

# COMPARISON OF DIFFERENT CLINICAL OUTCOMES AMONG ASTHMATIC AND NON-ASTHMATIC COVID-19 PATIENTS IN AN INTENSIVE CARE UNIT SETTING

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## ABSTRACT

**Objectives:** To compare the different clinical outcomes among asthmatic and non-asthmatic patients having COVID-19 in an ICU setting

**Materials and Methods:** A cross-sectional study was conducted in the Covid ICU of Hayatabad Medical Complex Peshawar from April 2021 to September 2022. WHO validated questionnaire was used among 220 study participants who were selected in this study. A modified questionnaire was tested for validation through a pilot study. A Cronbach alpha of less than 0.80 was considered acceptable. A significant P value was considered as < 0.05. SPSS version 22 was used for data analysis.

**Results:** Out of a total of 220 participants, 10.9% (n= 24) were asthmatic while 89.1% (n= 196) were non-asthmatic. The majority of participants were non-asthmatic male 118 (60.2%, p-value 0.86). Different comorbidities were seen in different patients, most of the non-asthmatic patients, 81 (41.3%, p-value 0.57) had more than one co-morbidity. Most of the non-asthmatic patients, 178 (90.8%, p-value 0.40) had consolidation on their chest X-rays while 23 asthmatics (95.8%, p-value 0.40) had consolidation on their chest X-rays. The majority of the non-asthmatic patients, 161 (82.1%, p-value 0.23) had high D-dimer levels. Ventilator use in the hospital was found in the majority of the non-asthmatic patients (183/93.4%, p-value 0.75) while, 22 asthmatic patients (91.7%, p-value 0.75) were found to be on a ventilator. The majority of non-asthmatic patients had high levels of serum LDH, D-dimer, and Ferritin. Twenty asthmatic patients (83.3%, p-value 0.21) had severe ARDS, and 169 non-asthmatic patients (86.2%, p-value 0.21) had severe ARDS. The number of days of hospitalization was found more among the majority of the asthmatic patients (23/95.8%, p-value 0.61) and in non-asthmatic patients, 176 (89.8, p-value 0.61) were admitted to the hospital for 20 days.

**Conclusion:** COVID-19 disease was found higher among non-asthmatic patients as compared to asthmatic patients. The presence of other significant comorbidities also increases COVID-19 infection severity.

**Key Words:** Asthmatic, Non-Asthmatic, COVID-19, Comorbidities, Ventilator.

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## INTRODUCTION

Novel Coronavirus (SARS COV-2) resulted in a pandemic that was considered as most health-hazardous disease of the era after World War II. The coronavirus disease 2019 (COVID-19) has emerged as an extraordinary global threat. It is believed that COVID-19 is the third outbreak. Above 50,000 people have died, and over a million more have been infected globally. In March 2020, the WHO (World Health Organization) labeled the disease as a global pandemic.<sup>1</sup> Current research conducted on COVID-19

severity allergy disorders and asthma is conflicting.

The prevalence of COVID-19 in patients with asthma or allergy history is very low, according to a large case series study conducted in Wuhan on adults and children in China.<sup>1</sup> Similarly, in another study conducted in New York City, asthma was not found to be a predisposing factor for endotracheal intubation in COVID-19 patients.<sup>2</sup> COVID-19 results are linked to underlying disorders or circumstances that may alter immunity, exacerbating the illness.

Factors such as age (>65 years), patients with lung and kidney diseases, diabetes, cardiovascular disease, obesity, smoking, and suffering from HIV infection all are known as epidemiologic risk factors for COVID-19. In previous investigations, COVID-19 patients having asthma were linked to poor prognosis evident in data from UK Biobank and Seattle, but it was not linked to poor clinical results in Wuhan. Although allergic conditions like atopic dermatitis, asthma, and allergic rhinitis all are associated with the severity of viral respiratory diseases.<sup>3</sup>

COVID-19 has severe outcomes such as hospitalization or death among patients who have old age and have co-morbidities. Lung problems, such as respiratory failure and ARDS, are common causes of severe outcomes.<sup>4</sup> Coronavirus spreads through two different routes. Droplet inhalation, often known as the aerosol pathway, is the direct pathway via which infection occurs. Moreover, the infection can be spread through persons by contaminating objects by touching them, or by droplets through sneezing, coughing, or exhaling, providing a medium for infection spreading from contaminated objects to individuals, resulting in new cases, this is referred to as the indirect pathway.<sup>5</sup>

