

Relation between liver, kidney function, and lipid profile in glycaemic control among type 2 diabetic patients in Al Baha City

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Background: Every year the incidence of type 2 diabetes mellitus (T2DM) rises, bringing with it a greater health and financial burden. It is still challenging for diabetics to achieve glycaemic control, with only 9–15% reaching the ideal glucose level. Previous studies have discussed the influence of and correlation between glycated haemoglobin levels and kidney and liver profile functions. This study aimed to assess whether lipid irregularities and liver profile function are associated with high hemoglobin A1c (HbA1c) in T2DM and demonstrate the variation in vital organ parameters between diabetic and nondiabetic patients.

Methods: This retrospective observational study, comprising 129 diabetic patients and 130 non-diabetic patients, was conducted at King Fahd Hospital in Saudi Arabia. Data including kidney and liver parameters and glycated haemoglobin were obtained from the patients' records after ethical approval was received from the King Fahd Hospital Ethical Committee.

Results: Ferritin, blood urea, creatinine, alanine transaminase (ALT), and triacylglycerides (TGs) showed significantly greater levels in diabetic than nondiabetic patients, whereas uric acid ($P=0.01$), albumin ($P=0.002$), and alkaline phosphatase (ALP) ($P<0.001$) were significantly lower in the diabetic patient group. Glycated haemoglobin showed positive and negative correlations with cholesterol and uric acid, respectively. Overall, the results of this study highlight the significant association between glycated haemoglobin level and the parameters reflecting the function of vital organs, which will give insight into the role of glycated haemoglobin levels in diabetic and nondiabetic patients.

Conclusions: A significant increase in kidney profile parameters in diabetic patients, such as uric acid ($P=0.01$), urea ($P=0.001$), and creatinine ($P<0.001$), was seen, which could lead to diabetic kidney disease. In addition, HbA1c showed a positive correlation with uric acid ($P=0.007$) and cholesterol ($P=0.01$) in diabetic patients. The results of this work highlight the critical relation between poor glycaemic control and increasing the parameters of glycated haemoglobin in the function of vital organs, such as the kidney. These findings give insight into the need to regularly investigate the glycated haemoglobin level in prediabetics and diabetic patients in terms of lipid, liver, and kidney profile reading.

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Introduction

The rise in the prevalence of diabetes in the Kingdom of Saudi Arabia from 6% in 1996 to over 20% recently is primarily due to changes in lifestyle (1,2). These rates place Saudi Arabia in the top 10 highest countries in terms of diabetes prevalence (2). Globally, around 366 million individuals were diagnosed as diabetics in 2011, and this number is expected to reach 552 million by 2030 (3,4). Approximately 380 million individuals are estimated to suffer from type 2 diabetes mellitus (T2DM), with an additional 400 million having impaired glucose tolerance (IGT).

The utilisation of hemoglobin A1c (HbA1c) to analyse prediabetes and T2DM provides valuable insights into the progression of the disease. HbA1c levels above 48 mmol/mol (6.5%) are indicative of T2DM, while levels of 39–46 mmol/mol (5.7–6.4%) suggest prediabetes (1). The prediabetes category includes subjects with a fasting glucose level of 5.6–6.9 mmol/L and a 2-hour post-prandial

glucose level of 7.8–11.0 mmol/L after a 75-gram oral glucose tolerance test (OGTT). It is important to note that people with HbA1c-characterised prediabetes develop diabetes when an excess of multiple visits with typical HbA1c levels is recorded, indicating a clear progression (2). The pathophysiology of prediabetes, characterised as IGT and impaired fasting glycaemia (IFG), has been extensively studied and shows lipid and apolipoprotein changes (3).

An atypical lipid profile, often seen in patients with T2DM, is characterised by elevated levels of triglycerides (TGs) and lipoproteins rich in fatty substances, reduced high-density lipoprotein (HDL) cholesterol levels, and an increased proportion of low-density lipoprotein (LDL) (4). These lipid irregularities are not only a cause for concern, but also a significant risk factor for cardiovascular diseases, which are a well-documented and serious issue among diabetic populations (5).

