Original Article

Association of Comorbid and Metabolic Factors with Optimal Control of Type 2 Diabetes Mellitus

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Abstract

Background: Type 2 diabetes mellitus (T2DM) is a poorly controlled epidemic worldwide that demands active research into mitigation of the factors that are associated with poor control. **Aims:** The study was to determine the factors associated with suboptimal glycemic control. **Materials and Methods:** Electronic medical records of 263 adult patients with T2DM in our suburban internal medicine office were reviewed. Patients were divided into two groups: Group 1 [optimal diabetes control with glycosylated hemoglobin (HbA1c) of 7% or less] and Group 2 (suboptimal diabetes control with HbA1c greater than 7%). The influence of factors such as age, gender, race, social history, comorbid conditions, gestational diabetes, family history of diabetes, diabetes management, statin use, aspirin use, angiotensin convertase enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB) use, body mass index (BMI), blood pressures, lipid profile, and urine microalbumin level were analyzed in the two groups. **Results:** In the suboptimal diabetes control group (N = 119), the majority (86.6%) of the patients were 41-80 years old. Factors associated with the suboptimal control were male gender [odds ratio (OR) 2.6, 95% confidence interval (CI), 1.579-4.321], Asian ethnicity (OR 1.4, 95% CI, 0.683-3.008), history of peripheral arterial disease (PAD; OR 3.9, 95% CI, 1.017-14.543), history of congestive heart failure (CHF; OR 3.9, 95% CI, 1.017-14.543), elevated triglycerides (OR 1.004, 95% CI, 1.000-1.007), and elevated urine microalbumin level of 30 mg/24 h or above (OR 4.5, 95% CI, 2.446-8.380). Patients with suboptimal diabetes control had a 3.8 times greater odds (95% CI, 1.493-6.885) of receiving the insulin and oral hypoglycemic agent together. **Conclusions:** In adult patients with T2DM, male gender, Asian ethnicity, CHF, PAD, management with insulin along with oral hypoglycemic agents, hypertriglyceridemia, and microalbuminuria were associated with suboptimal control.

Keywords: Asian ethnicity, male gender, congestive heart failure (CHF), hypertriglyceridemia, microalbuminuria, peripheral arterial disease (PAD), suboptimal control of type 2 diabetes, type 2 diabetes mellitus (T2DM)

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Introduction

Type 2 diabetes mellitus (T2DM) is a multifactorial genetic disease that causes substantial morbidity and mortality in the United States (USA) and worldwide. Despite population-based and pharmacologic interventions that have decreased mortality from heart disease, stroke, and accidents over the past 40 years, T2DM continues to increase as a cause of mortality.[1] T2DM remains the most common cause of lower-limb amputation, adult blindness, and end-stage renal disease in the USA, each with their own excess of disability and health care-related

Access this article online

Quick Response Code:

Website: www.najms.org

DOI: 10.4103/1947-2714.175197

How to cite this article: Roy S, Sherman A, Monari-Sparks MJ, Schweiker O, Jain N, Sims E, *et al.* Association of comorbid and metabolic factors with optimal control of type 2 diabetes mellitus. North Am J Med Sci 2016;8:31-9.

costs. With a current estimate of over 29 million persons in the USA affected with T2DM, it is estimated that 1 out of every 3 adults in the USA will be diagnosed with diabetes by 2050.[2] It is apparent that T2DM is a poorly controlled epidemic that demands active research into methods for the prevention and mitigation of disease in order to prevent its complications. As the pathogenesis of T2DM is multifaceted, successful management should include social interventions, pharmacologic therapies, and surgical therapies that address the multitude of pathophysiologic aberrations causing hyperglycemia and consequent vascular damage.[3,4]

Large, population-based, prospective trials have shown that intensive glucose management can dramatically decrease the rate of microvascular complications in diabetes mellitus as well as protect against macrovascular complications to some degree.[5] The increasing prevalence of T2DM has been largely attributable to lifestyle changes and obesity,[2] therefore the identification and modification of these factors is paramount. While the benefit of intensive lifestyle intervention for prevention of diabetic complications is difficult to demonstrate empirically,[6] it is a promising, cost-effective treatment modality.[7,8]

To this end, we sought to determine which metabolic and behavioral factors were associated with optimal glycemic control, defined as glycosylated hemoglobin (HbA1c) of 7% or less.[9] In this single-center cohort in our suburban office, we also sought to understand which comorbid and metabolic factors influence glycemic control so as to inform which groups may benefit from closer T2DM screening.

