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**Original Article**

# Atherogenic index of Plasma and LDL/HDL ratio in Patients with Chronic Obstructive Pulmonary Disorder with Special Reference to Risk of Cardiovascular Diseases

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## ABSTRACT

**Background:** Atherogenic index of plasma (AIP) and LDL/HDL ratio was considered as a strong predictor in the development of cardiovascular diseases (CVDs) particularly in patients with chronic obstructive pulmonary disease (COPD). The present study aimed to determine the AIP and LDL/HDL ratio in patient with COPD and to find out the risk of CVDs in these patients.

**Materials and Methods:** This single centered cross-sectional study was conducted in the department of pulmonology, Khyber Teaching Hospital Peshawar. 150 COPD patients were enrolled in the study according to the GOLD guidelines. Fasting blood sample was withdrawn for biochemical analysis. Body mass index (BMI), atherogenic index of plasma (AIP) and LDL/HDL ratio were calculated as per protocols previously described. All the data was entered in SPSS version 22.0. Independent sample t-test and Pearson correlation was applied to establish was applied to determine any correlation between study variables.

**Results:** Mean age was 57.34 ± 9.6 years. Out of 150 COPD patients, 62 (41.3%) were females while 88 (58.7%) were males. Strong association between dyslipidemia and AIP and LD/HDL ratio with p-value <0.001 was observed. Strong positive correlation was observed between BMI and total cholesterol (TC) (r=0.31), triglycerides (TGs) (r=0.52), low density lipoprotein (LDL) (r=0.26), very low density lipoprotein (VLDL) (r=0.52), AIP (r=0.4) and LDL/HDL ratio (r=0.27) where as strong negative correlation with disease duration (r=-0.24) and weak correlation with high density lipoprotein (HDL) level (r=0.04). There was a strong positive correlation observed in AIP and BMI (r=0.4), TGs (r=0.81), VLDL (r=0.81) and HDL (r=0.60). LDL/HDL ratio was also strongly positive correlated with BMI (r=0.27), TC (r=0.58), TGs (r=0.27), LDL (r=0.77), VLDL (r=0.27) and AIP (r=0.48) while strongly negative correlated with age (r= -0.2) and HDL (r= -0.46).

**Conclusion:** In our study, COPD patients are at higher risk of developing CVDs.

**Key words:** COPD, Dyslipidemia, Cardiovascular Diseases, LDL/HDL ratio

## Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by chronic airflow limitation and a range of pathological changes in the lungs [1]. Chronic airflow limitation is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, particularly cigarette smoke [2]. The main causes of morbidity and mortality among COPD patients are cardiovascular disease (CVD) and lung cancer [3].

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COPD is one of the major health problems in patients with age 40 years and above and considered as the 4th leading cause of death worldwide [4]. COPD and CVD are associated as both share common risk factors and pathophysiological processes [5]. COPD progression leads to pulmonary hypertension, ventricular dysfunction, coronary disease and dysrhythmia. Thus patients with COPD are more prone to develop cardiovascular disease as compared to patient without COPD.[5] Different studies reported variable prevalence of CVD in patient with COPD ranges from 14% to 33% [6, 7]. Coronary artery disease (CAD), stroke and sudden cardiac death is associated with reduce force expiratory volume in 1 second (FEV1). For every 10% decrease in FEV1, the chances of CVD related mortality is increases by 28%. Furthermore, patients with COPD are also associated with increase aortic pulse wave velocity (arterial stiffness) [8]. Administration of corticosteroids in the treatment of COPD also affects lipid values in such patients [9]. Dyslipidemia related to increase plasma levels of total

cholesterol (TC) or low density lipoprotein (LDL) and triglycerides (TGs) and low concentrations of high density lipoprotein (HDL) [10]. Various studies reported that dyslipidemia is prevalent in COPD [8, 10] and is one the major risk factors for the development of CVDs [11]. The positive association between increase levels of TC, LDL and low levels of HDL are strongly associated with CVDs. Therefore, the ratio of LDL/HDL is often calculated to estimate CVDs risk. Furthermore, the Atherogenic index of plasma (AIP) is also considered as a strong marker to predict atherosclerosis and CVDs risk [12].

