Original Article

Dyslipidemia and Its Components Across Body Mass Index Levels Among Type II Diabetic Patients in the West of Iran

Abstract

Background: The combination of dyslipidemia, obesity, and hyperglycemia can accelerate the progression to cardiovascular disease. Therefore, this study aimed to investigate dyslipidemia and its components across body mass index (BMI) levels among type II diabetic patients. **Methods:** The data for this cross-sectional study were extracted from the records of diabetic patients during 2014 to 2015. About 2,300 diabetic patients had been registered, and finally, the records of 2,110 patients which were fully completed were investigated. Dyslipidemia was defined based on the NCEP/ATP III classification of lipid profile. In order to investigate about nonlinear relationship between BMI and dyslipidemia, and its components, restricted cubic spline method was used. **Results:** The median age of patients was 55 (IQR = 14) years. 61.11% was females. The median of BMI, triglyceride, cholesterol, HDL-Chol, and LDL-Chol were 28.3 kg/m^2, 167, 193, 41, and 110 mg/dL in patients, respectively. The prevalence of dyslipidemia was 91.29% (95% CI: 90.05–92.54). Being overweight, diabetic patients were associated with an increased risk of dyslipidemia (OR = 1.87–2.78), hypertriglyceridemia (OR = 1.64; 95% CI: 1.29–2.09), and hypo-HDL (OR = 1.55; 95% CI: 1.20–2.01). Similarly, obesity also increased the risk of dyslipidemia (OR = 1.94; 95% CI: 1.28–2.95), hypertriglyceridemia (OR = 1.66; 95% CI: 1.29–2.12), and hypo-HDL (OR = 1.86; 95% CI: 1.41–2.43). The nonlinear dose–response relationship was associated with a significant increase then decrease in the risk of dyslipidemia, hypertriglyceridemia, and hypo-HDL in men and women as per 1 kg/m^2 increase in BMI. **Conclusions:** With regards to the result, we know that there is no linear relationship between lipid profiles and BMI, the bell-shape association between dyslipidemia, hypertriglyceridemia, and hypo-HDL needs to be further investigated in both diabetic and general population in men and women separately. In addition, for public health section, an appropriate intervention is of most important priorities.

Keywords: *Body mass index, diabetic, dyslipidemias, lipids*

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Introduction

Dyslipidemia is a major and primary risk factor for coronary heart disease (CHD) and the causal association between atherosclerotic cardiovascular disease (CVD) and dyslipidemia is well established.[1,2] It encompasses abnormal changes in lipid profile, i.e., change in the size and density and covers the broad spectrum of lipid abnormalities.[3] The hypercholesterolemia, elevations of triglyceride (TG) and low-density lipoprotein cholesterol (LDL-Chol) and low high-density lipoprotein cholesterol (HDL-Chol) levels are components of dyslipidemia.[4] In a meta-analysis study, the estimated prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-Chol, and low HDL-Chol levels in Iranian people were 41.6%, 46.0%, 35.5%, and 43.9%, respectively.[5] In addition, in Chinyere *et al*. study, the overall prevalence of dyslipidemia in the study population was 58.1%.[6]

In diabetes, the lipid abnormalities are most common and diabetic patients have elevated the risk of coronary artery disease associated with abnormal serum lipids. In Sarfraz *et al*. study, the prevalence of dyslipidemia in hyperglycemic patients was 95% (99.13% in males and 89.14% in females) and the majority of people suffered from high LDL (88%) followed by low HDL (71.5%).[7]

Obesity, by increasing the likelihood of lipid profile abnormalities, increases atherosclerotic cardiovascular disorders, hypertension, respiratory disorders, stroke,

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type II diabetes, and dyslipidemia.[8,9] Different studies have shown that obesity and fat were related to high plasma TG levels.[8,10] In Sheth *et al*. study, a significant linear association was observed between central obesity along with dyslipidemia in type II diabetic patients.[11]

In diabetes, the combination of dyslipidemia, obesity, and hyperglycemia can accelerate the progression to CVD.[12] Early detection and treatment of dyslipidemia in diabetic patients decreases the likelihood of major comorbidities resulted from such lipid abnormalities, such as CVD.[13] Therefore, this study aimed to investigate dyslipidemia and its components across body mass index (BMI) levels among type II diabetic patients.