Materials and Methods

Study selection

This study was a retrospective case-control electronic medical record review that observed the association between a multitude of factors and the control of T2DM. Patients who were seen between January 1, 2014 and December 31, 2014 were included in this study. The study was reviewed and approved by the Institutional Review Board of the Cooper Health System, Camden, New Jersey, USA.

Subjects were adult patients of age 18 years or older with T2DM. Any patients under the age of 18 years or without T2DM were excluded. There were 260 subjects included in this study in order to provide 80% power to the study hypothesis, based on the rationale that for a retrospective case-control study looking at multiple risk factors, assuming there is a 25% prevalence of nonoptimal control in the study population, a minimum of 260 subjects, of whom at least 97 have nonoptimal control, would be required. Furthermore, it was based on detecting an odds ratio (OR) of 2 for potential risk factors with alpha = 0.05 and 80% power.

Data collection

The following data were collected for each patient: Age, gender, race (Caucasian, African American, Alaska Native, American Indian, Asian American, Hispanic, Pacific Islander American, or other), social history (tobacco use, alcohol use, and/or recreational drug use), comorbid medical conditions (coronary artery disease, cerebrovascular accident, carotid stenosis, aortic aneurysm, peripheral arterial disease (PAD), hypertension, hyperlipidemia, hypothyroidism, obesity, overweight, obstructive sleep apnea, depression, congestive heart failure (CHF), chronic obstructive pulmonary disease, chronic kidney disease, osteoarthritis, history of gestational diabetes, and/or family history of diabetes), method of management of T2DM (oral hyperglycemic agent only, insulin only, both, or none), current use of a statin, current use of aspirin, current use of angiotensin convertase enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB), body mass index (BMI), systolic and diastolic blood pressures (SBP and DBP, respectively), most recent HbA1c level, total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and urine microalbumin level (less than 30 mg/24 h, 30-300 mg/24 h, or greater than 300 mg/24 h).

Statistical study

Collected data were entered into a Microsoft Excel (2013, Redmond, Washington, USA) spreadsheet. Statistical analysis was done using SPSS (Statistical Package for the Social Sciences, version 15.01, IBM, Armonk, New York, USA). Subjects were divided into two groups. Group 1 represented the control group, which was defined as patients with optimal T2DM control with HbA1c of 7% or less. Group 2 represented the case group, which was defined as patients with suboptimal T2DM control with HbA1c greater than 7%. We compared each factor and its influence on the two groups in order to find any significant difference. Case and control group characteristics (demographic, clinical) of the study population were compared using independent *t*-tests or the Wilcoxon rank sum test for continuous data and Fisher's exact test for categorical data. Single and multiple variable logistic regression analysis were carried out to evaluate potential risk factors as predictive of inadequately controlled T2DM (HbA1c greater than 7%). ORs with 95% confidence intervals (CIs) were calculated for each risk factor using single variable logistic regression. Significant predictors from

the univariate analysis were included in the multiple variable logistic regression. Adjusted ORs from the final multivariate model were tested for significance and calculated with 95% CIs. Where appropriate, receiver operating characteristic (ROC) curves were calculated with area under the ROC curve and cut points for continuous predictors. In this study, significance was defined as a $P < 0.05$.

Results

A total of 263 patients were included in the study. The age range of our study population was 22-95 years, with an average age of 60.9 years. There was no statistically significant difference in the mean age between the patients with optimal T2DM control with HbA1c of 7% or less (Group 1) and the patients with suboptimal T2DM control with HbA1c greater than 7% (Group 2) [Table 1]. The majority of the patients (86.6%) in the suboptimal T2DM control group were 41-80 years old [Figure 1].

