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GENDER-RELATED DIFFERENCES IN LIPID PROFILE AND ATHEROGENIC INDICES IN PATIENTS WITH TYPE 2 DIABETES MELLITUS IN JEDDAH, SAUDI ARABIA

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ABSTRACT
Coronary artery disease (CAD) is the epidemic of modern civilization in which dyslipidemia contributes significantly to its pathogenesis. Dyslipidemia is elevation of serum total cholesterol (TC), triglycerides (TG), or both, or low high-density lipoprotein cholesterol (HDL-c) level that contributes to the development of atherosclerosis, which is a hallmark of diabetes. The patients with diabetes have a type of dyslipidemia that is related to insulin resistance. The aim of this study was to verify and document, role and correlation of lipid disorders (dyslipidemia) and hyperglycemia in the pace of progress and appearance of cardiovascular diseases in patients with type 2 diabetes mellitus (T2 DM). This retrospective, cross-sectional study examined a total of 150 T2 DM patients of which 72 were males and 78 were females and 25 – 65 years of age. Total cholesterol were more than 200mg/dl in more than 51% of studied patients, while HDL-c less than 40 mg/dl in 67.3% patients, whereas LDL-c level greater than 100mg/dl in 64.0% of patients. Triglyceride level was higher than 150mg/dl in 65.3% of all patients. The results revealed that female patients had higher serum total cholesterol and lower serum HDL-c in comparison with male patients, whereas LDL-c and TG were significantly increased compared with male patients. AIP of both male and female patients were higher than normal value. CRR and AC of both genders were greater than normal value, although atherogenic indices of female were higher than those for male. Thus, T2 DM diabetic females have a more adverse atherogenic profile as compared to male. The monitoring of the lipid profile of newly diagnosed female T2 DM patients is warranted so that early intervention is possible to reduce cardiovascular complications and mortality.

KEYWORDS: Diabetes, lipid profile, dyslipidemia, atherogenic indices, cardiovascular risk, gender.

INTRODUCTION

Type 2 diabetes mellitus (T2 DM) is the commonest form of diabetes constituting 90% of the diabetic population. Diabetes is a global endemic with rapidly increasing prevalence in both developed and developing countries and there is a high risk of cardiovascular disease (CVD) in people with T2 DM[1]. Saudi Arabia ranks seventh worldwide and the first in the Gulf in terms of diabetes rates. Over 25% of the adult population is suffering from diabetes mellitus (DM) and that figure is expected to be more than double by 2030[2]. The burden of DM and CVD is on the rise in all developing countries. In Saudi Arabia, CVD accounts for over 22% of deaths each year, and other estimates showed over 42% of all deaths are attributed to CVD in Saudi Arabia[3]. The risk of developing CVD is 2-4 times higher among people with diabetes as compared to people without diabetes [4]. Mortality due to CVDs account for 65-75% of all deaths among DM patients[5]. Globally, several studies have examined gender-based differences in the distribution of cardiovascular risk factors and risk of CVD among patients with diabetes, which indicate excess risk factor clustering among females, thus rendering them at an increased risk of CVD and CVD mortality as compared to men[6-8]. The reported magnitudes of the diabetes-related coronary heart disease (CHD) in men and women vary widely between different studies [9]. Although the mechanism underlying this excessive CHD risk in women with T2 DM has not been fully elucidated yet, several hypotheses suggest that diabetes per se may be a stronger CHD risk factor in the female gender, determining a more unfavorable CHD risk profile [10-12]. This could lead to more complex risk factors and/or disease management in women with T2 DM as compared to men.

