

# Assessment of Cardiovascular Risk Factors in Patients with Type 2 Diabetes in Upper Egypt Villages

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**Background:** A large percentage of diabetic patients also have other components of metabolic syndrome, which is a group of cardiovascular (CV) hazard factors related to both diabetes mellitus (DM) and cardiovascular diseases (CVD). We do not know about the prevalence of CV risk factors in diabetic patients in Upper Egypt. We aimed to assess the CV risk factors in type 2 diabetic patients in Upper Egypt villages.

**Methods:** We conducted a cross-sectional study that included 800 patients with type 2 DM. We classified the participants into three groups according to the hemoglobin A1c (HbA1c) levels. We assessed the prevalence of other cardiovascular risk factors and their association with HbA1c levels through a detailed history, full clinical examination, and laboratory tests.

**Results:** We found that 75% of the participants were males, 25.5% elderly, 60.25% had hypertension, 60.75% had dyslipidemia, 33.25% were overweight or obese, 19.75% had a family history of coronary artery disease (CAD), 55.75% had established CVD, 42.5% were smokers, and only 12.25% were physically inactive. We found that 84% of the participants had  $\geq$  two cardiovascular risk factors other than DM. HbA1c level was  $\geq$  7% in 77% of patients. After multivariate regression analysis, we found a significant association of higher systolic blood pressure (BP), more elevated diastolic BP, higher body mass index (BMI), increased waist circumference, old age, long duration of DM, and an increase in the number of clustered CV risk factors with a higher HbA1c level. At the same time, insulin therapy was significantly associated with a lower HbA1c level.

**Conclusion:** All type 2 diabetic patients in Upper Egypt villages have other associated CV risk factors. The clustering of cardiovascular risk factors showed a significant association with higher HbA1c levels. These findings require the thought of associated CV risk factors in choosing medical treatments to optimize glycemic control and multifactorial intervention to improve CV risk.

**Keywords:** DM, HbA1c, CV risk factors, CVD

## Introduction

Many diabetic patients also have metabolic syndrome,<sup>1</sup> a group of CV hazard factors related to both DM and CVD.<sup>2</sup> The cardiovascular risk factors are considered as clinical markers of macro and microvascular DM complications.<sup>3</sup>

Patients with type 2 DM have two-to triple more danger of CV events compared to subjects without DM, and CVD causes about 80% of the mortality in type 2 DM.<sup>4</sup> Hyperglycemia is a weak hazard factor for CVD. The significant advantage of lessening plasma glucose levels in type 2 DM is the reduction of long-term microvascular complications and, to a lesser degree, macrovascular complications

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that may occur only in young patients with short diabetes duration, no prevalent CVD, and followed-up for more than ten years.<sup>5,6</sup> Mediations concentrated on lessening plasma glucose have failed to essentially diminish CV hazard and mortality, especially in the secondary prevention trials.<sup>7,8</sup>

Cardiometabolic risk refers to a higher lifetime hazard for CVD. The specific factors that can make this expanded hazard include obesity, hyperglycemia, high blood pressure (BP), insulin resistance, and dyslipidemia. When patients are physically inactive or smokers and have at least one cardiometabolic risk factor, this markedly increases the cardiometabolic risk. Also, clustering of these risk factors can markedly increase the risk of CVD. Diseases that frequently share the above risk factors, such as type 2 DM, can also increase cardiometabolic risk.<sup>9</sup>

Some of the cardiometabolic risk factors that contribute to the development of DM are non-modifiable, as age, sex, race/ethnicity, and family history. However, many other risk factors, as overweight and obesity, smoking, sedentary life, dyslipidemia, high BP, insulin resistance, and inflammation, are modifiable through lifestyle changes and treatment.<sup>10</sup>

A multifactorial intervention to improve CV hazard factors decreased cardiovascular events and mortality in type 2 DM patients. For example, lowering BP and improving the lipid profile leads to a more prominent CVD risk reduction than lowering plasma glucose in diabetic patients.<sup>11</sup>

We do not know about the prevalence of CV risk factors in diabetic patients in Upper Egypt. We conducted this study to assess the cardiovascular risk factors in type 2 diabetic patients in Upper Egypt villages.

