

Association of atherosclerosis with dyslipidemia and co-morbid conditions: A descriptive study

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Abstract

Background: Dyslipidemia (Dys), the commonest cause of cardiovascular diseases, leads to lipid deposits on the arterial wall, thereby aggravating the process of atherosclerosis. To assess the impact of Dys and other co-morbid conditions on atherosclerosis (i.e., increased intimo medial thickness (IMT) or plaques) in the common carotid arteries (CCAs) we studied the incidence and association of plaques and increased IMT in dyslipidemic patients from North Indian population (south-west of Punjab, India). **Materials and Methods:** A cross-sectional study consisting of 88 (male-39 and female-49) dyslipidemic patients (age group 30-80 years); was designed. Blood pressure, waist circumference (WC), hip circumference (HC) were measured and fasting lipid profile, renal function, and liver function tests were performed. B-mode sonography, for CCA, was performed to assess IMT. **Results:** Average value (mg/dl) of total cholesterol, triglyceride, low density lipoprotein and high density lipoprotein in males and females was 220.30 versus 231.93, 240.3 versus 242.14, 125.29 versus 133.62 and 44.33 versus 46.09 respectively ($P > 0.05$, all), while WC, HC, systolic blood pressure and diastolic blood pressure were 101.8 versus 96.53 cm, 98.23 versus 99.53 cm, 143.23 versus 138.98 mmHg and 91.53 versus 88.97 mmHg respectively. Increased IMT and atherosclerotic plaques were observed in 36.36% cases ($n = 32$, male - 14 and female - 18) and 29.54% cases ($n = 26$, male 14, female 12) respectively. Odd ratio (OR) for plaques was more for Dys with coronary artery disease (CAD; 11.43) and Dys with CAD (Dys-CAD) + hypertension (HT) (24) respectively vs isolated Dys. **Conclusion:** Dyslipidemia patients have higher waist and HCs than normal subjects. Incidence and OR of plaques is higher in Dys-CAD or Dys-CAD + HT when compared to isolated Dys or Dys with HT. Hence, treatment of dyslipidemic patients' needs to be intensified if more than one risk factor(s) is present simultaneously.

Key words: Cardiovascular diseases, carotid intimo-medial thickness, common carotid arteries, co-morbid conditions, hip circumference, hypertension, risk factors, waist circumference

INTRODUCTION

Cardiovascular disorders (CVD) are major noncommunicable diseases worldwide and atherosclerosis is the major risk factor for morbidity and mortality associated with CVD.^[1-3] Dyslipidemia (Dys), cigarette smoking, hypertension (HT), diabetes, obesity and sedentary lifestyle are the modifiable risk factors for CVDs that promote atherosclerosis.^[1-4]

Of these, Dys stands out prominently as it enhances the deposition of the fats in the arteries, thereby narrowing the lumen, obstructing the blood supply, leading to thrombo-embolic episode(s) such as stroke, transient ischemic attack (TIA), ischemic heart disease, pulmonary embolism, etc.^[1-6] Patients with CVDs have silent atherosclerotic plaque(s) or increased intimo-medial thickness (IMT) prior to the incidence of thrombo-embolic events.^[1,7] Due to genetic or environmental variations, Indians have different kinds of risk factors,^[6,8] with only a few studies been reported. Hence, this study was designed involving North Indian subjects from the Malwa-region of Punjab (near Indo-Pak Border of Punjab), wherein socioeconomic background and living standards are considerably different from western nations. The study was designed to explore the risk factors and their association with atherosclerosis (increased IMT or plaques), in patients with Dys. Other co-morbid

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conditions were also studied, and patients were categorized according to risk factors/co-morbid conditions for efficient clinical management. We aimed to see the incidence of plaques and increased IMT in dyslipidemic patients and association of these atherosclerotic changes with Dys and co-morbid diseases in North Indian population from the Malwa-region of Punjab.

MATERIALS AND METHODS

A cross-sectional study with participants recruited from Medicine Department (outpatients and inpatients) of Guru Gobind Singh Hospital attached to Guru Gobind Singh Medical College, Faridkot was designed. Subjects in the age group of 30-80 years, having Dys with or without HT or coronary artery disease (CAD), were enrolled during a period of 3 months. A patient was diagnosed dyslipidemic according to NCEP-ATP III criteria as below:^[6] Total cholesterol (TC) >240 mg/dl or low density lipoprotein-cholesterol (LDL-C) >160 mg/dl or high density lipoproteins cholesterol (HDL-C) <40 mg/dl (male) or <50 mg/dl (female) or triglycerides (TGs) >200 mg/dl.