Our population has not been evaluated for the determination of AIP, LDL/HDL ratio and lipid profile especially in COPD patients. The present study aim to determine the lipoprotein levels in patients with COPD and to calculate AIP, LDL/HDL ratio and to find the CVD risk in these patients.

## Material and Methods

This single centered cross-sectional study was conducted in the department of pulmonology, Khyber Teaching Hospital Peshawar. After ethical approval and patients consent, COPD patients were enrolled in the study. The COPD confirmed patients according to the global initiative of chronic obstructive pulmonary disease (GOLD) guidelines of either gender were included in the study [4]. Samples of 150 COPD patients were included in the study. The sample size was calculated using WHO sample size calculator with 80 powers of study and 95% confidence interval. The demographics were recorded on purposefully designed proforma. After detailed history, 5cc Fasting blood sample was withdrawn from each patient, properly labeled and stored for biochemical analysis. Patients not willing to participate in the study, known cardiovascular diseases, history of other chronic disorders and patients receiving lipid lowering drugs were excluded from the study.

The BMI was calculated using the formula previously described and BMI was categorized as normal BMI (18-24.9), overweight (25-29.9) and obese (>30) [12]. The atherogenic index of plasma (AIP) was also calculated as previously described as logarithmic transformation of TG to HDL ratio [13]. Where AIP value -0.3-0.1 is considered lower risk, 0.-0.24 intermediate risk and >0.24 as high cardiovascular risk [12]. The lipid profile was analyzed using cobas 6000 analyzer c501 series Roche diagnostics. Patients were classified as dyslipidemia positive and dyslipidemia negative according to the criteria previously described [11].

All the data were entered in SPSS 22.0. Numerical variables were expressed as mean ± standard deviation (SD) while frequency and percentages were used for categorical variables. Independent sample t test was used to find the possible association between dyslipidemia and AIP values and LDL/HDL ratio. Pearson correlation was applied to determine any correlation between the study parameters. All the results were recorded as 2 tail method and p-values <0.05 were considered significant.

## Results

This study enrolls total 150 COPD patients. The mean age was 57.34 ± 9.6 years where the minimum and maximum age was recorded as 40 years and 70 years respectively. The mean BMI, CHO, TGs, HDL, LDL, VLDL was 25.49 ± 3.0, 166.57 ± 36.7, 129.93 ± 51.1, 43.85 ± 11.5, 106.93 ± 35.3 and 25.99 ± 10.2 mg/dl respectively. Similarly, the mean duration of disease in years was 7.61 ± 4.2 years. The mean AIP was recorded as 0.45 ± 0.21 while the mean LDL/HD ratio was 2.55 ± 0.94. Further details of each variable are summarized in table 1 below.

**Table 1: Demographics of study population**

| Variable | Minimum value | Maximum value | Mean ± SD |
|---|---|---|---|
| Age (years) | 40 | 70 | 57.34 ± 9.6 |
| BMI | 20 | 40 | 25.49 ± 3.0 |
| TC(mg/dl) | 87 | 291 | 166.57 ± 36.7 |
| TGs (mg/dl) | 46 | 376 | 129.93 ± 51.1 |
| HDL (mg/dl) | 17 | 104 | 43.85 ± 11.5 |
| LDL (mg/dl) | 39 | 204 | 106.93 ± 35.3 |
| VLDL (mg/dl) | 9 | 75 | 25.99 ± 10.2 |
| Disease duration (years) | 2 | 18 | 7.61 ± 4.2 |
| AIP | -0.19 | 1.05 | 0.45 ± 0.21 |
| LDL/HDL ratio | 0.65 | 5.63 | 2.55 ± 0.94 |

In total 150 COPD patients, 62 (41.3%) were females while 88 (58.7%) were males. Furthermore, 63 (42%) patients were overweight followed by 17 (11.3%) patients which were obese. Higher levels of TC were recorded in 22 (14.7%) patients while 45 (30%) of the patients have higher TGs levels. HDL levels were low in 143 (95%) patients and LDL and VLDL were high in 35 (23.3%) and 45 (30%) respectively. The AIP was high in 134 (89.3%) COPD patients. According to the LDL/HDL ratio, 45 (30%) of the total patients have moderate cardiovascular risk while 2 (1.3%) have high

risk. Dyslipidemia was positive in 44 (29.3%) of the total patients. All the details are shown in table 2.

