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Original Research

# A STUDY ON THE OCULAR MANIFESTATIONS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS WITH HISTORY OF SMOKING

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## Abstract

**Background:** Chronic obstructive pulmonary disease is associated with various systemic manifestations. Objective: The objective of this study was to evaluate the prevalence of ophthalmological changes in chronic obstructive pulmonary disease (COPD) patients. **Materials and Methods:** This study was conducted at the Department of Ophthalmology, Chalmeda Anand Rao Institute of Medical Sciences from October 2021 to March 2022. Total of 40 patients with COPD (study group) and 40 healthy controls satisfying inclusion and exclusion criteria were included, and 160 eyes were analysed. All patients were subjected to detailed systemic and ophthalmic examination. **Result:** The prevalence of ophthalmological changes in both groups was significantly different. COPD patients had mean IOP of 18±3.4 mmhg, while the control group had mean IOP of 15±2.89 mmhg ($p<0.001$). 15 (36.4%) patients among the case group presented with cataract, while 2 (4.5%) persons in the control group had cataract ($p = 0.0003$). 18 (45.5%) individuals from the case group presented with ARMD, whereas only 2 (4.5%) individuals from the control group presented with ARMD. **Conclusion:** In this study, it can be concluded that the prevalence of a higher mean IOP, cataract, and ARMD in smokers diagnosed with COPD is significant. This reinforces the need for referral of these patients to the ophthalmologist.

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a serious public health problem.[1] COPD affects about 300 million people worldwide, resulting in approximately 64 million disability-adjusted life years.[17] The incidence of COPD was 174 million in 2015, and there were around 3.2 million deaths worldwide because of COPD.[18] It is a non-communicable chronic disease.[2] According to the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD, 2018), the spirometric diagnostic criteria for this disease is the ratio of forced expiratory volume in the first second / forced vital capacity (FEV1/FVC) of less than 0.7 after the bronchodilator. Then patients were divided into four categories based on the degree of bronchial obstruction according to the established spirometric criteria.[3] It is associated with various systemic manifestations like heart disease, diabetes, osteoporosis, GERD, and depression.[4,5] So, ocular complications are unrecognized manifestations, and may be potentially serious or irreversible if not treated in time, such as glaucoma, hypertensive retinopathy, retinal hemorrhage, age-related macular degeneration, changes in nerve fiber layer, etc.[6,7,8,9] The aim of this study was to evaluate the ocular manifestations in patients with COPD who have a history of smoking and compare the findings with a group of normal subjects who are non-smokers and don't have COPD.

## MATERIALS AND METHODS

A case-control study was conducted in the Department of Ophthalmology OPD at Chalmeda Anand Rao Institute of Medical Sciences. Permission was obtained from the Institute Ethics Committee, CAIMS, Karimnagar. An informed consent was obtained from subjects willing to participate in the study. The study was carried out from October 2021 to March 2022. Total of 80 individuals, out of which 40 are patients with COPD (study group) and 40 are healthy controls, participated in the study for a span of 6 months. 160 eyes were analyzed.


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**Inclusion Criteria**

Patients male or female aged 40 years or more, chronic obstructive pulmonary disease patients with history of smoking

**Exclusion Criteria**

Patients presenting with lung carcinomatoses, hemoglobinopathies, patients who are taking anticoagulants History of all the individuals was taken. Ocular examination including visual acuity using Snellen chart, slit lamp examination, and fundus examination using slit lamp biomicroscopy 90D and indirect ophthalmoscopy was done. IOP was measured using Goldmannapplanation tonometry. Optical coherence tomography and fundus fluorescein angiography was done wherever necessary. Spirometry and chest imaging was done. Sampling technique and sample size: Simple random sampling was done to gather all the participants of the study. According to Brandt et. al. study, prevalence of ophthalmic changes (cataract) among the cases observed was 36%, and among the controls was 4%.[38] By using G*Power software for sample size calculation, taking alpha as 5% and power of test as 95%, sample size calculated for cases and controls was.[39] After rounding off, we have included 40 samples in each group.Statistical Analysis: The collection of data was entered in the Microsoft Excel 2016, for further statistical analysis. Qualitative data was presented by frequency and percentages, association between variables was assessed by using chi-square test. P-value <0.05 was considered as statistical significance. Analysis was done by using statistical software SPSS Version.[25]

## RESULTS

In this study, 80 individuals were examined and the following assessments were made.