Methods

Data source and data collection

This cross-sectional study was performed on records of diabetic patients registered in a diabetes clinic in Kermanshah province of Iran from April 2014 to March 2015. In this center, each person's information was recorded after the diagnosis of diabetes. Diabetic clinic in Kermanshah University of Medical Sciences is located in Taleghani hospital. After filling a standard questionnaire on demographic data, all referred patients will be visited by a trained nurse and then by a general physician for required measurements such as height, weight, blood pressure, and general physical examination. Patients will be referred to specialists based on a request by general physicians and on a regular basis for periodic checkup to neurologist, ophthalmologists, endocrinologists, nutritionist, and other subspecialties. The result of all medical treatments, interventions, and other medical advice will be recorded in the patient's files. In regards to biochemical specimens and laboratory data, a central laboratory located in the clinic is responsible to perform all biochemical exams. The necessary data were extracted from these records using a data collection form based on the records of diabetic patients. Data collection form included age, sex, family history, type of treatment, and laboratory information including lipid profiles (total cholesterol, triglycerides, and LDL and HDL cholesterol). During the study period, about 2,300 diabetic patients had been registered in the center and 190 patients with less than 80% of their information were excluded, and finally, the records of 2,110 patients which were fully completed, were investigated.

Anthropometric measurements and blood pressure in the diabetes center

Using the Seca mechanical column scale, the weight of all patients was measured while they had the least clothes. In order to measure the height, people stand beside the wall, without shoes, and using the tape measure with a precision about 1 cm, while the shoulders, heel, and hips were in contact with the wall. In addition, the systolic and diastolic blood pressure of all patients was measured twice using a calibrated OMRON blood pressure monitor and their mean were recorded.

Definitions

Dyslipidemia was defined as hypercholesterolemia, hypertriglyceridemia, hyper-LDL, and/or hypo-HDL based on the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) classification of lipid profile.[4] Hypercholesterolemia, hypertriglyceridemia, hyper-LDL, and hypo-HDL were defined as Chol ≥200, TG ≥150 mg/dL, LDL ≥130 mg/dL, and HDL <40 mg/dL in males, respectively. The corresponding values for women were <50 mg/dL in all lipid components. Hypertension was defined as systolic blood pressure ≥130 mmHg and diastolic ≥85 mmHg. In order to measure obesity, we calculated BMI by weight (kg) over square of height (m^2). According to the WHO guidelines, we classified the participants to underweight (BMI <18.5 kg/m^2), normal (18.5≤ BMI <25 kg/m^2), overweight (BMI ≥25 kg/m^2 and <30 kg/m^2) and obese (BMI ≥30 kg/m^2).[14]

Statistical analysis

In order to investigate about non-normal distribution of quantitative variables, we used Shapiro–Wilk test and in this case, median (interquartile range [IQR]) and count (percentage) were used to describe quantitative and qualitative variables, respectively. The Mann–Whitney test was used to compare the differences between median of age, weight, BMI, lipid profile, and blood pressure among males and females, and also the investigation the difference in prevalence of dyslipidemia, its components (hypercholesterolemia, hypertriglyceridemia, hyper-LDL, and hypo-HDL), hypertension and overweight/obesity among males and females were done by Chi-square test.

We implemented multiple imputations to impute values for weight with missing information (N = 1894, 95.8% of data) using age, sex, and height covariates. The adjusted prevalence was estimated by taking the predicted marginal. We used logistic regression to estimate the age, sex, family history and hypertension adjusted prevalence of dyslipidemia, hypercholesterolemia, hypertriglyceridemia, hyper-LDL, and hypo-HDL across BMI levels. The association between dyslipidemia and its component and BMI levels were examined using univariate and multivariate logistic regression. To investigate about a nonlinear relationship between BMI and dyslipidemia and its components, we used restricted cubic spline method. Different models with varying knots (nknot = 3–7) were fitted to evaluate a nonlinear relationship and the best model was chosen according to the AIC and BIC. Data were analyzed by the R software (version 3.4.1) and "lrm" [logistic regression model] function in "rms" [response-surface methods] package (2017). For all statistical tests, $P < 0.05$ was considered statistically significant.

Results

The median age of patients was 55 (IQR = 14) years (range from 21 to 93 years). 61.11% (1207) of patients were female (sex ratio: 1.57 women/men). Type of treatment in 76.88% of patients was oral (74.39% in males and 78.51% in females). About 58.08% of patients (1132 patients) reported a family history of diabetes. While the lipid profiles and BMI were significantly higher in women than in men, the mean of age, systolic, and diastolic blood pressure did not show any significant difference between two sexes. The distribution of age, weight, BMI, lipid profile and blood pressure by dyslipidemia among patients has been shown in Table 1.