## Methods

### Design of the Study

We conducted a cross-sectional study in 12 villages in Upper Egypt. We selected villages randomly at Sohag, Beni Suef, and Qena Governorates and involved 800 patients with type 2 DM. We recruited the participants at primary care unit clinics. We classified the participants into three groups according to the HbA1c level, group 1; Patients have HbA1c below 7, group 2; Patients have HbA1c 7 to less than 9, and group 3; Patients have HbA1c  $\geq 9$ . We conducted the study from May 2018 to March 2020.

All subjects provided written informed consent to participate in the study. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. The ethics committee at Sohag, Beni Suef, and Qena faculty of medicine approved the study protocol.

## We Subjected the Participants to the Following

### Detailed history

Detailed history, including age, sex, education level, income, smoking history, hypertension, family history of DM, family history of CAD, duration of DM, history of established CVD, physical activity, and type of anti-glycemic used (oral hypoglycemic, insulin therapy or no anti-glycemic drugs).

### Full Clinical Examination with Particular Emphasis on the Following Items

**Blood Pressure Measurement.** We measured BP while the patient in the sitting position after a rest for 5 minutes and used a standardized mercury sphygmomanometer. We considered the average of three readings taken as the estimated systolic and diastolic blood pressures.

The Joint National Committee VIII (JNC VIII) criteria defined systemic hypertension as a BP  $\geq 140/\geq 90$  mmHg and/or on current antihypertensive drugs.<sup>12</sup>

### Anthropometric Measurements

**BMI.** We calculated BMI by the following equation: -

$$BMI(kg/m^2) = \text{weight in kilograms} / (\text{height in meters})^2$$

We estimated weight with the subject delicately shut to the closest 0.5 Kg, and estimated height without shoes to the closest 0.5 cm. BMI was considered elevated  $\geq 25$  kg/m<sup>2</sup>.<sup>13</sup>

**Waist Circumference.** Measured using a measuring tape around the bare stomach and just above the right iliac crest parallel to the floor. Abdominal obesity defined as a waist circumference of  $\geq 102$  cm for men and  $\geq 88$  cm for women.<sup>13</sup>

### Laboratory Investigation

1- HbA1c level, Complete blood count, and serum creatinine.

2- Lipid profile: we measured 12 hours overnight fasting serum triglycerides (TG), high-density lipoprotein cholesterol (HDL) levels, total serum cholesterol, and low-

density lipoproteins (LDL). We considered the TG level elevated as TG of  $\geq 150$  mg/dl. HDL cholesterol was considered low  $< 40$  mg/dl in males and  $< 50$  mg/dl in females. LDL level was considered elevated  $\geq 100$  mg/dl.<sup>14</sup>

3- Resting 12 leads surface Electrocardiogram to identify signs of myocardial ischemia (ST-segment and T wave abnormalities and pathological Q waves.

## Diagnosis of Type 2 DM

In this study, we considered the participant as previously diagnosed as being diabetic if (1) A physician once told him/her that he/she had DM in a setting other than during pregnancy or (2) On regular anti-diabetic treatment.

We considered the participants as newly diagnosed diabetics if they had one of the following:

1 - (Fasting plasma glucose  $>$  or  $= 126$  mg/dl) and/or (Random glucose  $>$  or  $= 200$  mg/dl) on two successive days.

2 - Hyperglycemia  $> 200$  mg/dl plus classic symptoms of diabetes: polyuria, polydipsia, and Loss of weight.

The recommendation of the American Diabetes Association (ADA) to include the use of HbA1c to diagnose diabetes, using a cut point of 6.5%, was not used in this study, as many labs in our area are not adequately standardized.<sup>14</sup>

—The following formula used to calculate the minimum size of the required sample:

$$n = (z)^2 p(1 - p) / d^2$$

Where n shows the sample size, z demonstrates the level of confidence according to the standard normal distribution (for a level of confidence of 95%,  $z = 1.96$ ), p shows the estimated proportion of the population that presents the characteristic (about 16%), d demonstrates the tolerated margin of error (for example, we want to know the real proportion within 5%).

Utilizing the past equation for the sample size calculation  $(n) = (1.96)^2 \times 0.16(1 - 0.16) / (0.05)^2 = 206.52$ . Therefore, the minimum sample size is 207 participants.

## Participant Characteristics

All patients with type 2 diabetes, except those with hematologic diseases (could affect HbA1c values), were selected to participate in the study.

