Original Research Article

Evaluation of lipid profile pattern and atherogenic index of plasma (AIP) having type-2 diabetes mellitus in Bangladesh

Mahfuza Anjum[1], Md. Salah Uddin[1], Naima Ahmed Tamanna[2], Md. Abdullah Al-Zobair[3], A. T. M. Mijanur Rahman[1]*

[1]Department of Applied Nutrition and Food Technology, Islamic University, Kushtia, Bangladesh
[2]Department of Statistics, Jagannath University, Dhaka, Bangladesh
[3]Department of Otolaryngology and Head Neck Surgery, Bangabandhu Sheik Mujib Medical University, Dhaka, Bangladesh

*Correspondence:
Dr. A. T. M. Mijanur Rahman,
E-mail: mijananftiubd@gmail.com

ABSTRACT

Background: Dyslipidemia has been noted to play an integral role in the pathogenesis and progression of micro and macrovascular complications in Diabetes Mellitus (DM) patients. The study was aimed to evaluate the prevalence and pattern of dyslipidemia and atherogenic index of plasma (AIP) in type 2 diabetes mellitus patients as it has not been reported previously in Bangladesh

Methods: This cross-sectional study was conducted at Armed Forces Institute of pathology, Bangladesh from November 2016 to October 2017. A total number of 300 patients having diabetes in the age group of 30-60 years have been selected using a non-probability method. Fasting plasma glucose (FPG), serum total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and triglyceride (TG) levels were estimated by laboratory tests.

Results: The prevalence of dyslipidemia in at least one lipid parameter was found in 282 patients (94%), while 18 patients (6%) had no dyslipidemia. High levels of TC, TG and LDL-C were found in 134 (47.3%), 230 (76.7%) and 124 (41.3%) patients, respectively. On the other hand, low levels of HDL-C were found in 180 patients (60%). An increased risk of AIP was found in 298 patients (99.3%), whereas only 2 patients (0.7%) were in low risk. FPG was positively correlated with TC, TG, LDL-C and AIP, while negatively correlated with HDL-C. A significant positive correlation was also observed between FPG and AIP.

Conclusions: The Study revealed that dyslipidemia is very common in type 2 diabetic patients and the most common abnormality observed was increased serum triglyceride levels followed by decreased serum HDL-C levels. The AIP is also significantly higher in type 2 diabetic patients.

Keywords: Atherogenic index of plasma, Bangladesh, Dyslipidemia, Type 2 diabetes

INTRODUCTION

Diabetes mellitus was the 8th leading cause of death, accounting for 4% (1.5 million) of all deaths under the age of 70 in 2012 globally.[1,2] Additionally, the most recent data from WHO revealed that 422 million adults are living with diabetes mellitus.[2] The disease is caused in most cases by a deficiency or complete lack of the hormone insulin, which is produced in the pancreas, or by an inability of the body to respond appropriately to insulin (i.e., insulin resistance). The result of both conditions can include chronically elevated blood glucose

levels, excessive excretion of glucose in the urine, and the accumulation of certain acidic substances in the blood. If not prevented or treated properly, these changes can lead to coma and even death. Other adverse events associated with diabetes include the increased risks of associated complications e.g. heart disease, stroke, kidney failure, accounting for another 2.2 million deaths worldwide.[2,3] Especially, cardiovascular disease (CVD) has been the leading cause between 50% and 80% of deaths in people with diabetes in which type 2 diabetes makes up about 85-90% of all cases.[4,5] Dyslipidemia is an important component of the metabolic syndrome observed in type-2 diabetes patients.

It is characterized by high levels of total cholesterol (TC), high density lipoprotein-cholesterol (LDL-C) and triglycerides (TG), and low level of high density lipoprotein-cholesterol (HDL-C). Worsening of glycemic control has been reported to deteriorate this dyslipedemias along with elevated TC and LDL-C.[6] The prevalence of lipid abnormalities among diabetic patients are due to insulin resistance or deficiency which affects key enzymes and pathways in lipid metabolism.[7]

Therefore, diabetes mellitus with poor glycemic control is an important risk factor for atherosclerosis and coronary heart disease. The composition of lipid particles in diabetic dyslipedemia has been proposed to be more atherogenic than other types of dyslipidemia which means that even normal lipid concentrations might be more atherogenic in diabetic than non-diabetic people.[8] The associated hyperglycemia, obesity and insulin changes in diabetes have been found to be highly accelerated the progression to atherosclerosis.