Nursing mothers or pregnant subjects, or subjects having hepatitis or cirrhosis of the liver, bronchial asthma, HIV, tuberculosis, chronic inflammatory disease, thyroid disorders, diabetes mellitus, renal failure or on corticosteroids, oral contraceptive pills, hormonal replacement therapy, alcoholism, tobacco chewing or smoking were excluded from the study. A total of 88 out of 100 individuals with Dys underwent physical examination and ultrasonography of the carotid arteries. We excluded 12 individuals who didn't fit the inclusion criteria. All individuals underwent a detailed medical history by a standardized questionnaire to obtain information about current and past medication(s) use, presence of CVDs (HT, CAD, stroke, TIA, etc.) and habits of smoking and alcohol. Patients underwent general physical examination including measurement of waist circumference (WC), Hip circumference (HC) and systemic blood pressure of both arms (systolic and diastolic, taken by a sphygmomanometer). Under aseptic conditions venous blood was collected after overnight fasting for lipid profile, serum glucose, blood urea, serum creatinine and other tests [Figure 1]. All the B-mode ultrasonographic measurements of common carotid arteries (CCAs) and internal carotid arteries were performed by a single blinded expert reader. The Institutional Ethical Committee approved the protocol, and all the subjects gave written informed consent before participating in the study.

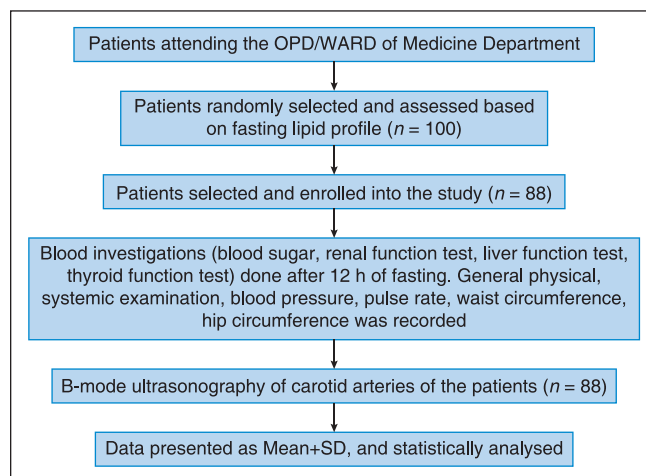


Figure 1: Study design

Carotid duplex sonographic of common carotid arteries

Carotid ultrasonography followed by a duplex color Doppler examination was performed on patients in the supine position with Philips Envisor unit with a linear probe of 7.5-12 MHz. Both left and right CCA were analyzed in longitudinal and transverse planes. IMT was measured at mid-CCA, about 10 mm proximal to the carotid bulb, between the leading edge of first echogenic line (lumen intima interface) and second echogenic line (upper layer of adventitia), in the far and near walls of the artery [Figure 2].^[9,10] The mean value of three readings in the mid-segment of CCA was recorded as IMT. A plaque is defined as a focal structure that encroaches into the arterial lumen of at least 0.5 mm or 50% of the surrounding IMT value or demonstrates a thickness >15 mm as measured from the media-adventitia interface to the intima lumen interface [Figure 3], and an IMT of <8 mm as normal while >8 mm considered to be increased IMT [Figure 4].^[9]

Statistical analysis

Data are represented as mean and standard deviation for continuous variable and frequency and column percentages for categorical variables. Participant's demography was stratified by gender and Student's *t*-test applied. Data were categorized into four groups according to risk factors/co-morbid conditions. The Chi-square test and Fischer exact test for categorical data were used to evaluate the association between variables. $P < 0.05$ was considered to be significant.

RESULTS

The average age of the study population was 55.14 ± 9.25 years (male- 55.89 ± 10.92 and female- 54.55 ± 7.74). Detailed clinical characteristics of the patients are listed in Table 1. As per the observations the patients were categorized into four groups that are, patients with isolated Dys, Dys with

