Short Communication

Assessment of G6PD Level among Type 2 Diabetes Mellitus Patients and Its Relationship to Demographic and Clinical Data

Widad Waleed Ali [1], Najlaa Al-Awadi [2, *]

[1] Iraqi Board Pathology, Hematology, National Center of Teaching Laboratories, Medical City Hospital, Iraq.

[2] Department of Pathology and Forensic Medicine, College of Medicine, University of Babylon, 51002 Babylon, Iraq.

[*] Corresponding author: med.najlaa.alawady@uobabylon.edu.iq

Submission: April 30, 2025 Accepted: June 20, 2025 Published: June 30, 2025

Abstract

Background: Glucose-6-phosphate dehydrogenase is the rate-limiting enzyme of the pentose phosphate pathway. Because it produces the coenzyme nicotinamide adenine dinucleotide phosphate, the major cellular reductant and fuel for glutathione recycling within the cells, it is necessary for antioxidant defense. Diabetes mellitus is a metabolic disorder marked by hyperglycemia caused by insulin metabolism problems. Type 2 diabetes mellitus, which was previously referred to as non-insulin dependent diabetes mellitus (NIDDM) or "adult-onset diabetes" is claimed to be caused by insulin resistance, a disease in which cells fail to adequately utilize insulin, which can be paired with an absolute insulin deficit or diminished insulin output. It was discovered that diabetes mellitus and high glucose levels reduce G6PD activity. **Objectives:** The aim of the study is to assess the G6PD level among type 2 DM patients and correlate the G6PD level with demographic and clinical data. **Materials and Methods:** This cross-sectional study included 100 patients with type 2 DM who are receiving therapy at the Diabetic Center of Marjan Teaching Hospital in Babylon. The current study included patients with established diagnosis of type 2 DM and HbA1c ≥ 7%. Demographic and clinical data include (age, sex, body mass index, physical activity, alcoholic intake, smoking, duration and type of treatment for DM, medical history include Family history of G6PD, hematological disease (sickle cell trait\disease, thalassemia), adrenal disorder, autoimmune disease (lupus, rheumatoid arthritis), hypertension, coronary artery disease, thyroid disease , splenectomy and chronic use of other drugs).Investigations (G6PD level, FPG,2-h PG, HbA1c and lipid profile) will be collected at the time of the sampling. **Results:** There was no significant difference (P value < ٠,٣٠٦) in G6PD level according to age of type 2 DM patients. There was no significant difference (P value < 0.721) in G6PD level according to sex of type 2 DM patients. There was significant negative correlation between G6PD level and study markers of glycemic control among type 2 DM patients. There was no significance correlation between G6PD level and lipid profile among type 2 DM patients. There was no significant difference of G6PD level according to history of hypertension among type 2 DM patients. **Conclusions:** Poor glycemic control was associated with lower G6PD activity which may be associated with several health problems.

Keyword: G6PD, Type 2 Diabetes Mellitus, Glycemic Control, Antioxidant, Lipid Profile.

Introduction

Glucose-6-phosphate dehydrogenase (G6PD) is involved in the production of nicotinamide adenine dinucleotide phosphate (NADPH), which protects the cell from oxidant injury triggered by certain drugs or infections by ensuring a reduced state of glutathione (GSH). G6PD is the most common enzyme in the Hexose monophosphate (HMP) pathway that causes hemolytic anemia [1]. Its deficiency mostly affects red blood cell (RBC). RBC does not have alternative pathways for NADPH production. In NADPH deficiency, hemolysis occurs by precipitation of hemoglobin (Heinz body) in RBC by oxidative stress and damaging the RBC membrane [1]. G6PD deficiency leads

to episodic or chronic non-spherocytic hemolytic anemia (CNSHA). It affects more than 400 million people around the world; its prevalence in the world is 4.9%. It is common in males due to its X-linked inheritance [2]. Diabetes mellitus (DM) is the most common endocrine disease of carbohydrate metabolism is considered a free radical disease owing to the increase in the production of free radicals [3]. G6PD plays a key role in cell metabolism and has been linked to various conditions; numerous observations have demonstrated highly significant decreases in G6PD activity due to hyperglycemia or diabetes in liver, kidney, brain, endothelial cells, red blood cells, and other cells and tissues [4]. The cause of reduced G6PD activity in diabetic patients without a gene mutation remains unclear. G6PD deficiency could arise not only from genetic mutations but also from changes in factors that regulate G6PD activity, including Hormones or growth factors such as insulin, estrogen, and epidermal growth factor (EGF). Oxidative stress, Post-translational regulation [5]. The relationship between G6PD deficiency and diabetes remains under investigation. Experimental studies indicate that hyperglycemia may lead to reduced G6PD activity. Screening has revealed a higher prevalence of G6PD deficiency in individuals with diabetes compared to the general population [5]. The aim of the study is to assess the G6PD level among type 2 DM patients and correlate the G6PD level with demographic and clinical data.