The atherogenic index of plasma (AIP) has recently been regarded as a strong marker for plasma atherogenicity and is positively correlated with cardiovascular disease risk.[9-15] Since it considers the elevated levels of triglycerides as an important risk factors.[16] It has been suggested that an AIP value of under 0.11 is associated with low risk of CVD; the values between 0.11 to 0.21 and upper than 0.21 are associated with intermediate and increased risks, respectively.[17,18] The prevalence of diabetes epidemic is growing rapidly, particularly in low- and middle-income countries including Asia and Africa.[19]

However, few studies have investigated the interrelationship between dyslipidemia, atherogenic index of plasma (AIP) and type-2 diabetes mellitus especially in Asians. The prevalence of diabetes among adults in Bangladesh had increased substantially, from 4% in 1995 to 2000 and 5% in 2001 to 2005 to 9% in 2006 to 2010. The International Diabetes Federation (IDF) estimated that the prevalence will be 13% by 2030.[20] This explosion in diabetes prevalence will place Bangladesh among the top ten countries in terms of the number of people living with diabetes in 2025. To the best of our knowledge, no previous study has described the distribution pattern of

lipid profiles, the atherogenic index of plasma (AIP) and type-2 diabetes mellitus in Bangladesh.

The aim of the present study was to evaluate the prevalence and pattern of dyslipidemia and AIP in type 2 diabetic patients. The study group comprised of 300 patients having type 2 diabetes in the age group of 30-60 years. The patients have been selected from the Armed Forces Institute of pathology (AFIP), Dhaka, Bangladesh. Among patients, 50% were men and 50% were women. Personal data and history of co-existing medical conditions were collected by data collection sheet. Fasting plasma glucose (FPG), serum total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and triglyceride (TG) were determined by laboratory tests.

METHODS

Study participants

It was a cross-sectional study involving 300 patients of type 2 diabetes. The study was conducted in the Department of Biochemistry, Armed Forces Institute of pathology (AFIP), Dhaka cantonment, Bangladesh. Patients who were in the age group of 30-60 years were selected using a non-probability method and the duration of the study period was from November 2016 to October 2017.

Patients with history of renal impairment, liver disease, malignant disease, hypothyroidism, pregnancy and those intake lipid lowering drugs were excluded from the study. After selection of appropriate study subjects, written informed consent for participation was obtained from all participants attending at AFIP.

Data collection

Personal data and history of co-exiting medical conditions were collected by data collection sheet. Laboratory investigations of all patients in the age group of 30-60 years were subsequently performed to determine their fasting plasma glucose (FPG) and serum lipid profiles including serum total cholesterol (TC), HDL-C, serum triglyceride TG), calculated LDL-C, and detailed estimates of the percent of persons with high blood cholesterol.

Analytical techniques

The quantitative estimation of fasting plasma glucose was done by glucose oxidase method. Serum triglyceride, total cholesterol and HDL cholesterol were also estimated by enzymatic method. LDL cholesterol (LDL cholesterol = Total cholesterol-(1/5TG+HDL cholesterol) was calculated by Friedewald formula. The AIP was calculated as log (TG/HDL-C) using the Czech online calculator of atherogenic risk.

Statistical analysis

The subject groups were divided into two categories according to gender i.e. male and female. Furthermore, the subjects were divided into three categories according to age i.e., 30-39years, 40-49years and 50-59years. To compare the result between male and female and among different age groups variables, Student's t-test or the chi-square test was used. Pearson's correlation analysis was used to correlate between FPG with lipid profile and AIP. Differences were considered to be significant at P values less than 0.05 and the confidence interval was 95%. All statistical studies were carried out using the SPSS program (version 22.0; SPSS Inc., Chicago, Illinois, USA).

RESULTS

The distribution of patients according to age groups and gender is shown in Table 1. Of the 300 patients, 24 patients (16%) were male and 20 patients (13.3%) were female in the age group of 30-39 years, 66 patients (44%) were male and 66 patients (44%) were female in the age range of 40-49 years, and 60 patients (40.0%) were male and 64 patients (42.7%) were female in the age range of 50-59 years.

The group consisted of equal number of men (50%) and women (50%). There was no significant difference (p = 0.782) between male and female and age group.