Crude prevalence of dyslipidemia and its components

The prevalence of dyslipidemia was 91.29% (95% CI: 89.9–92.4) (86.33%, 95% CI: 83.7–88.58 for males, and 94.45%, 95% CI: 93–95.6 for females), and the prevalence of hypercholesterolemia, hypertriglyceridemia, hyper-LDL, and hypo-HDL was 43.94% (95% CI: 41.75–46.13), 58.44% (95% CI: 56.26–60.61), 28.68% (95% CI: 26.64–30.72), and 70.55% (95% CI: 68.53–72.57), respectively. Also, the prevalence of dyslipidemia and all its components in females was significantly higher than males. The prevalence of dyslipidemia was 91.16% for <40-year patients, 92.55% for 40–60 year, and 88.43% for ≥60-year patients [Table 2].

Adjusted prevalence of dyslipidemia and its components

The highest adjusted prevalence of dyslipidemia (by age, gender, and family history of hypertension) was among those who were overweight (92.8%). The prevalence of dyslipidemia, hypercholesterolemia, hypertriglyceridemia, and hyper-LDL are higher among patients who are underweight compared with normal BMI patients, although they were statistically nonsignificant [Table 3].

Association of dyslipidemia and its components with BMI

Using univariate and multivariate logistic regression, there was no significant association between

Table 1: Distribution of age, weight, BMI, lipid profile, and blood pressure by dyslipidemia among diabetic patients (2014-2015)

Dyslipidemia	Median (Q1-Q3)			*P**
	Yes (*n*=1,805)	No (*n*=172)	Total (*n*=1,977)	
Age (year)	55 (47-62)	57 (50-64)	55 (48-62)	0.01
Weight (kg)	73 (65-82)	71 (62-81)	73 (65-82)	0.18
BMI (kg/m^2)	28.3 (25.5-31.2)	26.7 (23.3-30.7)	28.3 (25.4-31.2)	<0.001
Triglyceride (mg/dL)	176.5 (128-247)	101 (84-122)	167 (120-237)	<0.001
Cholesterol (mg/dL)	196 (165-230)	167 (145-186)	193 (162-227)	<0.001
HDL-Chol (mg/dL)	40 (34-46.7)	52 (45-58)	41 (34-48)	<0.001
LDL-Chol (mg/dL)	113 (88-136)	91.5 (72-110)	110 (86-134)	<0.001
Systolic-BP (mmHg)	135 (120-150)	130 (120-150)	135 (120-150)	0.26
Diastolic-BP (mmHg)	80 (70-90)	80 (70-90)	80 (70-90)	0.06

*Based on Mann-Whitney test

Table 2: The prevalence of overweight/obesity, hypercholesterolemia, hypertriglyceridemia, hyper-LDL, hypo-HDL, dyslipidemia and hypertension by sex and age group among diabetic patients (2014-2015)

Variable	*n* (%)						
	Overweight/ obesity	Hypercholesterolemia	Hypertriglyceridemia	Hyper-LDL-Chol	Hypo-HDL-Chol	Dyslipidemia	Hypertension
Sex							
Male	513 (69.05)	284 (37.12)	430 (56.21)	186 (25.48)	456 (60)	663 (86.33)	207 (26.95)
Female	975 (83.19)	582 (48.26)	721 (59.78)	357 (30.75)	920 (77.25)	1140 (94.45)	312 (25.85)
Total	1488 (77.7)	866 (43.94)	1151 (58.40)	543 (28.71)	1376 (70.5)	1803 (91.29)	519 (26.28)
*P**	<0.001	<0.001	0.04	0.01	<0.001	<0.001	0.58
Age group							
<40 year	137 (77.84)	85 (47.22)	110 (60.77)	52 (29.71)	135 (74.59)	165 (91.16)	28 (15.47)
40-60 year	936 (78.99)	545 (44.64)	745 (61.07)	334 (28.55)	862 (71.30)	1131 (92.55)	311 (25.45)
≥60 year	407 (74.82)	231 (41.25)	293 (52.32)	154 (28.68)	372 (67.51)	497 (88.43)	175 (31.14)
Total	1480 (77.69)	861 (43.91)	1148 (58.54)	540 (28.69)	1369 (70.5)	1793 (91.25)	514 (26.16)
*P**	0.09	0.26	0.002	0.95	0.12	0.01	<0.001