Frequent hand hygiene and social distancing are important, but they aren't enough to defend against viruses present in airway microdroplets emitted into the air by infected persons.<sup>6</sup> Although the chance of severe COVID-19 infection is thought to be higher in patients with asthma, particularly non-allergic asthma. Still, it is unclear whether asthmatic patients are vulnerable to SARS-CoV-2 infection. There is also less information on whether COVID-19 can cause asthma exacerbation and how to treat asthma exacerbation caused by COVID-19.<sup>7</sup> COPD, hypertension, diabetes, cancer, obesity, immune suppression, and kidney diseases all are associated with an increased risk of death in patients with COVID-19.<sup>8</sup> Studies have been conducted which reveal that asthma did not influence mortality, this study included 744 asthmatics and 8151 non-asthmatic.<sup>9</sup>

Due to a lack of data, no firm conclusions about asthma and clinical results could be drawn. In an analysis of 17,694 subjects, the researcher concluded that COVID-19 is not linked with an increased likelihood of asthma when compared to non-severe COVID-19 cases, and therefore it is not linked to increased deaths in COVID-19 patients. Asthma was not overrepresented among COVID-19 patients who required more intense

therapy, had more severe clinical symptoms, or had a poorer prognosis.<sup>10</sup>

No study has been conducted in Pakistan to evaluate the associated factors linked with asthma and COVID-19. So, this study will not only provide local guidelines for the health care workers but will also provide lessons learned for the asthmatic patients suffering from recent COVID-19 infection. The objective of the study was to compare the different clinical outcomes among asthmatic and non-asthmatic patients having COVID-19 infection.

## MATERIALS AND METHODS

This cross-sectional study was carried out from April 2021 to September 2022 at Hayatabad Medical Complex (HMC) in Peshawar, where all the patients suffering from COVID-19 disease in the intensive care unit of Hayatabad Medical Complex were selected. Using the WHO sample size calculator, the total sample size was 220 with 90.6% frequency of patients without asthma among all COVID-19 patients. Keeping a 95% confidence interval and 4% margin of error the sample size was calculated. Consecutive nonprobability sampling technique was used.

Selected patients were admitted to the intensive care unit (ICU) for COVID-19 infection in Hayatabad Medical Complex, Peshawar. Written and oral consent was taken from the attendants of the selected patients. They were guided for the study objectives and confidentiality of the data.

A modified questionnaire was being tested for validation through a pilot study. A Cronbach alpha of less than 0.80 was taken as acceptable. Inclusion and exclusion criteria were strictly followed to avoid biases. An ethical approval was taken from the ethical committee (No:125/HMC/B&PSC/2021) of Hayatabad Medical Complex (HMC) Peshawar, Pakistan". SPSS version 22 was used for data analysis. Numerical variables were presented in the form of mean and standard deviation while categorical variables were presented in the form of frequency and percentages.

The chi-square test was applied by taking the type of group (Asthmatic & Non-asthmatic) as the outcome variable with all other independent variables. A significant p-value of  $\leq 0.05$  was taken as significant.

## RESULTS

Out of a total of 220 participants, 10.9% (n= 24) were asthmatic while 89.1% (n= 196) were non-asthmatic. Almost 60% (n= 132) were male while 40% (N=88) were female. As Table 1(a) shows Out of all, 56.4% (n=124) were non obese while 43.6% (n=96) were obese. The majority of participants, 78.2% (n=172) had high white blood cell count, 20.9% (n=46) had normal white blood cell count and 0.9% (n=2) had low WBC level. Different co-morbidities were seen in the patients. 28.6% (n= 63)

had no comorbidity. 2.7% (n=6) had a history of allergy. 1.8% (n= 4) had cerebrovascular disease. 1.8% (n=4) had a history of coronary artery disease. 13.6% (n=30) had a history of hypertension. 8.6% (n=19) had a history of diabetes and the majority of participants 42.7% (n= 94) had more than one disease. The majority of patients 93.2% (n= 205) used CPAP masks during hospitalization.

The mean age of the participants was  $58.9 \pm 13.5$ , the Mean intubation time in days was  $0.60 \pm 1.8$ , the mean total household income was  $126095.4 \pm 559475.9$  while the mean number of days of hospitalization was  $9.9 \pm 9.8$  respectively. These four were converted by dividing the range into three equal intervals of width in each class. The age of the participants was classified into three categories. The first category was 15-39 years and 2nd category were 39.1-63 while the third category was more than 63 years.