The cause of greater relative risk of CHD in diabetic women still remains incompletely understood, but several explanations have been offered. First, adverse changes induced by T2 DM in some cardiovascular risk factors, such as high-density lipoprotein (HDL-c) cholesterol, triglycerides (TG) low-density lipoprotein (LDL) particle size and blood pressure have been found to be more pronounced in women than men[9,13]. In addition, DM in women may interfere with protective mechanisms in the vascular wall and thereby lead to enhanced atherogenesis. Cardiovascular disease is a multifactorial condition and major risk factors (i.e., obesity, hypertension, and dyslipidemia) have all demonstrated to contribute to its occurrence[12]. Diabetic dyslipidemia is characterized by [14]:

i) High triglyceride (TG) concentrations
ii) Low high-density lipoprotein cholesterol (HDL-c) concentrations
iii) Increased low-density lipoprotein cholesterol (LDL-c) concentrations

An early intervention to normalize circulating lipids has been shown to reduce cardiovascular complications and mortality[9,15]. The atherogenic index (AI) is an emerging index that is fulfilling the criteria to be used as a stand-alone index for cardiac risk stratification[16]. Lipid profile and atherogenic index have been shown to be significant predictors for metabolic abnormalities including dyslipidemia, atherosclerosis, hypertension and cardiovascular disease. Changes in the levels of lipids make the individuals more inclined to develop these atherosclerotic cardiovascular diseases and endothelial dysfunction[17,18]. Atherogenic Index of Plasma (AIP) is based on two important parameters TG and HDL-c, both of which are independent risk factors for CAD [19]. Cardiac Risk Ratio (CRR) calculated as (TC/HDL-c) is another fraction which involves independent risk factors for CAD [20]. Atherogenic Coefficient (AC) calculated as {(TC - HDL-c)/HDL-c} is yet another ratio relying on the significance of HDL-c in predicting the risk of CAD [21]. These are the calculated fractions which can be used in the critical setting for assessing the risk of cardiovascular disease beyond the routinely done lipid profile.

The purpose of the present study was to evaluate the effect sex on lipid abnormalities and also on the prevalence of cardiovascular risk factors among patients with type 2 diabetes attending King Abdulaziz University health clinic, Jeddah (Saudi Arabia).

MATERIALS & METHODS

A total of 150 patients (72 males and 78 females) with T2 DM were enrolled in this retrospective, cross-sectional study. The age limits was 25 to 64 years. The diagnosis of DM was based on the American Diabetes Association criteria for type 2 DM (fasting plasma glucose level higher than 126 mg/dl and/or glucose level exceeding 200mg/dl at 2 hours in the 75 g oral glucose tolerance test). For each patient a questionnaire including epidemiological data such as age, gender, occupation, duration of DM, hypertension and history of smoking was completed. Information was obtained about demographic characteristics and medical history of all patients concerning their age, sex and duration of DM, hypertension, smoking, medications, and co-morbidities. Patients' drug history such as taking anti-hypertensive and lipid lowering drugs was not considered as a restriction for inclusion.

After eliciting history, detailed physical and systemic examination anthropometric measurement were done. Patients with elevated serum creatinine (1.3 mg/dl for women and 1.5 mg/dl for men), clinical evidence of congestive heart failure (CHF) or liver insufficiency, poor blood glucose control, and systemic or local infections were excluded. Informed consent was sought and obtained from individuals before enrolment into the study. The study protocol was approved by institutional ethical committee.

Venous blood samples were collected from each patient after at least 10 hours fasting into centrifuge tubes. Serum was separated by centrifugation at 3000 rpm for 15 minutes. The sera were analyzed for total cholesterol (TC), triglycerides (TG), and high density lipoprotein cholesterol (HDL-c) using an autoanalyzer (Roche Modular P-800, Germany). Serum low density lipoprotein cholesterol (LDL-c) was calculated by Friedewald's formulas shown below [22,23]:

$$LDL\text{-}c = TC - [(HDL\text{-}c) + (TG/5)]$$

The atherogenic indices were calculated as follows [22-26]:

Atherogenic Index of Plasma (AIP) = log (TG / HDL-c)

Cardiac Risk Ratio (CRR) = TC / HDL-c

Atherogenic Coefficient (AC) = (TC – HDL-c) / HDL-c

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS 15.0 for windows). Means are presented as values ± standard deviation. Student's t-test was used to compare quantitative data between two groups. Analysis of variance (ANOVA) was used as appropriate. P value < 0.05 was considered statistically significant.

RESULTS

A total 150 patients with T2 DM were recruited for the study comprising of 72 males and 78 females to assess the alteration in lipid profile and atherogenic indices. The distribution of patients according to age groups is illustrated in Table 1 which revealed that there was highly significant difference in the prevalence of diabetes mellitus type 2 among different age groups.

