

A Comparative Analysis of Clinical Characteristics, Laboratory Findings, and Radiological Manifestations of Hospitalized COVID-19 Patients with and without Atopy: A Single-Center Cross-Sectional Study with Matched Controls

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Abstract

Background: The coronavirus Disease 2019 (COVID-19) pandemic emerged in December 2019, resulting in a high number of deaths worldwide. There is a need to investigate how this condition affected people with different diseases, particularly atopy.

Objectives: This study aimed to compare clinical symptoms, laboratory test results, radiological manifestations, and clinical outcomes between hospitalized COVID-19 patients with and without atopy.

Methods: This single-center cross-sectional study with matched controls was conducted on 106 (out of 334) COVID-19 patients hospitalized in Baqiyatallah Hospital, Tehran, Iran, from March 24 to April 24, 2020. Among them, there were 40 and 66 cases with and without atopy, respectively. The non-atopic patients were also matched with the atopic patients in terms of age, gender, Body Mass Index (BMI), and the prevalence of comorbidities, particularly hypertension and diabetes. Patients' clinical characteristics, laboratory findings, and radiological features, recorded upon their admission, and the outcomes were then compared between both study groups.

Results: Compared with the non-atopic group, weakness, myalgia, and chills were more frequent in the patients affected with atopy ($P < 0.05$), and neutrophil count, Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), bilateral lung involvement, bilateral pneumonia, and Ground-Glass Opacity (GGO) were among the laboratory test results and radiological manifestations that were observed significantly less in atopic patients ($P < 0.05$). No significant difference was further detected regarding the COVID-19 outcomes in both study groups ($P > 0.05$).

Conclusion: This study showed that atopic conditions were capable of increasing the frequency of some COVID-19 clinical symptoms and reducing the severity of COVID-19 with regard to laboratory findings and radiological features on admission. In addition, atopy was not correlated with COVID-19 outcomes in atopic patients.

Keywords: Atopy, Clinical Characteristics, COVID-19, Hospitalized Patient

1. Background

The Coronavirus Disease 2019 (COVID-19) pandemic, caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), is still a global public health issue.¹ The virus utilizes Angiotensin-Converting Enzyme 2 (ACE2) for its attachment and entry into lung cells.²

There are some treatments available for patients with COVID-19 as well as effective vaccines that can prevent serious illness,^{3,4} but the disease continues to affect people throughout the world.⁵

Atopy is one of the comorbidities that can occur during COVID-19,⁶ which is defined as an immunological

sensitivity to allergens that can give rise to CD4+ helper T-cell type 2 (Th2) differentiation. Such cells lead to elevated levels of immunoglobulin E (IgE), which finally induce an excessive response to allergens.⁷

Reports about the relationship between atopy and COVID-19 are still contradictory. Despite the results of some studies suggesting that atopy is not a risk factor for COVID-19,^{8,9} some cases have thus far shown the attenuating effect of this condition on COVID-19 severity.^{10,11} Furthermore, a nationwide cohort study of Korean patients indicated that allergy can result in aggravated clinical outcomes.¹² Reports on the protective effect of atopic conditions against COVID-19 have further demonstrated fewer severe complications and decreased length of stay in hospitals among atopic patients compared to non-atopic patients.^{10,11} The protective effect of atopic conditions against COVID-19 can result from the decreased level of ACE2 in airway epithelial cells of people with atopy,¹³ or the Th2-mediated attenuation of inflammation caused by Th1 following virus infection.¹¹

2. Objectives

Much more information about the effects of atopic conditions on COVID-19 patients is thus needed to understand the relationship between these two diseases. Furthermore, COVID-19 scientific data are important for future possible pandemics. The main purpose of the present study was to compare the clinical characteristics, laboratory findings, and radiological manifestations on admission and the outcomes between hospitalized COVID-19 patients with and without atopy.