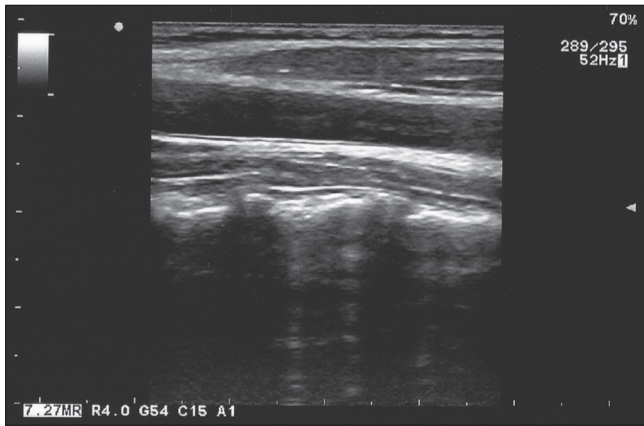


Figure 2: Carotid sonography showing normal intimo-medial thickness

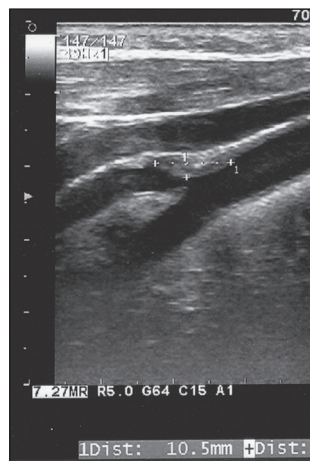


Figure 3: Carotid sonography showing plaque at near wall at bifurcation

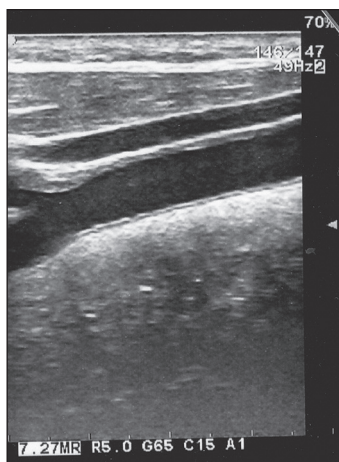


Figure 4: Carotid sonography showing increased intimo-medial thickness

HT (Dys-HT), Dys with CAD (Dys-CAD), and Dys-HT and CAD (Dys-HT-CAD) [Table 2]. Table 2 shows mean and standard deviation of age, TC, TGs, LDL, VLDL, HDL, WC and HC, systolic blood pressure (SBP) and diastolic blood pressure (DBP), number of plaques and IMT in these categories. Average value (mg/dl) of TC,

TG, LDL and HDL in males and females was 220.30 versus 231.93, 240.3 versus 242.14, 125.29 versus 133.62 and 44.33 versus 46.09 respectively ($P > 0.05$, all), whereas WC, HC, SBP and DBP were 101.8 versus 96.53 cm, 98.23 versus 99.53 cm, 143.23 versus 138.98 mmHg and 91.53 versus 88.97 mmHg respectively [Table 1]. Increased IMT was seen in 36.36% cases ($n = 32$, male-14 and female-18) while plaques in 29.54% cases ($n = 26$, male-14, female-12) [Table 1]. Odds ratio (OR) for plaques was 24.00 ($P < 0.01$) for Dys-HT-CAD patients when compared to isolated dyslipidemic patients. Incidence of plaque and OR was significantly higher in the Dys-HT-CAD category when compared to Dys, Dys-HT and Dys-CAD categories [Table 3]. Plaques in CCA were observed in 5.9% subjects with Dys, 25% with Dys-HT, 41.7% with Dys-CAD, and 60% with Dys-HT-CAD [Table 4] indicating that CCA plaques are higher in dyslipidemic subjects having multiple co-morbid conditions vis-a-vis Dys alone or Dys with a single co-morbid disease.

DISCUSSION

All the patients in our study group had higher average WC compared to normal values (male-90 cm and female-80 cm, respectively).^[11] Average age of male and female subjects in our study group was higher^[8] and lower^[12] compared with previous reports. However, our data is consistent with the previous report suggesting a higher incidence of Dys and other risk factors at an early age of their life as compared to the Western population. Genetic factors or lifestyle may be major factors responsible for such early Dys events which are a cause for concern. Further the average age of patients in isolated Dys (50.06 ± 8.89 years) was less as compared to Dys-HT (55.6 ± 9.08 years), Dys-CAD (57.64 ± 8.23 years) and Dys-HT-CAD (58.73 ± 10 years) respectively, indicating an early role of Dys in progression of cardiovascular pathology. The increased blood pressure observed in our study group is consistent with previous reports.^[13] Both SBP and DBP was higher in patients with Dys-HT (147.3 ± 21.95 and 94 ± 13.3) and Dys-HT-CAD (144.4 ± 15.06 and 93.6 ± 6.74) as compared to Dys (131.9 ± 17.21 and 83.1 ± 8.73), Dys-CAD (123.8 ± 17.67 and 80.9 ± 13.8) respectively. Thus, further supporting the primary role of Dys in development of cardiovascular hemodynamics. The plasma levels of TC and LDL was less, while TGs was higher in our study group, which is consistent with the previous report^[13] and suggests that our study group is more prone to hypertriglyceridaemia than hypercholesterolemia in contrast to the Western population.