The prevalence of different types of dyslipidemia in all of the patients and in males and females are shown in Table 2. For serum lipid reference level, National Cholesterol Education Programme (NCEP) Adult Treatment Panel (ATP III) guideline was referred[27,28]. According to NCEP-ATP III guideline, hypercholesterolemia is defined as TC > 200 mg/dl, high LDL-c when value is >100 mg/dl, hypertriglyceridemia as TG >150 mg/dl and low HDL-c when value is <40 mg/dl. Dyslipidemia was defined by the presence of one or more than one abnormal serum lipid concentration. In our study, total cholesterol were more than 200 mg/dl in 77 (51.3%) and HDL-c were less than 40 mg/dl in 101 (67.3%) of all patients. LDL level higher than 100 mg/dl were present in 96 (64%) , while 98 (65.3%) of all patients had triglyceride level higher than 150 mg/dl.

TABLE 1: Distribution of diabetic patients according to age range

Age range (years)	Number of patients	p-value
25 - 34	8	
35 - 44	33	
45 - 54	56	p = 0.002*
55 - 64	53	
Total	150	

* Highly significant

TABLE 2: Pattern of dyslipidemia in studied diabetic patients

Lipid type		All patients	Female	Male	p-value
TC	Normal	48.7%	41.4%	56.4%	
	High	51.3%	58.6%	43.6%	0.041**
TG	Normal	34.7%	34.3%	46.7%	
	High	65.3%	65.6%	53.3%	0.312*
HDL	Normal	32.7%	29.8%	56.5%	
	Low	67.3%	70.1%	43.5%	0.001***
LDL	Normal	36.0%	28.1%	42.2%	
	High	64.0%	71.9%	57.8%	0.083*

*Not significant ** Significant ***Highly significant

Table 3 shows the mean ±SD values of lipid profiles (mg/dl) of males and females. The results in Table 3 revealed that diabetic females had higher level of TC (211.44 mg/dl vs. 192.56 mg/dl) ($p < 0.05$) and lower level of HDL-c (38.92 mg/dl vs. 46.42 mg/dl) ($p < 0.01$) compared to matched male patients, whereas LDL-c and TG were significantly increased in females (134.80 mg/dl, 71.9%; 181.40 mg/dl, 65.6%) in comparison to males (114.10 mg/dl, 57.8% ; 169.27 mg/dl, 53.3%) respectively ($p < 0.05$).

TABLE 3: Gender differences in terms of lipid profile

Gender	Mean conc. of TC (mg/dl)	Mean conc. of TG (mg/dl)	Mean conc. of HDL (mg/dl)	Mean conc. of LDL (mg/dl)
Male	192.56 ± 8.65	169.27 ± 12.89	46.42 ± 8.53	114.10 ± 9.16
Female	211.44 ± 14.39	181.40 ± 13.50	38.92 ± 6.72	134.80 ± 11.81

TABLE 4: Comparison of Atherogenic Index of Plasma (AIP) of both genders

Gender	No. of patients	Mean of AIP	SD	p-value
Male	74	0.605	0.051	
Female	76	0.649	0.063	p = 0.383*
Baseline value		0.214		p = 0.000**

*Not significant, ** highly significant

TABLE 5: Comparison of AIP values for diabetic patients according to duration of disease

Duration of disease (years)	No. of patients	Mean values of AIP	SD	p-value
1 - 4	88	0.589	0.048	
5 - 8	33	0.625	0.061	(ANOVA)
9 -12	19	0.632	0.042	p = 0.412*
13-16	10	0.643	0.046	

***Not significant**

TABLE 6: Atherogenic indices for both genders

Atherogenic indices	Male	Female	Baseline value	p-value
Cardiac risk ratio (CRR)	4.726*	5.038*	4.494**	p > 0.05* N.S
Atherigenic coefficient (AC)	3.726 *	4.038*	3.494**	p > 0.05** N.S
Atherogenic index of plasma (AIP)	0.605*	0.649*	0.214***	p= 0.000*** H.S

N.S – Not significant, H.S - Highly significant

Table 4 shows the comparison of AIP values between male and female diabetic patients. The results revealed that AIP value of female was greater than that for male, although statistically no significant difference. There was a highly significant difference in mean percent of AIP for both male and female (0.605; 0.649) respectively in comparison with baseline value[22,29] of (0.214) at p= 0.000.