Among all the patients, 144 (53.6%) were male and 46.4% were female. Male gender was associated with suboptimal T2DM control with 66.4% male patients in group 2 compared to 43.1% in group 1 ($P < 0.001$). On the contrary, female gender was associated with optimal T2DM control with 56.9% female patients in group 1 compared to 33.6% in group 2 ($P < 0.001$). Univariate analysis showed that males were at a significantly increased risk of suboptimal T2DM control with OR 2.612 (95% CI, 1.579-4.321).

The analysis of the race factor showed that the majority of the patients were Caucasian (63.1%), followed by African American (13.3%), Asian (12.2%), and Hispanic (8.4%). Three percent identified as of "other race" [Table 1]. Intergroup comparison showed no statistically significant difference in each race category between the two groups [Table 1]. Univariate analysis showed that the Asian ethnicity was associated with higher odds of suboptimal T2DM control (OR = 1.433, 95% CI, 0.683-3.008). Eight patients (3%) were grouped under the "other race" category, among them one identified as Pacific Islander, 1 as Alaskan native, and 6 as undeclared. Seventy-five percent of the patients in the other race category had suboptimal T2DM control.

Social factors such as alcohol intake, cigarette smoking, and use of recreational drugs were observed in 37.9%, 26.2%, and 3.0% of all patients, respectively. Intergroup comparison showed no statistically significant difference in each social factor category between the two groups [Table 1].

We found that hypertension, hyperlipidemia, and obesity were the most common associated comorbid conditions in all patients (74.9%, 74.1%, and 54.7%, respectively) followed by overweight, osteoarthritis, coronary artery

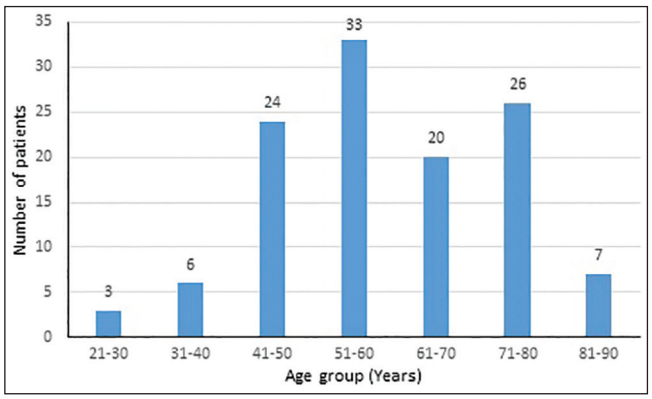

Figure 1: Age distribution of patients with suboptimal T2DM control

Table 1: Baseline characteristics

Variable	Variable	All ($N = 263$)	Group 1 HbA1c ≤7% ($N = 144$)	Group 2 HbA1c >7% ($N = 119$)	P Group 1 vs Group 2
Age (year)	Mean (SD)	60.9 (14.4)	61.9 (14.6)	59.7 (14.1)	0.1711*
Gender					
	Male (*N* %)	144 (53.6)	62 (43.1)	79 (66.4)	<.001†
	Female (*N* %)	121 (46.4)	82 (56.9)	40 (33.6)	<.001†
Race					0.3802†
	Caucasian (*N* %)	166 (63.1)	93 (64.6)	73 (61.3)	
	African American (*N* %)	35 (13.3)	21 (14.6)	14 (11.7)	
	Asian American (*N* %)	32 (12.2)	15 (10.4)	17 (14.3)	
	Hispanic (*N* %)	22 (8.4)	13 (9.0)	9 (7.6)	
	Other (*N* %)	8 (3.0)	2 (1.4)	6 (5.1)	
Social factors					
	Alcohol (*N* %)	99 (37.9)	55 (38.2)	44 (37.6)	1.0000†
	Cigarettes (*N* %)	69 (26.2)	36 (25.0)	33 (27.7)	0.6734†
	Drugs (*N* %)	5 (1.9)	5 (3.5)	0 (0.0)	0.0658†