## Analysis of Data

Data were analyzed using SPSS version 19. We analyzed the quantitative data using the analysis of variance

(ANOVA) to compare the three groups' means. We compared the qualitative data using the Chi-square test. We used Fisher's exact correction when the expected cell count is less than five. We used the Pearson correlation to study the correlation between HbA1c level and other variables. We performed univariate and multivariate regression analyses between cardiovascular risk factors and HbA1c groups after adjustment for confounding factors.

We also analyzed the association between clustering of cardiovascular risk factors and HbA1c level using estimated risks (odds ratios (OR)) from the logistic regression analysis. We applied Bonferroni correction, and thus we considered the p-value as significant at or below 0.0167.

The outcome variables were the CV risk factors and the HbA1c level.

## Results

Out of the 800 participants in our study, 75% were males, 25.5% were elderly, 60.25% were hypertensives, 60.75% had dyslipidemia, 33.25% were overweight or obese, 19.75% had a family history of CAD, 42.5% were smokers, and only 12.25% were physically inactive. [Table 1](#)

**Table 1** Distribution of Cardiovascular Risk Factors in Participants

Cardiovascular Risk Factors	N (%)
<b>Age</b>	
Middle age (35–65 years)	596 (74.5%)
Old age ( $> 65$ years)	204 (25.5%)
<b>Sex</b>	
Female	200 (25%)
Male	600 (75%)
<b>Hypertension</b>	
Yes	482 (60.25%)
<b>Dyslipidemia</b>	
Yes	486 (60.75%)
<b>BMI, kg/m<sup>2</sup></b>	
$< 25$ kg/m <sup>2</sup>	534 (66.75%)
$\geq 25$ kg/m <sup>2</sup>	266 (33.25%)
<b>Family history of CAD</b>	
Yes	158 (19.75%)
<b>Smoking</b>	
Yes	340 (42.5%)
<b>Physical inactivity</b>	
Yes	98 (12.25%)

**Abbreviations:** BMI, body mass index; CAD, coronary artery disease; N, number.

**Table 2** Distribution of Other Cardiovascular Risk Factors Than DM in Participants

Cardiovascular Risk Factors	N (%)
No other risk factors	0
One risk factor	128 (16%)
Two other risk factors	296 (37%)
Three other risk factors	196 (24.50%)
Four other risk factors	180 (22.50%)

**Abbreviations:** DM, diabetes mellitus; N, number.

We found that no one had type 2 DM without any other CV risk factors, and 84% of the participants had  $\geq$  two CV risk factors other than DM. [Table 2](#), [Figure 1](#)

HbA1c level was  $\geq 7\%$  in 77% of patients. We found that 446 (55.75%) patients had a history of established CVD. After multivariate regression analysis, both old age and long duration of DM were independent factors associated with a higher HbA1c level, while insulin therapy was an independent factor associated with a lower HbA1c level. Sex, low education level, low income, smoking, positive family history of DM, and history of established CVD were dependent risk factors that affect HbA1c in the presence of other risk factors only ([Tables 3](#) and [4](#)).

HbA1c level was significantly higher in participants with higher systolic BP (OR 1.53, 95% CI 0.88:2.36,  $p < 0.001$ ), higher diastolic BP (OR 1.71, 95% CI 1.09:2.37,  $p < 0.001$ ), higher BMI (OR 1.39, 95% CI 0.74:2.35,  $p < 0.001$ ), and increased waist circumference (OR 1.29, 95% CI 0.65:1.99,  $p < 0.001$ ). ([Tables 5–7](#))

