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Impact Of Obstructive Airway Diseases On The Outcome Of Covid 19.

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Abstract

Background: The prevalence of obstructive airway diseases (OADs) including Asthma, Chronic Obstructive Pulmonary Disease (COPD) and Asthma-COPD overlap (ACO) in COVID-19 patients may range from 1.1-36.3%, 0.7-70.6% and 0.4-29.4% respectively. The effect of OAD on severity and outcome of COVID-19 has been published with varied results. Although few studies have shown that coexistence of obstructive airway diseases with COVID-19 have increased the morbidity and mortality in COVID-19, other studies have shown no effect on the morbidity and mortality.

Aims and Objectives: Our study aimed to determine the outcome of COVID-19 infections in patients with OADs and to compare the outcome of COVID-19 infection in patients with OADs with that of the patients without OADs.

Materials and Methods: Our study was a case-control study conducted in a tertiary care hospital. We included patients who were either recently diagnosed or having a history of OADs and were COVID-19 positive (based on Reverse Transcription Polymerase Chain Reaction (RT-PCR) or Rapid Antigen Test (RAT) who were admitted in the hospital. COVID-19 patients with OADs were considered as **cases** while patients without OADS were taken as **control**. All the patients were followed-up during the hospital stay. Statistical analyses were performed using the

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Statistical Package for the Social Sciences (SPSS) version 19 for windows. $P < 0.05$ was considered significant

Results: A total of 102 patients were included in the study, out of which 52 patients were cases; another 50 patients were included in control group. The mean age of patients among cases and control group were 57.29 ± 14.49 and 50.38 ±12.71 years respectively (p=0.012). Among the patients with OADs, asthma was the most common (51.9%). Among the cases, 36.5% had severe disease while only 14% patients in the control group developed severe disease (p=0.009). 15 (28.8%) of the cases and 8 (16%) controls required mechanical ventilation in their course of hospitalization (p=0.06). 14 (26.9%) patients among case group and 4 (8%) patients of control group died during course of hospitalization (p=0.006).

Conclusion: Our study determined that patients with OADs have a longer hospital stay, more severe radiological involvement, higher need for mechanical ventilation and higher mortality when infected with COVID-19.

Keywords: asthma, COPD, COVID-19, mortality

INTRODUCTION:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first detected in Wuhan, China.[1] It was the causative agent of the coronavirus disease 2019 (COVID-19) pandemic. [2] The pandemic created havoc throughout the world with high mortality in many countries including India. COVID constituted 29% of deaths from June 2020 to July 2021, corresponding to 3.2 M (3.1 to 3.4) deaths, of which 2.7 M (2.6 to 2.9) occurred in April to July 2021. [3] Most of these deaths were reported in patients in co-morbidities. Fifty percent of COVID-19 patients have been found to have at least one comorbidity. [4] As per the previous studies, prevalence of obstructive airway diseases (OADs) including Asthma, Chronic Obstructive Pulmonary Disease (COPD) and Asthma-COPD overlap (ACO) in COVID-19 patients ranges from 1.1-36.3%, 0.7-70.6%[6,7] and 0.4-29.4% respectively. [5-9] Few studies have shown that coexistence of obstructive airway diseases with COVID-19 have increased the morbidity and mortality in COVID-19. [10,11] Other studies, however, have shown that these diseases neither increase the mortality rate nor are the risk factors for the same. [12-15]

Aims and objectives:

a. To study the outcome of COVID-19 infections in patients with OADs.

b. To compare the outcome of COVID-19 infection in patients with OADs with that of the patients without OADs.

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Materials and Methods:

Type of study: It was a case-control study conducted in COVID hospital of a tertiary care hospital.

Inclusion criteria: Patients either recently diagnosed or having a history of OADs and were COVID-19 positive who were admitted in the hospital were included in the study.

Exclusion criteria:

1. Patients having other chronic diseases like chronic kidney disease (CKD), chronic liver disease (CLD) and cardiac disease.
2. Patients unwilling to give consent.