Table 1: Distribution of patients according to age groups and sex.

Age groups Gender				
Years	Male	Female	Total	P value
30-39	24 (16.0)	20 (13.3)#	44 (14.7) #	0.514*
40-49	66 (44.0)	66 (44.0)	132 (44.0)	1.00
50-59	60 (40.0)	64 (42.7)	124 (41.3)	0.639
Total	150 (100.0)	150 (100.0)	300 (100.0)	0.782

Chi-square test was done to measure the level of significance. #Figure within parentheses indicates percentage.

Table 2: Mean values of lipid profiles, AIP and diabetes related characteristics of all patients.

Variables	Mean ± SD	Min-max
FPG (mmol/l)	9.81±3.08	7.00-22.80
TC (mg/dl)	199.48±42.73	112.00-376.00
TG(mg/dl)	229±118.66	45.00-747.00
HDL-C (mg/dl)	38.03±7.63	21.00-65.00
LDL-C (mg/dl)	121.44±38.55	39.00-293.00
AIP	0.73±0.23	0.08-1.41

FPG: Fasting plasma glucose, TC: total cholesterol, TG: triglyceride, HDL-C: high-density lipoprotein-cholesterol, LDL-C: low-density lipoprotein-cholesterol, AIP: atherogenic index of plasma (AIP): DM (FPG ≥7mmol/L), dyslipidemia (TC: >200mg/dL, TG: >150 mg/dL, HDL-C: <40mg/dL, LDL-C: >130 mg/dL

Table 3: Mean values of lipid profiles, AIP and diabetes related characteristics by sex.

Gender			
Variables	Male	Female	P value
FPG (mmol/l)	10.04±3.35	9.58±2.78	0.200*
Cholesterol (mg/dl)	201.4±39.6	197.5±45.6	0.428
LDL-C (mg/dl)	234.7±122.1	224.0±115.2	0.434
HDL-C (mg/dl)	36.6±6.4	39.4±8.4	0.001
Triglyceride (mg/dl)	123.0±37.4	119.8±39.6	0.471
AIP	0.76±0.21	0.70±0.24	0.023

Chi-square test was done to measure the level of significance.

As can be observed in Table 2, the mean FPG was 9.81±3.08 mmol/L. Mean serum total cholesterol, triglyceride, HDL-C, and LDL-C levels were 199.48±42.73 mg/dL, 229±118.66 mg/dL, 38.03±7.63 mg/dL and 121.44±38.55 mg/dL, respectively. The mean ±SD of AIP was 0.73±0.23. Statistically there was no significant difference in FPG, TC, TG and LDL-C levels;

however, HDL-C levels and AIP were significantly different between male and female (Table 3).

Distribution pattern of dyslipidemia in study subjects

As can be seen in Table 4, the prevalence of dyslipidemia in at least one lipid parameter was 282 (94%) and the 95% confidence interval (CI) were found to be 91.26% to

96.74%. Of the patients, 18 patients (6%) were found to have no dyslipidemia (95% confidence interval, 3.26% to 8.74%), while 56 patients (19%) had single dyslipidemia (95% confidence interval, 14.48% to 23.52%) and 226 patients (75%) had multiple dyslipidemia (95% confidence interval, 70.00% to 80.00%). The most frequent type of single dyslipidemia was hypertriglyceridemia (60.7%), while in the case of multiple dyslipidemia, it was hypertriglyceridemia with low HDL-C (35.4%) (Table 5).

Table 4: Distribution pattern of dyslipidemia in study subjects.

Pattern of lipid profile	Frequency	%	95% confidence interval (Cl)
Normal	18	6	3.26-8.74%
Single dyslipidemia	56	19	14.48-23.52%
Multiple dyslipidemia	226	75	70.00- 80.00%

Table 5: Distribution pattern of single and multiple dyslipidemia.

		Percentage	95% confidence interval (Cl)
Single dyslipidemia: 56 (19%)	High triglyceride (TG)	60.7%	47.64% to 73.76%
	Low HDL-C	35.7%	22.90% to 48.50%
	Others	3.6%	-1.38% to 8.58%
Multiple dyslipidemia: 226 (75%)	High TG & low HDL-C	35.4%	29.04% to 41.76%
	High TG, high TC & high LDL-C	22.1%	16.58% to 27.62%
	High TG, high TC, high LDL-C & low HDL-C	19.5%	13.94% to 24.46%
	Others	22.8%	17.22 % to 28.38%

Table 6: Distribution pattern of lipid profiles and AIP by sex.