Moreover, non-alcoholic fatty liver disease (NAFLD) is notably more prevalent in individuals with T2DM (6) and, to a lesser extent, in those with prediabetes (7), as indicated by plasma glucose measurements. NAFLD is worsened by obesity (6), dyslipidemia (8), and diabetes (9) and is regarded as the liver-related consequence of metabolic dysfunctions resulting from insulin resistance. Importantly, the overall death rate among NAFLD patients is remarkably higher than that of the general population (10). HbA1c has been the subject of extensive research, with numerous investigations focusing on stratifying patients based on their diabetes status and comparing renal outcomes between diabetic and nondiabetic groups (11). However, there is a lack of data on the impact of non- or prediabetes on renal outcomes assessed by estimated glomerular filtration rate (eGFR) (12,13). Given that diabetes can remain undiagnosed for years and that even glycaemia within the prediabetes range may contribute to the development of end-organ diseases, it is crucial to assess the reliability and adequacy of baseline measurements for predicting the long-term risk of new-onset chronic kidney diseases and the progression of existing ones (14). Therefore, this study aims to investigate whether lipid abnormalities and

Highlight box

Key findings

- Significant increase in the levels of creatinine and urea in diabetic patients compared with the control group.
- Significant increase in triglyceride level in diabetic patients compared with control group.
- Ferritin (a biomarker of inflammation) have a positive correlation with increasing liver enzymes.

What is known and what is new?

- Although it was previously known that elevated hemoglobin A1c (HbA1c) level is linked with high lipid profile as well as high liver and kidney functions tests. Our study is novel as it showed the association between elevated glycated haemoglobin and high liver, kidney and lipid profiles in a single study at Al Baha region, suggesting primarily management strategies to control risk factor of liver, kidney and heart diseases by improving patients knowledge regarding HbA1c.

What is the implication, and what should change now?

- Effective health education for diabetic patients by life style modification and intensive programme screening is recommended.

liver function profiles are associated with elevated HbA1c levels in individuals with T2DM. We present this article in accordance with the STROBE reporting checklist (available at <https://jlp.m.amegroups.org/article/view/10.21037/jlp.m-24-41/rc>).

Methods

Participants

Patients with T2DM were recruited in this study. Specifically, 259 participants [129 diabetic patients and 130 nondiabetic (control) patients] were collected retrospectively from the medical records of the last 3 years (from 1 January 2021 to 31 December 2023). A convenience sample method was used to include patients who matched the inclusion criteria and have history of T2DM of 8 years or more for last 3 years. All patients were above 18 years of age, did not have chronic diseases, especially liver and kidney diseases, and were defined in the medical records as having T2DM according to the criterion used in the hospital, namely, HbA1c $\geq 6.5\%$. HbA1c is recommended as a standard of care (SOC) for testing and monitoring diabetes, specifically, T2DM. Both group (129 diabetic patients and 130 nondiabetic control) were matched in criteria and number of cases per control.

Study design

The current observational retrospective study was conducted at King Fahd Hospital's clinical chemistry laboratory in Al Baha City, Saudi Arabia. The sociodemographic data were collected retrospectively from medical records of up to 3 years ago (from 1 January 2021 to 31 December 2023). Patients with history of T2DM of 8 years or more and nondiabetic patients were selected using a random sampling method.

Exclusion criteria

Patients taking medication for chronic liver and kidney diseases and smokers (based on their medical files) were excluded from this study, as were patients below the age of 18 years old.

Study parameters measured

The study analysed the lipid and liver profiles of diabetic

patients, focusing on crucial factors such as total cholesterol (TC), HDL, LDL, TGs, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), and albumin. In addition, kidney profile tests were analysed, such as ferritin, C-reactive protein (CRP) uric acid, sodium, potassium, chloride, blood urea, and creatinine. The study considered the HbA1c levels of the diabetic patients as the independent variable, while age and gender were treated as confounding variables. HbA1c $>6.5\%$ was used to diagnose diabetic patients.

Ethical approval

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ethical Research Committee on Publication Ethics at King Fahd Hospital at Al-Baha City (KFH/IRB04072024/5) and individual consent for this retrospective analysis was waived.

Statistical analysis

The data were analysed using the powerful SPSS version 28. Numbers and percentages were used to illustrate qualitative data and the median [range] to capture numerical variables. Correlations were determined by Spearman correlation, and the Chi-squared and Mann-Whitney tests were used to compare the qualitative and quantitative data, respectively. A result with a P value of 0.05 or less was considered significant.

Results

The study considered 129 diabetic and 130 nondiabetic (control) patients. The median age [range] were 58 [29–68] and 40 [37–80] years in the diabetic and nondiabetic patients, respectively. There was higher proportion of males ($n=68$; 52.7%) among the diabetic than among the nondiabetic patients ($n=51$; 39.2%), whereas females were more prevalent among the nondiabetics than the diabetics.