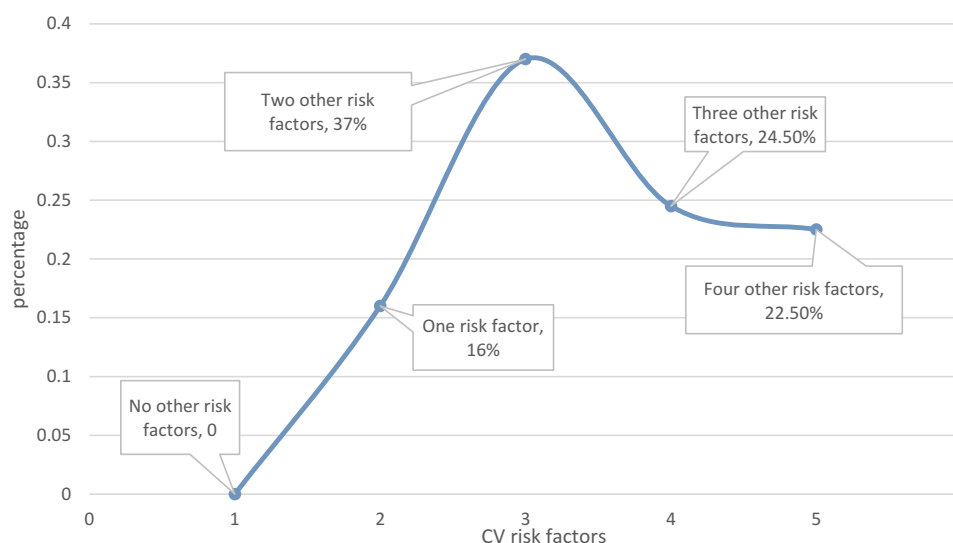
Age, systolic BP, diastolic BP, BMI, and waist circumference have shown a statistically significant positive correlation with HbA1c level ( $p < 0.0167$ ). ([Table 8](#))

Regression analysis showed that the increased number of clustered CV risk factors is statistically significantly associated with the increased HbA1c levels. ([Table 9](#))

## Discussion

Out of the 800 diabetic participants in our study, 25.5% were elderly, and 75% were males. Most of them have hypertension (60.25%), dyslipidemia (60.75%), and a history of established CVD (55.75%). 33.25% were overweight or obese, 19.75% had a family history of CAD, 42.5% were smokers, and only 12.25% were physically inactive. The case of being truly active by the majority of subjects is justifiable because the major economic activity in this community is farming, and all residents, irrespective of age and gender, engage in farming daily. The case of being genuinely active by most subjects, together with low economic state and certain dietary habits, may explain the low percentage of overweight and obesity in these communities. Also, we found that no one had type 2 diabetes without any other CV risk factors, and 84% of the participants had  $\geq$  two cardiovascular risk factors other than DM. This finding means that most diabetic patients in Upper Egypt villages are considered at high-risk for CVD.

We found that 77% of the patients had uncontrolled DM (HbA1c  $\geq 7\%$ ). Old age and longer duration of DM

**Figure 1** Distribution of CV risk factors other than DM in participants.

**Abbreviations:** CV, cardiovascular; DM, diabetes mellitus.

**Table 3** Distribution of Baseline Sociodemographic Characteristics and Detailed History of DM

Variables	HbA1c Level			P-value
	<7 N=184 (23%)	7–9 N=220 (27.5%)	≥9 N=396 (49.5%)	
<b>Age</b> Mean ± (SD)	45.24 ± (10.70)	52.67 ± (9.69)	58.21 ± (11.80)	<0.001
<b>Sex</b> Females Males	84 (42%) 100 (16.66%)	40 (20%) 180 (30%)	76 (38%) 320 (53.33%)	<0.001
<b>Education level</b> Illiterate Primary/Secondary Higher	52 (17.63%) 85 (20.78%) 47 (48.96.25%)	78 (26.44%) 115 (28.12%) 27 (28.13%)	165 (55.93%) 209 (51.10%) 22 (22.92%)	0.009
<b>Income</b> Low moderate High	25 (7.89%) 61 (19.43%) 98 (57.99%)	96 (30.28%) 85 (27.07%) 39 (23.08%)	196 (61.83%) 168 (53.50%) 32 (18.93%)	0.006
<b>Smoking</b> Yes	32 (9.41%)	104 (30.59%)	204 (60%)	0.003
<b>Type of treatment</b> No treatment Oral hypoglycemic Insulin therapy	12 (13.64%) 116 (19.60%) 56 (46.67%)	32 (36.36%) 172 (29.05%) 16 (13.33%)	44 (50%) 304 (51.35%) 48 (40%)	0.01
<b>Duration of DM (years)</b> Mean ± (SD)	3.34 ± (3.47)	4.35 ± (4.05)	5.36 ± (4.50)	0.002
<b>Positive family history of DM</b>	48 (12.06%)	92 (23.12%)	258 (64.82%)	<0.001
<b>History of established CVD</b>	67 (15.02%)	126 (28.25%)	253 (56.73%)	0.01