**Table 2: demographics presentation of categorical variables**

| Variables | | Frequency | %age |
|---|---|---|---|
| Gender | Female | 62 | 41.3 |
| | Male | 88 | 58.7 |
| BMI | Normal BMI | 70 | 46.7 |
| | Overweight | 63 | 42.0 |
| | Obese | 17 | 11.3 |
| TC | Normal | 128 | 85.3 |
| | High | 22 | 14.7 |
| TGs | Normal | 105 | 70.0 |
| | High | 45 | 30.0 |
| HDL | Normal | 7 | 4.7 |
| | Low | 143 | 95.3 |
| LDL | Normal | 115 | 76.7 |
| | High | 35 | 23.3 |
| VLDL | Normal | 105 | 70.0 |
| | High | 45 | 30.0 |
| AIP categories | Lower risk | 9 | 6.0 |
| | Intermediate risk | 7 | 4.7 |
| | Increase risk | 134 | 89.3 |
| LDL/HDL ratio | Low risk | 103 | 68.7 |
| | Moderate risk | 45 | 30.0 |
| | High risk | 2 | 1.3 |
| Dyslipidemia | No | 104 | 70.7 |
| | Yes | 44 | 29.3 |

Independent sample t test reveals that there is a strong association between dyslipidemia and AIP with p-value <0.001. Similarly, strong association was observed between dyslipidemia and LD/HDL ratio with p-value <0.001. Further details are shown in table 3.

Table 3: Association between dyslipidemia and LD/HDL ratio

| Variable | Dyslipidemia | N | Mean | P value | 95% CI |
|---|---|---|---|---|---|
| AIP | Yes/No | 54 / 96 | 0.60 / 0.37 | <0.001 | -(0.28 – 0.16) |
| LDL/HDL ratio | Yes/No | 54 / 96 | 3.2/ 2.1 | <0.001 | -(1.3 – 0.85) |

Correlation analysis reveals that age is significantly negative correlated with the BMI (r= -0.2) and LDL (r= -0.16) but positively correlated with disease duration (r=0.73). Similarly, BMI is strongly positive correlated with TC (r=0.31), TGs (r=0.52), LDL (r=0.26), VLDL (r=0.52), AIP (r=0.4) and LDL/HDL ratio (r=0.27) where as strong negatively correlated with disease duration (r=-0.24) and weakly correlated with HDL level (r=0.04). Furthermore, TC is strongly positive correlated with TGs (r=0.32), HDL (r=0.35), LDL (r=0.91), VLDL (r=0.32) and LDL/HDL ratio (r=0.58). There is a strong positive correlation observed in AIP and BMI (r=0.4), TGs (r=0.81), VLDL (r=0.81) and HDL (r=0.60). The LDL/HDL ratio is also strongly positive correlated with BMI (r=0.27), TC (r=0.58), TGs (r=0.27), LDL (r=0.77), VLDL (r=0.27) and AIP (r=0.48) while strongly negative correlated with age (r= -0.2) and HDL (r= -0.46). All the details of each variable are summarized in table 4.

**Table 4: Correlation of different study variables**

| Variables | BMI | TC | TGs | HDL | LDL | VLDL | Disease duration | AIP | LDL/HDL ratio |
|---|---|---|---|---|---|---|---|---|---|
| Age | -0.2** | -0.15 | -0.14 | 0.10 | -0.16* | -0.14 | 0.73** | -0.15 | -0.20* |
| BMI | 1 | 0.31** | 0.52** | -0.04 | 0.26* | 0.52** | -0.24** | 0.4** | 0.27** |
| TC | | 1 | 0.32** | 0.35** | 0.91** | 0.32** | -0.15 | 0.08 | 0.58** |
| TGs | | | 1 | -0.11 | 0.20* | 1.0*** | -0.08 | 0.81** | 0.27** |
| HDL | | | | 1 | 0.11 | -0.11 | -0.02 | 0.60** | -0.46** |
| LDL | | | | | 1 | 0.20* | -0.17* | 0.10 | 0.77** |
| VLDL | | | | | | 1 | -0.08 | 0.81** | 0.27** |
| Disease duration | | | | | | | 1 | -0.03 | -0.13 |
| AIP | | | | | | | | 1 | 0.48** |
| LDL/HDL ratio | | | | | | | | | 1 |