HbA1c = Glycosylated hemoglobin, SD = Standard deviation, *Wilcoxon two-sample test, †Fisher's Exact Test

disease, depression, hypothyroidism, obstructive sleep apnea, and chronic kidney disease (36.6%, 20.2%, 19%, 18.8%, 18.6%, 10.7%, and 10.7%, respectively). The prevalence of these associated comorbid conditions were similar in Group 1 and Group 2, and there was no statistically significant difference [Table 2]. We did observe that more than two-third of patients with hypothyroidism had optimal T2DM control, but the difference was not statistically significant.

Although cerebrovascular accidents, chronic obstructive pulmonary disease, CHF, PAD, carotid artery stenosis, and aortic aneurysm were associated in 7.6%, 6.1%, 4.6%, 4.6%, 2.7%, and 2.7% of all patients, only CHF and PAD were associated with suboptimal T2DM control ($P < 0.05$). Twelve patients (4.6%) had PAD and 75% of them had suboptimal T2DM control ($P < 0.05$). Similarly, 12 patients (4.6%) had CHF and 75% of them had suboptimal T2DM control ($P < 0.05$). Univariate analysis showed that the patients with CHF had a 3.9 times greater chance of suboptimal T2DM control (OR = 3.845, 95% CI, 1.017-14.543). Similarly, the patients with PAD had a 3.9 times greater chance of suboptimal T2DM control (OR = 3.845, 95% CI, 1.017-14.543). Multivariate analysis showed an estimated OR for CHF of 2.619 (95% CI, 0.511-13.419) and for PAD of 1.783 (95% CI, 0.347-9.152) of having suboptimal T2DM control.

An association of family history of diabetes and a personal history of gestational diabetes mellitus was seen in 46.8% and 2.3% of all patients, respectively, which was similar and comparable between the two groups.

In our study, 18.3% of all patients with T2DM were managed with diet alone. About half (49.8%) of all the patients were treated with an oral hypoglycemic agent (OHA), which was comparable between Group 1 and Group 2. A significantly higher number of patients in Group 2 were treated with insulin without or with OHA ($P < 0.0005$) [Table 3]. Multivariate analysis showed an estimated OR for management with insulin and OHA 3.207 (95% CI, 1.493-6.885) of having suboptimal T2DM control. Among all the patients with T2DM, 60% were on a statin, 36.5% were on aspirin, and 51.7% were on an ACE-I or ARB agent. There percentages were similar in the two groups.

In all patients, mean BMI was 32.2 kg/m^2, mean SBP was 127 mmHg and mean DBP was 77 mmHg. Group 1 and Group 2 had similar vital parameters, and there were no statistically significant differences in the mean BMI, SBP, and DBP between the two groups [Table 3].

The mean HbA1c of group 1 was 6.24% and of group 2 was 8.87%. The mean total cholesterols of Group 1 and 2 were 169.0 mg/dL and 173.1 mg/dL, respectively, which showed no significant difference. Similarly, the mean HDL-C and LDL-C levels of Group 1 and 2 were 47.5 mg/dL and 45.4 mg/dL (HDL-C), and 92.5 mg/dL and 96.3 mg/dL (LDL-C), respectively, which showed no significant differences. We found a significant difference between the mean triglyceride levels in Group