**Abbreviations:** CVD, cardiovascular disease; DM, diabetes mellitus; HbA1c, hemoglobin A1c; N, number; SD, standard deviation.

were independent factors associated with a higher HbA1c level, while insulin therapy was an independent factor

**Table 4** Multivariate Regression Analysis of Baseline Sociodemographic Characteristics and Detailed History of DM for HbA1c Level

Variables	OR (95% Confidence Intervals)	P-value
<b>Age/year</b>	2.23 (1.03:4.42)	<0.001
<b>Type of treatment</b>		
Insulin therapy	1	<0.001
Oral hypoglycemic	1.55 (0.93:2.22)	<0.001
No treatment	2.96 (1.63:4.89)	<0.001
<b>Duration of DM/ year</b>	2.71 (1.12:4.91)	<0.001

**Abbreviations:** CI, confidence interval; DM, diabetes mellitus; HbA1c, hemoglobin A1c; OR, odds ratio.

associated with a lower HbA1c level. Sex, low education level, low income, smoking, positive family history of DM, and history of established CVD were dependent risk factors that affect HbA1c in the presence of other risk factors only. HbA1c level was significantly higher in patients with more elevated systolic BP, higher diastolic BP, higher BMI, and increased waist circumference.

We found a positive correlation between age, systolic BP, diastolic BP, BMI, and waist circumference, and the HbA1c level. Also, we demonstrated that the clustering of cardiovascular risk factors significantly increased with a higher HbA1c level. So, it is required to pay more attention to type 2 diabetic patients in Upper Egypt. We should create periodic screening programs for early detection and multifactorial intervention of associated cardiovascular risk factors besides controlling DM. Patients should use anti glyceic agents, which improve insulin



**Table 5** Distribution of Cardiometabolic Risk Factors as Regards to HbA1c Level

Variables	HbA1c Level			P-value
	< 7 N=184 (23%)	7–9 N=220 (27.5%)	≥ 9 N=396 (49.5%)	
<b>Systolic BP (mm Hg)</b> Mean ± (SD)	130.18 ± (2.90)	135.31 ± (4.31)	138.26 ± (3.68)	<0.001
<b>Diastolic BP (mm Hg)</b> Mean ± (SD)	78.18 ± (2.90)	82.31 ± (4.31)	84.26 ± (3.68)	<0.001
<b>BMI (kg/m<sup>2</sup>)</b> Mean ± (SD)	21.18 ± (2.90)	23.31 ± (4.31)	26.26 ± (5.68)	<0.001
<b>Waist circumference (cm)</b> Mean ± (SD) Mean ± (SD)	88.18 ± (2.90)	94.31 ± (4.31)	102.26 ± (5.96)	<0.001
<b>Total Cholesterol</b> Mean ± (SD)	227.08 ± (63.06)	237.87 ± (66.24)	235.32 ± (61.07)	0.49
<b>TG</b> Mean ± (SD)	274.89 ± (89.65)	259.85 ± (84.41)	247.18 ± (88.85)	0.16
<b>LDL</b> Mean ± (SD)	113.63 ± (34.76)	112.45 ± (32.79)	112.35 ± (33.13)	0.97
<b>HDL</b> Mean ± (SD)	45.56 ± (10.29)	44.49 ± (9.90)	43.94 ± (8.49)	0.69

**Abbreviations:** BMI, body mass index; BP, blood pressure; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; N, number; SD, standard deviation; TG, triglycerides.

sensitivity and various components of insulin resistance syndrome, ie, hypertension, dyslipidemia, and endothelial dysfunction, that reduce CVD risk in type 2 diabetes, independent of its glucose-lowering action. GLP-1 receptor agonists, SGLT2 inhibitors, and pioglitazone should be considered to reduce CVD risk in type 2 diabetes, independent of its glucose-lowering action, along with metformin, over other agents with similar lowering effect on HbA<sub>1c</sub> but not reduce CV risk.<sup>15–18</sup>

In our study, 49.5% of diabetic patients showed an HbA<sub>1c</sub> level ≥ 9%, while Bogdan et al showed in their study that only 18.3% of the diabetic participants had an HbA<sub>1c</sub> level > 9%.<sup>19</sup> This finding indicates that patients in Upper Egypt villages have a significantly higher rate of poor diabetes control that may be explained by low economic and education levels, higher smoking rates, and CVD besides poor health services.

