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A Comparative Study of Carotid Intima-Medial Thickness (CIMT) Among Smokers and Non-Smokers

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Abstract

BACKGROUND:
Atherosclerosis is one of the most common causes of mortality throughout the world and continues to be the leading cause of morbidity in industrialized countries in population more than 45 years of age. The carotid intima-media thickness (IMT) is a widely used surrogate marker for atherosclerosis worldwide. Thickening of the intima-media is identified as the initial stage in the pathogenesis of atherosclerosis and it is also a predictor of future cardiovascular and cerebrovascular events.

AIMS AND OBJECTIVES:
To study the modulating effect of smoking on atherosclerosis, by assessing and comparing carotid intima-medial thickness among smokers and non-smokers.

METHODOLOGY:
This study is a hospital based comparative cross-sectional study conducted in a tertiary care hospital in Salem district of Tamilnadu. Study population identified were Smokers (50) and non-smokers (50) attending the General medicine outpatient department (OPD). The inclusion criteria for the study were Individuals aged between 20-50 years. Smokers and non-smokers without any vascular diseases. Smokers, smoking ≥ 10 cigarette per day for a duration of ≥ 5 years. The patients with any vascular disorders/diabetes mellitus/familial dyslipidemia/alcoholic and patients who are already on statins are excluded from the study. After getting the written and informed consent carotid doppler was done and CIMT was measured. In addition to that lipid profile was also done and results were analyzed.

RESULTS:
In this study, 52% of the smokers had a pack year of ≤ 15, 38% had 16-25 pack years and 10% of the smokers had a pack year > 25. Almost three fourth (74%) of them had increased CIMT and only 34% of the non-smokers had increased CIMT. We also found a significant association between carotid intima media thickness and smoking with smokers having 5.52 times more risk of having high carotid intima media thickness compared to non-smokers. And also, there was a significant association between CIMT and total cholesterol & triglyceride value whereas VLDL and HDL were found to be non-significant.

CONCLUSION:
The current study demonstrates that cigarette smoking is associated with increased atherosclerosis as indicated by increased CIMT in smokers as compared to non-smokers. Our results emphasize the importance of prevention and cessation of cigarette smoking behavior.

KEYWORDS: Smoking, Carotid doppler, Carotid intima-medial thickness (CIMT), Lipid Profile.

Introduction

Atherosclerosis is one of the most common causes of mortality throughout the world and continues to be the leading cause of morbidity in industrialized countries in population more than 45 years of age. The carotid intima-media thickness (IMT) is a widely used surrogate marker for atherosclerosis worldwide Carotid ultrasonography allows the measurement of not only the carotid IMT but also the presence and characteristics of plaques and the severity of carotid stenosis. Hence, in this study we would like to evaluate the modulating effect of smoking on atherosclerosis, by assessing and comparing carotid

intima medial thickness among smokers and non-smokers.

Methodology:

Study design:

This study is a hospital based comparative cross-sectional study conducted in a tertiary care hospital in India.

Study population:

Study population identified were Smokers (50) and non-smokers (50) attending the General medicine outpatient department of a tertiary care hospital in India.

Study period:

The study was carried out from November 1st 2020 – April 31st 2021 for a period of 6 months.

Inclusion criteria:

1. Individuals aged between 25-50 years.
2. Smokers and non-smokers without any vascular diseases.
3. Smokers, smoking ≥ 10 cigarettes per day for a duration of ≥ 5 years.
4. Individuals who gave written informed consent for participation.