Table 2: Associated comorbid conditions

Diagnosis	All ($N = 263$)	Group 1 HbA1c ≤7% ($N = 144$)	Group 2 HbA1c >7% ($N = 119$)	P (Group 1 vs Group 2)
CAD (*N* %)	50 (19.0)	29 (20.1)	21 (17.7)	0.6388[†]
CVA (*N* %)	20 (7.6)	10 (6.9)	10 (8.4)	0.8159[†]
Carotid stenosis (*N* %)	7 (2.7)	3 (2.1)	4 (3.4)	0.7048[†]
Aortic aneurysm (*N* %)	7 (2.7)	4 (2.8)	3 (2.5)	1.0000[†]
PAD (*N* %)	12 (4.6)	3 (2.1)	9 (7.6)	0.0406[†]
Hypertension (*N* %)	197 (74.9)	109 (75.7)	88 (73.9)	0.7763[†]
Hyperlipidemia (*N* %)	195 (74.1)	109 (75.7)	86 (72.3)	0.5726[†]
Hypothyroidism (*N* %)	49 (18.6)	33 (22.9)	16 (13.5)	0.0568[†]
Obesity (*N* %)	144 (54.7)	75 (52.1)	69 (57.9)	0.3841[†]
Overweight (*N* %)	96 (36.6)	60 (41.9)	36 (30.3)	0.0544[†]
OSA (*N* %)	28 (10.7)	12 (8.3)	16 (13.5)	0.2285[†]
Depression (*N* %)	39 (18.8)	24 (16.7)	15 (12.6)	0.3878[†]
CHF (*N* %)	12 (4.6)	3 (2.1)	9 (7.6)	0.0406[†]
COPD (*N* %)	16 (6.1)	9 (6.3)	7 (5.9)	1.0000[†]
CKD (*N* %)	28 (10.7)	11 (7.6)	17 (14.3)	0.1075[†]
Osteoarthritis (*N* %)	53 (20.2)	31 (21.7)	22 (18.5)	0.5409[†]
History of GDM (*N* %)	6 (2.3)	5 (3.8)	1 (0.8)	0.2262[†]
Family hx DM (*N* %)	123 (46.8)	61 (42.4)	62 (52.1)	0.1364[†]

CAD = Coronary artery disease, CVA = Cerebrovascular accident, PAD = Peripheral arterial disease, OSA = Obstructive sleep apnea, CHF = Congestive heart failure, COPD = Chronic obstructive pulmonary disease, CKD = Chronic kidney disease, GDM = Gestational diabetes mellitus, DM = Diabetes mellitus, HbA1c = Glycosylated hemoglobin, [†]Fisher's exact test

Table 3: Diabetes management, vitals, and diagnostic test characteristics

Variable	Variable	All (*N* = 263)	Group 1 HbA1c ≤7% (*N* = 144)	Group 2 HbA1c > 7% (*N* = 119)	*P* Group 1 vs Group 2
Management					
	OHA alone (*N* %)	131 (49.8)	75 (52.1)	56 (47.1)	NS[ǂ]
	Insulin alone (*N* %)	30 (11.4)	12 (8.3)	18 (15.1)	0.0016[ǂ]
	OHA and Insulin (*N* %)	54 (20.5)	16 (11.1)	38 (31.9)	0.0016[ǂ]
	No medication (*N* %)	48 (18.3)	41 (28.5)	7 (5.9)	0.0016[ǂ]
	Statin (*N* %)	158 (60.0)	85 (59.0)	73 (61.3)	0.7067[ǂ]
	Aspirin (*N* %)	96 (36.5)	54 (37.5)	42 (35.3)	0.7970[ǂ]
	ACE-I or ARB (*N* %)	136 (51.7)	70 (48.6)	66 (55.5)	0.3214[ǂ]
Vitals					
	BMI (kg/M^2), mean (SD)	32.2 (7.3)	31.6 (7.5)	32.9 (7.1)	0.7711[*]
	SBP (mmHg), mean (SD)	127 (13.9)	125 (11.9)	129 (15.6)	0.1242[*]
	DBP (mmHg), mean (SD)	77 (10.3)	76.9 (9.9)	77 (10.7)	0.5686[*]
Lab tests					
	HbA1c (%), mean (SD)	7.4 (1.8)	6.24 (0.47)	8.87 (1.69)	<.0001[*]
	TC (mg/dL), mean (SD)	170.9 (41.5)	169.0 (39.8)	173.1 (43.4)	0.3260[*]
	TG (mg/dL), mean (SD)	152.6 (87.8)	139.4 (72.3)	168.8 (101.4)	0.0203[*]
	HDL-C (mg/dL), mean (SD)	46.5 (14.4)	47.5 (15.7)	45.4 (12.6)	NS[*]
	LDL-C (mg/dL), mean (SD)	66.2 (16.6)	92.5 (34.1)	96.3 (35.7)	0.5059[*]
	UMA < 30 mg/24 h (*N* %)	205 (77.9)	130 (90.1)	75 (63.0)	<.0001[ǂ]
	UMA 30-300 mg/24 h (*N* %)	50 (19.0)	13 (9.0)	37 (31.1)	<.0001[ǂ]
	UMA > 30 mg/24 h (*N*, %)	8 (3.1)	1 (0.7)	7 (5.9)	<.0001[ǂ]