Overweight/obesity was defined as BMI ≥25; hypercholesterolemia was defined as Chol ≥200; hypertriglyceridemia was defined as TG ≥150 mg/dL; hyper-LDL was defined as LDL ≥130 mg/dL; hypo-HDL was defined as HDL <40 mg/dL in male and <50 mg/dL in female; and hypertension was defined as systolic ≥130 and Diastolic ≥85. *Based on Chi-square test

hypercholesterolemia and hyper-LDL with BMI levels ($P > 0.05$). Being overweight, diabetic patients were associated with an increased risk of dyslipidemia (OR = 1.87; 95% CI: 1.26–2.78), hypertriglyceridemia (OR = 1.64; 95% CI: 1.29–2.09), and hypo-HDL (OR = 1.55; 95% CI: 1.20–2.01). Similarly, obesity also increased the risk of dyslipidemia (OR = 1.94; 95% CI: 1.28–2.95), hypertriglyceridemia (OR = 1.66; 95% CI: 1.29–2.12), and hypo-HDL (OR = 1.86; 95% CI: 1.41–2.43). Although nonstatistically significantly, the risk of dyslipidemia and hypo-HDL and hypertriglyceridemia among overweight diabetic patients were higher than those who were obese, even after adjustment for age, gender, family history, and hypertension [Table 4].

Table 3: Adjusted prevalence of dyslipidemia and it's component by BMI among diabetic patients (2014-2015)

Variable	BMI Group	Prevalence (%)[a]	95% CI
Dyslipidemia	Underweight	88.54	73.18-100
	Normal	88.97	86.05-91.90
	Overweight	92.87	91.10-94.64
	Obese	92	89.73-94.27
Hypercholesterolemia	Underweight	44.55	16.29-72.81
	Normal	45.27	40.26-50.28
	Overweight	43.20	39.73-46.68
	Obese	44.20	40.33-48.07
Hypertriglyceridemia	Underweight	52.86	24.71-81.01
	Normal	51.10	46.09-56.10
	Overweight	61.91	58.51-65.30
	Obese	60.80	56.94-64.66
Hyper-LDL	Underweight	34.90	7.60-62.20
	Normal	29.77	25-34.54
	Overweight	29.36	26.07-32.66
	Obese	28.05	24.49-31.62
Hypo-HDL	Underweight	54.91	27.33-82.50
	Normal	65.65	60.98-70.32
	Overweight	72.24	69.14-75.34
	Obese	73.04	69.48-76.61

[a]Adjusted for age, sex, family history, and hypertension

Dose–response association between dyslipidemia, hypertriglyceridemia, and hypo-HDL with BMI

In order to investigate about nonlinear relationship between BMI level and dyslipidemia, hypertriglyceridemia, and hypo-HDL in each sex groups, restricted cubic spline method was used. In general, there was a significant nonlinear association between the above-mentioned outcomes and level of BMI in both men and women (P for nonlinearity <0.05). Accordingly, after adjustment for age, family history of diabetes and hypertension, the nonlinear association between BMI and the risk of dyslipidemia in men and women changed significantly by an increase of 1 kg/m^2 in BMI. The reference group for the odds ratio was the median of the normal range for BMI (BMI = 23.5 kg/m^2).

The odds ratio for dyslipidemia risks indicated a significant decrease, and then increase and eventually decrease in the risk of dyslipidemia along with BMI increase in men and women [Figure 1]. Also, the odds ratio related

Table 4: The association between dyslipidemia and its components with BMI levels among diabetic patients using logistic regression