Parameters Gender				
Serum total cholesterol (mg/dl)	**Male**	**Female**	**Total**	**P value**
<200 (desirable)	76 (50.7)	82 (54.70)	158 (52.7) [#]	0.488*
200-239 (borderline-high)	44 (29.3)	50 (33.3)	94 (31.3)	0.455
≥240 (high)	30 (20.0)	18(12.0)	48 (16.0)	0.059
Total	150 (100.0)	150 (100.0)	300 (100.0)	0.164
Serum triglyceride (mg/dl)				
<150	32 (21.3)	38 (25.3)	70 (23.3) [#]	0.413*
150-199	40 (26.7)	36 (24.0)	76 (25.3)	0.595
200-499	72 (48.0)	70 (46.7)	142 (47.3)	0.817
≥500	6 (4.0)	6 (4.0)	12 (4.0)	1.000
Total	150 (100.0)	150 (100.0)	300 (100.0)	0.861
HDL-C				
<40	98 (65.3)	82 (54.7)	180 (60.0)[#]	0.059*
40-59	52 (34.7)	64 (42.7)	116 (38.7)	0.155
≥60	0 (.0)	4 (2.7)	4 (1.3)	0.044
Total	150 (100.0)	150 (100.0)	300 (100.0)	0.036
LDL-C (mg/dl)				
<100	44 (29.3)	44 (29.3)	88 (29.3) [#]	1.000*
100-129	42 (28.0)	46 (30.7)	88 (29.3)	0.162
130-159	38 (25.3)	44 (29.3)	82 (27.3)	0.437
160-189	18 (12.0)	8 (5.3)	26 (8.7)	0.040
≥190	8 (5.3)	8 (5.3)	16 (5.3)	1.000
Total	150 (100.0)	150 (100.0)	300(100.0)	0.346
AIP				
<0.11	0 (0.0)	2 (1.3)	2 (0.7) [#]	
0.11-0.20	0 (0.0)	0 (0.0)	0 (0.0)	
≥0.21	150 (100.0)	148 (98.7)	298 (99.3)	
Total	150 (100.0)	150 (100.0)	300 (100.0)	0.0156

*Chi-square test was done to measure the level of significance. Figure within parentheses indicates percentage. Normal total cholesterol: less than 200 mg/dL, borderline high: above 200 mg/dL, high: above 240; Normal TG: under 150 mg/dL, borderline high: 150-199 mg/dL, high: 200-499 mg/dL, very high: 500 mg/dL or higher; HDL-C: less than 40 mg/dL: risk of heart disease is high, best: 60 mg/d; Optimal LDL-C: less than 100 mg/dL, very high:above90 mg/dL; AIP: low risk < 0.11, intermediate risk: 0.11-0.21, increased risk: above 0.21.

Distribution patterns of lipid profile and AIP according to sex and age groups

The distribution patterns of lipid profile and AIP according to sex and age groups are shown in Table 6 and Table 7. In the present study, 142 patients (47.3%) had high serum TC as can be observed in Table 6. However, among the patients, 94 patients (31.3%) had borderline-high and 48 patients (16.0%) had high levels of serum TC cholesterol. On the other hand, 158 patients (52.7%) had desirable serum TC. There was no significant difference of TC between male and female (p= 0.164) and among different age groups (p = 0.473). Out of 300 patients, serum TG levels were found to be normal in 70 patients (23.3%). On the other hand, 230 patients (76.7%) had high level of TG, among them, 76 patients (25.4%) had borderline high, 142 patients (47.3%) had high and 12 patients (4%) had very high levels of TG. There was no significant difference of TG level between male and female (p = 0.861) and among different age groups (p= 0.094). Meanwhile, 180 patients (60%) had low HDL-C.