Exclusion criteria:

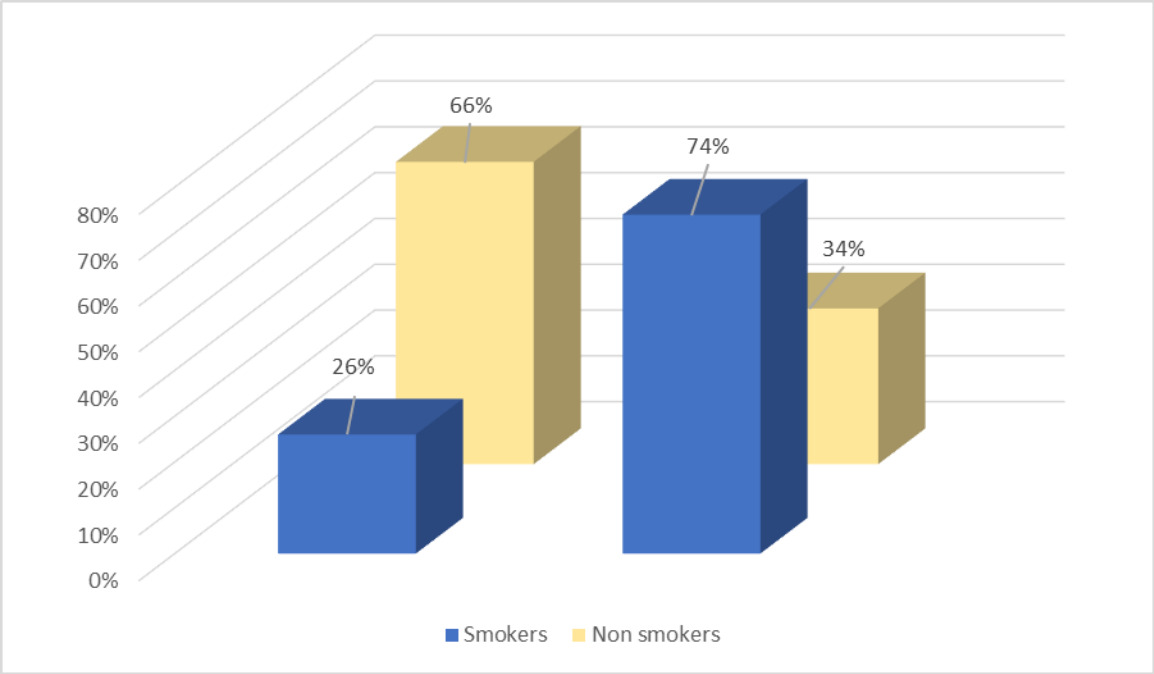
1. Patients with diabetes mellitus.
2. Patients with Coronary artery disease/Cardiovascular disease/Chronic kidney disease.
3. Individuals with Familial dyslipidemia
4. Patients on statins /fibrates were excluded from the study.

Sample size and Sampling method:

Sample size was calculated based on the study by Maillane-Vanegas using a correlation coefficient of 0.34 with 80% power at 95%confidence interval. The sample size included was 100. About 50 smokers and 50 non-smokers fulfilling the inclusion and exclusion criteria were selected using purposive sampling method until the desired sample size is reached.

Study tool:

A semi structured questionnaire was used as study tool for data collection, by interviewing the study participants. The interview was conducted by the investigator himself and their responses were recorded in the questionnaire.



Among the smokers, 74% of them had increased carotid intima media thickness and only 34% of the non-smokers had increased carotid intima media thickness.

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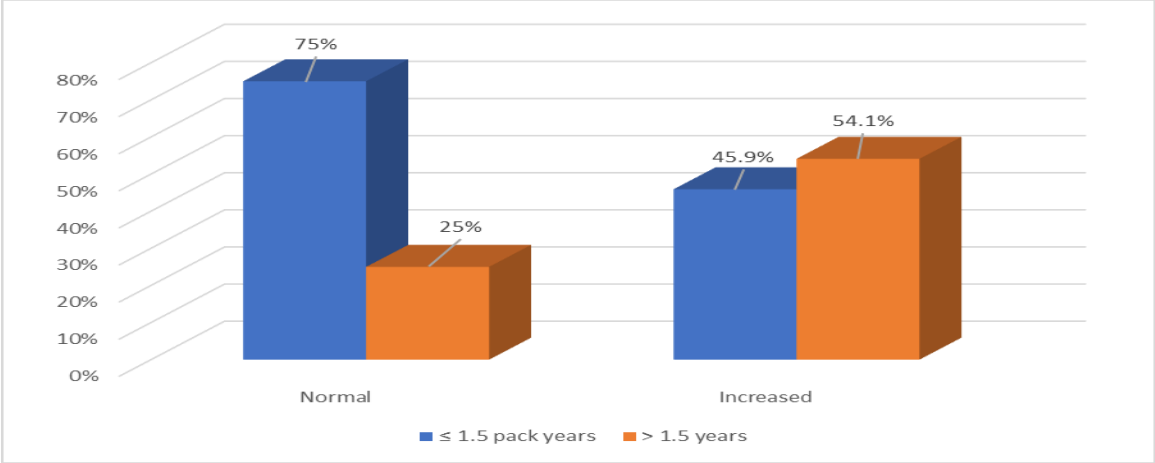
Distribution of carotid artery intima media thickness as per pack years of smoking (N-50)

