ASSESSING THE SERUM LIPID PROFILE AND ITS ASSOCIATION WITH PREDIABETES AND DIABETES IN INDIAN SUBJECTS

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ABSTRACT

Background: In subjects with type 2 diabetes mellitus, one of the most commonly seen disorders is dyslipidemia. The association of type 2 diabetes mellitus and dyslipidemia is established in the Caucasian subjects. However, the data establishing this link in the Indian subjects is scarce in the literature.

Aim: The present study was conducted to assess the serum lipid profile parameters and their association with glucose intolerance status in prediabetics and type 3 diabetes mellitus subjects in Indian subjects.

Methods: The present cross-sectional study included 1146 subjects from both genders. For all the subjects, demographics, fasting serum lipids including HDL-C (high-density lipoprotein cholesterol), LDL-C (low-density lipoprotein cholesterol), TG (triglycerides), and TC (total cholesterol), blood pressure, fasting glucose, and 2-hour OGTT (oral glucose tolerance test).

Results: Odds ratio for 95% confidence interval for type 2 diabetics was 0.61 for LDL-C, 2.15 for HDL-C, 3.89 for triglycerides and 2.41 for total cholesterol. This was non-significant for LDL-C with p-value of 0.107. However, for HDL-C, triglycerides, and total cholesterol, these values were statistically significant with respective p-values of 0.04, <0.001, and <0.001. For prediabetics, odds ratio for LDL-C, HDL-C, triglycerides, and total cholesterol was 1.42, 2.95, 1.98, and 0.92 respectively. For LDL-C and total cholesterol, this was statistically non-significant with respective p-values of 0.733 and 0.194. However, for HDL-C and triglycerides, this difference was statistically significant with p-values of <0.001 and 0.01 respectively. For category 0, 1, 2, and 3 there were 6.02% (n=69), 1.04% (n=12), 63% (n=722), and 28.97% (n=332) cases. In diabetics, for category 0, 1, 2, and 3 there were 1.44%

(n=1), 16.66% (n=2), 4.01% (n=29), and 16.86% (n=56) events. This was statistically significant for category 3 with p<0.001 and non-significant for category 1 and 2 with p-values of 0.007 and 0.08 respectively. Events for prediabetics were 2.89% (n=3), 8.33% (n=1), 8.03% (n=58), and 12.11% (n=39) respectively for category 0, 1, 2, and 3. This was statistically significant for category 2 and 3 with p-values of 0.03 and 0.002 respectively.
Conclusion: The present study concludes that high levels of triglycerides and HDL-C parameter of dyslipidemia are seen in subjects with diabetes mellitus which increase proportionally with the increase in glucose intolerance. This points to regular lipid parameter monitoring in subjects with type 2 diabetes mellitus.
Keywords: Cholesterol, Diabetes, HDL-C, LDL-C, Lipid Profile, Prediabetes

INTRODUCTION

Cardiovascular diseases and complications in subjects with type 2 diabetes mellitus are well-established in subjects with type 2 diabetes mellitus and pose a high global burden on the healthcare sector. The risk of coronary artery disease and other cardiovascular complications are 2 to 4 times higher in subjects with diabetes mellitus as compared to healthy subjects which is also a leading cause of death in diabetic patients. However, the modifiable risk factor in diabetics includes hypertension and dyslipidemia which constitute>87% morbidity and disability in middle and low-income countries. Another vital risk factor for increased risk of cardiovascular disease is prediabetes which is a metabolic state between type 2 diabetes mellitus and normoglycemia.[1]
Diabetic dyslipidemia denoting lipid abnormalities in diabetics is often described by low HDL-C, high total cholesterol, triglycerides, and LDL. LDL-C (Low-density lipoprotein cholesterol) may be normal or increased. Diabetic dyslipidemia is also seen in prediabetics. However, dyslipidemia levels pattern for different lipid parameters may show health care access, economic status, and ethnicity. Recent literature data suggest abnormal lipid parameters are correlated with poor glycemic control. Also, in subjects with type 2 diabetes mellitus, an association is seen between low HDL-C and triglycerides with coronary artery disease compared to solely assessed lipid parameters.[2]
In comparison with Caucasians, in Asian subjects, diabetes is seen at lower waist circumference and BMI (body mass index). Owing to this finding, IDF (International Diabetes Federation) and WHO (World Health Organization) collaboration recommended specific waist circumference cut-off for Asian subjects. Low BMI causing similar diabetes in Asians compared to Caucasians can be attributed to different fat distribution in the body. Visceral adipose cells risk is higher in South Asians which is a reason for type 2 diabetes mellitus and insulin resistance than with general adipose cells increase. In Asian subjects, Indians have a high risk for coronary artery disease compared to other countries. Compared to western countries, cardiovascular complications and type 2 diabetes mellitus develop nearly years earlier and have high mortality rates in young subjects. High mortality rates of nearly 7%, 18%, and 36% are seen with type 2 diabetes mellitus, stroke, and coronary artery disease are seen.[3]
Data concerning lipid abnormalities in Indian subjects is scarce in the literature. However, India is considered a country with an increased risk of coronary artery disease and type 2

diabetes mellitus. Increased lipid disorder prevalence is seen in both rural and urban Indian populations.

