

Association of Dyslipidemia and Comorbidities with Risk Factors Among Diabetic Patients: A Retrospective Analysis

This article was published in the following Dove Press journal:
Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy

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Purpose: To find out the association of dyslipidemia and comorbidities with risk factors among type-2 diabetes mellitus (T2DM) patients attending King Abdulaziz University Hospital (KAUH) Jeddah, Saudi Arabia (SA).

Patients and Methods: Three hundred and twenty-five T2DM patients were enrolled from the electronic record of the KAUH. The patients' existing comorbidities and dyslipidemia correlation with demographic, clinical, and available laboratory data were sought. Statistical analysis was performed on SPSS-23.

Results: Of the total 325 T2DM patients with a mean age of 60.13±10.5 years [males 95 (29.23%) and females 230 (70.77%)] were included from the electronic record. Poor glycemic control was observed in 222 (68.31%) subjects (HbA1c > 7%), and 154 (47.39%) subjects had DM for more than ten years. Among our study subjects, 103 (31.69%) were hypertensive (HTN), 112 (34.46%) had ischemic heart disease (IHD), 45 (13.85%) were obese, 8(2.46%) had a stroke and 269 (82.77%) had dyslipidemia. Of the total 269 dyslipidemic patients, 168 (62.45%) were on hypolipidemic treatment. On comparison of study variables according to dyslipidemia versus normal lipid levels, the lipid profile, including HDLc, LDLc, TC, and TG, revealed a highly significant difference (p-value <0.001) whereas many variables were not significantly different. HbA1c, FBG, and RBG were significantly higher in dyslipidemic subjects. Logistic regression analysis of risk factors and comorbidities in our patients revealed that age 60–69 years and 70–79 years had a significant association with comorbidities. Similarly, logistic regression analysis of risk factors and dyslipidemia in our patients revealed no statistically significant association.

Conclusion: Our results observed that the comorbidities were associated with increasing age and common comorbidities were HTN, IHD, dyslipidemia. Our study has highlighted the current trends in T2DM symptomatology and comorbidities. Efficient management and control by early screening and developing healthy lifestyles in our patients can be very helpful in the prevention of all these highly morbid complications of this preventable disease.

Keywords: dyslipidemia, DM, IHD, cholesterol, comorbidities, HbA1c, hypertension

Introduction

Diabetes mellitus (DM) being a metabolic disorder presenting mostly with hyperglycemia due to either relative or absolute deficiency of insulin. The world over there is a progressive rise in the number of patients of DM. It is estimated that around 350 million people would be diabetic by year 2030.¹ According to a WHO report,

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DM is ranked to be the potential seventh leading cause of death by the next ten years. Diabetic complications are seen in around 66% of patients of long-standing DM. Lifestyle in Saudi Arabia is changing so rapidly that according to a recent study, the incidence of obesity has been reported to be around 54% in the adult population of Saudi Arabia.² A Saudi Arabia study published in 2017 reported the incidence of type II DM from 17.7–25.7% in adults with more incidence in females.³ Saudi Arabia is having the highest prevalence of DM in the Middle east.⁴ A large number of complications have long been associated with DM, including disturbed cholesterol metabolism, hypertension, cardiac complications, retinal and renal disorders, and peripheral neuropathies. In 2015, DM & its complications resulted in more than one million deaths.⁵

Increased risk of heart diseases is mostly associated with dyslipidemias leading to atherosclerosis.⁶ Myocardial infarction due to coronary atherosclerosis has been mentioned as a leading cause of mortality in almost 80% of diabetics, the world over.⁷ The patients of T2DM often have other metabolic derangements resulting in enhanced morbidity and mortality.⁸

Comorbidity, by definition, is the occurrence of multiple chronic disorders in the same person due to one index disease is commonly seen in DM. Multiple diseases adversely affect the quality of life of an individual, and the patient has got an overall depressive element.⁹ The occurrence of multiple health-related problems in an individual poses a heavy burden on the individual, family, and the healthcare providing system of the society. Only a few studies have been carried out in Saudi Arabia regarding this aspect of the disease, and we hope that our effort would be helpful in raising the concern and awareness against this disease.^{10,11} The present study aimed to find out the association of dyslipidemia and comorbidities with risk factors among T2DM patients attending KAUH, Jeddah, SA.