Intubation time in days was classified into three categories. The first category was 01-08 days and 2nd category were 8.1-16 days while the third category was more than 16.1 days. Total household income was classified into three categories. The first category was 0-300000 Pakistani rupees while the second and third categories were 3.1-600000 Pakistani rupees and more than 600000 Pakistani rupees, respectively.

Number of days of hospitalization was classified into three categories. The first category was 01-20 days and 2nd category were 20.1-40 days while the third category was more than 40 days as shown in Table 1(b).

The chi-square test to see the association of our dependent variable (asthmatic/non-asthmatic) among demographic variables and lab-based results as demonstrated in Table 2. The majority of participants were non-asthmatic male 118 (60.2%, p-value 0.86). The majority of the participants were non-asthmatic 98(50.0%, p-value 0.63) and their ages were between 39.1-63 years. Most of the non-obese were non-asthmatic 112(57.1%, p-value 0.50). Asthmatic were the same in both obese and non-obese people 10(50.0%, p-value 0.50). Different co-morbidities were seen in different patients, most of the non-asthmatic patients 81(41.3%, p-value 0.57) had more than one co-morbidity. The majority of the non-asthmatic patients 151(77.0%, p-value 0.48) had high white blood cell count as compared to asthmatic patients. Table 3 presents a comparison between asthmatic and non-asthmatic individuals concerning various clinical outcomes. The analy-

sis encompasses the utilization of ventilators, noninvasive ventilation, non-rebreather masks, CPAP masks, serum LDH and ferritin levels, P/F ratio based on ARDS severity, invasive ventilation, intubation time, household income, and duration of hospitalization. Despite some variations observed, particularly in the utilization of noninvasive ventilation and serum LDH levels, statistical analysis yielded non-significant p-values, suggesting minimal differences between the two groups across these clinical parameters.

## DISCUSSION

The objectives of this study were to determine the different clinical outcomes among patients with COVID-19 having asthma and having no asthma. The majority of them were non-asthmatic males 118 of them were 39.1-63 years old. Among them most were non-obese n=112. The majority of the non-asthmatic 81 "had more than one co-morbidity. The majority of the non-asthmatic 151 patients had high leukocyte counts. Among these majority of the patients had high neutrophils count of 188, normal monocytes of 152(77.6%) eosinophil 194(99.0%), and basophils count of 196(100.0%), and low lymphocytes count of 189(96.4%, p-value 0.40). The majority of the non-asthmatic patients 164 (83.7%, p-value 0.57) had positive PCR reports with consolidation on their chest X-rays 178 (90.8%, p-value 0.40). Most of the non-asthmatic patients had high inflammatory markers i.e. D-dimer 161 (82.1%), serum LDH 189 (96.4%), and serum Ferritin 179 (91.3%, p-value 0.53).

Ventilator in the hospital setting was used by the majority of the non-asthmatic patients i.e. 183 (93.4%). In the hospital setting, non-invasive ventilation was used by the majority of the non-asthmatic patients which included Non-rebreather Mask 194 (99.0%) and CPAP 183 (93.4%). During hospitalization, the majority of the non-asthmatic patients 146 (74.5%) did not use invasive ventilation. Intubation days in the hospital were classified in which most non-asthmatic patients were intubated for 08 days 195 (99.5%). Stay in the hospital setting was also classified in which most of the non-asthmatic patients 176 (89.8) were admitted for 20 days. The severity of ARDS was seen in which majority of the non-asthmatic patients i.e. 169 (86.2%). Total household income was categorized in which the majority of non-asthmatic patients 195(99.5%) had an income of less than 30000 per month.

In our study, it was found that 118(60.2%) of the

**Table No 1(a): Descriptive statistics of study population**

	Categories	Frequency (Percentages)
Type of group	Asthmatic	24 (10.9)
	Non-Asthmatic	196 (89.1)
Gender	Male	132 (60.0)
	Female	88 (40.0)
Obese	No	124 (40.0)
	Yes	96 (43.6)