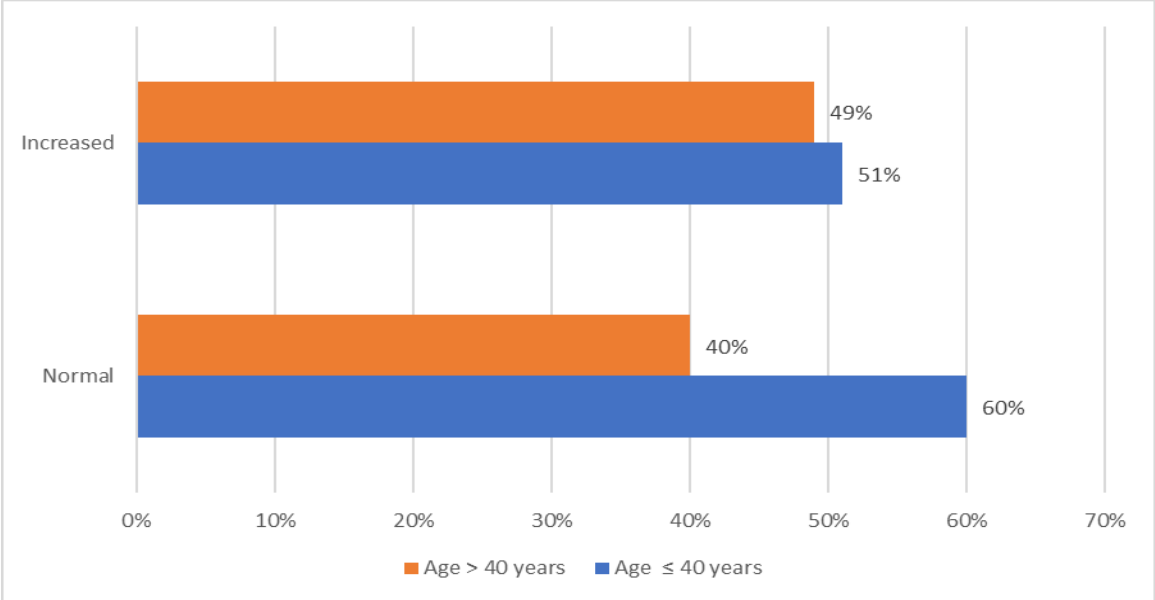
S.No	CIMT	Pack years ≤ 1.5		Pack years > 1.5	
		Frequency	Percentage	Frequency	Percentage
1.	CIMT				
	Normal	9	75%	3	25%
	Increased	17	45.9%	20	54.1%

According to the above table it can be inferred that among smokers with pack years of smoking > 1.5 54.1% had increased carotid artery intima thickness and about 75% of those with pack years of smoking ≤ 1.5 had normal CIMT values.

Distribution of carotid artery intima media thickness as per pack years of smoking (N-50)



Distribution of carotid artery intima media thickness as per age



Among the study participants with increased carotid intima media thickness about 51% belonged to age ≤ 40 years of age and 49% belonged to age > 40 years of age.