Materials and Methods

This retrospective study was conducted from Feb 2017 to March 2018 at the KAUH, Jeddah, SA. All the T2DM patients were included in the study were selected from their electronic record and patients suffering from Type1DM were not included in the study as the comorbidities and complications of Type 1 DM are different from T2DM. Relevant records were obtained from the hospital's central electronic medical records for clinical data and relevant investigative findings. For this study, permission was granted by the Ethics Research Committee at KAU, Jeddah (Reference No. 373–18). Being a retrospective

nature of the study, the consent of the patient was waived by the committee and we also maintained the confidentiality of all the patients. All the procedures and measures were in accordance with the international ethical standards and the latest (2008) version of the Helsinki Declaration of 1975.

The data regarding the type of DM, age, gender, BP, weight, height, educational level, FBG, RBG, lipid profile, serum creatinine, HbA1c values, complications, and associated problems were noted. Family history of dyslipidemia was not found in their record. All the biochemical investigations were done at KAUH laboratory by using kits. In our study only those patients were included who were taking anti-diabetic treatment excluding insulin and for selecting patients “American Diabetes Association (ADA) criteria (FBG ≥ 126 mg/dL, HbA1C $\geq 6.5\%$, or RBG ≥ 200 mg/dL)” was followed.¹² The patients we were divided into two groups according to their HbA1c values and patients having HbA1c ≤ 7 good glycemic control, and HbA1c > 7 poor glycemic control.¹³ Our study subjects were also divided into dyslipidemic and normal and for the study, dyslipidemia was considered as “having 1 or more of the following: TC ≥ 5.18 mmol/L, TG ≥ 1.7 mmol/L, LDL ≥ 3.37 mmol/L or HDL ≤ 1.04 mmol/L.”¹⁴ The MI was diagnosed from the patients' medical records and confirmed by the treating physician. The ADA criterion was used to diagnose hypertension among T2DM subjects, i.e., SBP ≥ 140 mmHg and DBP ≥ 90 mmHg measured on multiple visits.¹⁵

All biochemical parameters were determined in the KAUH biochemistry laboratory. The blood glucose, lipid profile serum creatinine, and HbA1c levels were investigated on an autoanalyzer (Roche Modular P-800, Roche Diagnostics, Germany).

Statistical Analysis

Analysis of study data was performed by SPSS (Statistical Package for Social Sciences) version 23. Mean \pm SD was mentioned for quantitative values. Frequency and percentages were mentioned for qualitative variables. The Student's *t*-test was used to compare the mean of age, BMI, systolic & diastolic BP (mm Hg), HDLc, LDLc, TG, serum creatinine, HBA1c, random and fasting blood glucose between dyslipidemia and non-dyslipidemic diabetic patients. The logistic regression analysis was also done to find out the association between variables. A *p*-value ≤ 0.05 was considered as significant.

Results

Our study cohort included 325 patients of T2DM with a mean age of 60.13 ± 10.5 years [males 95 (29.23%) and

females 230 (70.77%)). Poor glycemic control was observed in 222 (68.31%) subjects (HbA1c > 7%), and 154 (47.39%) subjects had DM for more than ten years. Among our study subjects, 103 (31.69%) were hypertensive (HTN), 112 (34.46%) had ischemic heart disease (IHD), 45 (13.85%) were obese, 8(2.46%) had a stroke, and 269 (82.77%) had dyslipidemia. Of the total 269 dyslipidemic patients, 168 (62.45%) were on hypolipidemic treatment. Most of the participants 214 (67.3%), were non-Saudi. The study subjects belonged to different educational background and age categories (Table 1). On comparison of study variables according to dyslipidemia versus normal lipid levels, the lipid profile, including HDLc, LDLc, TC, and TG revealed a highly significant difference (p-value <0.001) whereas many variables like age, BP, serum creatinine were not significantly different. HbA1c, FBG, and RBG were significantly higher in dyslipidemic subjects (Table 2). Logistic regression analysis of risk factors and comorbidities in our patients revealed that age 60–69 years and 70–79 years had a significant association with comorbidities. Similarly, the duration of diabetes >10 years was significantly associated with comorbidities, but the association was lost after adjusting other factors. Females, educational levels, weight, height, blood pressure, HbA1c >7, dyslipidemia, and hypolipidemic treatment had no significant relationship with comorbidities (Table 3). Similarly, logistic regression analysis of risk factors and dyslipidemia in our patients revealed no statistically significant association (Table 4).