The mean value of carotid IMT in our study group was higher as compared to previous reports from

Table 1: Baseline characteristics of the population

Variable	Mean (n = 88)	SD	Male (n = 39)	Female (n = 49)	Male versus female (Students' t-test)
Age (years)	55.14	9.25	54.89±10.92	54.55±7.74	>0.05
TC (mg/dl)	226.78	51.57	220.30±51.61	231.93±51.48	>0.05
TGs (mg/dl)	241.32	89.51	240.3±83.17	242.14±95.09	>0.05
LDL (mg/dl)	129.92	49.41	125.29±46.44	133.62±51.82	>0.05
VLDL (mg/dl)	49	18.2	47.42±16.67	48.39±19.16	>0.05
HDL (mg/dl)	45.32	5.97	44.33±6.139	46.09±5.78	>0.05
WC (cm)	98.86	10.22	101.8±12.29	96.53±7.56	<0.01
HC (cm)	98.95	8.607	98.23±8.62	99.53±8.63	>0.05
SBP (mmHg)	140.84	21	143.23±20.67	138.98±21.53	>0.05
DBP (mmHg)	125	12.05	91.53±12.03	88.97±13.26	>0.05
CCA Nearwall (cm)					
Right	0.765	0.09	0.75±0.06	0.78±0.01	>0.05
Left	0.8	0.14	0.82±0.14	0.78±0.01	>0.05
CCA Farwall (cm)					
Right	0.78	0.11	0.77±0.01	0.79±0.011	>0.05
Left	0.805	0.15	0.82±0.16	0.79±0.014	>0.05
CCA (cm) (mean of Nearwall and Farwall)					
Right	0.7725	0.01	0.76±0.08	0.785±0.10	>0.05
Left	0.8025	0.14	0.82±0.15	0.785±0.12	>0.05
ICA (cm) (mean of Nearwall and Farwall)					
Right	0.755	0.07	0.75±0.08	0.76±0.06	>0.05
Left	0.785	0.13	0.81±0.16	0.76±0.09	>0.05
Total IMT of CCA+ICA	0.739	0.01	0.733±0.01	0.774±0.01	>0.05
Percentage of plaques (n)	29.54 (26)	—	35.89 (14)	24.49 (12)	>0.05
Percentage of IMT (>0.8 mm) of CCA (n)	36.36 (32)	—	35.89 (14)	36.74 (18)	>0.05

TC: Total cholesterol, TGs: Triglycerides, LDL: Low density lipoprotein, VLDL: Very low density lipoprotein, HDL: High density lipoprotein, WC: Waist circumference, HC: Hip circumference, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CCA: Common carotid arteries, ICA: Internal carotid arteries, SD: Standard deviation, IMT: Intima medial thickening

Table 2: Categorization of the participants according to risk factors/co-morbid conditions

Variables	Dyslipidemia	Dyslipidemia with HT	Dyslipidemia with CAD	Dyslipidemia with HT and CAD	Plaques in the carotid arteries
n	17	44	12	15	26
Age (years)	50.06±8.89	55.6±9.08	57.64±8.23	58.73±10.4	59.08±8.85
TC (mg/dl)	237.1±45.81	223.9±54.19	242±62.24	209.9±37.52	232±61.09
TGs (mg/dl)	298±133.7	235.5±74.81	190.5±55.3	224.5±51.7	260.6±81.53
LDL (mg/dl)	132.6±49.04	128.5±49.26	157.7±59.82	119.6±38.2	134.5±51.3
VLDL (mg/dl)	58.28±27.31	46.78±15.24	38.07±11.11	44.85±10.3	51.93±16.28
HDL (mg/dl)	45.56±5.05	44.51±5.82	45±7.6	47.91±5.97	44.92±6.59
WC (cm)	94.1±8.14	99±9.71	98.7±10.8	103±14.2	96.4±8.96
HC (cm)	98.43±8.27	99.27±9.45	96±6.43	99.59±8.63	95.72±6.71
Number of plaques (percentage within the group)	01 (5.9)	11 (25)	05 (41.7)	09 (60)	26 (100)
Bilateral plaques	Nil	3	2	Nil	05
SBP (mm Hg)	131.9±17.21	147.3±21.95	123.8±17.67	144.5±15.1	145.4±20.77
DBP (mm Hg)	83.1±8.73	94±13.3	80.9±13.8	93.6±6.74	92.97±10.4
CCA (average of Nearwall and Farwall)					
Right	0.765±0.09	0.782±0.73	0.749±0.07	0.77±0.10	0.78±0.05
Left	0.820±0.17	0.803±0.13	0.771±0.10	0.86±0.17	0.87±0.18

