

ORIGINAL RESEARCH

Evaluation of prevalence of cardiac risk in diabetic patients: An original research

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ABSTRACT

Aim: The purpose of the present research was to assess the prevalence of cardiac risk factors in case of diabetic patients.

Methodology: 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

The International Diabetes Federation (IDF) estimates that worldwide, 415 million people have diabetes, 91% of whom have type 2 diabetes mellitus (T2DM). People with diabetes comprise 8.8% of the world's population, and IDF predicts that the number of cases of diabetes will rise to 642 million by 2040.¹ The prevalence of T2DM has been steadily increasing over time. Using data from the Framingham Heart Study, Abraham et al.² noted that the overall annualized incidence rates of the disease per 1000 persons increased from 3.0 in the 1970s to 5.5 in the first decade of the 2000s. That change represented an increase in the incidence of T2DM of 83.3% and was higher in males than females by a factor of 1.61. Cardiovascular disease (CVD) is a major cause of death and disability among people with diabetes.^{1,3} Adults with diabetes historically have a higher prevalence rate of CVD than adults without diabetes³, and the risk of CVD increases continuously with rising fasting plasma glucose levels, even before reaching levels sufficient for a diabetes diagnosis.⁵ T2DM reduces life expectancy by as much as 10 years, and the main cause of death for patients with T2DM is CVD.^{1,3} Furthermore, people with T2DM are disproportionately affected by CVD compared with nondiabetic subjects. Haffner et al. reported death rates due to cardiovascular causes over a 7-year period in patients with and without T2DM.⁶ In persons with T2DM, the death rates were 15.4% for those with no prior myocardial infarction (MI) and 42.0% in patients having a history of MI. In contrast, patients who did not have T2DM, the death rates due to cardiovascular causes were 2.1 and 15.9%, respectively. In the Framingham Heart Study, Fox reported that, along with the increasing T2DM prevalence, the attributable risk of CVD due to T2DM increased from 5.4% in the period 1952–1974 to 8.7% in the period 1975 and 1998.⁷ In a longitudinal study of 881 patients with T2DM over 10 years, van Hateren et al. indicated that the hazard ratio for death due to CVD was constantly increasing each year.⁸ Thus, an increasing burden of diabetes will likely be followed by an increasing burden of CVD. Given the clinical burden that CVD complications have on T2DM patients, there has been an increased focus on the joint management of T2DM and CVD. Good glycemic control remains the main foundation for managing T2DM. Although the importance of intensive glycemic control for protection against microvascular complications and CVD in people with T1DM is well established,^{9,10} its role for reducing cardiovascular risk has not been established as clearly in people with T2DM.¹¹⁻¹³ The assessment of the utility of risk biomarkers involves several statistical tests beyond the statistical association. Indeed, the presence of a statistically significant association between a risk marker and the disease is mandatory, but does not guarantee the improvement in risk prediction. Recent literature has proposed the use of measures of discrimination and calibration to test the prediction capacity of a risk marker. Discrimination is the capacity to identify the subject who will present the event of interest from the one who will not. The area under the receiver operating-characteristic (ROC) curve (AUC) is a popular metric of discrimination. The AUC represents the area under the plot of sensitivity (true positive rate) versus one minus specificity (true negative rate), and means the probability that a given test or predictive model assigns a higher probability of an event to those who actually develop the event. Due to the poor performance of various risk markers on their ability to increase the AUC, researchers have also tested other approaches to analyse the predictive utility of a marker, such as the reclassification. The reclassification evaluates the capacity of a new test when added to a model, to properly reassign a subject to a higher or lower category of risk.^{14,15}

AIM OF THE PRESENT STUDY

The purpose of the present research was to assess the prevalence of cardiac risk factors in case of diabetic patients.

METHODOLOGY

We conducted a cross-sectional study and involved 800 patients with type 2 DM between May 2020- May 2021. 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. 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. 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). All patients with type 2 diabetes, except those with hematologic diseases (could affect HbA1c values), were selected to participate in the study. Data were analyzed using SPSS version 25.0. 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 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. 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 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 (24.5%)
Four other risk factors	180 (22.5%)

* DM, diabetes mellitus; N, number

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. 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, $p < 0.001$). Regression analysis showed that the increased number of clustered CV risk factors is statistically significantly associated with the increased HbA1c levels. (Table 2)

Table 2- Multivariate Regression Analysis of Baseline Sociodemographic Characteristics and Detailed History of DM for HbA1c Level

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

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

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. 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. In our study, 49.5% of diabetic patients showed an HbA1c level \geq 9%, while Bogdan et al showed in their study that only 18.3% of the diabetic participants had an HbA1c level $>$ 9%.¹⁶ 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.¹⁷ 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,¹⁸ 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,¹⁹ 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,²⁰ systemic inflammation,²¹ oxidative stress,²² and platelet activation.²³ 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.²⁴ 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.