Table 5 shows the comparison of AIP values in diabetic patients according to duration of disease. The mean percent of AIP were increased with progression in duration of disease (Table 5). But no significant difference ($p > 0.05$) was observed in mean percent of AIP according to duration of disease.

The values of atherogenic indices (CRR, AC and AIP) for both gender are presented in Table 6. All these values were higher than the baseline value. The results revealed that there were a highly significant difference in percent of AIP of both gender comparing with baseline value, while no significant difference was observed in mean percent of

cardiac risk ratio (CRR) and atherogenic coefficient (AC) of both gender in comparison with baseline value. In spite of the fact that the mean percent of CRR and AC exceed the baseline value, these results are statistically non-significant.

DISCUSSION

Diabetes mellitus is associated with a greater incidence of morbidity and mortality from cardiovascular disease, the risk of which becomes substantially elevated when complications develop. Detection and treatment of dyslipidemia in diabetes is one major step towards reducing the risk of CVD associated with diabetes. Though the pathogenesis of CVD in diabetes is multifactorial, dyslipidemia is found to be a powerful risk factor[13]. In diabetes, long-term hyperglycemia causes generalized vascular endothelial damage, which reduces functional lipoprotein lipase, leading to increase in triglycerides and a decrease in HDL. Increased levels of VLDL, triglycerides and LDL cholesterol mediate the progression of atherosclerosis[30]. Lipid ratios and AIP have been reported to indicate atherogenic dyslipidemia. A number of lipid related parameters have been used to predict the risk of CAD. According to Grover *et al.* [31], either the ratio of LDL-c / HDL-c or TG / HDL-c is the best related predictor of future cardiovascular events. Later, TG / HDL-c was shown to be a more accurate predictor to CHD. The logarithmically transformed ratio of plasma TG / HDL-c (AIP) correlated closely with the LDL-c particle size and could serve as an indicator of the atherogenic lipoprotein phenotype[32]. Tan *et al.* [33] compared the results of AIP analysis with those of a TG / HDL-c ratio analysis used in another study [34]. The p-values for AIP were consistently lower than those for TG / HDL-c. An AIP of < 0.11 is considered as low risk, 0.11 – 0.21 intermediate risk and > 0.21 as high risk [28]. AIP has been used as a significant and independent predictor of CHD [33]. Type 2 diabetes risk increases with age. The incidence of diabetes increases with age until about age 65 years, after which both incidence and prevalence seem to level off [35]. In our study, the prevalence of diabetes was highest in 45-54 age group (Table 1) and the lowest in the 25-34 age group. This finding was consistent with the observations reported by other researchers [36,37]. One study found the peak incidence of diabetes in Nigeria and Tanzania to be recorded after age 45-50, and also to increase with age, similar to the findings in this study. In Nigeria, the risk of diabetes increases 3-4 times after the age of 44 years [38]. Globally, the greatest numbers of people with diabetes are aged between 40 and 59 years [39], as observed in this study. The worsening of insulin resistance with age, increased inactivity and longevity of diabetes patients due to improved care were the reasons given for the rising prevalence of T2 DM with age [36,40].