A statistically significant variation was found among the diabetic and nondiabetic patients in some kidney, liver, and lipid profile parameters, as shown in *Table 1*.

Tables 2,3 show Pearson's correlation of HbA1c with CRP and ferritin revealed a significant correlation with some of the laboratory data shown in *Table 2* for the diabetic patients and *Table 3* for the non-diabetic patients. CRP and ferritin (inflammation biomarkers) were selected

Table 1 Participants' laboratory results

Lab parameters	Diabetic (n=129)	Nondiabetic (n=130)	Normal range	P value
Kidney profile tests				
Ferritin (ng/mL)	63.4 [2.4–756.3]	32.9 [2.6–363.7]	Male: 30–400 Female: 13–150	<0.001
CRP (mg/L)	0.5 [0.1–34.8]	0.4 [0.1–23.3]	0–0.8	0.49
Uric acid (μmol/L)	288.7 [132.2–596]	365 [185–542.7]	155–357	0.01
Sodium (mmol/L)	139 [134–141]	138 [126–143]	135–150	0.75
Potassium (mmol/L)	4.1 [3–5]	4 [3–5]	3.5–5	0.80
Chloride (mmol/L)	104.8 [95–109]	105 [91–108]	96–106	0.96
Blood urea (mmol/L)	71.5 [34–831]	64 [19–129]	2.8–7.2	0.001
Creatinine (μmol/L)	5.1 [3–19.4]	4.3 [1.6–11.1]	53–88	<0.001
Liver profile				
Albumin (g/L)	40.7 [21.6–56]	42.7 [20–51.2]	35–52	0.002
ALT (U/L)	25.7 [7.1–103.1]	18.8 [5–130.1]	0–50	<0.001
AST (U/L)	19.6 [7.5–85.9]	19.5 [10.1–97]	0–50	0.88
ALP (mmol/L)	68.5 [27–149]	85 [48–306]	30–120	<0.001
Lipid profile				
Cholesterol (mmol/L)	4.6 [2.2–8.7]	4.9 [3.1–8.4]	<5.2	0.85
Triglyceride (mmol/L)	1.6 [0.6–5.6]	1.1 [0.6–2.9]	<1.7	0.001
HDL-C (mmol/L)	1.1 [0.5–1.8]	1.1 [0.5–1.8]	>1.55	0.21
LDL-C (mmol/L)	3 [1–7]	3.1 [1.4–5.8]	<2.59	0.94

Data are presented as median [range]. CRP, C-reactive protein; ALT, alanine transaminase; AST, aspartate transaminase; ALP, alkaline phosphatase; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol.

specifically to present the correlation with HbA1c, as the strong correlation between increasing HbA1c levels and CRP reflects increased systemic inflammation, according to previous research (15). More importantly, CRP is an additional marker for better glycaemic control and also correlates with dyslipidaemia, and it is a good indication for further complications in and consequences for the liver, kidney, and lipid profiles.

Discussion

The present study investigated whether lipid abnormalities and liver function profile are associated with HbA1c levels in individuals with T2DM. The main finding in the present study was a significant increase in the levels of creatinine, urea, and TG in the diabetic patients compared with those

in the control group. Ferritin (a biomarker of inflammation) showed a positive correlation with increasing liver enzyme. This study found a positive correlation between HbA1c and high cholesterol level.

In a comparison made between diabetic and non-diabetic groups, diabetic patients demonstrated higher serum ferritin levels (P<0.001). This result agrees with a previous study that found serum ferritin and body iron store levels were significantly higher in diabetic patients than in the control group (16). This might be related to the up-regulation mechanisms of transferrin, glucose, and insulin-like growth factor 2 receptors on the cell membrane. Thus, insulin in diabetic patients may mediate glucose transportation, increase the expression of transferrin receptors on the cell membrane, and increase extracellular iron uptake. This may increase the risk of insulin resistance to T2DM due to iron overload (17).