Discussion

The T2DM patients expect to experience several life-threatening and debilitating complications throughout the world, including SA.¹⁶ Lack of proper diabetic control and chronicity of the disease, are the main aggravating factors of these complications. The simultaneous presence of two or more complications, i.e., comorbidity, produces devastation health effects because of multiple organ involvement.¹⁷ Patients' education and dedication in proper management are the key factors in better control of this potentially fatal disorder. Commitment & willingness of health care professional has been well acknowledged in medical literature in the reduction of diabetes-related comorbidities in Saudi Arabian patients.¹⁸

In T2DM, the basic mechanism is thought to be the developing insulin resistance in the body. This mechanism leads to various derangements in the lipid metabolism resulting in various dyslipidemias.¹⁹ In our present study,

Table 1 Demographic, Comorbid and Essential Investigational Characteristics of Our Study Cohort

Variables	N(%)
Age (Years) Mean±SD	60.13 ± 10.5
< 40 years	15 (4.6)
40–49 years	46(14.15)
50–59 years	110 (33.84)
60–69 years	88(27.07)
70–79 years	49(15.7)
80+ years	17(5.23)
Gender	
Male	95(29.23)
Female	230(70.77)
Marital Status	
Single	17(5.23)
Married	295(90.77)
Divorced/Widowed	14(4.30)
Nationalities	
Saudi	111(32.7)
Non-Saudi	214(67.3)
Education	
Primary	67(20.61)
Intermediate	85(26.15)
High School	89(27.38)
Graduate	73(22.46)
Post Graduate & Above	11(3.38)
Duration of Diabetes Mellitus	
≤ 10 years	171(52.61)
> 10 years	154(47.39)
Smoker	
Yes	49(15.08)
No	276(84.92)
DM with One or More Comorbidities	
No co-morbid condition	57(17.54)
HTN	103(31.69)
IHD	112(34.46)
Obesity	45(13.85)
Stroke	8(2.46)
Dyslipidemia	
Yes	269(82.77)
No	56(17.23)
Dyslipidemia According to Duration of DM	
Duration of DM ≤ 10 years	
Dyslipidemia	143(83.6)
Normal	28(16.4)
Duration of DM > 10 years	
Dyslipidemia	126(81.8)

(Continued)

Table 1 (Continued).

Variables	N(%)
Normal	28(18.2)
Dyslipidemia Treatment	
Yes	168(62.45)
No	101(37.55)
HbA1c (%)	
≤ 7	103(31.69)
> 7	222(68.31)

Abbreviations: HTN, hypertension; IHD, Ischemic heart disease; HbA1c, Hemoglobin A1c.

Table 2 Comparison of Study Variables According to Dyslipidemia and Normal Lipid Values

Variables	Dyslipidemia N=269	Normal N=56	p-value
Age (years)	60.12 ± 10.6	59.83 ± 10.5	0.85
BMI (Kg/m ²)	32.2 ± 6.5	30.7 ± 6.3	0.12
Systolic BP (mm Hg)	138.7 ± 24.7	136.6 ± 25.8	0.59
Diastolic BP (mm Hg)	73.0 ± 12.8	70.9 ± 11.3	0.27
HDL (mmol/l)	0.99 ± 0.31	1.3 ± 0.26	<0.001
LDL (mmol/l)	3.3 ± 0.8	2.1 ± 0.3	<0.001
Cholesterol (mmol/l)	5.1 ± 1.1	3.51 ± 0.3	<0.001
TG (mmol/l)	2.31 ± 1.1	1.3 ± 0.3	<0.001
Serum creatinine (μmol/L)	67.1 ± 21.9	68.6 ± 26.6	0.654
HB A1C (%)	8.2 ± 1.9	6.8 ± 1.6	<0.001
FBG (mmol/l)	8.1 ± 2.7	7.3 ± 1.9	0.035
RBG (mmol/l)	11.3 ± 4.3	9.6 ± 3.4	0.005

Abbreviations: BMI, body mass index; HDLc, high-density lipoprotein cholesterol; LDLc, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride; HbA1c, Hemoglobin A1c; FBG, fasting blood glucose; RBG, random blood glucose.

we included Type II diabetic patients, both the Saudi nationals and expatriates, most of whom are working here in different capacities. Most of the participants 214 (67.3%) were non-Saudi and about one-third of our subjects were Saudi Arabian origin, whereas 52% of them belonged to nearby Middle Eastern countries and 14.7% from African origin. The recent studies in KSA, when examining the comorbidities in diabetic patients, have a similar multinational distribution of patients.^{20,21}