We found a significant association between higher systolic or diastolic BP and a higher HbA<sub>1c</sub> level. Bower et al reported a significant association of higher HbA<sub>1c</sub> values with increased hypertension risk during long-term follow-up.<sup>20</sup> In their study, Kathryn A Britton et al concluded that the HbA<sub>1c</sub> level in non-diabetic women was significantly

associated with more risk of hypertension after adjustment for the majority of traditional hypertension and CAD risk factors. However, this association was no longer significant after adjustment for BMI.<sup>21</sup> Other studies also reported a significant positive association between HbA<sub>1c</sub> level and hypertension.<sup>22,23</sup> The presence of shared risk factors, especially adiposity, may explain the positive association between hyperglycemia and hypertension. Furthermore, inflammatory processes play a role in both the development of hyperglycemia and hypertension.<sup>24</sup> In contrast, some studies have shown a better blood pressure profile among diabetic individuals receiving anti glycemic treatment.<sup>25,26</sup>

In our study, BMI and waist circumference showed a significant positive correlation with HbA<sub>1c</sub> level that matches with the results of a large prospective cohort study, conducted on 17,638 individuals by Chris Power and Claudia Thomas in England 2011; they concluded that excessive increase in BMI at all life stages was associated with elevated HbA<sub>1c</sub> levels.<sup>27</sup> Another study conducted by Leah M Lipsky et al showed that the role of greater BMI in diabetes management in youth with type 1 diabetes might relate specifically to increase hyperglycemia

**Table 6** Adjusted Univariate Regression Analysis of Cardiometabolic Risk Factors Regards to HbA1c Level

Variables	OR (95% CI)	P-value
<b>Systolic BP (mm Hg)</b> Mean (SD)	1.67 (0.93:2.42)	<0.001
<b>Diastolic BP (mm Hg)</b> Mean (SD)	1.77 (1.12:2.41)	<0.001
<b>BMI (kg/m<sup>2</sup>)</b> Mean (SD)	1.45 (0.75:2.15)	<0.001
<b>Waist circumference (cm)</b> Mean (SD)	1.25 (0.58:1.92)	<0.001
<b>Total Cholesterol</b> Mean (SD)	0.77 (−0.53:2.06)	0.25
<b>TG</b> Mean (SD)	0.52 (−0.15:1.19)	0.13
<b>LDL</b> Mean (SD)	0.85 (−0.32:2.01)	0.15
<b>HDL</b> Mean (SD)	0.63 (−0.24:1.31)	0.21

**Abbreviations:** BMI, body mass index; BP, blood pressure; CI, confidence interval; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; OR, odds ratio; SD, standard deviation; TG, triglycerides.

**Table 7** Adjusted Multivariate Regression Analysis of Cardiometabolic Risk Factors Regards to HbA1c Level

Variables	OR (95% CI)	P-value
<b>Systolic BP (mm Hg)</b> Mean (SD)	1.53 (0.88:2.36)	<0.001
<b>Diastolic BP (mm Hg)</b> Mean (SD)	1.71 (1.09:2.37)	<0.001
<b>BMI (kg/m<sup>2</sup>)</b> Mean (SD)	1.39 (0.74:2.35)	<0.001
<b>Waist circumference (cm)</b> Mean (SD)	1.29 (0.65:1.99)	<0.001

**Abbreviations:** BMI, body mass index; BP, blood pressure; CI, confidence interval; HbA1c, hemoglobin A1c; OR, odds ratio; SD, standard deviation.

excursions.<sup>28</sup> Many other studies have shown similar findings.<sup>29,30</sup> These findings explained by the accumulation of visceral fat after some time may enhance insulin resistance, potentially through dysregulation of adipokines released from visceral fat, resulting in diabetes.<sup>31</sup>

Our study did not find a significant relation between HbA1c level and lipid profile, which was different from the results obtained by some other studies showing that