Materials and Methods

This is a descriptive cross-sectional study performed on 100 patients (44 males, 56 females; age range 40-80 years) who were enrolled in this study.A full clinical assessment was obtained by a standardized questionnaire. Demographic and clinical data include (age, sex, BMI, physical activity, alcoholic intake, smoking, duration and type of treatment for DM, medical history include Family history of G6PD,hematological disease(sickle cell trait\disease,thalassemia), adrenal disorder, autoimmune disease (lupus,rheumatoidarthritis), hypertension, coronary artery disease,thyroid disease , splenectomy and chronic use of other drugs). The study took place at the Diabetic Center at Marjan Teaching Hospital, Babylon, from January 2024 to December 2024, verbal consent was obtained from the patient himself/herself before enrollment in the study. Also, the study was approved by the ethical committee of the Scientific Council of Pathology at the Iraqi Board for Medical Specializations and by the research ethics committee of the Health Babylon Directorate . T2DM were evaluated according to ADA criteria 2022 [6].

Inclusion Criteria

Patients of either gender with an established diagnosis of T2DM with HbA1C ≥ 7% were eligible for this study.

Exclusion Criteria

Subjects with any of the following conditions were excluded from this study:

1. Obesity (BMI ≥ 30).
2. Pregnancy (gestational DM).
3. Type 1 DM.
4. History of Hemolytic disorder (excluding G6PD deficiency).
5. Sever liver disease.
6. Chronic kidney disease stage 4-5.
7. Current use of hemolysis-inducing medication (e.g., dapsone, primaquine, sulfa drugs).
8. Blood transfusion in the last 3months.

Blood collection and sample preparation*:*

From each participant, a sample of blood would be withdrawn from the antecubital vein, after an

overnight fast. First (6 ml) of whole blood was transferred into vacuum collection tubes containing EDTA and mixed thoroughly for determination of HbA1c and used also for estimation of G6PD activity.Then the same sample centrifuged immediately at 3000 rounds per minute for 15 minutes, with resulting plasma separated and kept at room temperature for the estimation of FPG within minutes. Second (2 ml) of whole blood was transferred into vacuum collection gel tubes then centrifuged at 4000 round per minute for 15 minutes to obtain serum which then had been aspirated for measurement of lipid profile (total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C)). Third sample collected after 2hr post prandial, (2 ml) whole blood was aspirated in EDTA tube, centrifuged immediately at 3000 rpm for 15 minutes with resulting plasma used for measurement of 2 hrs Plasma sugar.

Methods

G6PD assay

Principle of the Assay

G6PD catalyzes the oxidation of glucose-6-phosphate (G6P) to 6-phosphogluconate, reducing NADP+ (nicotinamide adenine dinucleotide phosphate) to NADPH in the process. The rate of NADPH formation, which is directly proportional to G6PD activity, is measured spectrophotometrically.

Assay range of G6PD in EDTA blood: >1300 U\L

Other laboratory tests*:*

HbA1c was measured using Bio-Rad Variant II Turbo (HbA1c analyzer) by Roche Diagnostic, Germany. Lipid profile and blood Glucose were measured based on an enzymatic method using an analyzer by Siemens Diagnostic, Germany.

Statistical analysis

Statistical analysis was carried out using SPSS version 27. Categorical variables were presented as frequencies and percentages. Continuous variables were presented as (Means ± SD). The Student's t-test was used to compare means between two groups. ANOVA test was used to compare means among four groups. Pearson correlation coefficient was used to assess the relationship between two continuous variables. $P \leq 0.05$ was considered as significant.

Ethical approval

The study was registered and approved by College of Medicine, University of Babylon and informed consents were taken from the parents.

Results

Demographic data

Age of patients

Correlation between G6PD level and age of patient in T2DM and there was no significant differences of G6PD level in them (Table 1).

Table 1: The mean differences of G6PD level (U/L) according to age of T2DM.

Study variable	Age (years)	No.	Mean ± SD	F-test	P-value
G6PD level (U/L)	40- 50	28	3396.14 ± 962.423	1.22	0.306
	50-60	34	3019.74 ± 586.024		
	60-70	30	2931.57 ± 1278.707		
	70-80	8	2981.80 ± 1257.512		

Sex of patient

Correlation between G6PD level and sex of patient in T2DM and there was no significant differences of G6PD level (Table 2).