The commonest lipid abnormality noted in this study was low HDL-c (67.3%) followed by hypertriglyceridemia (65.3%) (Table 2). This is the common trend in majority of type 2 DM patients. The importance of this parameter stems from the growing evidence that reduced HDL-c is a powerful predictor of premature CHD[30,41]. HDL-c acts by enhancing the removal of cholesterol from the peripheral tissues and so reduces the body's cholesterol pool. Type 2 DM was usually associated with low plasma levels of HDL-c. Low HDL-c concentrations are often accompanied by elevated TG levels as seen in this study and others [41-44], and this combination has been strongly associated with an increase in the risk of coronary heart disease (CHD) [24,28,30,31,45]. The relative insulin deficiency that occurs in type 2 diabetes impairs the action of lipoprotein lipase and results in lower HDL-c levels and higher TG levels, which may improve with improved glycemic control [46]. Thus, HDL hypocholesterolemia in type 2 diabetes patients is mainly due to insulin resistance-linked lipoprotein lipase deficiency [47]. Type 2 DM is also associated with low plasma level of HDL-c. It is well documented that reduced HDL-c levels are associated with an increased risk of coronary heart disease [22,24]. Clinical studies showed that increasing plasma HDL-c concentration decreases cardiovascular risk, and vice versa. High HDL-c exerts a protective effect by decreasing the rate of entry of cholesterol into the cell via LDL-c and increasing the rate of cholesterol release from the cell by enhancing reverse cholesterol transport by scavenging excess cholesterol from peripheral tissues, and inhibiting the oxidation of LDL-c as well as the atherogenic effects of oxidized LDL-c by virtue of its antioxidant and anti-inflammatory property[24,48]. In the present study, the HDL-c levels below 40 mg/dl were present in 70.1% and 43.5% of the female and male respectively [Table 2]. This finding is in agreement with the previous studies which showed that reduced HDL-c were more common in females than males [9,13,22,42,49]. Studies showed that for each milligram-per-deciliter increase in HDL, there was ~2% decrease in CHD risk in men, but a 3% decrease in women [50,51].

The levels of TC, TG, and LDL-c were significantly higher in female patients as compared to male type 2 diabetic patients [Table 3]. Previous studies indicated that dyslipidemia was more marked in women than men [9,13,22,42.52]. Hyperlipidemia in females may be attributed to the effects of sex hormones on body fat distribution, which leads to differences in altered lipoproteins [9,22,53].

It has been reported that type 2 DM increased the risk of CHD more markedly in women than in men [9,54,55]. A diverse changes induced by T2 DM in some cardiovascular risk factors such as HDL-c, TC, TG, LDL particle size and blood pressure have been found to be more pronounced in women than in men [9,13,54 ,55]. Juutilainen et al. in their study of 1059 type 2 diabetic subjects aged between 45-65 years found considerably higher diabetes related relative risk factor for a major CHD event in diabetic women than in men [55].

A strong clustering of risk factors for coronary artery disease has been observed in diabetic subjects [56,57]. In this study, clustering of CAD risk factors such as higher level of total cholesterol, TG, LDL-c, and abnormal HDL-c levels were more pronounced in women compared to men. There are many theories proposed to account for the excess risk from diabetes in women. These include differences in coagulation, the pattern of obesity between men and women, and possible role for hyperinsulinemia. Diabetes may also alter estrogen related protective mechanisms. Furthermore, low grade inflammation may have a greater role in perturbing insulin action in women or inflammatory factors may interact with female sex hormones, resulting in a decrease of protective effects of estrogens on body fat distribution and insulin action

[13,49,58]. The Atherogenic Index of Plasma (AIP) is being used by some practitioners as a significant predictor of atherosclerosis. The AIP is a mathematical relationship between TG and HDL-c and an additional index for assessing cardiovascular (CV) risk factors[59]. The association of TGs and HDL-c in this simple ratio reflects the balance between risk and protective lipoprotein forces. The AIP of male and female in this study was observed to be significantly increased when compared with baseline value (Table 4). Our finding was similar to the results of different investigators [22,60,61]. It has been suggested that AIP values of -0.3 to 0.1 are associated with low, 0.1 to 0.24 with medium and > 0.24 with high Cardiovascular risk [26,62]. Different investigators concluded that AIP has a better prediction of coronary artery disease than individual lipids, and / or TC/HDL-c, LDL-c/HDL-c ratios [24,26,28,62]. This is because AIP is positively correlated with the fractional esterification rate of HDL (FERHDL), and also inversely correlated with LDL particle size. FERHDL predict size in HDL and LDL, which in turn predicts the risk of coronary heart disease. The simultaneous use of TG and HDL as AIP is useful in predicting plasma atherogenicity. This ratio has a strong predictor of myocardial infarction [24]. AIP provides information about the atherogenicity of plasma and quantifies the response to therapeutic intervention. Also AIP correlates inversely with insulin sensitivity measurement[62,63]. Moreover, studies have shown that in situations where other atherogenic risk parameters like TG and HDL-c appear normal, AIP may be the diagnostic alternative [63]. Studies have shown its role in predicting cardiovascular risk and effectiveness of therapy [64]. In view of different studies, AIP can be more reliable in predicting the risk for development of atherosclerosis in diabetes mellitus patients [26,59,65].