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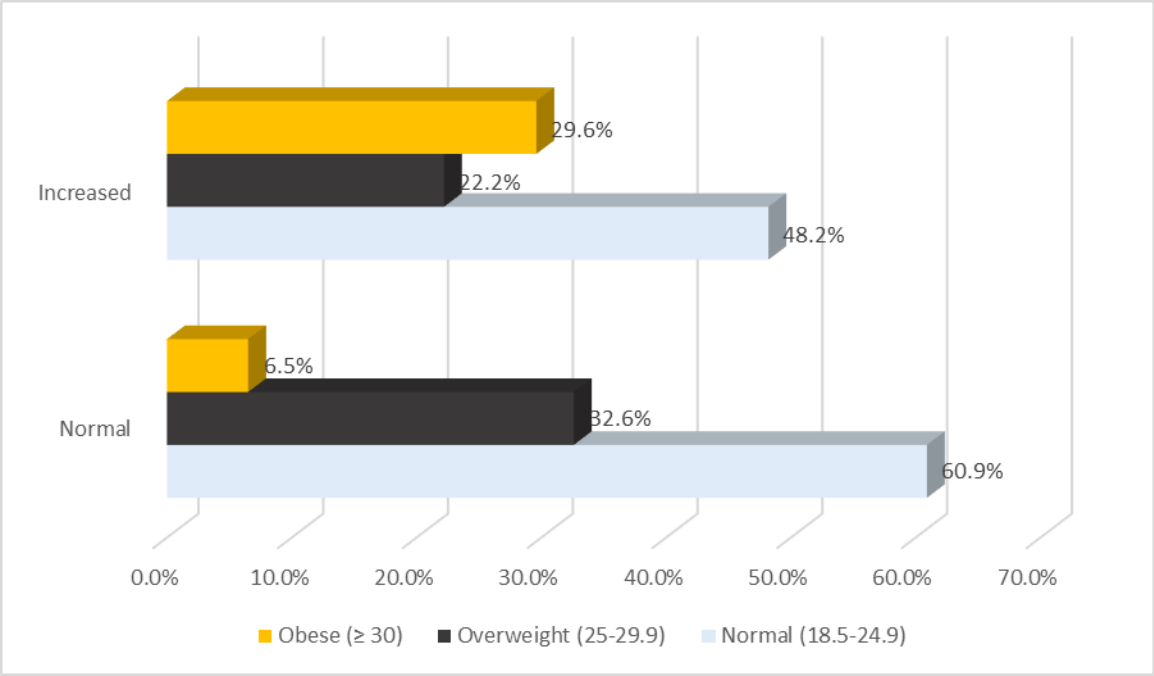
Distribution of carotid artery intima media thickness as per BMI Category



Among the study respondents with increased carotid intima media thickness, 48.2% had normal BMI and 29.6% were obese. Nearly 60.9% of those with normal carotid intima media thickness were belonging to normal BMI category and 32.6% were overweight.

Distribution of carotid artery intima media thickness as per BMI Category

S.No	CIMT	Normal		Overweight/Obese	
		Frequency	Percentage	Frequency	Percentage
1.	CIMT				
	Normal	28	60.9%	18	39.1%
	Increased	26	48.2%	28	51.8%

Mean and standard deviation of selected variables

S.No	Variable	Mean	Standard deviation	Minimum	Maximum
1.	Age (Years)	37.18	8.045	25	50
2.	BMI	25.39	4.383	19	40
3.	Duration of smoking (Years)	9.72	3.709	5	20
4.	Cigarettes smoke per day	16.70	2.418	12	20
5.	No of packs of cigarettes smoked per	1.67	0.242	1	2