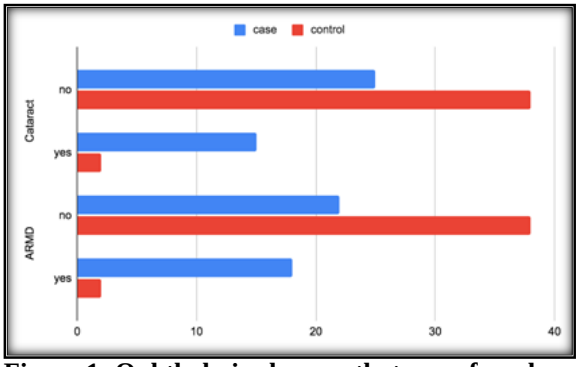


**Figure 1: Ophthalmic changes that were found**

**Table 1: Demographic features, comorbidities and habits**

| Variables | | Groups | | Total | p-Value |
|---|---|---|---|---|---|
| | | Case | Control | | |
| Sex | | 29(72.7%) | 25(63.6%) | 55(68.2%) | 0.33 |
| | | 11(27.3%) | 15(36.4%) | 25(31.8%) | |
| Age | | 65.4±8.0 | 68.4±7.2 | - | 0.378 |
| HTN | | 18(45.5%) | 25(63.6%) | 44(54.5%) | 0.11 |
| | | 22(54.5%) | 15(36.4%) | 36(45.5%) | |
| DM | | 33(81.8%) | 40(100%) | 73(90.9%) | 0.023 |
| | | 7(18.2%) | 0(0.0%) | 7(9.1%) | |
| Smokers | | 0(0.0%) | 38(95.5%) | 38(47.7%) | <0.001 |
| | | 27(68.2%) | 0(0.0%) | 27(34.1%) | |
| | | 2(4.5%) | 2(4.5%) | 4(4.5%) | |
| | | 11(27.3%) | 0(0.0%) | 11(13.6%) | |

It was observed that among the cases, 72.7% were females and 27.3% were males. The p-value was 0.33. The average age among cases was 65.4±8.0 years and controls was 68.4±7.2 years. The p-value was 0.378. 54.5% of cases and 36.4% of controls were hypertensive. The p-value is 0.11. 81.8% of cases were diabetic and the p-value was 0.023. Among the cases, 68.2% were ex-smokers, 4.5% were ex-smokers and 27.3% were heavy active smokers. The p-value is <0.001. Significant difference was not present in relation to gender, age, or hypertension among cases and controls [Table 1].

**Table 2: Ophthalmic examination**

| Variables | | Groups | | Total | p-Value |
|---|---|---|---|---|---|
| | | Case | Control | | |
| Anterior segment | Normal | 17(21.25%) | 48(60%) | 65(40.62%) | <0.001 |
| | Not Normal | 63(78.75%) | 32(40%) | 95(59.37%) | |
| Retina | Normal | 36(46.3%) | 76(95.5%) | 112(71.8%) | <0.001 |
| | Not Normal | 42(53.7%) | 4(4.5%) | 46(28.2%) | |
| Tonometry | Average | 18±3.4 | 15±2.89 | - | <0.001 |

Anterior segment was not normal in 78.75% of cases and 40% of controls. Retina was not normal in 53.7% of cases and 4.5% of controls. The mean IOP of the case group (18±3.4 mmhg) was higher than that of the control group (15±2.89 mmhg). The p-value was <0.001 [Table 2].


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**Table 3: Ophthalmic changes that were found**

| Variables | | Groups | | Total | p-Value |
|---|---|---|---|---|---|
| | | Case | Control | | |
| Cataract | No | 25(63.6%) | 38(95.5%) | 64(80%) | 0.0003 |
| | Yes | 15(36.4%) | 2(4.5%) | 16(20%) | |
| Age Related Macular Degeneration | No | 22(54.5%) | 38(95.5%) | 60(75%) | 0.000036 |
| | Yes | 18(45.5%) | 2(4.5%) | 20(25%) | |

In the case group, the incidence of cataract (36.4%) was more compared to the control group. The p-value was 0.0003 which is statistically significant. In the case group, age-related macular degeneration (ARMD) (45.5%) was more compared to the control group. The p-value was 0.000036 which is statistically significant [Table 3].

## DISCUSSION

**Demographic features, comorbidities and habits**

There was no significant difference in relation to gender, age, or hypertension among cases and controls. 81.8% of the cases were diabetics. Majority of the cases were ex-smokers (68.2%).According to the National Heart, Lung, and Blood Institute, COPD most often occurs in individuals more than 40 years of age who smoke or have done so earlier in life.[19,20] Therefore, individuals more than 40 years of age were included in the study.The mean age among cases was 68.4 ± 8.0 years. Holm KE et. al. conducted a study to know the impact of age on psychological and clinical outcome in alpha-1 antitrypsin deficiency-associated COPD. The mean age of the participants was 59.9 years, which is similar to the present study.[23]Among the cases, 72.7% were females and 27.3% were males. Lisspers K et. al. conducted a study to gather evidence regarding gender differences among COPD patients. It was observed that COPD was more frequent among women (53.8%), which corroborates with the present study.[22]In recent times, COPD is known to be more prevalent in women. Increase in tobacco consumption may explain the increase in incidence, there may be other factors such as differential susceptibility to tobacco, anatomic and hormonal differences, etc.[21]Ophthalmic examination: It was seen that there are changes in the anterior segment and retina associated with the presence of smoking and COPD. The mean IOP of the case group (18±3.4 mmhg) was higher than that of the control group (15±2.89 mmhg). Similar results were observed in previous studies. Lee et al. conducted a study to compare the intraocular pressure in smokers, past smokers, and non-smokers. It was observed that compared with never smokers, current and past smokers showed a statistically significantly higher IOP by 0.92 mmHg (95% confidence interval [CI], 0.88–0.95 mmHg) and 0.77 mmHg (95% CI, 0.75–0.79 mmHg), respectively.[10]Yoshida M. et. al. conducted a study to know whether smoking was associated with elevated intraocular pressure. It was observed that the IOP level may be substantially affected by smoking habits in middle-aged and older Japanese men.[24] Mukherji S. et. al. conducted a study to know the correlation between smoking and raised intraocular pressure in males. The results showed that there was a positive correlation between intraocular pressure and smoking overall.[25]Verma et. al. conducted a study on the effect of inhaled tiotropium on intraocular pressure in patients with chronic obstructive pulmonary disease. It is a long acting antimuscarinic agent (LAMA) used in the treatment of COPD. It has a number of effects such as dryness of mouth, urinary retention, and raised intraocular pressure. It causes pupillary dilation which can lead to angle closure glaucoma in susceptible patients. It was observed that there was statistically significant change in mean IOP at the end of study compared to baseline.[36]A significantly higher mean IOP was observed in the case group when compared to the control group. This could be because smoking causes immediate increase in IOP by vasoconstriction, which increases the episcleral vein pressure and leads to reduced aqueous outflow causing increase in IOP.[11] Therefore, this is an important risk factor for developing glaucoma in the future.