As per the general age group involved in T2DM, almost all our patients (95.4%) were 40 plus, with nearly 61% in 50–69-years of age group. In our study, for diabetic patients, the odds of having comorbidities are 7.33 and 20.14 times higher in the age group 60–69 years and 70–79 years, respectively, as the odds for age less than 40

years having comorbidities. This OR remained significant after adjusting other risk factors. We do not find any proper explanation for this high OR value in this age group. Nevertheless, the possible reason for this association could be that with increasing age, all other body systems weaken, and the person is prone to develop comorbidities. Moreover, in diabetic subjects with increasing age, diabetic complications also appear. Alzaheb & Altemani mentioned similar age group experiences of T2DM in Gulf countries and especially in SA.²² Chronicity of the disease is well associated with increasing age in diabetic patients and being a multi-disciplinary disease, mostly comorbidities are observed in varying proportions. We also found that dyslipidemia was associated with the duration of the DM. It can be explained that with increasing duration of T2DM, the insulin resistance increases, and that consequently influences carbohydrate and lipid metabolism.

We observed comorbid conditions among HTN, IHD, and varying levels of dyslipidemias. Hussain et al mentioned adverse prognostic effects on diabetics in the case of comorbidity of HTN & ICH.²³ Around 14% of the patients had coexisting obesity that further complicated the picture and SA among the countries having the highest prevalence of diabetes and obesity.²⁴ Our study observed that the majority of the obese patients had a comorbidity of HTN, Stroke, and IHD in varying proportions and this group had HbA1c levels >7, showing relatively poor diabetic control.

A high incidence of MI, associated dyslipidemias, and cerebrovascular accidents (CVA) were found in our patients. CVA is otherwise well correlated with DM and hypertension. A multicenter study revealed a clear association of high morbidity and mortality due to these coexisting disorders of T2DM.²⁵ As observed in many previous studies, we also noted the rising incidence of comorbidities in elderly patients and a positive association with the increasing age.^{26–28}

Microvascular complications involving end artery organs like selected neuropathies, retinopathy, and nephropathies are mostly associated with long-standing hyperglycemia, especially in poorly controlled T2DM. There is a clear-cut association of hypertension, long-standing T2DM with nephropathy, incidence getting as high as 60% in patients of T2DM with hypertension, while the incidence of retinopathy is higher in normotensive patients of long-standing T2DM.²⁹

Table 3 Logistic Regression Analysis of Risk Factor and Comorbidities in Diabetic Patients

Variables	Odds Ratio (95% Confidence Interval)	p-value	Adjusted Odds Ratio (95% Confidence Interval) ^a	p-value
Age Group				
< 40 years	1		1	
40–49 years	3.24 (0.87–12.06)	0.080	2.85 (0.59–13.65)	0.191
50–59 years	2.42 (0.75–7.81)	0.140	2.54 (0.60–10.64)	0.204
60–69 years	7.33 (2.02–26.66)	0.002	8.35 (1.59–43.97)	0.012
70–79 years	20.14 (3.38–120.22)	0.001	16.97 (2.05–140.2)	0.009
80+ years	5.14 (0.81–32.77)	0.083	3.85 (0.46–32.11)	0.212
Gender				
Male	1		1	
Female	1.06 (0.56–2.02)	0.852	0.70 (0.27–1.84)	0.467
Educational Level				
Primary	1		1	
Intermediate	0.64 (0.23–1.79)	0.396	0.76 (0.22–2.59)	0.661
High School	0.55 (0.22–1.52)	0.251	1.23 (0.34–4.44)	0.748
Graduate	0.35 (0.13–0.96)	0.040	0.65 (0.19–2.24)	0.494
Post graduate & above	0.36 (0.06–2.20)	0.269	0.51 (0.06–4.44)	0.540
Height	0.047 (0.002–1.199)	0.064	0.02 (0.00–2.75)	0.117
Weight	1.00 (0.99–1.03)	0.627	1.03 (1.00–1.05)	0.049
Systolic BP	1.00 (0.99–1.01)	0.991	0.99 (0.97–1.01)	0.328
Diastolic BP	0.99 (0.97–1.01)	0.989	1.00 (0.97–1.04)	0.863
HbA1c				
≤ 7	1		1	
> 7	0.68 (0.35–1.32)	0.256	0.50 (0.21–1.17)	0.111
Duration of DM				
≤ 10 years	1		1	
> 10 years	2.11 (1.15–3.89)	0.017	1.60 (0.71–3.62)	0.258
Dyslipidemia				
No	1		1	
Yes	1.17 (0.55–2.52)	0.680	1.33 (0.58–3.08)	0.500
Hypolipidemic Treatment				
No	1		1	
Yes	0.91 (0.47–1.77)	0.773	0.89 (0.43–1.84)	0.744

Notes: ^aOdds ratios were adjusted for age, gender, BP, weight, height and educational level, HbA1c, duration of diabetes, dyslipidemia and hypolipidemic treatment.