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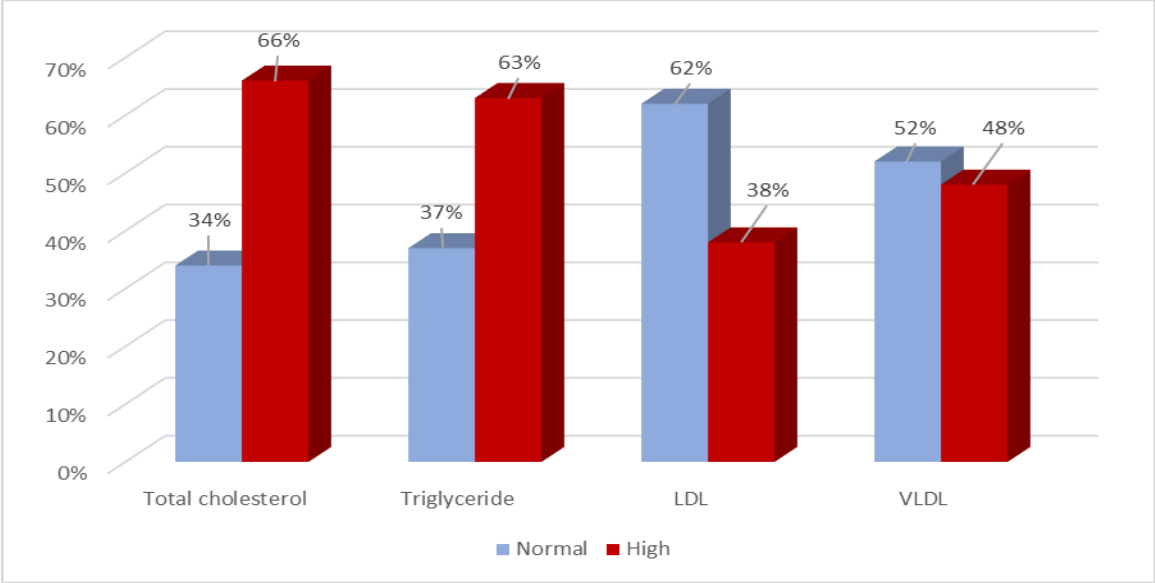
	day				
6.	Pack years	16.16	6.48	7	34
7.	Total cholesterol (mg/dl)	216.99	33.033	147	294
8.	Triglycerides (mg/dl)	165.24	30.576	104	266
9.	HDL (mg/dl)	47.09	10.768	21	68
10.	LDL (mg/dl)	125.44	14.858	100	159
11.	VLDL (mg/dl)	28.67	7.711	15	42

Among the study participants the mean age was 37.18±8.045 years and mean BMI was 25.39±4.383. Mean duration of smoking was 9.72±3.709 years. Mean total cholesterol and triglyceride values were 216.99±33.033 mg/dl and 165.24±30.576 mg/dl respectively.

Distribution of lipid profile among the study participants



Among the study participants 66% and 63% of them had high total cholesterol and triglyceride value. About 62% had normal LDL values and 52% had normal VLDL values in this study.

Distribution of lipid profile as per age

S.No	Lipid profile	Age ≤ 40 years		Age > 40 years	
		Frequency	Percentage	Frequency	Percentage
1.	**Total cholesterol**				
	Normal	17	50%	17	50%
	High	39	59.1%	27	40.9%
2.	**Triglyceride**				
	Normal	21	56.8%	16	43.2%
	High	35	55.5%	28	45.5%

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3.	**HDL**				
	Normal	7	70%	3	30%
	Low	49	54.4%	41	45.6%
4.	**LDL**				
	Normal	37	59.7%	25	40.3%
	High	19	50%	19	50%
5.	**VLDL**				
	Normal	31	%	21	%
	High	25	%	23	%

Among the participants with high cholesterol 59.1% were ≤ 40 years of age and 40.9% were belonging to > 40 age category. About 55.5% of those with high triglyceride value belong to age ≤ 40 and 45.5% were of age > 40. Nearly 54.4% of those with low HDL values belonged to age ≤ 40 and 50% of those with high LDL values belonged to > 40 years of age.

Distribution of lipid profile as per sex

S.No	Lipid profile	Male		Female	
		Frequency	Percentage	Frequency	Percentage
1.	**Total cholesterol**				
	Normal	29	85.3%	5	14.7%
	High	59	84%	7	16%
2.	**Triglyceride**				
	Normal	33	89.2%	4	10.8%
	High	55	82.1%	8	17.9%
3.	**HDL**				
	Normal	9	90%	1	10%
	Low	79	87.8%	11	12.2%
4.	**LDL**				
	Normal	57	91.9%	5	8.1%
	High	31	81.6%	7	18.4%
5.	**VLDL**				
	Normal	46	88.5%	6	11.5%
	High	42	87.5%	6	12.5%

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In this study, among those with high total cholesterol 84% were males and 16% were females and similarly those with high triglyceride values 82.1% were males and 17.9% were females. Among those with low HDL values 87.8% were male and 12.2% were females. Those with high LDL values 81.6% were male and 18.4% were female.