There was significant difference in HDL-C level between male and female (p = 0.036); however, no significant difference was observed among different age groups (p=0.211). High serum LDL-C levels were found to be in 124 (41.3%) diabetic patients, among them, 82 patients (27.3%) had borderline high, 26 patients (8.7%) had high and 16 patients (5.3%) had very high level of LDL-C. However, 88 patients (29.3%) had optimal and 88 patients (29.3%) had near or above normal level of LDL-C. Although there was no significant difference of serum LDL-C level between male and female (p= 0.346), significant difference was observed among different age groups (p= 0.005). Additionally, 298 diabetic patients (99.3%) were found to have high AIP (95% confidence interval level, 98.5% to 100%) and only 02 patients (0.7%) had low AIP (95% confidence interval level, 0.26% to 1.66%). There was significant difference in AIP between male and female (p = 0.156), however, no significant difference was observed among different age groups (p = 0.278).

Table 7: Distribution pattern of lipid profiles and AIP by age groups.

Parameters Age (years)					
Serum total cholesterol (mg/dl))	30-39	40-49	50-59	Total	P value
<200 (desirable)	24 (54.5)	64 (48.5)	70 (56.6)#	158 (52.7)	0.427*
200-239 (borderline high)	14 (31.8)	48 (36.4)	32 (25.8)	94 (31.3)	0.190
≥240(high)	6 (13.6)	20 (15.2)	22 (17.7)	48 (16.0)	0.766
Total	44 (100.0)	132 (100.0)	124 (100.0)	300 (100.0)	0.473
Serum triglyceride (mg/dl)					
<150	12 (27.3)	34 (25.8)	24 (19.4)#	70 (23.3)	0.384*
150-199	10 (22.7)	32 (24.2)	34 (27.4)	76 (25.3)	0.769
200-499	22 (50.0)	56 (42.4)	64 (51.6)	142 (47.3)	0.315
≥500	0 (0.0)	10 (7.6)	2 (1.6)	12 (4.0)	0.0188
Total	44 (100.0)	132 (100.0)	124 (100.0)	300 (100.0)	0.094
HDL-C					
<40	26 (59.1)	80 (60.6)	74 (59.7)#	180 (60.0)	0.980*
40-59	18 (40.9)	52 (39.4)	46 (37.0)	116 (38.7)	0.882
≥60	0 (0.0)	0 (.0)	4 (3.2)	4 (1.3)	0.056
Total	44 (100.0)	132 (100.0)	124 (100.0)	300 (100.0)	0.211
LDL-C (mg/dl)					
<100	14 (31.8)	28 (21.2)	46 (37.1)#	88 (29.3)	0.019*
100-129	12 (27.3)	44 (33.3)	32 (25.8)	88 (29.3)	0.396
130-159	12 (27.3)	46 (34.8)	24 (19.4)	82 (27.3)	0.021
160-189	6 (13.6)	10 (7.6)	10 (8.1)	26 (8.7)	0.443
≥190	0 (0.0)	4 (3.0)	12 (9.7)	16 (5.3)	0.014
Total	44 (100.0)	132 (100.0)	124 (100.0)	300 (100.0)	0.005
AIP					
<0.11	0 (0.0)	2 (1.5)	0 (0.0)#	2 (0.7)	
0.11-0.20	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
≥0.21	44 (100.0)	130 (98.5)	124 (100.0)	298 (99.3)	
Total	44 (100.0)	132 (100.0)	124 (100.0)	300 (100.0)	0.278*

*Chi-square test was done to measure the level of significance. Figure within parentheses indicates percentage.

Table 8: Correlation of fasting plasma glucose with lipid profile and AIP.

Lipid profiles	R value	P value
Serum total cholesterol (mg/dl)	0.169	0.003
Serum triglyceride (mg/dl)	0.421	<0.001
Serum HDL-C (mg/dl)	-0.049	0.397
Serum LDL-C (mg/dl)	0.077	0.185
AIP	0.123	0.033

The Pearson correlation analysis showed significant and positive associations of FPG with TC (r=0.169, p= 0.003), TG (r=0.421, p=<0.001), LDL-C (r= 0.077, p=0.185) and AIP (r=0.123, p= 0.033), respectively. On the other hand, a non-significant and inverse correlation was found between FPG and HDL-C (r= -0.049, p= 0.397).