We compared multiple important variables in our cohort presenting with dyslipidemia with the T2DM patients do not have dyslipidemia. There was a significant difference in tests of the lipid profile series, ie, HDLc, LDLc, TC, and TG between the groups. The HbA1c, FBG, RBG values were significantly high in the dyslipidemic individuals. The probable reason for these differences could be the deranged metabolism of the lipids and carbohydrates among such patients. The T2DM is a metabolically complex situation, varied findings have been mentioned by Fung et al.³⁰

Our study provides a comparison of a multimorbid population of SA. Our study cohort belonged to SA and many neighboring countries having quite varied living setups. The health system in SA provides efficient care to the patients presenting with a chronic disorder like T2DM. Provision of better health care and awareness campaigns for the patients having a chronic disorder like T2DM is the key factor in better care and avoidance of multiple morbidities. However, there is also a need for an extensive move for public awareness regarding the importance of healthy living styles and regular physical activities so that this deadly but potentially preventable disease could be prevented.³¹

Table 4 Logistic Regression Analysis of Risk Factor and Dyslipidemia in Diabetic Patients

Variables	Odds Ratio (95% Confidence Interval)	p-value	Adjusted Odds Ratio (95% Confidence Interval) ^a	p-value
Age Group				
< 40 years	1		1	
40–49 years	0.60 (0.11–3.17)	0.548	0.62 (0.11–3.51)	0.588
50–59 years	1.32 (0.26–6.61)	0.740	1.53 (0.28–8.34)	0.624
60–69 years	1.02 (0.20–5.15)	0.980	1.33 (0.22–7.93)	0.751
70–79 years	0.71 (0.14–3.73)	0.685	0.83 (0.13–5.42)	0.843
80+ years	1.09 (0.13–9.12)	0.936	1.51 (0.16–14.78)	0.721
Gender				
Male	1		1	
Female	1.29 (0.67–2.48)	0.444	1.51 (0.63–3.64)	0.357
Educational Level				
Primary	1		1	
Intermediate	0.71 (0.28–1.76)	0.456	0.54 (0.20–1.49)	0.234
High School	0.83 (0.33–2.14)	0.705	0.63 (0.21–1.85)	0.396
Graduate	1.22 (0.44–3.34)	0.700	1.04 (0.34–3.21)	0.941
Post graduate & above	0.50 (0.09–2.93)	0.442	0.41 (0.06–2.79)	0.359
Height	0.53 (0.02–15.9)	0.716	1.12 (0.01–110.1)	0.961
Weight	1.02 (0.99–1.04)	0.184	1.02 (0.99–1.04)	0.200
Systolic BP	1.00 (0.99–1.02)	0.592	1.00 (0.99–1.02)	0.897
Diastolic BP	1.02 (0.99–1.04)	0.273	1.01 (0.98–1.04)	0.398
HbA1c				
≤ 7	1		1	
> 7	1.28 (0.68–2.41)	0.446	1.20 (0.60–2.41)	0.600
Duration of DM				
≤ 10 years	1		1	
10 years	9.94 (0.52–1.73)	0.852	0.82 (0.39–1.70)	0.587
Comorbidities				
No	1		1	
Yes	1.17 (0.55–2.52)	0.680	1.36 (0.59–3.11)	0.474

Notes: ^aOdds ratios were adjusted for age, gender, BP, weight, height and educational level, HbA1c, duration of diabetes and comorbidities.

Limitations

Like all the retrospective studies, we received data from the central registry and did not have direct exposure to the patients. A number of questions remained unanswered like the dietary and exercise habits and management associated problems faced by elderly diabetics.

Conclusion

Our results observed that the comorbidities were associated with increasing age, and common comorbidities were HTN, IHD, dyslipidemia.

Our study has highlighted the current trends in T2DM symptomatology and comorbidities. Efficient management and control by early screening and developing healthy

lifestyles in our patients can be very helpful in the prevention of all these highly morbid complications of this preventable disease.

Acknowledgments

The authors are thankful to all hospital staff that helped us in data collection.

Disclosure

The authors report no conflicts of interest in this work.

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