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.

REFERENCES

1. International Diabetes Federation. *idf diabetes atlas*. 7th ed. Brussels: International Diabetes Federation; 2015.
2. Abraham TM, Pencina KM, Pencina MJ, Fox CS. Trends in diabetes incidence: the Framingham heart study. *Diab Care*. 2015;38:482–7.
3. International Diabetes Federation. *Diabetes and cardiovascular disease*. Brussels: International Diabetes Federation; 2016. p. 1–144.
4. Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Angelantonio D, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *emerging risk factors collaboration*. *Lancet*. 2010;375:2215–22.
5. Singh GM, Danaei G, Farzadfar F, Stevens GA, Woodward M, Wormser D, Kaptoge S, Whitlock G, Qiao Q, Lewington S. The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: a pooled analysis. *PLoS ONE*. 2013;8:e65174.
6. Haffner SM, Lehto S, Rönnekaa T, Pyörälä K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med*. 1998;339:229–34.
7. Fox CS, Pencina MJ, Wilson PW, Paynter NP, Vasan RS, D'Agostino RB. Lifetime risk of cardiovascular disease among individuals with and without diabetes stratified by obesity status in the Framingham heart study. *Diab Care*. 2008;31:1582–4.
8. Van Hateren KJ, Landman GW, Kleefstra N, Logtenberg SJ, Groenier KH, Kamper AM, Houweling ST, Bilo HJ. The lipid profile and mortality risk in elderly type 2 diabetic patients: a 10-year follow-up study (ZODIAC-13). *PLoS ONE*. 2009;4:e8464.
9. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329:977–86.
10. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, Raskin P, Zinman B. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med*. 2005;353:2643–53.
11. ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med*. 2008;358:2560–72.
12. UK Prospective Diabetes Study. (UKPDS) Group: intensive blood glucose control with sulphonyl ureas or insulin compared with conventional treatment and risk of

- complications in patients with type 2 diabetes (UKPDS 33). UK prospective diabetes study (UKPDS) group. *Lancet*. 1998;352:837–53.
13. Action to Control Cardiovascular Risk in Diabetes Study. Group: effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med*. 2008;358:2545–59.
 14. Wang TJ. New cardiovascular risk factors exist, but are they clinically useful? *Eur Heart J*. 2008;29(4):441–4.
 15. Pencina MJ, D'Agostino RB Sr, D'Agostino RB Jr, Vasan RS. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. *Stat Med*. 2008;27(2):157–72.
 16. Bogdan T, Oana A. The relationship between hemoglobin a1c and chronic complications in diabetes mellitus. *Romanian J Diab Nutrition Metabolic Diseases*. 2012;19:2.
 17. Ray KK, Seshasai SR, Wijesuriya S, et al. Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomized controlled trials. *Lancet*. 2009;373:1765–1772.
 18. Peng G, Lin M, Zhang K, et al. Hemoglobin A1c can identify more cardiovascular and metabolic risk profile in OGTT-negative chinese population. *Int J Med Sci*. 2013;10(8):1028–1034. doi:10.7150/ijms.590536.
 19. Okosun I, Annor F, Dawodu E, et al. clustering of cardiometabolic risk factors and risk of elevated HbA1c in non-hispanic white, non-hispanic black, and mexican-American adults with type 2 diabetes. *Diab Metab Syndrome*. 2014;8:88–90. doi:10.1016/j.dsx.2014.04.02637.
 20. Lorbeer R, Empen K, Dorr M, et al. Association between glycosylated haemoglobin A (1c) and endothelial function in an adult non-diabetic population. *Atherosclerosis*. 2011;217:358–363. doi:10.1016/j.atherosclerosis.2011.04.00738.
 21. Natali A, Toschi E, Baldeweg S, et al. Clustering of insulin resistance with vascular dysfunction and low-grade inflammation in type 2 diabetes. *Diabetes*. 2006;55:1133–1140. doi:10.2337/diabetes.55.04.06.db05-107639.
 22. Zheng F, Lu W, Jia C, et al. Relationships between glucose excursion and the activation of oxidative stress in patients with newly diagnosed type 2 diabetes or impaired glucose regulation. *Endocrine*. 2010;37:201–208. doi:10.1007/s12020-009-9296-640.
 23. Shah B, Sha D, Xie D, et al. The relationship between diabetes, metabolic syndrome, and platelet activity as measured by mean platelet volume: the National Health And Nutrition Examination Survey, 1999–2004. *Diab Care*. 2012;35(5):1074–1078. doi:10.2337/dc11-172441.
 24. Gaede P, Lund-Andersen H, Parving HH, et al. effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med*. 2008;358(6):580–591.