TC: Total cholesterol, TGs: Triglycerides, LDL: Low density lipoprotein, VLDL: Very low density lipoprotein, HDL: High density lipoprotein, WC: Waist circumference, HC: Hip circumference, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CCA: Common carotid arteries, HT: Hypertension, CAD: Coronary artery disease

Korea,^[14] Japan,^[14] and Mexican American population.^[15] However, the IMT was lower compared to previous reports from the western population.^[13,16] Plaques in CCA were observed in 29.54% cases in the present study and were both lower^[13] and higher^[16] than previous reports from the western population. TC, LDL, WC

and HC were highest in Dys-HT-CAD patients as compared to other categories while TGs and VLDL-C levels were higher in Dys patients as compared to Dys-CAD (242 ± 62.24), Dys-HT (235.5 ± 74.81) and Dys-HT-CAD (224.5 ± 51.7) respectively. Dys-HT-CAD patients had a higher percentage of plaques, WC and

Table 3: Risk of plaque formation among subgroups of dyslipidemia

Category	Plaques		95% CI	Odds ratio	P*
	Yes	No			
Dys HT (vs.)	11	33	0.63-44.99	5.33	>0.05
Dys	1	16			
Dys CAD (vs.)	5	7	1.12-116.70	11.43	<0.05
Dys	1	16			
Dys CAD HT (vs.)	9	6	2.48-232.09	24.00	<0.01
Dys	1	16			
Dys CAD (Vs.)	5	7	0.56-8.14	2.14	>0.05
Dys HT	11	33			
Dys CAD HT (vs.)	9	6	1.30-15.52	4.50	<0.05
Dys HT	11	33			
Dys CAD HT (vs.)	9	6	0.45-9.84	2.10	>0.05
Dys CAD	5	7			

*Fischer exact test (one tailed), CI: Confidence interval, HT: Hypertension, CAD: Coronary artery disease

Table 4: Different co-morbid conditions and plaques in common carotid arteries

Risk factors/co-morbid condition(s)	Plaques in common carotid arteries		
	Present (%)	Absent (%)	Total
Dyslipidemia and dyslipidemia+HT*	12 (19.67)	49 (80.33)	61
Dyslipidemia+CAD	5 (41.7)	7 (58.3)	12
Dyslipidemia+HT+CAD	9 (60)	6 (40)	15
Total	26 (29.5)	62 (70.5)	88
Chi-square value (P)	10.39 (0.005)		

*Chi-square value has been calculated by merging of values of both dyslipidemia and dyslipidemia + HT categories, HT: Hypertension, CAD: Coronary artery disease

HC as compared to Dys-CAD, Dys-HT and isolated Dys respectively. OR and incidence of plaques were significantly higher in the Dys-CAD-HT and Dys-CAD categories as compared to Dys and Dys-HT categories, respectively. Our observations suggest that plaques have a strong association with co-morbid conditions viz. Dys-HT-CAD and this association becomes progressive when more than one co-morbid condition exists simultaneously in the dyslipidemic patient. ACC/AHA Cardiovascular Risk Assessment Guidelines (2013)^[5] recommend hs-C-reactive protein, coronary artery calcium score, microalbuminuria, etc. as better tools for risk assessment of CVDs, but in developing countries like India because of the cost and limited availability of these investigations, ultrasonographic assessment of IMT and plaques in the arteries is a cost effective and easily available modality for risk assessment of dyslipidemic patients. Limitations of the study: As the study design was cross-sectional, and hospital based, performed in a relatively small sample size of patients, the results need to be confirmed in a large, population based study. Nevertheless dyslipidemic patients should be explored for other CVD risk factors such as HT, obesity, increased IMT and plaques in CCA with noninvasive B-mode Ultrasonography for early

detection of progressive cardiovascular pathology, which can help initiate early therapy to prevent development of serious CVDs complications and improve therapeutic outcome.

In conclusion, dyslipidemic patients have higher waist and HCs. Incidence and OR of plaques is higher in patients who have Dys-CAD or. Dys-HT-CAD as compared to those having isolated Dys or Dys-HT. Hence, dyslipidemic patients should be treated accounting for the existence of simultaneous risk factor(s).

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