

Original article

# The Effect of elevated HbA1 Levels on Kidney and Liver Function

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## ABSTRACT

**Background and aims.** Diabetes is a chronic illness. The comorbidities that can be linked to elevated blood sugar levels must be understood. The purpose of this study was to evaluate the impact of elevated hemoglobin subunit alpha 1 (HbA1) on renal and hepatic functioning in individuals with diabetes in Al-Jabal Al-Akhdar, Libya. **Methods.** From January to December 2022, blood samples from 18 patients with high HbA1 level and 37 with normal values were analyzed in the laboratories located in Al Bayda city, Libya. **Results.** According to the findings, patients with high HbA1 levels had higher results on tests measuring liver function, but these increases were not statistically significant when compared to participants with normal HbA1 levels. Additionally, there were notable variations between the first and second groups' glutamic Oxaloacetic transaminase enzyme levels. **Conclusion.** HbA1 should only be assessed in conjunction with fasting plasma, post-meal glucose, liver and kidney function tests for accurate monitoring of diabetes patients' long-term glycemic management.

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## INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterised by abnormally high blood glucose levels. Diabetes is linked to a number of illnesses, including liver dysfunction and an increased risk of hepatocellular carcinoma. [1]. Adults' liver enzyme functions are substantially correlated with commonly reported diabetic indicators like HbA1. It is likely that diabetes could be a predictor of liver health in adults [2]. The relationship between a significant type 2 diabetes consequence and liver damage has been acknowledged for decades [3,4]. Both the World Health Organization (WHO) and the American Diabetes Association (ADA) consider HbA1c to be the most accurate chemical test for controlling blood sugar in type 2 diabetes (T2DM) [5]. Alkaline phosphatase (ALP) levels are another marker of hepatocyte integrity, in addition to aminotransferases [6].

Compared to other causes of renal failure, roughly 40% of diabetic patients eventually acquire kidney disease [7]. Diabetes affects the efficiency of the kidneys in removing toxins and excreting excess fluids from the body, thus their accumulation in the blood [8]. Many tests are considered guides to indicate kidney function and detect morbidity in diabetic patients, including measuring the concentration of urea, creatinine, uric acid, total protein, albumin, sugar, and HbA1 [9].

Tests for protein are indicators of kidney and liver disease; compared to other tests, the creatinine test is more accurate. Its concentration is influenced by age and weight, which alter the glomerular filtration rate and raise its concentration in situations of renal failure and urine retention [10]. Thus, the purpose of this study was to evaluate how high HbA1 affects kidney and liver function in diabetes patients.

## METHODS

### *Experimental design and Procedure*

We examined the association between liver, kidney function tests, and HbA1 levels in a group of 55 individuals, consisting of 18 individuals with diabetes and 37 individuals without the disease who served as controls. All individuals between the ages of 16 and 86 who attended medical laboratories in the Libyan city of Al-Bayda between January and December 2022.

### *Sample collection*

Whole blood samples were collected from each participant using the standard methods.

### *Glycosylated hemoglobin HbA1 and Blood glucose*

Blood glucose was estimated by using glucose MR kit (LNEAR CHEMICALS, Montgat, Barcelona, Spain). Glycosylated hemoglobin HbA1 was estimated by chromatographic spectrometric Ionexchange method.

### *Liver function testing*

Blood was taken from non-diabetic individual without who had no accumulated HbA1 and those who had elevated HbA1 level. Samples were allowed to clot in a plain tube at room temperature for 20 minutes. The serum was separated using centrifugation for ten minutes at 3000 rpm. The plasma levels of alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (direct and indirect bilirubin) were measured using an automated analyzer kit approach. Using spectrophotometers (Humalyzer Junior), commercially available test kits (Analytic on Biotechnologies, Germany) were used, following the manufacturer's instructions.

### *Kidney function testing*

All participants without accumulated HbA1 and those who had elevated HbA1 level blood were donated blood for kidney function test to measure serum creatinine levels. The Jaffe reaction, which forms a colour complex when creatinine is deproteinized in an alkaline picrate solution [11], was used to determine creatinine levels. Serum urea was measured enzymatically using kits from Biomarhreb, Germany, and a spectrophotometer from Humalyzer Junior for both tests [12].

### *Statistical analysis*

All data are expressed as mean  $\pm$  standard deviation (M $\pm$ SD). An unpaired t-test was applied to test the significance of variance ( $p < 0.05$ ) of the parameters under study between patients with high HbA1 levels and controls.