Distribution of lipid profile as per BMI

S.No	Lipid profile	Normal		Overweight/Obese	
		Frequency	Percentage	Frequency	Percentage
1.	**Total cholesterol**				
	Normal	17	50%	17	50%
	High	37	56.1%	29	43.9%
2.	**Triglyceride**				
	Normal	21	56.8%	16	43.2%
	High	33	52.4%	30	47.6%
3.	**HDL**				
	Normal	6	60%	4	40%
	Low	48	53.3%	42	46.7%
4.	**LDL**				
	Normal	33	53.2%	29	46.8%
	High	21	55.3%	17	44.7%
5.	**VLDL**				
	Normal	28	53.8%	24	46.2%
	High	26	54.2%	22	45.8%

In our study among the respondents with high total cholesterol value 56.1% had normal BMI and 43.9% were either overweight or obese. Likewise, among the respondents with low HDL 53.3% had normal BMI and 46.7% were overweight or obese. Among those with high VLDL values 54.2% had normal BMI and 45.8% were overweight or obese.

Distribution of Lipid Profile Among Smokers and Non-Smokers

S.No	Lipid profile	Smoker		Non-smoker	
		Frequency	Percentage	Frequency	Percentage
1.	**Total cholesterol**				
	Normal	8	23.5%	26	76.5%
	High	42	65.5%	24	34.5%
2.	**Triglyceride**				
	Normal	10	27%	27	73%

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	High	40	63.5%	23	36.5%
3.	**HDL**				
	Normal	3	30%	7	70%
	Low	47	52.2%	43	47.8%
4.	**LDL**				
	Normal	30	48.4%	32	51.6%
	High	20	52.6%	18	47.4%
5.	**VLDL**				
	Normal	16	30.8%	36	69.2%
	High	34	70.8%	14	29.2%

Among the study participants with high triglyceride value, 65.5% were smokers and 34.5% were non-smokers. Similarly, those with high LDL values 52.6% were smokers and 47.4% were non-smokers. Among the respondents with low HDL values 52.2% and 47.8% were smokers and non-smokers respectively. About 70.8% of those with high VLDL values were smokers and 29.2% were non-smokers.

Association between CIMT and smoking

Variable	**CIMT**		**P value**	**Odds ratio**	**95% Confidence interval (CI)**
	Increased	**Normal**			
Smoker	37	13	**0.0001****	5.52	2.33-13.07
Non smoker	17	33			
** p value < 0.01is highly significant					

In this study on testing the association between carotid intima media thickness and smoking there was a highly significant statistical association (p value-0.0001, OR- 5.52). It also can be inferred that smokers have 5.52 times more chance of having high carotid intima media thickness compared to non-smokers.

Association between CIMT and lipid profile

Variable	**CIMT**		**P value**	**Odds ratio**	**95% Confidence interval (CI)**
	Increased	**Normal**			
Total cholesterol					
Normal	24	10	**0.016***	2.88	1.19-6.96
High	30	36			
Triglyceride					
Normal	26	11	**0.013***	2.95	1.24-6.99
High	28	35			
LDL					

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Normal	20	42	**<0.0001****	0.05	0.01-0.17
High	34	4			
VLDL					
Normal	26	26	0.404	0.71	0.32-1.57
High	28	20			
HDL					
Normal	5	5	0.789	0.83	0.22-3.09
Low	49	41			
* p value < 0.05 is significant and **p value < 0.01 is highly significant					

On testing the association between carotid intima media thickness and lipid profile statistically significant association was found between carotid intima media thickness and total cholesterol (p value-0.016), triglyceride value (p value-0.013) and LDL (p value <0.0001). VLDL and HDL were found to be non-significant.