Previous literature data also suggest an association of dyslipidemia with hypertension, prediabetes, and type 2 diabetes mellitus. A better understanding of the association between glucose intolerance stages and serum lipid profile is vital for health and clinical aspect, and this association can form the basis for future programs for diabetes prevention and prevention of associated complications.[4]

The present study was conducted to assess the serum lipid profile parameters and their association with glucose intolerance status in prediabetics and type 3 diabetes mellitus subjects in Indian subjects.

MATERIALS AND METHODS

The present cross-sectional study was conducted to assess the serum lipid profile parameters and their association with glucose intolerance status in prediabetics and type 3 diabetes mellitus subjects in Indian subjects. The study population was comprised of the subjects visiting the Outpatient Department of the Institute. The study included a total of 1146 subjects from both genders with an age of more than 20 years. After explaining the detailed study design, informed consent was taken from all the study subjects in both written and verbal form.

The inclusion criteria for the study were subjects with prediabetes and diabetes, aged 20 years or more, and were willing to participate in the study. The exclusion criteria for the study were subjects with mental illness, pregnant females, acute physical illness, and subjects who did not agree to give consent. Among 1680 screened subjects, 1146 who met the inclusion criteria were finally included in the study. After final inclusion, detailed history included demographics were recorded followed by detailed clinical examination.

In all the included subjects, 8ml intravenous blood after overnight fasting was collected under the aseptic and sterile condition from the antecubital vein for assessing the insulin, lipid profile, and fasting blood glucose (FBS). After 2 hours of 75gm glucose, 3ml blood was collected. The glucose oxidase method was used to assess plasma glucose levels. Enzymatic procedures were used to evaluate serum lipid levels including HDL-C, LDL-C, triglycerides, and total cholesterol.

All the parameters were assessed in the same laboratory. A pre-structured questionnaire was given to all the subjects for assessing clinical, anthropometric, and sociodemographic data. Bodyweight (kg) and height (cm) were assessed to calculate BMI, and waist circumference was measured and rounded using tape in the iliac crest and lower rib margin. Two readings were taken to monitor blood pressure. Obesity was taken as BMI of ≥25kg/m2. For waist circumference of ≥80 and ≥90 cm was considered obesity for females and males respectively. For prediabetes, fasting plasma glucose of >6.1 to <7mmol/L and for diabetes, fasting plasma glucose levels of ≥7/ 2hour glucose of ≥11mmol/L was considered. For diastolic and systolic blood pressure of ≥90mmHg and ≥140mmHg was considered hypertension. Concerning serum lipid parameters, cut-off values were ≥3.4mmol/L, ≥1.7mmol/L, and ≥5mmol/L respectively for LDL-C, triglycerides, and total cholesterol. For low HDL-C, <1.3mmol/L for females and <1.04mmol/L for males were taken as the cut-off. With these cut-offs, 4 categories of 0=normal HDL-C and triglycerides, 1= normal HDL-C and high triglycerides, 2= normal triglycerides and low HDL-C, and 3=high triglycerides and low HDL-C were made. Homeostatic model assessment for insulin resistance (HOMA-IR) was assessed by fasting serum insulin in µU/mL X FPG/22.5 by Matthews et al.[5]

RESULTS

The present cross-sectional study was conducted to assess the serum lipid profile parameters and their association with glucose intolerance status in prediabetics and type 3 diabetes mellitus subjects in Indian subjects. The study included a total of 1146 subjects from both genders with an age of more than 20 years. The demographic characteristics of the study subjects are listed in Table 1. The mean age of the study subjects was 45.6, 44.4, and 41.3 years for Type 2 DM, prediabetics, and normal subjects respectively ($p<0.001$). Gender has a significant difference in the three groups with 43.97% (n=73) males in the Type 2 DM group p=0.003. High TG low HDL-C, LDL-C, and LDL-C ≥3.4mmol/l was highest in subjects with type 2 diabetes mellitus followed by prediabetics, and normal subjects with respective p-values of <0.001, 0.01, and 0.01 respectively. High HDL-C was seen in prediabetes followed by diabetes (p=0.003). TG, TG≥1.7mmol/L, TC, and TC≥5.2mmol values were highest for the diabetes group followed by prediabetes and normal subjects with a respective p-value of <0.001. HOMA-IR values were 4.12 for diabetics, 2.34 for prediabetics, and 1.48 for normal subjects ($p<0.001$). Fasting insulin, 2h Plasma glucose, Fasting plasma glucose, hypertension, Waist M≥90, F≥80, and BMI≥25kg/m2 was also significantly higher for diabetics followed by prediabetics and normal subjects with $p<0.001$ (Table 1).