Methodology:

After considering the inclusion and exclusion criteria, patients with COVID-19 positive by Reverse Transcription Polymerase Chain Reaction (RT-PCR) or Rapid Antigen Test (RAT) were included in the study. COVID-19 patients with OADs were considered as **cases** while patients without OADS were taken as **control**. Detailed history along with clinical examination was carried out. Routine investigations and chest X-ray was performed for all cases; High Resolution Computed Tomography (HRCT) thorax was done when required.

The patients were followed up closely during the entire period of hospitalization and the following parameters were recorded:

1. Duration and course of hospital stay.
2. Need for ventilator support and its type.
3. Outcome of hospitalization in terms of mortality.

Case definition: Definition of COVID-19 disease severity as per COVID-19 Treatment Guidelines was followed:

• Asymptomatic or presymptomatic infection: Individuals who test positive for SARS-CoV-2 using a virologic test (i.e., a nucleic acid amplification test [NAAT] or an antigen test) but have no symptoms consistent with COVID-19.

• Mild illness: Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but do not have shortness of breath, dyspnea, or abnormal chest imaging.

• Moderate illness: Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation measured by pulse oximetry (SpO2) ≥94% on room air at sea level.

• Severe illness: Individuals who have SpO_2 30 breaths/min, or lung infiltrates >50%.

• Critical illness: Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction [16].

Ethical clearance: The study was approved by the Institutional Ethics Committee (KIIT/KIMS/IEC/718/2021)

Statistical analysis: Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 19 for windows. Continuous variables were presented as mean ± standard deviation and categorical variables as percentages. Chi-square test was used to

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determine the associations between categorical variables. Evaluation of group differences in means for continuous variables was done using the unpaired student's *t* test and for categorical variables by Chi-square test. $P < 0.05$ was considered significant

Results:

A total of one hundred two patients were included in the study, out of which 52 patients were cases; another 50 patients were included in control group. The mean age of patients among cases and control group were 57.29 ± 14.49 and 50.38 ±12.71 years respectively (p=0.012) [Table 1].

Among the patients with OADs, asthma was the most common (51.9%) followed by COPD (48.1%)

Mean duration of symptoms among cases and control group were 7.35±4.5 days and 6±2.6 days respectively (p=0.072). There was no significant difference in clinical features among cases and controls (p=0.075). Shortness of breath was the most common complaint in both groups. Among the cases, 36.5% had severe disease while only 14% patients in the control group developed severe disease; this was statistically significant (p=0.009) [Table 2].

The occurrence of consolidation in radiology was seen in 30.8% cases and 24% of controls (p=0.7). The occurrence of ground glass opacities along with consolidation was seen in 14 (27%) cases and only 1 (2%) control (p=0.00019) [Table 2].

Among the cases, 20 (38.5%) cases required O_2 supplementation via nasal cannula while 21 (43.4%) required non-re breather mask for oxygen supplementation among cases. On the other hand, 35 (70%) patients required nasal cannula for oxygenation and nine (18%) patients required non-re breather mask for oxygenation among control group.

It was found that 19 (36.54%) patients among case group and 4 (8%) patients among controls required mechanical ventilation in their course of hospitalization (p=0.06). Among patients requiring mechanical ventilation among cases, median duration of invasive mechanical ventilation was four days while patients in the control group had a duration of 1.5 days (p=0.072). Fourteen (26.9%) patients among case group and four (8%) patients of control group died during course of hospitalization (p=0.006) [Table 2].

Discussion:

Our study aimed to determine the outcome of COVID-19 in patients with obstructive airway disease. We included 50 and 52 patients each in the study and control group respectively. These patients were followed up throughout their stay in the hospital.

Studies of COVID-19 on bronchial asthma and other OADs is scarce and most of the published literature is based on COPD patients. The available literature in asthma patients shows these patients to be no more susceptible to COVID-19 (17, 18)

Estimation of the risk of contracting COVID-19 and its outcome in patients with COPD has been a challenging job due to various reasons. First, the published studies have been primarily based on admitted patients with moderate or severe disease. Secondly, the underdiagnosis of COPD in the community could lead to erroneous results (19). The prevalence of COVID-19 in hospitalized

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patients with COPD has been reported to be almost similar in many studies from around the world. (20-26).