Table 2 Correlation between HbA1c, CRP, and ferritin with laboratory data for diabetic patients

Lab parameters	HbA1c (mmol/mol)		CRP (mg/L)		Ferritin (ng/mL)	
	r	P value	r	P value	r	P value
Ferritin (ng/mL)	0.098	0.27	0.048	0.58	–	–
CRP (mg/L)	0.095	0.28	–	–	–	–
Uric acid (μmol/L)	–0.250	0.007	0.016	0.86	0.261	0.005
Sodium (mmol/L)	–0.663	0.03	–0.528	0.11	–0.804	0.005
Potassium (mmol/L)	–0.491	0.15	–0.200	0.58	–0.770	0.009
Chloride (mmol/L)	–0.399	0.25	–0.448	0.19	–0.448	0.14
Blood urea (mmol/L)	–0.098	0.28	–0.009	0.91	0.266	0.003
Creatinine (μmol/L)	–0.112	0.22	0.043	0.63	0.294	0.001
Albumin (g/L)	–0.106	0.25	–0.388	<0.001	0.144	0.12
ALT (U/L)	0.0075	0.41	–0.305	0.001	0.270	0.003
AST (U/L)	0.108	0.23	–0.275	0.002	0.165	0.07
ALP (mmol/L)	0.097	0.35	0.233	0.02	0.098	0.34
Cholesterol (mmol/L)	0.228	0.01	0.043	0.64	0.171	0.06
Triglyceride (mmol/L)	0.154	0.11	0.036	0.69	0.264	0.004
HDL-C (mmol/L)	0.029	0.76	–0.055	0.55	–0.100	0.28
LDL-C (mmol/L)	0.175	0.06	0.040	0.67	0.161	0.08

HbA1c, hemoglobin A1c; CRP, C-reactive protein; ALT, alanine transaminase; AST, aspartate transaminase; ALP, alkaline phosphatase; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol.

The present study showed a highly significant increase in creatinine ($P<0.001$) and urea levels ($P=0.001$). Subsequently, uncontrolled blood glucose level mostly led to an increase in serum urea and creatinine, thus increasing the risk of diabetic nephropathy. This result is supported by a previous study that revealed that hyperglycaemia is fundamental in increasing the incidence of renal diseases (18,19).

In the present study, urea ($P=0.001$) and creatinine ($P<0.001$) were significantly high in the diabetic patient group. Our results are supported by a previous study that found the levels of serum urea and creatinine were more significant in people with diabetes than in a nondiabetic control group; the mean urea levels were 18.31 ± 4.55 and 29.22 ± 20.32 mmol/L in the control and diabetic patients, respectively. Creatinine levels in the diabetic group were 1.13 ± 0.77 μmol/L, and in the control group, they were 0.89 ± 0.21 μmol/L (17).

The liver plays a significant role in carbohydrate metabolism. Patients with T2DM lose the direct effect of insulin on the liver. Thus, it is crucial to monitor and

measure the liver profile parameters of diabetic patients. Patients with T2DM showed a significant increase in albumin, ALT, and ALP levels compared to the control group ($P=0.002$, $P<0.001$) respectively. Siddiqua *et al.* [2023] supported our results by reporting a significant increase in liver function tests (39.20%) in diabetic patients. They found a significant association between blood glucose and HbA1c with liver function tests (20). Wang *et al.* [2016] reported that liver function tests can be a good predictor for T2DM (21).

Moreover, TGs in the current study revealed a significant increase in the diabetic group compared with the control group. This phenomenon might be due to insulin resistance, which causes the accumulation of lipids, toxicity to liver cells, and diminished hepatic synthetic capacity (22). This was confirmed by a previous study, which found that 40–70% of diabetic patients were affected by fat accumulation in the liver in the form of TG due to enhanced fat transport to the liver, increased hepatic fat synthesis, and diminished oxidation of hepatic fat, causing

Table 3 Correlation between HbA1c, CRP, and ferritin with laboratory data for non-diabetic patients

Lab parameters	HbA1c (mmol/mol)		CRP (mg/L)		Ferritin (ng/mL)	
	r	P value	r	P value	r	P value
Ferritin (ng/mL)	0.344	0.046	−0.062	0.48	–	–
CRP (mg/L)	0.082	0.60	–	–	−0.062	0.48
Uric acid (μmol/L)	0.378	0.14	−0.213	0.30	0.208	0.31
Sodium (mmol/L)	0.295	0.38	−0.058	0.62	0.108	0.36
Potassium (mmol/L)	0.292	0.33	0.003	0.98	0.044	0.71
Chloride (mmol/L)	0.457	0.11	0.011	0.92	0.064	0.59
Albumin (g/L)	−0.075	0.69	−0.467	0.10	0.288	0.006
ALT (U/L)	−0.016	0.93	−0.135	0.17	0.421	0.20
AST (U/L)	0.048	0.79	−0.109	0.29	0.163	0.14
ALP (mmol/L)	−0.316	0.13	0.219	0.052	−0.063	0.57
Cholesterol (mmol/L)	0.234	0.30	0.290	0.09	0.116	0.51
Triglyceride (mmol/L)	0.403	0.07	0.020	0.91	0.178	0.32
HDL-C (mmol/L)	0.074	0.75	−0.200	0.56	−0.052	0.76
LDL-C (mmol/L)	0.247	0.28	0.372	0.03	0.131	0.47
Blood urea (mmol/L)	0.023	0.89	−0.111	0.23	0.476	0.30
Creatinine (μmol/L)	0.190	0.27	−0.115	0.02	0.507	0.30