Model		Univariate			Model A			Model B		
Variable	BMI	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Dyslipidemia	Underweight	0.71	0.15-3.36	0.67	0.76	0.15-3.65	0.73	0.86	0.17-4.19	0.85
	Normal	1	-	-	1	-	-	1	-	-
	Overweight	1.87	1.26-2.78	0.002	1.67	1.12-2.50	0.01	1.62	1.07-2.44	0.02
	Obese	1.94	1.28-2.95	0.002	1.45	0.94-2.24	0.09	1.43	0.91-2.24	0.11
Hypercholesterolemia	Underweight	0.97	0.30-3.11	0.96	0.99	0.30-3.21	0.99	0.95	0.29-3.10	0.94
	Normal	1	-	-	1	-	-	1	-	-
	Overweight	1.04	0.82-1.32	0.73	0.98	0.77-1.25	0.91	0.91	0.71-1.17	0.47
	Obese	1.15	0.90-1.48	0.24	1.002	0.77-1.29	0.98	0.93	0.71-1.22	0.63
Hypertriglyceridemia	Underweight	1.02	0.32-3.24	0.96	0.96	0.30-3.07	0.95	1.001	0.31-3.20	0.99
	Normal	1	-	-	1	-	-	1	-	-
	Overweight	1.64	1.29-2.09	<0.001	1.60	1.25-2.03	<0.001	1.55	1.21-1.99	0.001
	Obese	1.66	1.29-2.13	<0.001	1.57	1.21-2.03	<0.001	1.46	1.12-1.91	0.005
Hyper-LDL	Underweight	1.26	0.37-4.27	0.70	1.28	0.37-4.37	0.68	1.25	0.36-4.27	0.71
	Normal	1	-	-	1	-	-	1	-	-
	Overweight	1.03	0.79-1.35	0.80	0.99	0.76-1.30	0.97	0.97	0.73-1.28	0.85
	Obese	1.03	0.78-1.35	0.83	0.92	0.69-1.23	0.61	0.90	0.67-1.21	0.51
Hypo-HDL	Underweight	0.60	0.19-1.90	0.39	0.64	0.20-2.08	0.46	0.63	0.19-2.04	0.44
	Normal	1	-	-	1	-	-	1	-	-
	Overweight	1.55	1.20-2.01	0.001	1.43	1.10-1.85	0.006	1.37	1.05-1.79	0.01
	Obese	1.86	1.41-2.43	<0.001	1.51	1.14-1.99	0.004	1.43	1.07-1.91	0.01

Model A=Adjusted for age and sex; Model B=Adjusted for age, sex, family history and hypertension; OR=Odds ratio; CI=Confidence interval

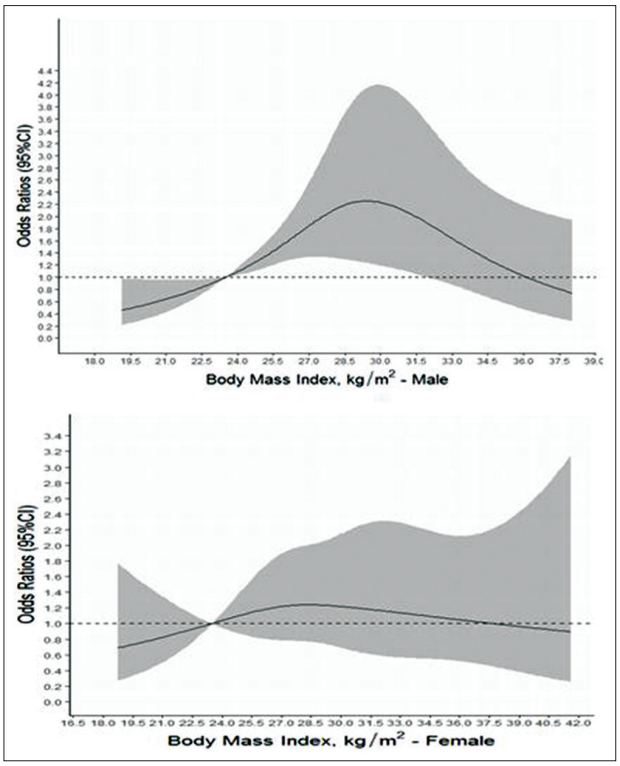

Figure 1: The dose–response relationship of BMI and dyslipidemia by sex based on the restricted cubic spline model (four knots were located at the 21.6, 26.5, 29.9, and 36.4 kg/m²); solid line represents the fitted nonlinear trend and colored area represent the 95% confidence interval

to hypertriglyceridemia and hypo-HDL was similar to dyslipidemia.

Discussion

There are several social, behavioral, and public health factors contributing to global increase of diabetes mellitus. According to the report from The Institute for Health Metrics and Evaluation (IHME), in 2015, diabetes contributed to 3.77% (3.24%–4.35%) of the total burden of diabetes in Iran with an annual change of 3.54% from 1990 to 2015.[15] While contribution of hypercholesterolemia to ischemic heart disease and stroke has not changed over the last 25 years (53.2% and 11.4% in 2015, respectively), because of increase in the burden of ischemic heart disease and stroke, the contribution of dyslipidemia to the total burden has increased over the last decades.[15] According to our results, from a total of patients with diabetes who are registered in the diabetic center, 77.7% are suffering from overweight/obesity and 91.29% from dyslipidemia. In addition, dyslipidemia, hypo-HDL, and hypertriglyceridemia had a non-linear dose–response relationship with BMI.