OHA = Oral hypoglycemic agent, ACE-I = Angiotensin convertase enzyme inhibitor, ARB = Angiotensin receptor blocker, BMI = Body mass index, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, HbA1c = Glycosylated hemoglobin, TC = Total cholesterol, TG = triglyceride, HDL-C = High density lipoprotein cholesterol, LDL-C = Low-density lipoprotein cholesterol, UMA = Urine microalbumin, NS = Not significant, SD = Standard deviation, [*]Wilcoxon two-sample test, [ǂ]Fisher's exact test

1 (139.4 mg/dL) and Group 2 (168.8 mg/dL) ($P < 0.05$). Multivariate analysis showed an estimated OR for elevated triglyceride 1.004 (95% CI, 1.000-1.007) of having suboptimal T2DM control. Further analysis by ROC showed low predictive value of elevated triglyceride level for suboptimal T2DM control.

We observed a significant difference in the association of elevated urine microalbumin levels of 30 mg/24 h or above in 9.7% of patients in Group 1 and in 37.0% of patients in Group 2 ($P < 0.001$) [Table 3]. Univariate analysis showed that the patients with an elevated urine microalbumin level of 30 mg/24 h or above had a 4.5 times greater risk of suboptimal T2DM control (OR = 4.528, 95% CI, 2.446-8.380). Multivariate analysis showed an estimated OR for elevated urine microalbumin level 4.594 (95% CI, 2.323-9.084) of having suboptimal T2DM control.

Finally, specific cut point analysis showed a statistically significant association with suboptimal T2DM control and SPB greater than 146 mmHg, but the ROC analysis indicated low predictive value of SBP for suboptimal T2DM control.

Discussion

Diabetes is responsible for a significant disease burden in the USA and worldwide,[2,10] hence many studies have looked for factors that affect glycemic control favorably or adversely.

Many risk factors have been associated with the development and progression of T2DM, such as weight above the normal range, abnormal fat distribution, inactivity, family history of T2DM, race, age, history of prediabetes, history of gestational diabetes, polycystic ovarian syndrome, HDL-C below 35 mg/dL, triglyceride above 250 mg/dL, hypertension, acanthosis nigricans, and presence of cardiovascular disease.[11]

We found a significant association between poor or suboptimal control of T2DM and some factors such as male gender, Asian ethnicity, CHF, PAD, management with insulin and one or more oral hypoglycemic agent(s), elevated triglyceride level and elevated urine microalbumin level of 30 mg/24 hour or above [Figure 2].

In our study, males had a 2.6 times increased risk of suboptimal control of T2DM. Our result, however, differs from the findings of several studies. One study found that at the end of 1 year, males had better fasting blood glucose levels than females ($P < 0.07$).[12] Another study found that female diabetic subjects had higher HbA1c than males ($P < 0.0075$).[13] A study in Israel found that in the well-controlled T2DM group there were more