DISCUSSION

Dyslipidemias are one of the most common metabolic diseases seen in clinical practice. A number of chronic squeal including coronary heart disease, dermatological manifestations, pancreatitis, neurological and ocular anomalies may result from dyslipidemias.[21] The present study shows very high prevalence of dyslipidemia (94%), because patients were on oral hypoglycemic agents to improve glycemic control, however, they didn't take any lipid lowering agents. Consequently, a significant proportion of them had abnormal lipid profile. This is in agreement with findings of other studies which have also shown high prevalence of dyslipidemia (90.3%, 86.98%, respectively).[22,23] By contrast in Senegal and in Nigeria reported a low prevalence of dyslipidemia (63.8%, 60.5%, respectively).[24,25] Therefore, the overall prevalence of dyslipidemia varies from one country to another. The increasing prevalence of dyslipidemia in this study may be attributed to the current trend toward urbanization and adoption of western diet and lifestyle which have inadvertently resulted in the higher incidence of type 2 diabetes mellitus with its attendant metabolic abnormalities.

Considering both single and multiple dyslipidemia, hypertriglyceridemia (76.7%) was the most common lipid abnormality in this study followed by low HDL-C (60%). This is a common trend for patients with diabetes mellitus and has been associated with high risk of CHD morbidity and mortality in this group of patients. The prevalence of hypertriglyceridemia (76.7%) is very close to the results reported in Pakistan where the prevalence of hypertriglyceridemia was 78%.[21] However, the prevalence of this study is higher than the one of Osuji et al in Nigeria who had found 34.1% and the one of Sharma et al in India who found 16.60%.[25,26] A high level of triglycerides may be the result of the unbalanced metabolic state of diabetes. The percent of patients (60.6%) having low HDL-C is very close to the results reported in Nigeria who had found 62%.[27] However, the prevalence of HDL-C in women aged 40 to 49 years is lower than the one of Gupta et al in India who found 48.8%.[28] However, higher than the one reported by Sharma et al. (2013) in India which was 13.70%.[26] The study denotes that there is significant difference (p= 0.001) in serum HDL-C level between male and female. The female sex hormone estrogen tends to raise HDL cholesterol, and as a rule, women have higher HDL cholesterol levels than men, which may help explain why premenopausal women are usually protected from developing heart disease.[29] The prevalence of hypercholesterolemia 47.3% is lower than the one of Gomina et al who found 53.03%.[23] However, the present data are in accordance with previous study by Fatma et al, which has shown that the prevalence of hypercholesterolemia was 48%. Our result is higher than those found by Sharma et al. (2013) in India i.e. 34%, Osuji et al (2010) and Odenigbo et al (2008) in Nigeria which were respectively 31.4% and 23% among adult populations.[25-27] This difference in cholesterol level may be due to the fact that it depends on other factors like weight, sex, age and eating habits which are variable from one region to another. No significant difference was observed between serum cholesterol level with respect to sex and age groups. The prevalence of LDL hypercholesterolemia was 41.3% in our study. This result is similar to the findings of previous studies were carried out in Nigeria that showed the prevalence of hypercholesterolemia were 47.72% and 37.1%, respectively.[30] By contrast, it is higher than the one of studies who had found 72%.[31]

A significant positive correlation was observed between FPG and AIP (r=0.123, p=0.033) in type 2 diabetes mellitus patients. This finding is in agreement with a previous study, which has also showed a significant association between AIP and FBS.[32] AIP was significantly increased with increasing TC, TG and LDL-C and decreasing HDL-C. Prolonged hyperglycemia and insulin resistance increase the lipogenesis and increase TG concentrations and decrease the HDL-C and therefore, may contribute to elevation of AIP levels in diabetic patient.[15,33,34,32] There is a significant difference in AIP level between male and female (p= 0.023). AIP, being HDL-C based parameter, well correlates with the HDL-C findings in this case. Therefore, AIP has been shown to be a strong marker for predicting the risk of cardiovascular disease in this study which was also supported by previous studies.[32,35,36]

CONCLUSION

The most common abnormality observed in the present study was increased serum TG levels followed by decreased HDL-C levels. A significant positive correlation was also observed between FPG and AIP. The level of AIP was found to be higher in type 2 diabetic patients. Therefore, correlation of lipid abnormalities in patients with diabetes is necessary to prevent pancreatitis (due to hypercholesterolemia) and to reduce risk of macrovascular complications. Initial approaches to lower

the levels of lipids in subjects with diabetes mellitus should therefore include glycemic control, diet, weight loss and exercise. A limitation of the study is the small sample of 300 patients with type 2 diabetes mellitus may not reflect the exact situation of the country. These findings could be further strengthened if large number of patients from different places could be included and conducted the study in healthy population as well as diabetic subjects.

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