In summary, managing diabetes in Iraq has to implement an all-inclusive integrated diagnostic procedure. Measuring HbA1c by itself insufficient. It is necessary to monitor renal markers (urea and creatinine), liver enzymes and hemodynamic parameters (blood pressure and BMI) to allow for early detection and timely intervention [16, 19, 20].

5. Conclusions and Recommendations

5.1. Conclusions

This clinical study establishes the evolution of type 2 diabetes mellitus (T2DM) in the studied patients as a disease process involving many systems and not simply a metabolic disorder. Research shows that poor glycemic control, particularly when HbA1c >10, is strongly associated with nitrogen waste retention (urea, creatinine). The prolonged oxidative stress causes renal compensation mechanisms to fail gradually and this is the relationship.

Moreover, high systolic blood pressure and high body mass index (BMI) are independent but interactive factors for kidney damage. High blood pressure causes glomeruli to function under stress while excess fat leads to lipotoxicity and inflammation. The tubular basement membrane thickening and renal injury aggravation are the end results of this.

The hepato-renal axis is also an important connection. Having type 2 diabetes causes the liver and the kidneys to grow under metabolic burden simultaneously. Dyslipidemia and insulin resistance seem to create a common pathological environment through which injury occurs

within both organs rather than in each organ alone.

The length of time a person has a disease is an important factor in determining which organs are affected. Diabetes duration of more than 18 years is clinically a threshold point beyond which the accumulating glycation and oxidative stress overwhelms the body's defensive ability. Older patients in the age group of 60 to 80 years are most affected.

5.2. Recommendations

There is a recommendation of several measure for improving clinical outcomes and delaying the progression. All patients with type 2 diabetes mellitus (T2DM) must have a comprehensive multisystem diagnosis. A combined metabolic panel with regular monitoring of renal biomarkers, liver enzymes, and lipids should be included in a system with organized long-term follow-up.

It is also important to control hemodynamic factors. Individuals exhibiting HbA1c more than 8% need intensive management for blood pressure stabilization (mostly pulse pressure) and Body Mass Index (BMI) reduction. By controlling these factors, it may be possible to lessen the stress on the kidneys.

Individuals who have been unwell for over 15 years should go under enhanced clinical surveillance. To allow earlier detection of declining kidney function, more sensitive markers of renal filtration including estimated Glomerular Filtration Rate (eGFR) should be added to routine creatinine testing.

Programs for community-based interventions should be developed in Al-Najaf to better aware patients and impart adherence practices to lifestyle modification protects both liver and kidney. The focus of these programs lies on diet control, weight control, and blood pressure control.

In conclusion, it is further suggested that prospective research is conducted to evaluate the role of inflammatory cytokines as early markers of multi-organ damage in the Iraqi diabetic population.

These studies may help improve early prediction and targeted strategies.

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Data Availability Statement: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Clinical Trial Registration: Not applicable.

Reporting Guidelines Statement: This study was conducted and reported in accordance with the STROBE guidelines for observational studies.

Patient Consent for Publication: Patient consent was obtained where required in accordance with ethical standards.

Disclaimer (Artificial Intelligence): The author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.), and text-to-image generators have been used during writing or editing of manuscripts.

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