As per the reports from multiple studies, COPD may be considered as a risk factor for severe COVID-19 disease (27, 28). This has been attributed to the ease of entry of the virus into the cell. The envelope protein of SARS CoV-2 fuses with angiotensin converting enzyme-2 (ACE-2) receptors present on cells that facilitates its entry into the cell (29, 30). These ACE-2 receptors have been found in high concentration in patients with COPD as well as in current smokers. (31, 32). This phenomenon has not been confirmed in patients with asthma (33). Also, this being associated with more severe disease has not been adequately studied. It is believed that this along with a decreased host antiviral defense and immune system dysfunction results in increased severity of disease in COPD patients. Evidence suggests that interferons are dampened in patients with COPD resulting in more severe disease (34). Similarly, there is an overexpression of programmed cell death protein 1 and decreased expression of T-cell receptor in patients with COPD indicating T-cell dysfunction.

In our study, patients with OADs had a higher age of presentation (57.29±14.49 years; p=0.012), and a longer duration of hospitalization (10.15± 6.24 days; p= 0.53).

Hypoxia is a common feature in COVID-19. This arises due to various reasons like alveolar edema causing ventilation-perfusion (V/Q) mismatch and extensive pulmonary intravascular clots. The V/Q mismatch leads to intrapulmonary shunting causing pulmonary vasoconstriction and thus hypoxia. This vasoconstriction also increases the shear stress in pulmonary vessels leading to platelet aggregation and thrombus formation. These aggravate the hypoxia in patients with COPD who already suffer from V/Q mismatch (35).

Our study also showed increased oxygen requirement and need for mechanical ventilation in patients with OAD. This has been supported by many other studies (19-21).

Conclusion:

Our study determined that patients with OADs have a longer hospital stay, more severe radiological involvement, higher need for mechanical ventilation and higher mortality when infected with COVID-19. The results were almost like previous pandemics caused by viral infections. Hence, these patients need more aggressive management and care in scenarios of viral pandemics.

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ANNEX (TABLES)

Table 1: Demographic, Laboratory and Radiological Parameters of Patients with and without Obstructive Airway Disease

Group	Non OAD (n=50)		OAD (n=52)		p
	Mean	Std. Deviation	Mean	Std. Deviation	
Age (years)	50.38	12.71	57.29	14.49	0.012
Duration of Illness (days)	6.00	2.66	7.35	4.55	0.072
Saturation of Oxygen (SpO_2)	88.60	5.81	85.88	8.16	0.057
Total Blood Count (cells/mm^3)	8542.00	3960.68	9970.19	9051.41	0.308
Neutrophil/Lymphocyte (N/L) ratio	6.80	6.91	10.13	14.22	0.138
C-reactive protein (mg/litre)	73.33	81.22	83.94	83.80	0.518
D-dimer (ug/ml)	2.59	3.25	11.43	59.67	0.298
CT score	14.08	6.13	16.90	6.32	0.024
Duration of Hospitalisation (days)	9.46	4.76	10.15	6.24	0.530

Table 2: Comparison of Clinical and Radiological features and treatment outcome

Category		Non-OAD group (n= 50)	%	OAD group (n= 52)	%	p
Clinical features	Fever	43	86	39	75	0.08
	Cough	43	86	42	80.8	0.24
	SOB	45	90	52	100	0.009
COVID-19 category	Moderate	43	86	33	63.5	0.0045
	Severe	7	14	19	36.5	0.0045
Co-morbidities	HTN	25	50	32	61.5	0.12
	DM	10	20	15	28.8	0.15
Radiological findings	None	4	8	1	1.9	0.078

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	Ground-glass opacities	34	68	30	57.7	0.14
	Consolidation	11	22	2	3.8	0.003
	Both ground glass opacities+ consolidation	0	0	5	9.6	0.012
	Pleural effusion	1	2	14	26.9	0.0002
Need for ventilation	NIV	4	8	9	17.3	0.07
	IV	4	8	19	36.54	0.0003
Outcome of disease	Discharge	46	92	38	73.1	0.006
	Death	4	8	14	26.9	0.006

**HTN: hypertension; DM: diabetes mellitus; NIV: non-invasive ventilation; IV: invasive ventilation*