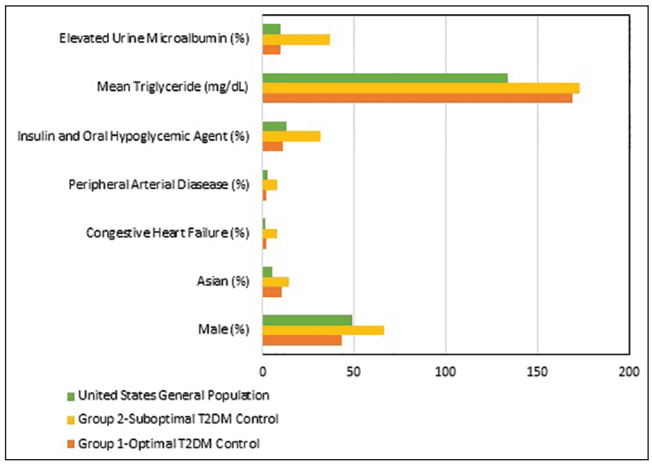

Figure 2: Frequency of factors influencing control of T2DM

males than females (52% vs 43.8%, $P < 0.001$).[14] Another cross-sectional observation study reported that men were more likely to reach a HbA1c level of less than 7% than women.[15] Conversely, several studies have shown that diabetic women have better glycemic control than men.[16,17] One study reported that diabetic women had a 19% greater chance of reaching a HbA1c level of less than 7.0% compared to men.[18] The study revealed that while men were more physically active than women, they were less adherent to the recommendations from their physicians with respect to diet and checking blood glucose levels.[18] We believe that in our suburban population, the lack of daily exercise and less adherence to physicians' recommendations might be key factors associated with 2.6 times increased risk of poor control of T2DM in males.

In the race category, we found that the Asian ethnicity was associated with higher odds of suboptimal T2DM control. Our observation was markedly different than other studies that looked into the influence of ethnicity. A cross-sectional study of 1,350 adult subjects found that poor glycemic control was associated with the non-Hispanic black and Hispanic races.[19] Another longitudinal observational study found that better glycemic control was associated with the Asian race.[20]

We found that patients with PAD had a 3.9 times greater chance of suboptimal control of T2DM. Our findings correspond with the analysis of 2,174 National Health and Nutrition Examination Surveys (NHANES) surveys during 1999-2000 that showed that PAD (ankle-brachial index less than 0.9) was more than twice as common in adult T2DM patients as compared to those without T2DM (OR 2.71, 95% CI 1.03-7.12).[21] Another prospective cohort study of 1,895 individuals with diabetes showed a strong positive correlation between HbA1c and PAD in diabetic adults.[22] Patients with poor glycemic control were 5 times more likely to develop intermittent claudication compared to the patients with HbA1c under 6%.[22] Conversely, one study found no statistically significant difference in the ankle-brachial index values in patients with poor glycemic control compared to those with good glycemic control.[23] Our findings are supported by the majority of the studies.

In our study, patients with CHF had a 3.9 times greater chance of suboptimal control of T2DM. Our findings parallel the findings of other studies, such as the retrospective review of 9,591 medical records that showed that CHF was more common in patients with diabetes (11.8% vs 4.5%).[24] An association between diabetes and CHF was also found in the Framingham Heart Study.[25] While elevated HbA1c levels have a known association with increased cardiovascular risk, the effect of glycemic control on heart failure is not completely understood. The Candesartan in Heart failure Assessment of Reduction in Mortality and Morbidity (CHARM) study demonstrated that a HbA1c level is an independent risk factor for heart failure hospitalization, cardiovascular risk, and mortality in diabetic and nondiabetic patients. Patients with moderate glucose control had the lowest risk of mortality.[26] Other studies suggest an independent association between poor glycemic control and heart failure.

Studies have found that each 1% increase in HbA1c was associated with an 8% increased risk of heart failure[27] and 1.24-fold increased risk of mortality.[28] On the contrary, one study has revealed that stricter glycemic control was independently associated with developing CHF. It demonstrated that diabetic patients who developed CHF had lower HbA1c levels at follow-up compared to those who did not develop CHF.[24] These patients had similar baseline HbA1c levels prior to follow-up, thus suggesting that reduction in HbA1c in diabetic patients may lead to an increased risk of developing CHF.[24] In any case, our findings further enhance our understanding that CHF is a strong indicator of poor control of T2DM and it offers a 3.9 times greater chance of suboptimal control of T2DM.