On assessing the Different lipid parameters and associated risk for diabetes and prediabetes in the study subjects, it was seen that the odds ratio for 95% confidence interval for type 2 diabetics was 0.61 for LDL-C, 2.15 for HDL-C, 3.89 for triglycerides, and 2.41 for total cholesterol. This was non-significant for LDL-C with a p-value of 0.107. However, for HDL-C, triglycerides, and total cholesterol, these values were statistically significant with respective p-values of 0.04, <0.001, and <0.001. For prediabetics, the odds ratio for LDL-C, HDL-C, triglycerides, and total cholesterol was 1.42, 2.95, 1.98, and 0.92 respectively. For LDL-C and total cholesterol, this was statistically non-significant with respective p-values of 0.733 and 0.194. However, for HDL-C and triglycerides, this difference was statistically significant with p-values of <0.001 and 0.01 respectively as shown in Table 2.

Based on the 4 categories of 0=normal HDL-C and triglycerides, 1= normal HDL-C and high triglycerides, 2= normal triglycerides and low HDL-C, and 3=high triglycerides and low HDL-C, the status was assessed. For category 0, 1, 2, and 3 there were 6.02% (n=69), 1.04% (n=12), 63% (n=722), and 28.97% (n=332) cases. In diabetics, for category 0, 1, 2, and 3 there were 1.44% (n=1), 16.66% (n=2), 4.01% (n=29), and 16.86% (n=56) events. This was statistically significant for category 3 with $p<0.001$ and non-significant for category 1 and 2 with p-values of 0.007 and 0.08 respectively. Events for prediabetics were 2.89% (n=3), 8.33% (n=1), 8.03% (n=58), and 12.11% (n=39) respectively for category 0, 1, 2, and 3. This was statistically significant for category 2 and 3 with p-values of 0.03 and 0.002 respectively (Table 3).

DISCUSSION

The present cross-sectional study was conducted to assess the serum lipid profile parameters and their association with glucose intolerance status in prediabetics and type 3 diabetes mellitus subjects in Indian subjects. The study included a total of 1146 subjects from both genders with an age of more than 20 years. The mean age of the study subjects was 45.6, 44.4, and 41.3 years for Type 2 DM, prediabetics, and normal subjects respectively ($p<0.001$). Gender has a significant difference in the three groups with 43.97% (n=73) males in Type 2 DM group p=0.003. High TG low HDL-C, LDL-C, and LDL-C ≥3.4mmol/l was highest in subjects with type 2 diabetes mellitus followed by prediabetics, and normal subjects with respective p-values of <0.001, 0.01, and 0.01 respectively. High HDL-C was seen in prediabetes followed by diabetes (p=0.003). TG, TG≥1.7mmol/L, TC, and TC≥5.2mmol values were highest for the diabetes group followed by prediabetes and normal subjects with a respective p-value of <0.001. HOMA-IR values were 4.12 for diabetics, 2.34 for prediabetics, and 1.48 for normal subjects ($p<0.001$). Fasting insulin, 2h Plasma glucose, fasting plasma glucose, hypertension, Waist M≥90, F≥80, and BMI≥25kg/m2 was also significantly higher for diabetics followed by prediabetics and normal subjects with $p<0.001$. These demographics were comparable to the studies of Misra A et al[6] in 2017 and Badimon JJ et al[7] in 2015 where authors assessed diabetics and prediabetics with comparable demographics as the present study.

For the assessment of different lipid parameters and associated risk for diabetes and prediabetes in the study subjects, it was seen that the odds ratio for 95% confidence interval for type 2 diabetics was 0.61 for LDL-C, 2.15 for HDL-C, 3.89 for triglycerides, and 2.41 for total cholesterol. This was non-significant for LDL-C with a p-value of 0.107. However, for HDL-C, triglycerides, and total cholesterol, these values were statistically significant with respective p-values of 0.04, <0.001, and <0.001. For prediabetics, the odds ratio for LDL-C, HDL-C, triglycerides, and total cholesterol was 1.42, 2.95, 1.98, and 0.92 respectively. For LDL-C and total cholesterol, this was statistically non-significant with respective p-values of 0.733 and 0.194. However, for HDL-C and triglycerides, this difference was statistically significant with p-values of <0.001 and 0.01 respectively. These results were consistent with the studies of Aryal N et al[8] in 2017 and Gallego S[9] in 2015 where similar lipid parameters as in the present study were seen in subjects with diabetes and prediabetes.