**Ophthalmic changes that were found**

In the case group, the incidence of cataract (36.4%) and ARMD (45.5%) were more prevalent compared to the control group.Hemoglobinopathies can cause neovascularisation leading to vitreous hemorrhage and retinal detachment, as in sickle cell disease.[33] Risk of intraocular hemorrhage is present in those using anticoagulants. Patients with ischemic stroke, pulmonary embolism, deep vein thrombosis, and myocardial infarction are usually prescribed with anticoagulants.[34] Patients with lung carcinomatosis can undergo ocular metastases which usually present with blurred or loss of vision.[35] Therefore, patients with lung carcinomatosis, hemoglobinopathies and those taking anticoagulants were excluded from the study.There was a higher incidence of cataract among the case group patients. It can be explained by the indiscriminate use of corticosteroids during treatment.[12] Mechanism of steroid cataract formation is that glucocorticoids are covalently bound to lens proteins resulting in destabilization of the protein structure allowing further modification (i.e. oxidation) leading to cataract.[37] Similar observations were made in other studies. Ye et. al. conducted a meta-analysis to evaluate the relationship between smoking and age-related cataract. It was observed that there was an association between nuclear cataract and smoking.[13] Beltrán-Zambrano E et. al. conducted a


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meta-analysis to compare the risk of cataract between smokers and ex-smokers. It was observed that there was a risk of nuclear cataract in smokers.[26] Irie H. et. al. conducted a study to know the impact of cataract in the quality of life in chronic obstructive lung disease patients. The study concluded that COPD patients with cataract displayed worse health-related quality of life, and cataract was shown to be related to frequent COPD exacerbations.[32] The pathophysiology may be that smoking influences the changes in the level of metal ions that occur in normal ageing of tissues.[13] It can be prevented by a healthy diet which includes high-dose zinc and antioxidant vitamin supplements.[14] In this study, there was a higher frequency of ARMD in the case group. Previous studies have also shown similar results. Chutney et. al. conducted a study to determine whether chronic lung disease was associated with age-related macular degeneration. It was observed that patients with neovascular ARMD were more likely to have chronic lung disease compared to controls with no ARMD.[15] Vingerling JR et. al. conducted a study to assess the relation between cigarette smoking and age-related macular degeneration in a population of elderly persons. The results showed that there was a dose-response relationship between smoking and ARMD, particularly the neovasculartype.[28] A study was conducted by Tan JSL et. al. to assess the association between smoking and long term incidence ARMD. It was observed that smoking strongly increased the long-term risk of incident late ARMD.[29] A study was conducted by Dr. Deepak V.N. to assess the ocular manifestations in COPD patients. It was observed that the most common manifestations were cataract, followed by glaucoma and ARMD.[30] Bair et. al. conducted a population based cohort study on the risk of ARMD in patients with COPD. It was observed that COPD patients have a higher risk for developing ARMD.[31] The exact pathogenesis of ARMD is not clear but it may be due to a multifactorial interaction among genetic, metabolic, functional and environmental factors. It may be directly due to oxidative stress induced by nicotine or indirectly due to promotion of atherosclerosis.[27] It could also be due to its effect of decreasing macular pigment density.[16] Possible explanations for association of COPD are systemic inflammation and hypoxia. In inflammatory processes, para-inflammation can occur in the choroid, retinal pigment epithelium, and neuroretina. Hypoxia causes imbalance between oxidative stress induced cellular damage and the remodelling process. These mechanisms are essential for ARMD development and progression.

## CONCLUSION

With respect to the age, gender, hypertension there were no significant differences found in the variables. A significantly higher mean IOP was observed in the case group. The higher frequency of cataract among COPD patients was evident. There was an association between smoking and ARMD. The ophthalmic manifestations in COPD are infrequently recognised. This emphasizes that there is a need to refer these patients to an ophthalmologist.

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