The burden of dyslipidemia is high in patients with diabetes. One of the major risk factor for the development of CVD is dyslipidemia. Degree of dyslipidemia increases with increase in duration of diabetes [66,67]. In an analysis of diabetes duration and risk of major cardiovascular disease events and total mortality by Wannamethee et al. [68], only those with diabetes for more than eight years had an increased risk of cardiovascular disease death compared with those who had diabetes for less than two years. CAD risk in patients with diabetes escalates significantly with disease duration and approaches CAD risk equivalence only when disease duration is beyond eight years. The dependence of AIP on duration of disease in our study (Table 5) is consistent with the findings of Al-Qaicy [22]. The findings of a recent meta-analysis suggest that increased AIP is associated with an incremental increase in risk of T2 DM and also suggest that AIP may be used as a simple, easily calculated parameter in assessing the risk of T2 DM [69].

One of the major risk factor for the development of CVD is dyslipidemia. The ratio of TG and HDL- c was proved as strong predictor of Myocardial Infarction (MI). Cardio Risk Ratio (CRR) and Atherogenic Coefficient (AC) have a good predictive value for future cardiovascular events. Atherogenic Index of Plasma (AIP), which indicates the plasma atherogenecity, is also a significant independent predictor of CAD. AIP which can easily be calculated from standard lipid profile can act as an adjunct that significantly adds predictive value beyond that of the individual lipids, and / or TC / HDL-c, LDL-c / HDL-c ratios [63]. This parameter is easy to calculate every time a lipid profile is asked for, so that the cardiovascular risk of the patient can be assed [28,62]. Studies have also shown that in situations where TG and HDL-c appear normal, AIP may be the diagnostic alternative [63,70]. One study [70] suggests that AIP may be particularly useful as atherogenic risk predictor in newly-diagnosed type 2 diabetic patients. According to another study [71], the AIP was a superior index for predicting the CAD when compared to the most commonly used indices of atherogenicity in every day practice. AIP have the potential to emerge as the best cost effective marker of risk for CAD especially when the absolute values of individual lipoproteins seem normal [72]. In the current study, we observed that AIP was significantly higher in both gender as compared to baseline value. Similar results were also reported by previous investigators [22,60,61,72]. According to the value of AIP as previously mentioned (Table 4), this study showed that female participants were dominant in high risk AIP category and so they were at a higher risk of developing coronary heart disease. This finding was in agreement with the studies of different investigators [9,13,22,52,58,60].

In this study, the Cardiac risk ratio (CRR) calculated as the ratio of [TC / HDL-c], was found to be significantly increased in men and women compared to baseline value (Table 6). This is in accordance with the works of different authors [22,60,73,74]. When CRR of our patients were compared with the value of American Heart Association (≤3.5)[26,62], both male and females show greater propensity towards cardiovascular disease. Our results also show that the females are at a higher risk than males of developing cardiovascular disease. The Canadian working group had chosen the [TC / HDL-c] ratio as a secondary goal of therapy considering it to be a more sensitive and specific index of cardiovascular risk than total cholesterol, particularly in individuals with TG > 300 mg/dl [75]. We observed CRR in our male and female patients was > 4 in concordance with other studies [22,60,61,73,76]. Studies have shown the association of [TC / HDL-c] ratio with coronary plaque formation [26, 77].

In the present study we found a significant increase in the levels of Atherogenic coefficient (AC) in both male and female patients when compares to baseline value [Table 6]. This is in agreement with the works of different investigators [22,23,24, 26,62,72]. The observed values of AC for both male (3.726) and female (4.038) show a greater tendency towards cardiovascular disease [62,78]. Atherogenic Coefficient (AC), calculated as [(Non HDL-c) / HDL-c] or [(TC – HDL-c) / HDL-c] is a measure of cholesterol in LDL-c, VLDL-c, IDL-c lipoprotein fractions with respect to good cholesterol or HDL-c. It reflects atherogenic potential of the entire spectrum lipoprotein fractions and hence indicates the CV risk. The higher the values, higher the risk of developing cardiovascular diseases and vice versa. Non HDL-c is calculated as total cholesterol minus HDL-c. It is a single