Legends: *** correlation significance at 0.001, ** level of significance at 0.01, * level of significance at 0.05. BMI-body mass index, TC- total cholesterol, TGs- triglycerides, HDL- high density lipoprotein, LDL-low density lipoprotein, VLDL- very low density lipoprotein, AIP-atherogenic indices

## Discussion

This study evaluates the lipid profile and atherogenic index of plasma (AIP) in patients with COPD. Increase AIP, dyslipidemia and LDL/HDL ratio is considered as strong risk factors for the development of CVDs. The results of this study clearly show an imbalance between lipid profile, AIP and LDL/HDL ratio. In our study, the mean age recorded was 57.34 ± 9.6 years. In total 150 COPD patients, 58.7% were males while 41.3% were females. Various studies have been published, reported variable prevalence of men and women. Many studies reported no gender disparity in COPD while there are many studies reported conflicting results among men and women [14]. According to our results, levels of HDL were low in 95.3% of COPD patients. Similarly, TC, TGs, LDL and VLDL were high in 14.7%, 30%, 23% and 30% respectively. Similar studies were also done in the past reported elevated levels of TC, TGs, LDL and VLDL and low levels of HDL in COPD patients [15, 16]. Dyslipidemia was prevalent in 29.3% of COPD patients and was strongly positive associated with LDL/HDL ratio and AIP (p-value <0.001). Dyslipidemia is prevalent in patients with COPD as published by many researchers in the past [8, 10,17, 18]. High levels of LDL may be deposited with the artery wall and is involved in atherogenic process leading to increase CVD risk [19] while reducing LDL levels are associated with decrease CVD risk [20]. Although the association of high TGs levels also increases CVD risk and are involved in elevated levels of LDL and low levels of HDL [20]. Low levels of HDL also increases CVD risk by altering cholesterol efflux from the cells[21]. All these reports strongly associate abnormal lipid profile with CVD risk. Thus, these reports are consistent with the results of our findings. In our study, based on LDL/HDL ratio, 30% of the patients having moderate CVD risk while 1.3% patients have high CVD risk. LDL/HDL ratio is a useful marker to indicate CVD risk as reported by many studies [22, 23] as it combinedly evaluates both LDL and HDL levels. According to a recent study published in 2019, reported a positive correlation of LDL/HDL ratio and CVDs [24]. Another report published in 2022 found LDL/HDL ratio as a positive predictor of coronary atherosclerotic heart disease [25]. AIP is a novel marker to determine CVD risk and is composed of TGs and HDL. AIP is an optimal indicator of dyslipidemia and related of CVDs [13]. In our study, based on AIP, 89.3% of COPD patients have increase CVD risk. According to a recent study published in 2021 reported that AIP were high in patient COPD with CVDs [10]. Our results reveals that AIP is strongly positive correlated with increase BMI (r=0.4**) which is in consistent with the findings published previously [13]. Furthermore, AIP is also positive correlated with TGs (r=0.81**), HDL (r=0.60**), VLDL (r=0.81**) and LDL/HDL ratio (r=0.48**). Similar positive results were also reported by other researchers in the past where the AIP is significantly correlated with LDL and VLDL and was considered as a strong predictor of atherosclerosis [26, 27]. Thus both AIP and

LDL/HDL ratio is independently associated with increased risk of developing CVDs in patient with COPD.

## Conclusion

COPD patients with higher levels of AIP and LDL/HDL ratios are at high risk of developing CVDs. Thus minimizing these risk factors will result in reducing the risk of such diseases and will improve quality of life of the patients.

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| HISTORY | |
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**KEY FOR CONTRIBUTION OF AUTHORS:**

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C. Interpretation/ Analysis and Discussion

| CONTRIBUTION OF AUTHORS | |
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| Irum Mehmood | C |