Our report regarding the prevalence of different components of dyslipidemia in patients suffering from diabetes is much higher from reports from elsewhere,[11,16] but comparable to report from Rao *et al*. 2016.[17] In fact, the increase in the prevalence of lipid profile abnormality in diabetic patients is associated with poor outcome and one of the main goals for providing the health care for diabetic patients is to control dyslipidemia.[18] Our study focused on newly diagnosed patients; therefore, it is assumed that these patients had not been under the restrict control of lipid-lowering diets and treatments as well as health promotion programs. In fact, one may expect to see an acceptable lipid profile for diabetic patients after registration and implementation of health interventions. Research from elsewhere confirmed that the decrease in lipid profile abnormality can effectively decrease the death from CVD.[19] In addition, an increase in lipid profile abnormality is directly associated with long-term blood glucose control measured by HbA1C.

Our findings revealed that there is a nonlinear relationship between triglyceride, HDL-Chol, and overall dyslipidemia with overweight and obesity. There is a gradual increase in the likelihood of overall dyslipidemia, hypertriglyceridemia, and hypo-HDL-Chol by increase in BMI till 27–29 kg/m^2 and a gradual decrease afterward in both sexes (there is no decrease in the likelihood of hypo-HDL-Chol by an increase in BMI among women). Our findings are not in accordance with Rao W *et al*. (2016), as their results show a gradual increase with any plateau even after BMI of 32 kg/m^2.[17] Such nonlinear association, although noncausal, is in much interest of public health policymakers. But, there is no justification for the bell-shaped relationship between such lipid profiles and BMI.

The pathophysiology behind the obesity paradox might explain some of these reverse association between diabetes mellitus and dyslipidemia, hypo-HDL and hypertriglyceridemia.[20,21] Hashemi *et al*. also found that the hazard of CHD decreases with hypo-HDL in premenopausal women in the Iranian population. It might be because of the different percentages of different apo-lipoproteins in some populations.[22]

It might also be important to investigate the association between peripheral and visceral fat and dyslipidemia. Besides, nonsignificant, lower level of lipid profiles in diabetic obese patients compared to those who were overweight might be due to implementation of more restrict health promotion and treatment interventions in such patients even before registration in diabetes centers.

Our study has some limitations. First, our study has a cross-sectional design and therefore any relationship cannot guarantee the causal association. However, most of the studied risk factors are behavioral and therefore lasting for quite a long time and stable. In addition, due to a central laboratory that located in the clinic for the biochemical specimens and laboratory data and perform all biochemical exams, it can be said that the validity of information is

almost the same for all patients. Second, although our laboratory results are assumed to be on registration, this does not mean all patients were in the same stage of diagnosis. The center is a referral one and therefore patients may refer after some period of treatment and care by other healthcare providers. Third, we had no information about some of the important laboratory results such as HbA1C. This factor is an additional criterion for the quality of care provided to diabetic patients. Estimation of the relationship between obesity and lipid profiles adjusted by the level of HbA1C could provide a more in-depth feature of such association. We did not have any information about the body composition of overweight/obese patients and also detailed components of lipids. On the other hand, given the referral center, the presence of trained nurses, general physicians, specialists and central laboratory at the center as well as the high sample size of the study, it may be possible to claim that the study results have external validity.

Conclusions

With regards to fast change in lifestyle in developing countries toward western lifestyle which includes low physical activity, high protein and fat diet as well as an increase in prevalence of smoking and other behavioral risk factors, it is estimated that the prevalence of diabetes, overweight/obesity, and abnormal lipid profile will continue to increase in future. Synergistic effect of all these factors together can increase mortality and morbidity. Therefore, for public health section, an appropriate intervention is of most important priorities. Although, we know that there is no linear relationship between lipid profiles and BMI, the bell-shape association between dyslipidemia, hypertriglyceridemia, and hypo-HDL need to be further investigated in both diabetic and general population in men and women separately.

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Conflicts of interest

There are no conflicts of interest.

Ethical approval

All procedures performed in studies involving data extracted from existing information were in accordance with the ethical standards of the forensic medicine organization and Kermanshah University of Medical Sciences research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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