Based on the 4 categories of 0=normal HDL-C and triglycerides, 1= normal HDL-C and high triglycerides, 2= normal triglycerides and low HDL-C, and 3=high triglycerides and low HDL-C, the status was assessed. For category 0, 1, 2, and 3 there were 6.02% (n=69), 1.04% (n=12), 63% (n=722), and 28.97% (n=332) cases. In diabetics, for category 0, 1, 2, and 3 there were 1.44% (n=1), 16.66% (n=2), 4.01% (n=29), and 16.86% (n=56) events. This was statistically significant for category 3 with $p<0.001$ and non-significant for category 1 and 2 with p-values of 0.007 and 0.08 respectively. Events for prediabetics were 2.89% (n=3), 8.33% (n=1), 8.03% (n=58), and 12.11% (n=39) respectively for category 0, 1, 2, and 3. This was statistically significant for category 2 and 3 with p-values of 0.03 and 0.002 respectively. These results were in agreement with the findings of Li N et al[10] in 2014 and Siddiquee T et al[11] in 2015 where authors found similar triglyceride and HDL-C levels in their study population as in the present study.

CONCLUSION

Within its limitations, the present study concludes that high levels of triglycerides and HDL-C parameter of dyslipidemia are seen in subjects with diabetes mellitus which increase proportionally with the increase in glucose intolerance. This points to regular lipid parameter monitoring in subjects with type 2 diabetes mellitus. However, the present study had a few limitations including small sample size, cross-sectional nature, and geographical area biases. Hence, more longitudinal studies with larger sample size and longer monitoring period will help reach a definitive conclusion.

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TABLES

Characteristics	Type 2 diabetes mellitus (n=166)	Prediabetes (n=172)	Normal subjects (n=808)	p
Mean age (years)	45.6	44.4	41.3	<0.001
Gender % (n)				
Males	43.97 (73)	43.02 (74)	35.02 (283)	0.003
Females	56.02 (93)	56.97 (98)	64.97 (525)	
High TG low HDL-C % (n)	59.03 (98)	40.11 (69)	25 (202)	<0.001
LDL-C (mmol/L)	2.82	2.78	2.74	0.01
LDL-C ≥3.4mmol/l % (n)	15.66 (26)	15.69 (27)	11.01 (89)	0.01
HDL-C (mmol/L)	0.83	0.88	0.93	<0.001
High HDL-C % (n)	95.78 (159)	97.09 (167)	90.96 (735)	0.003
TG (mmol/L)	1.7	1.3	1.1	<0.001
TG≥1.7mmol/L % (n)	62.65 (104)	41.86 (72)	25.99 (210)	<0.001
TC (mmol/L)	4.7	4.3	4.1	<0.001
TC≥5.2mmol/ L%(n)	25.90 (43)	12.79 (22)	9.03 (73)	<0.001
HOMA-IR	4.12	2.34	1.48	<0.001
Fasting insulin (µIU/ml)	11.3	10.3	7.7	<0.001
2h Plasma glucose (mmol/L)	13.7	7.3	5.2	<0.001
Fasting plasma glucose (mmol/L)	9.3	5.5	4.5	<0.001
Hypertension % (n)	24.69 (41)	16.86 (29)	13.98 (113)	<0.001
Waist M≥90, F≥80 % (n)	62.04 (103)	56.97 (98)	36.01 (291)	<0.001
BMI≥25kg/m2 % (n)	40.96 (68)	43.02 (74)	23.01 (186)	<0.001

Table 1: Demographic and disease characteristics of the study subjects

Lipid parameters	Type 2 diabetes		Prediabetes	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
LDL-C	0.61	0.107	1.42	0.733
HDL-C	2.15	0.042	2.95	<0.001
Triglycerides	3.89	<0.001	1.98	0.01
Total cholesterol	2.41	<0.001	0.92	0.194

Table 2: Different lipid parameters and associated risk for diabetes and prediabetes in the study subjects

Status	Subgroup	Events % (n)	Cases % (n)	p-value
Type 2 diabetes (n=166)	**0**	1.44 (1)	6.02 (69)	
	1	16.66 (2)	1.04 (12)	0.007
	2	4.01 (29)	63.00 (722)	0.08
	3	16.86 (56)	28.97 (332)	<0.001
Prediabetes (n=172)	**0**	3 (2.89)	6.02 (69)	
	1	8.33 (1)	1.04 (12)	0.455
	2	8.03 (58)	63.00 (722)	0.03
	3	12.11 (39)	28.97 (332)	0.002

Table 3: Association of triglycerides and HDL-C in prediabetics and diabetics study subject