Table 2: The mean differences of G6PD level (U/L) according to sex of T2DM patients.

Study variable	Sex	No.	Mean ± SD	t-test	P-value
G6PD level (U/L)	Male	44	3052.45 ± 997.89	-0.358	0.721
	Female	56	3124.48 ± 1014.84		

Clinical data

G6PD level in T2DM

Percentage distribution of G6PD deficiency among 100 T2DM patients, categorized by severity. It includes gender distribution, mean ± SD of G6PD levels, and the overall range (Table 3).

Table 3: Percentage of G6PD Levels and Deficiency Categories in Male and Female Patients with T2DM, Including Mean and Range of G6PD Activity.

G6PD deficiency category	G6PD level range (U\L)	% of total patients (N=100)	Male (%)	Female (%)	Mean ± SD	Range
Severe deficiency (<10% of normal)	< 200	4	2	2	3093.41± 1003.23	101.0-5539.0
Moderate deficiency (10-60% of normal)	200 - 600	1	1	0		
Mild deficieny (>60%but below normal)	600 - 1350	5	3	2		
Normal	>1350	90				

Correlation between G6PD level and glycemic control markers in T2DM

Showing there was significant negative linear correlation between G6PD level and the glycemic control markers, in which G6PD level was lower with poor glycemic control and higher with improvement of glycemic control (Table 4)

Table 4: The correlation between G6PD level (U/L) and glycemic control markers among T2DM patients.

Study Variable	Markers of glycemic control	r	P-value
G6PD level (U/L)	HbA1c (%)	-0.195	0.049*
	FPG (mg/dl)	-0.231	0.02*
	2-h PG (mg/dl)	-0.247	0.012*

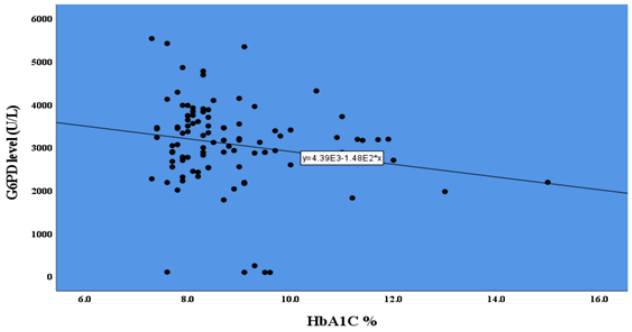

Figure 1: The correlation between G6PD level (U/L) and HbA1c (%) among T2DM patients (N=100, r = -0.195, P=0.049*).

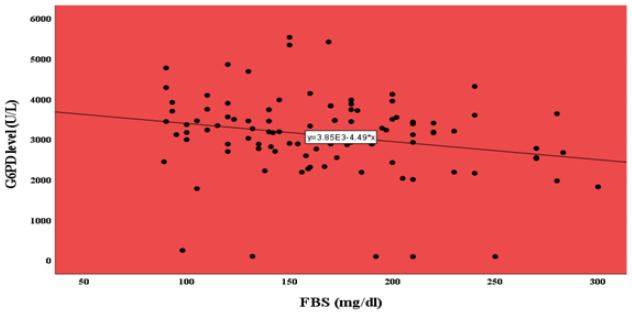

Figure 2: The correlation between G6PD level (U/L) and FPG (mg/dl) among T2DM patients (N=100, r = -0.231, P=0.02*).

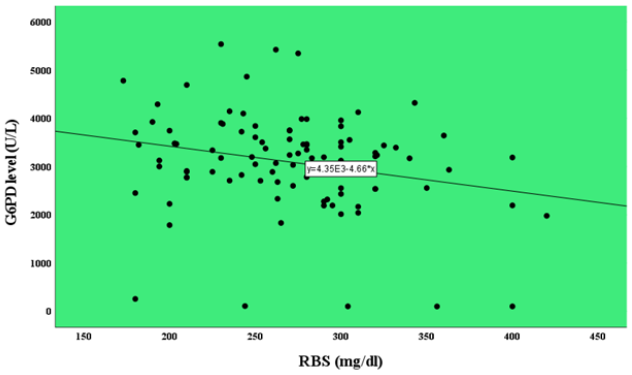

Figure (3): The correlation between G6PD level (U/L) and 2-h PG (mg/dl) among T2DM patients (N=100, r = -0.247, P=0.012*).

History of hypertension

Correlation between G6PD level and history of hypertension in T2DM.