White Blood Cells	Normal	46 (20.9)
	High	172 (78.2)
	Low	2(0.9)
Neutrophils	Normal	7 (3.2)
	High	211 (95.9)
	Low	2 (0.9)
Lymphocytes	Normal	8 (3.6)
	Low	211 (95.9)
	High	1 (0.5)
Monocytes	Normal	170 (77.3)
	High	7 (3.2)
	Low	43 (19.5)
Eosinophil	Normal	217 (98.6)
	High	2 (0.9)
	Low	1 (0.5)
Basophils	Normal	220 (100)
	Nil	63 (28.6)
	Allergy	6 (2.7)
	Cerebrovascular disease	4 (1.8)
	Coronary artery disease	4 (1.8)
	Hypertension	30(13.6)
	Diabetes	19 (8.6)
	More than one	94 (42.7)
PCR test during Hospitalization	Negative	37 (16.8)
	Positive	183 (83.2)
Consolidation on Chest X-ray	Present	201 (91.4)
	Absent	19 (8.6)
D Dimer Level	Normal	37 (16.8)
	High	183 (83.2)
Ventilator used during hospitalization	No	15 (6.8)
	Yes	205 (93.2)
Non-invasive ventilation used during hospitalization	No	1 (0.5)
	Yes	219 (99.5)
A rebreather Mask used during hospitalization	No	1 (0.5)
	Yes	219 (99.5)
CPAP Mask used during hospitalization	No	15 (6.8)
	Yes	205 (93.2)
Serum LDH Level	Normal	7 (3.2)
	High	213 (96.8)
Serum Ferritin	Normal	20 (9.1)
	High	200 (90.9)
P/F ratio	Mild	11 (5.0)
	Moderate	20 (9.1)
	Severe	189 (85.9)
Invasive ventilation used during hospitalization	No	167 (75.9)
	Yes	53 (24.1)

**Table No 1(b): Descriptive statistics for continuous variables**

	Mean	Standard deviation	Min-Max(range)
Age in years	58.93	13.50	15-88(73.0)
Intubation time in days	0.60	1.88	0-24(24)
Total household income	126095.45	559475.96	0-8000000(8000000)
Number of Days of Hospitalization	9.98	9.80	01-62(61)

**Table No 2: Comparison of Asthmatic and non-asthmatic with demographic and lab-based outcome**

	Categories	Asthmatic group (%)	Non-asthmatic (%)	P-Value
Gender	Male	14 (58.3)	118 (60.2)	0.86
	Female	10 (41.7)	78 (39.8)	
Age categories in the year	15-39	1 (4.2)	17 (8.7)	0.63
	39.1-63	14 (58.3)	98 (50.0)	
	More than 63	9 (37.5)	81 (41.3)	
Obese	No	12 (50.0)	112 (57.1)	0.50
	Yes	12 (50.0)	84 (42.9)	
Co-morbidities	Nil	7 (29.2)	56 (28.6)	0.57
	Allergy	1 (4.2)	5 (2.6)	
	Cerebrovascular disease	1 (4.2)	3 (1.5)	
	Coronary artery disease	0 (0.0)	4 (2.0)	
	Hypertension	1 (4.2)	29 (14.8)	
	Diabetes	1 (4.2)	18 (41.3)	
	More than one	13 (54.2)	81 (41.3)	
White Blood Cell	Normal	3 (12.5)	43 (21.9)	0.48
	High	21 (87.5)	151 (77.0)	
	Low	0 (0.0)	2 (1.0)	
Neutrophils	Normal	1 (4.2)	6 (3.1)	0.84
	High	23 (95.8)	188 (95.9)	
	Low	0 (0.0)	2 (1.0)	
Lymphocytes	Normal	2 (8.3)	6 (3.1)	0.40
	High	22 (91.7)	189 (96.4)	
	Low	0 (0.0)	1 (0.5)	
Monocytes	Normal	18 (75.0)	152 (77.6)	0.52
	High	0 (0.0)	7 (3.6)	
	Low	6 (25.0)	37 (18.9)	
Eosinophil	Normal	23 (95.8)	194 (99.0)	0.19
	High	1 (4.2)	1 (0.5)	
	Low	0 (0.0)	1 (0.5)	
Basophils	Normal	24 (100.0)	196 (100.0)	
PCR Testing during hospitalization	Negative	5 (20.8)	32 (16.3)	0.57
	Positive	19 (79.2)	164 (83.7)	
Consolidation on Chest X-ray	Present	23 (95.8)	178 (90.8)	0.40
	Absent	1 (4.2)	18 (9.2)	
D Dimer level	Normal	2 (8.3)	35 (17.9)	0.23
	High	22 (91.7)	161 (82.1)	