## RESULTS

According to the findings, individuals without cumulative diabetes had a normal HbA1 level ( $5.44 \pm 0.966$ ), while those with high cumulative diabetes had a high HbA1 level ( $9.10 \pm 2.49$ ). Comparing the results of kidney function analyses (Creatinine and blood urea) between individuals without diabetes and high-risk diabetic patients, it was found that those with normal HbA1 levels had higher levels of both creatinine ( $2.35 \pm 6.62$ ) and blood urea ( $26 \pm 15.8$ ). This increase was not statistically significant between the two groups Table 1.

Patients with diabetes who had high HbA1 level showed higher liver function outcomes, including total serum bilirubin, direct and indirect bilirubin, alkaline ALP, and glutamic pyruvic transaminase levels, in comparison to those who had normal HbA1 levels. Table 2 displays that all levels were not significantly different from the second group with high HbA1 values, with the exception of the glutamic oxaloacetic transaminase value, which was significantly different from the second group.

**Table 1. Comparison of Kidneys function among the two groups**

Test	Normal HbA1	High HbA1 patients	P-Value
HBA1C	5.44 $\pm$ 0.966	9.10 $\pm$ 2.49	<b>0.000</b>
Creatinine	2.35 $\pm$ 6.62	5.2 $\pm$ 10.2	<b>0.293</b>
Blood urea	26 $\pm$ 15.8	25.2 $\pm$ 13.2	<b>0.831</b>

**Table 2. Comparison of liver function among the two groups**

Test	Normal HbA1	High HbA1 patients	P-Value
HbA1c	5.44±0.966	9.10± 2.49	<b>0.000</b>
Total Serum Bilirubin	0.576±0.426	0.647± 0.434	<b>0.568</b>
Direct Bilirubin	0.214 ±0.313	0.228±0.208	<b>0.842</b>
Indirect Bilirubin	0.354±0.243	0.428±0.280	<b>0.348</b>
Alkaline ALP	123.5±65.3	163±132	<b>0.249</b>
Glutamic oxaloacetic transaminase GOT	17.11 ±6.60	29.3±19.4	<b>0.018</b>
Glutamic pyruvic transaminase GPT	17.6±11.3	21.11±7.99	<b>0.190</b>

## DISCUSSION

In the current study, we examined the relationship between participants with and without high cumulative diabetes and their liver, kidney function, and high HbA1 level. The useful information provided by a single HbA1c test has established it as a reliable biomarker for diabetes diagnosis [13].

Diabetes mellitus is a chronic disease that affects a large number of Libyans people and reflects the ineffectiveness of the body in using glucose properly [14]. Accumulated high blood sugar increases the risk of fatty liver disease and thus increases the risk of cirrhosis; The disease may progress to kidney disease and failure, because over the years, the cumulative rise in HbA1 level leads to sluggishness and damage to the kidney's microfiltration system. HbA1c is short for glycated haemoglobin. The test is also sometimes called haemoglobin A1c. HbA1c refers to glucose and haemoglobin joined together (the haemoglobin is 'glycated'). The amount of HbA1c formed is directly related to the amount of glucose in your blood. However, The ability to reflect the cumulative glycemic history of the previous two to three months makes HbA1c an essential biomarker of long-term glycemic control Therefore, patients with elevated levels of HbA1c need to have their liver and kidney function checked periodically every three to six month [2,15].

This study found a strong correlation between HbA1 and liver enzymes, which is consistent with earlier research that found an increase in the incidence of hepatocellular carcinoma. This increase is probably caused by the rising prevalence of metabolic syndrome, obesity, and type 2 diabetes mellitus (T2DM). Also, it is consistent with a number of other studies that found a substantial relationship between high HbA1 level and ALP, GOT, GPT, and total bilirubin [2,16]. The advancement of liver fibrosis has been linked to various putative biological causes, including elevated glucose [18] [19].

The results in table (1) showed a relationship between height HbA1 and renal function. Higher blood glucose levels are associated with an increase in glycated haemoglobin, which causes nephropathy, neuropathy, retinopathy, and cardiovascular disease because both urea and creatinine are trustworthy markers that help determine kidney function during diabetic nephropathy [16]. Our findings have been confirmed by other research, which proposed that inadequate insulin secretion-induced elevation in blood sugar levels is the cause of the rise in urea and creatinine levels [16, 17].

## CONCLUSION

HbA1c tests considered a trustworthy biomarker for the diagnosis and prognosis of diabetes. We recommend future studies and expansion of the sample size in the analysis be performed in patients with elevated HbA1 that long-term affects renal and hepatic function.

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