We found that the patients with suboptimal or poor control of T2DM had a 3.8 times greater chance of receiving insulin and OHA together. The American Diabetes Association (ADA) recommends a goal HbA1c of less than 7% to reduce the risk of microvascular and macrovascular complications of T2DM.[29] Intensive glycemic control reduces microvascular complications of T2DM, which was demonstrated by the United Kingdom Prospective Diabetes Study (UKPDS) trial.[30] For patients with uncontrolled diabetes, the consensus algorithms published by the ADA and the European Association for the Study of Diabetes (EASD) recommend lifestyle modification and insulin therapy as definitive treatment.[31] Studies show that there have been barriers to prescribing and taking insulin from the physicians

and the patients, respectively.[32,33] Conversely, a systemic review showed that insulin monotherapy and insulin combined with OHA provide similar improvements in glycemic control.[34] Our findings parallel the studies that show a strong association between poor control of T2DM and insulin use.[20,35]

An elevated mean triglyceride level was found in the patients who had suboptimal control of T2DM in our study. Although we found a significant difference between the mean triglyceride levels in the optimally controlled group and the suboptimally controlled group (139.4 vs 168.8 mg/dL; $P < 0.05$), multivariate analysis showed an estimated OR for elevated triglyceride 1.004 (95% CI, 1.000-1.007) of having suboptimal T2DM control and a low predictive value of elevated triglyceride level for suboptimal T2DM control, as deduced by the ROC analysis. Our findings were similar to a study that showed that elevated triglyceride levels were associated with poor glycemic control,[36] and other studies that observed triglycerides as a marker of poor glycemic control.[16] Although low HDL-C has been associated with poor glycemic control[9,37,38] we did not observe such an association in our study.

Our study also found that the patients with an elevated urine microalbumin level of 30 mg/24 h or above had a 4.5 times greater risk of suboptimal T2DM control (OR = 4.528, 95% CI, 2.446-8.380). A longitudinal observational study found a similar association.[20]

In addition to the major findings mentioned above, we observed some associations that are worth mentioning. The majority of the patients who had suboptimal control of T2DM were over the age of 40 years. Our finding differed from the findings of a retrospective study of 2,970 Hawaiian patients that showed that patients younger than 35 years old were more likely to have poorly controlled T2DM compared to the patients in the 50-64-years age group.[39] Data from the CDC found poor control of T2DM in young and middle-aged adults.[19] Another longitudinal observational study of 1,357 subjects found better glycemic control in younger patients.[20]

Another observation was related to cigarette smoking. Although the data from the National Diabetes Register in Sweden suggested that smoking is independently associated with elevated HbA1c levels ($P < 0.001$),[40] we found no statistically significant difference in the association of cigarette smoking between the optimal T2DM control group and the suboptimal T2DM control group. Lastly, all (100%) of our patients had an elevated BMI of greater than 25 kg/M^2, out of which 54.7% patients were obese. A survey of 2,894 adults with T2DM demonstrated that 80.3% of these individuals had elevated BMI and 49.1% were obese.

The prevalence of diabetes increased with increasing BMI.[41] Although our patients had elevated BMI, we found no significant difference in the impact of BMI on HbA1c levels between the optimally controlled and suboptimally controlled groups.

The strength of our study was selection of the patients who had more than one office visit in one location in the specified time period that allowed us to include the time-specific follow-up data regarding management as well as control of T2DM. Nevertheless, our study had several limitations, such as a relatively small number of subjects, retrospective analysis of only documented variables, lack of availability of additional variables, and analysis limited to a suburban outpatient population, which cannot be generalized.

We conclude that in adult patients with T2DM, suboptimal control is associated with factors such as male gender, Asian ethnicity, CHF, PAD, management with insulin and one or more oral hypoglycemic agent(s), elevated triglyceride level, and elevated urine microalbumin level of 30 mg/24 h or above. Further studies are needed in order to understand the impact of these factors and other factors, if any, on the suboptimal control of T2DM, as well as the impact of amelioration of such factors in optimal control of T2DM.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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