There was no significant differences of G6PD level according to history of hypertension among T2DM patients (Table 5).

Table (5): The mean differences of G6PD level (U/L) according to history of hypertension among T2DM patients (significant P value <0.05)

Study variable	History of hypertension	No.	Mean ± SD	t-test	P-value
G6PD level (U/L)	Present	56	3125.70 ± 818.37	0.357	0.722
	Absent	44	3054.11 ± 1198.96		

Lipid profile

Correlation between G6PD level and lipid profile among T2DM:

There was no statistically significant correlation between G6PD level and lipid profile among T2DM (Table 6).

Table (6): The correlation between G6PD level (U/L) and lipid profile among T2DM patients (N=100).

Study variable	Lipid profile	R	P-value
G6PD level (U/L)	Serum cholesterol (mmol/l)	0.056	0.576
	Triglyceride (mmol/l)	0.096	0.339
	HDL (mmol/l)	-0.113	0.257
	LDL (mmol/l)	0.155	0.119
	VLDL (mmol/l)	0.071	0.478

Discussion

This study showed that there were no significant differences (P value > 0.306) in G6PD level according to age in T2DM patients. This result disagreed with a study done by Heymann AD et al. at Maccabi Healthcare Services, Israeli, that revealed a significantly higher proportion of patients with G6PD deficiency among the diabetic population aged 45–64 years. This could

be due to the true strength of the association being underestimated because many people with G6PD deficiency might not have been tested for the condition (7). This study evaluated the correlation between G6PD activity and sex of patients in T2DM and didn't show any significant differences (P value > 0.721).

This result disagreed with a study done by Hamzah SA. et al. at the diabetic center in Erbil, Iraq, which revealed the activity of G6PD in males was greater than the activity of G6PD in females (8). Another disagreement with the result was done by A. Khanam et al. in Dhaka, Bangladesh, which found that G6PD activity decreased in males with diabetes, although this study focused only on male patients (9).

Another study done by Akter N. et al. at Dhaka, Bangladesh, revealed that a few percentage of diabetic females showed a deficiency of G6PD (10). The result of this study showed that there was a significant negative correlation between G6PD level and glycemic control markers (HbA1c, FPG, and 2-h PG) among T2DM; G6PD level will decrease with poor glycemic control. Similar results agreed with a study done by Ibrahim MA et al. in Kano, Nigeria, that revealed that reduced G6PD activity was linked to poor glycemic control in diabetic patients (11). Another agreement with a study done by Akter N et al. in Dhaka, Bangladesh, showed G6PD deficiency may be one of the risk factors for T2DM (10). Also, a study was done by Niazi GA et al. in Saudi Arabia that revealed a significantly greater prevalence of G6PD deficiency in diabetic patients (12). This result disagreed with a study done by Hamzah SA et al. at the Diabetic Center in Erbil, Iraq, that showed a significant positive correlation between HbA1c levels and G6PD activity ($r = 0.572$, $P < 0.001$). This indicated that the increase in G6PD activity with higher HbA1c levels is an adaptive response to the oxidative stress caused by chronic hyperglycemia in type 2 diabetes mellitus (8). The result of this study didn't show any significant difference in G6PD level with a history of hypertension among T2DM patients. These findings might be due to methodological factors that could affect the result, including assay limitations, sample size, or distribution of G6PD deficiency severity, or the lack of a direct physiological connection between these parameters.

The result of this study didn't reveal any significant correlation between G6PD level and lipid profile among T2DM patients. There are possible explanations for this result, including different sample sizes and different study populations that could impact the result and the complex nature of diabetes-related dyslipidemia, in which insulin resistance and hyperglycemia play dominant roles. While G6PD activity influences lipid metabolism indirectly, its impact may be minor or masked by other more prominent factors in the diabetic milieus.

Conclusion

The study concluded that poor glycemic control was associated with lower G6PD activity which may be associated with several health problems. It is suggested that: Patients with type 2 diabetes may be routinely screened for this enzymopathy to provide appropriate medical care. Controlling hyperglycemia may protect the patients from many risks. This highlights the necessity for a variety of approaches to manage type II diabetes, addressing lipid levels and glycemic control. Further studies are required to include multiple centers with larger number of participates to confirm other result. Another study is required to detect any causative role for G6PD deficiency in onset of diabetes mellitus. Determining oxidative

biomarkers to evaluate oxidative damage to lipids and proteins, such as protein carbonyl (PC), and determining antioxidant substances like reduced glutathione (GSH). Another study measures HbA1c and G6PD at a certain time.

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