Association between Total cholesterol and smoking

Variable	**Total cholesterol**		**P value**	**Odds ratio**	**95% Confidence interval (CI)**
	High	**Normal**			
Smoker	42	8	**0.0003****	5.68	2.22-14.52
Non smoker	24	26			
** p value < 0.01 is highly significant					

In this study, total cholesterol value was significantly associated with smoking (p value 0.0003). Smokers have 5.68 times more chance of having high total cholesterol value compared to non-smokers.

Association between Triglyceride and smoking

Variable	**Triglyceride**		**P value**	**Odds ratio**	**95% Confidence interval (CI)**
	High	**Normal**			
Smoker	40	10	**0.0006****	4.69	1.93-11.41
Non smoker	23	27			
** p value < 0.01 is highly significant					

In this study, triglyceride value was significantly associated with smoking (p value 0.0006). Smokers have 4.69 times more chance of having high triglyceride value compared to non-smokers.

Association between LDL and smoking

Variable	**LDL**		**P value**	**Odds ratio**	**95% Confidence interval (CI)**
	High	**Normal**			
Smoker	18	32	0.680	0.84	0.37-1.89
Non smoker	20	30			

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In this study, LDL value was not significantly associated with smoking (p value 0.680). Smokers and non-smokers had no difference in the LDL values.

Association between VLDL and smoking

Variable	VLDL		P value	Odds ratio	95% Confidence interval (CI)
	High	Normal			
Smoker	34	16	**0.0002****	5.16	2.18-12.20
Non smoker	14	36			
** p value < 0.01 is highly significant					

In this study, VLDL value was significantly associated with smoking (p value 0.0002). Smokers have 5.16 times more chance of having high total cholesterol value compared to non-smokers.

Association between HDL and smoking

Variable	HDL		P value	Odds ratio	95% Confidence interval (CI)
	Low	Normal			
Smoker	43	7	0.194	0.392	0.09-1.61
Non smoker	47	3			

In this study, HDL value was not significantly associated with smoking (p value 0.194). Smokers and non-smokers had no difference in the HDL values.

In our study, about 48% of the smokers belonged to 41-50 years of age and 24% of the non-smokers belonged to 31-40 years of age. Majority (88%) among smokers were male, almost three fourth (74%) of the smokers were using ≤ 15 cigarettes per day and nearly 60% of smokers were smoking for a duration of 5-10 years. These findings are parallel to a study done by Mahmoud MZ et al.

CIMT and Smoking:

Prior studies have demonstrated that smoking has a specific fibro genic effect which causes intimal thickening. The adverse effects of smoking on vascular wall structure have been historically evaluated by autopsy studies.

In this study, 52% of the smokers had a pack year of ≤ 15, 38% had 16-25 pack years and 10% of the smokers had a pack year > 25. Almost three fourth (74%) of them had increased carotid intima media thickness and only 34% of the non-smokers had increased carotid intima media thickness. We also Found a significant association between carotid intima media thickness and smoking with smokers having 5.52 times more risk of having high carotid intima media thickness compared to non-smokers [P value=0.0001, OR=5.52 (2.33-13.07)].

Li S et al,28 also observed similar findings where cigarette smokers had significantly higher CIMT when compared to non-smokers. Fan AZ et al, in their study found evidence that cigarette smoking and duration of smoking were positively Associated with markers of inflammation which may be one of the mechanisms of intimal injury from Smoking. In the Atherosclerosis Risk in Community (ARIC) study, it was observed progression of atherosclerosis among past smokers was higher than among never smokers, despite past smokers' non-smoking status over the period during their study and also no difference was found between past and current smokers after controlling for number of pack years of exposure. They suggested that the effect of smoking on atherosclerosis progression maybe cumulative, proportional to life time pack years of exposure and irreversible.