index of all the Atherogenic, apolipoprotein (apo) B-containing lipoproteins, Low Density Lipoprotein, Very Low Density Lipoprotein, Intermediate Density Lipoprotein and lipoprotein (a). Although apo B can be can be measured directly, measurement of Non HDL cholesterol is more practical, reliable and inexpensive and is accepted as a surrogate marker for apo B in routine clinical practice[62, 79]. Because of its simple calculation, the Non HDL cholesterol level is easily available with every lipid profile ordered and eliminating any additional costs[23]. Non HDL cholesterol serves as an index of cardiovascular risk in diabetic patients in whom LDL-c may not be elevated [80]. Non HDL-c is the second target of therapy after LDL-c as per ATP III guideline especially in individuals with hyper-triglyceridemia[26,27]. Studies have shown Non HDL-c being analogous to Apo-B in assessing atherogenic cholesterol and lipoprotein burden [23,26]. Non HDL-c has been observed to have the strongest relationship with small dense LDL-c (sdLDL-c) levels when compared with other lipid measurement[62]. The predictive value of Non HDL-c for cardiovascular risk and mortality is better than that of LDL-c[62]. The strong association between Non HDL-c and sdLDL-c adds additional support for using the Non HDL-c level as a predictor of CVD mortality [62].

The results of the present study revealed that all three atherogenic indices of female were higher than those for male. Similar observations were made by different investigators in their studies of male and female subjects [22,58,60,61,81,82]. These findings suggest that women may be more at risk of cardiovascular disease than men since the three indices were higher in them than their male counterparts. All physicians should be made aware that development of diabetes is associated with a greater increase in cardiovascular risk in women than in men so that they should, at the very least, treat women with diabetes as aggressively as they do with their male counterparts.

Lifestyle changes are widely advocated as a first line of treatment for dyslipidemia. The Canadian and the American lipid guidelines recommend dietary changes and regular physical activity for all individuals with dyslipidemia[83,84]. Thus lifestyle change, performing regular exercise and healthy diet modification is recommended for Saudi population. In economically advanced countries, results of screening the general population for blood lipids have led to the introduction of both physical exercise and pharmacological interventions in lowering blood lipids[60,61]. It is our opinion that the Saudi population should consider this approach at this early stage. In addition to epidemiological study of the general population, there is a need for education on healthier lifestyles such as good nutrition, weight reduction and smoking cessation, greater physical activity and regular medical check-up.

CONCLUSION

The present study shows that the derangement in the lipid profile in patients of type 2 diabetes mellitus is more adverse in females as compared to male patients. The management of dyslipidemia, a well-recognized and modifiable risk factor among patients with T2 DM, is an important element in the multifactorial approach to prevent coronary heart disease. It might be appropriate at this stage in Saudi Arabia to consider both physical activity and pharmacological interventions in lowering blood lipids. Early identification of dyslipidemia and aggressive management strategies, in addition to glycemic control, are necessary to delay the onset and progression to more serious and debilitating cardiac events. Thus the relevance of the present study lies in recognizing increased risk of dyslipidemia in female type 2 diabetic patients and hence monitoring of the lipid profile of newly diagnosed female type 2 diabetic patients, so that early intervention is possible. We recommend a gender-sensitive approach in planning interventions (counseling and treatment) to reduce the risk of cardiovascular disease.

CRR, AC, AIP are found to have a good implication prospect in daily practice to assess cardiovascular risk in type 2 diabetes mellitus. These indices can be calculated from the routinely done lipid profile parameters especially in centers where new tests are not possible due to cost factor. The atherogenic indices are powerful indicators for the risk of heart disease, the higher the values the higher the risk developing cardiovascular disease and vice versa. Thus, the use of these cardiovascular risk indices should be encouraged to complement the existing profile of tests for identifying high risk individuals for CAD and effective drug management. Preventive measures such as lifestyle modification with healthy diet, adequate physical activity, and decrease in stress could help prevent the twin epidemics of diabetes and CAD.

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