**Table 8** Correlation Between Continuous Variables and HbA1c Level

Variables	Correlation Coefficient	P-value
<b>Age/year</b>	0.23	0.002
<b>Systolic BP (mm Hg)</b> Mean (SD)	0.52	<0.001
<b>Diastolic BP (mm Hg)</b> Mean (SD)	0.59	<0.001
<b>BMI (kg/m<sup>2</sup>)</b> Mean (SD)	0.44	<0.001
<b>Waist circumference (cm)</b> Mean (SD)	0.43	0.002
<b>Total Cholesterol</b> Mean (SD)	0.09	0.18
<b>TG</b> Mean (SD)	−0.07	0.29
<b>LDL</b> Mean (SD)	−0.004	0.95
<b>HDL</b> Mean (SD)	−0.05	0.45
<b>Duration of DM</b>	0.14	0.047

**Abbreviations:** BMI, body mass index; BP, blood pressure; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; SD, standard deviation; TG, triglycerides.

**Table 9** Regression Analysis Showing the Association of Clustered Cardiovascular Risk Factors and the HbA1c Level

Number of Risk Factors	Regression Coefficient (95% Confidence Interval)	P-value
One	1	
Two	1.45 (0.55:2.36)	0.002
Three	3.13 (2.23:4.17)	<0.001
Four	3.20 (2.14:4.12)	<0.001

dyslipidemia is significantly associated with a higher HbA1c level.<sup>19,32</sup> This difference may be due to the effects of other confounding factors and the vast majority of our studied population's tendency to dyslipidemia and lack of patients with controlled lipid profile among our studied populations.

There was a significant positive correlation between age and HbA1c levels in our study. Dubowitz et al also supported our results. They said that the association of age

with higher HbA1c levels was consistent in their research, and age should be taken into consideration when using HbA1c for the diagnosis and management of diabetes and prediabetes.<sup>33</sup>

We demonstrated that patients receiving insulin showed significantly lower levels of HbA1c compared to other lines of treatment. Ray et al enrolled 33,040 patients and compared standard treatment effects to the intensive one on cardiovascular events and mortality in DM patients. They showed that the average HbA1c was 0.9% lower, the number of cardiovascular events was 15%, and myocardial infarction was 17% lower in intensively treated patients with insulin.<sup>34</sup>

We found the clustering of cardiovascular risk factors significantly associated with increased HbA1c levels. This finding is consistent with that showed by Peng et al,<sup>35</sup> in which subjects with HbA1c  $\geq 6.5\%$  had more unfavorable cardiovascular and metabolic risk profiles than those with HbA1c  $< 6.5\%$ . Also, Okosun et al,<sup>36</sup> concluded that cardiometabolic risk factors' clustering is positively associated with elevated HbA1c. Several kinds of research explained this finding in that long-term uncontrolled DM is associated with endothelial dysfunction,<sup>37</sup> systemic inflammation,<sup>38</sup> oxidative stress,<sup>39</sup> and platelet activation.<sup>40</sup> In type 2 diabetic patients at high CV risk, intensive intervention with multiple drug combinations and lifestyle changes had supported beneficial impacts as for vascular complications and on a CV, and any cause mortality rate.<sup>11,41</sup> This discovering requires the thought of comorbid cardiovascular risk factors in choosing medical treatments to optimize glycemic control and reduce CV risk in people with type 2 diabetes.

## Strengths of Our Study

To our knowledge, no previous study assessed the cardiovascular risk factors in type 2 diabetic patients in Upper Egypt villages.

## Limitations of Our Study

We did not consider some crucial cardiovascular risk factors like alcohol consumption, socioeconomic status, dietary habits, and adherence to prescribed drug regimens.

## Conclusion

All diabetic patients in Upper Egypt villages have one or more associated CV risk factors, with a high prevalence of hypertension, dyslipidemia, and established CVD. Old

age, longer duration of DM, hypertension, high BMI, increased waist circumference, and cardiovascular risk factors' clustering showed a significant association with higher HbA1c levels. These findings require the thought of associated cardiovascular risk factors in choosing medical treatments to optimize glycemic control in people with type 2 diabetes, together with multifactorial intervention, to improve CV risk.

## Abbreviations

BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; CVD, cardiovascular disease; DM, diabetes mellitus; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; HTN, hypertension; LDL, low-density lipoprotein; TG, triglyceride.

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## Disclosure

The authors report no conflicts of interest for this work.

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