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Conclusion:

In this study, about 48% of the smokers belonged to 41-50 years of age and 24% of the non-smokers belonged to 31-40 years of age. Majority (88%) among smokers were male, almost three fourth (74%) of the smokers were using ≤ 15 cigarettes per day and nearly 60% of smokers were smoking for a duration of 5-10 years. 52% of the smokers had a pack year of ≤ 15, 38% had 16-25 pack years and 10% of the smokers had a pack year > 25. Almost Three fourth (74%) of them had increased carotid intima media thickness and only 34% of the non-smokers had increased carotid intima Medial thickness. We also found a significant association between carotid intima media thickness and smoking with smokers having 5.52 times more risk of having high carotid intima media thickness compared to non-smokers [P value=0.0001, OR=5.52 (2.33-13.07)]. We observed a significant association between carotid intima media thickness and total cholesterol [p value-0.016, CI: 2.88 (1.19-6.96)], triglyceride value [p value-0.013; CI: 2.95 (1.24-6.99)] and LDL [p value <0.0001; CI: 0.05 (0.01-0.17)]. Association Between CIMT and VLDL and HDL were found to be non-significant. In this study, we observed that total cholesterol, triglyceride and VLDL value was significantly associated with smoking [p value=0.0003; CI: 5.68 (2.22-14.52)], (p value 0.0006 CI: 4.69 (1.93-11.41)], (p value 0.0002; CI: 5.16 (2.18-12.20)], respectively. There was no significant association between LDL and HDL value with smoking.

In conclusion, the current study demonstrates that cigarette smoking is associated with increased atherosclerosis as indicated by increased IMT in smokers as compared to non-smokers. Our results emphasize the importance of prevention and cessation of cigarette smoking behavior. Future longitudinal studies are needed to confirm the current findings and to evaluate the effects of cessation of cigarette smoking behavior.

Summary

Atherosclerosis is one of the most common causes of mortality throughout the world and continues to be the leading cause of morbidity in industrialized countries in population more than 45 years of age. It is a condition in which fatty material is deposited along the wall of arteries. This fatty material thickens, hardens and may eventually block the arteries. Atherosclerosis remains asymptomatic for decades and can lead to ischemic heart disease, cerebrovascular accidents and peripheral vascular diseases. The complications progress slowly and cumulatively.

Among various known risk factors for atherosclerosis, tobacco smoking is the most important one, and it is the most common preventable cause. The adverse effects of smoking on vascular wall structure have been historically evaluated by autopsy studies.

In this study, about 48% of the smokers belonged to 41-50 years of age and 24% of the non-smokers belonged to 31-40 years of age. Majority (88%) among smokers were male, almost three fourth (74%) of the smokers were using ≤ 15 cigarettes per day and nearly 60% of smokers were smoking for a duration of 5-10 years. 52% of the smokers had a pack year of ≤ 15, 38% had 16-25 pack years and 10% of the smokers had a pack year > 25. Almost three fourth (74%) of them had increased carotid intima media thickness and only 34% of the non-smokers had increased carotid intima media thickness. We also found a significant association between carotid intima media thickness and smoking with smokers having 5.52 times more risk of having high carotid intima media thickness compared to non-smokers [P value=0.0001, OR=5.52 (2.33-13.07)]. We observed a significant association between carotid intima media thickness and total cholesterol [p value-0.016, CI: 2.88 (1.19-6.96)], triglyceride value [p value-0.013; CI: 2.95 (1.24-6.99)] and LDL [p value <0.0001; CI: 0.05 (0.01-0.17)]. Association between CIMT and VLDL and HDL were found to be non-significant. In this study, we observed that total cholesterol, triglyceride And VLDL value was significantly associated with smoking [p value=0.0003; CI: 5.68 (2.22-14.52)], (p value 0.0006 CI: 4.69 (1.93-11.41)], (p value 0.0002; CI: 5.16 (2.18-12.20)], respectively. There was no significant association between LDL and HDL value with smoking.

In conclusion, the current study demonstrates that cigarette smoking is associated with increased atherosclerosis as indicated by increased IMT in smokers as compared to non-smokers. Our results emphasize the importance of prevention and

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cessation of cigarette smoking behavior. Future longitudinal studies are needed to confirm the current findings and to evaluate the effects of cessation of cigarette smoking behavior.

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