HbA1c, hemoglobin A1c; CRP, C-reactive protein; ALT, alanine transaminase; AST, aspartate transaminase; ALP, alkaline phosphatase; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol.

hepatic steatosis and impairment of liver function, which ultimately leads to liver cirrhosis (22,23).

In the present study, ferritin showed a positive correlation with uric acid, ALT, TG, urea, and creatinine. Cugy *et al.* also noted a significant relationship between increases in serum ferritin levels and elevated liver enzymes and hepatic inflammatory markers ALT, AST, and gamma-glutamyl transferase (GGT) (23). Our results align with this study, as we reported higher cholesterol, HDL-C, ALT, and TG values in diabetic patients than nondiabetics (24). In the current study, CRP showed a negative correlation with albumin ($P<0.001$) and ALT ($P=0.001$). Prospective study has indicated an association between baseline serum albumin concentration and the risk of T2DM (25), while other studies found no association between them (24,26). Low serum albumin concentration has been suggested as a potential marker of underlying subclinical diseases, such as malnourishment, anaemia, and hepatic or kidney disease (27), which could lead to false negative correlations

with T2DM and other chronic illnesses (28).

The current research was designed to investigate the relation between HbA1c and different parameters, such as lipid profile. Our results indicated a significant positive correlation between HbA1c and cholesterol parameters in diabetic patients. This is consistent with the study of Sharahili *et al.*, who found that HbA1c was significantly associated with high cholesterol and TG levels in T2DM (29). However, in the same study, no significant correlation was detected between HbA1c and other lipid profile parameters such as LDL, HDL, and TG or even liver and kidney profiles. This finding broadly supports other findings that noted no correlation between HbA1c and LDL and HDL (30). Few other researchers have reported a positive relationship between HbA1c and HDL and the liver profile (30,31).

The differences found between our study and other research concerning the relation between HbA1c and lipid profile parameters could be attributed to variances in the type of parameter, age, lifestyle, and nature of the population.

Conclusions

In conclusion, this study aimed to investigate the relationship between HbA1c and lipid profile, kidney profile, and liver profile. The main strength of this study is that it found kidney profile parameters to be significantly elevated in poor glycaemic control patients, such as uric acid ($P=0.01$), urea ($P=0.001$), and creatinine ($P<0.001$). According to the finding, patients with poor glycaemic control are more likely to have kidney disease, which is a common complication in diabetic patients that leads to high mortality and morbidity. Strikingly, HbA1c showed a positive correlation with uric acid ($P=0.007$) and cholesterol ($P=0.01$) in the diabetic patients. Unfortunately, this result indicates that diabetic patients are at high risk of dyslipidaemia, which may be a major factor in the development of cardiovascular disease. To reduce these complications, regular monitoring of blood glucose levels and kidney profile, liver profile, and lipid profiles and optimal therapy should be included early on in these patients' treatment plans.

Overall, this finding underlines the need for early screening of renal function, liver function, and lipid profiles in diabetic patients and the importance of early glucose management to delay the development of complications from diabetes.

The strength of this study is that it reports a complete picture of lipid, liver, and kidney profiles in diabetic and nondiabetic patients. Furthermore, this study provides the first comprehensive assessment of these three parameters (kidney, liver, and lipid profiles) in Al Baha City. This new understanding should help to improve the care of diabetic patients in hospitals in the Al Baha area. In addition, the statistical power in this report was appropriate to determine a significant association between HbA1c and other parameters. However, the main limitation is the sample size, as it is not possible to extrapolate the results to the entire population of the region. Future investigations could usefully screen different health centers in the same region.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://jlpn.amegroups.org/article/view/10.21037/jlpn-24-41/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ethical Research Committee on Publication Ethics at King Fahd Hospital at Al-Baha City (KFH/IRB04072024/5) and individual consent for this retrospective analysis was waived.

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