**Table No 3: Comparison of Asthmatic and non-asthmatic with clinical outcome**

Variable	Categories	Asthmatic group (%)	Non-asthmatic (%)	P-Value
Ventilator used during hospitalization	No	2 (8.3)	13 (6.6)	0.75
	Yes	22 (91.7)	183 (93.4)	
Noninvasive ventilation used during hospitalization	No	0 (0.0)	1 (0.5)	0.72
	Yes	24 (100.0)	195 (99.5)	
Non-rebreather mask is used during hospitalization	No	0 (0.0)	1 (0.5)	0.88
	Yes	24 (100.0)	194 (99.0)	
CPAP mask is used during hospitalization	No	2 (8.3)	13 (6.6)	0.75
	Yes	22 (91.7)	183 (93.4)	
Serum LDH level	Normal	0 (0.0)	7 (3.6)	0.34
	High	24 (100.0)	189 (96.4)	
Serum Ferritin Level	Normal	3 (12.5)	17 (8.7)	0.53
	High	21 (87.5)	179 (91.3)	
P/F ratio	Mild ARDS	0 (0.0)	11 (5.6)	0.21
	Moderate ARDS	4 (16.7)	16 (8.2)	
	Severer ARDS	20 (83.3)	169 (86.2)	
Invasive ventilation used during hospitalization	No	21 (87.5)	146 (74.5)	0.15
	Yes	3 (12.5)	50 (25.5)	
Intubation time in days	01-08	24 (100)	195 (99.5)	0.72
	08.1-16	0 (0.0)	0 (0.0)	
	More than 16.1	0 (0.0)	1 (0.5)	
Total household income	0-300000	24 (100)	195 (99.5)	0.72
	3.1-600000	0 (0.0)	0 (0.0)	
	More than 600000	0 (0.0)	1 (0.5)	
Number of Days of Hospitalization	01-20	23 (95.8)	176 (89.8)	0.61
	20.1-40	1 (4.2)	17 (8.7)	
	More than 40	0 (0.0)	3 (1.5)	

non-asthmatic were male. Similarly, in China, an epidemiologic study conducted on COVID-19 confirmed 44,672 cases and did not find asthma as a severity risk factor.<sup>11</sup> As indicated by the hospitalization, 6.8% of patients didn't utilize ventilators while a larger part of patients 93.2% used ventilators during hospitalization. A study conducted in which the majority of the patients used ventilators during hospitalization stay (Similarly, this study shows that asthma prevalence is (10.9%) which is much lower than non-asthmatic patients.<sup>12</sup> Regarding co-morbidities, according to our study hypertension (14.8%), diabetes (41.3%), and cardiovascular disease (1.5%) were the main reported diseases. There was no asthma diagnosis in any of the subjects because of poor health hygiene more people were involved in more than diseases in Pakistan.<sup>13</sup>

## CONCLUSION

Out of a total of 220 participants, 10.9% (n=24) were asthmatic while 89.1% (n=196) were non-asthmatic. Thus, our results indicate that COVID-19 in asthmatic patients is lower than those who have no asthma. It means asthma has no association with COVID-19. In asthmatic

COVID-19 patients, there is less possibility of deaths and ICU admissions.

The significant presence of co-morbidities accompanying COVID-19 infection severity; however, asthma does not contribute as a risk for admission to ICU with COVID-19. The majority of non-asthmatic were obese and had high leukocyte count, positive PCR report with consolidation on chest X-ray, high inflammatory markers, and used non-invasive ventilation. The health system should prioritize high-risk groups that include (obese, old age people, co-morbid patients i.e. COPD, diabetes mellitus, as well hypertension), and understated ethnic-community and their group as they are at high risk of contracting illnesses.

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**Authors Contribution:**

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Ullah Z	✓	✗	✓	✗	✓	✗
Ullah R	✓	✓	✗	✓	✓	✗
Khan MA	✗	✗	✓	✓	✗	✓
Haq F	✓	✓	✗	✗	✓	✗
Khan A	✓	✗	✓	✓	✗	✓
Khan MKS	✓	✓	✗	✓	✗	✓
Hussain I	✗	✓	✗	✓	✓	✓
Naeemullah	✗	✓	✓	✗	✗	✗
Ali F	✓	✗	✗	✗	✓	✓

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Ethical Approval:**

**This Manuscript was approved by the Ethical Review Board of Hayatabad Medical Complex, Peshawar. Vide No. 125/HEC/B&PSC/2021. Dated: 16 03 2021**



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