3. Methods

3.1. Study Design and Participants

This study was fulfilled using a single-center cross-sectional study design with matched controls. In total, 334 COVID-19 patients were screened as the study's participants. The inclusion criteria for selecting the atopic group members were (1) admission, with COVID-19 confirmed, to Baqiyatallah Hospital, Tehran, Iran, from March 24 to April 24, 2020, and (2) diagnosis with at least one of the atopic conditions, including allergic rhinitis, atopic dermatitis, or food allergy verified by skin prick or serum IgE testing upon admission. On the other hand, the exclusion criterion was taking one of the atopy-related drugs, such as corticosteroids or omalizumab, which could affect the COVID-19 clinical characteristics. The non-atopic group members were thus hospitalized COVID-19 patients matched with the atopic group in terms of age, gender, Body Mass Index (BMI), and the prevalence of some comorbidities, including hypertension and diabetes ($P > 0.05$). The COVID-19 diagnosis was further confirmed by Computed Tomography (CT) scan of the chest as well as nasal and/or pharyngeal swab

specimens for real-time reverse transcriptase polymerase chain reaction (real-time RT-PCR). Patients or variables with missing values were also excluded. Finally, the COVID-19 treatment regimen was in accordance with the Iranian National COVID-19 Treatment Protocol for both groups.

3.2. Data Collection and Study Procedure

All the data, which included patients' atopic status, demographic characteristics, clinical symptoms, laboratory test results, radiological features, and clinical outcomes, were initially transferred from their medical records to a preliminary checklist. The data were then imported into the computer database and crosschecked independently by the members of a group of trained physicians.

3.3. Statistical Analysis

Clinical symptoms, laboratory findings, radiological manifestations, and outcomes were compared between the two study groups. Statistical analysis was also conducted using the SPSS Statistics software package (ver. 22) (SPSS Inc., Chicago, IL, USA). The continuous variables were accordingly described as the mean \pm Standard Deviation (SD), and the categorical variables were illustrated as count and percentage, which were analyzed by t-test and Chi-square/Fisher's exact tests, respectively.

4. Results

In total, 106 hospitalized COVID-19 patients were selected out of 334 patients in the present study, including 40 COVID-19 patients with atopy and 66 non-atopic controls matched with the atopic group in terms of age, gender, BMI, and the prevalence of some comorbidities, including hypertension and diabetes.

Considering the atopic patients, as shown in Table 1, about 50% of the cases were men, their mean age (\pm SD) was 53.05 (13.15) years, and their mean BMI was 29.32 (4.54) Kg/m².

No statistically significant difference was found regarding the prevalence of comorbidities between the atopic and non-atopic groups ($P > 0.05$). As illustrated in Figure 1, the most prevalent comorbidities in these patients were hypertension, diabetes, kidney disease, and cardiovascular disease.

The clinical symptoms were recorded on admission. In the atopic group, fever (52.5%), cough (67.5%), dyspnea (72.5%), weakness (62.5%), myalgia (72.5%), and chills (70.0%) were the most prevalent symptoms. On the other hand, in the group without atopy, fever (54.5%), cough (54.5%), and dyspnea (60.6%) were the most frequent ones. There were also significant differences regarding the prevalence of chills ($P = 0.03$), myalgia (0.01), and weakness (0.021) in both groups (Figure 2).

Table 1. Demographic Data and Smoking Prevalence in Atopic and Non-atopic Patients Hospitalized with COVID-19

Characteristic		Atopic (n = 40)	Non-atopic (n = 66)	P value
Demographic data				
Sex	Male	20 (50.0%)	35 (53.0%)	0.762
	Female	20 (50.0%)	31 (47.0%)	
Age, years	Mean ± SD	53.05 ± 13.15	53.74 ± 12.90	0.791
	Min-Max	27-80	24-83	
BMI, Kg/m ²	Mean ± SD	29.32 ± 4.54	28.13 ± 3.68	0.151
	Min-Max	22.59-40.90	21.22-39.25	
Smoking		1 (2.5%)	2 (3.0%)	0.999

SD: standard deviation; BMI: body mass index. P values indicate differences between atopic and non-atopic patients. P < 0.05 was considered as statistically significant difference.

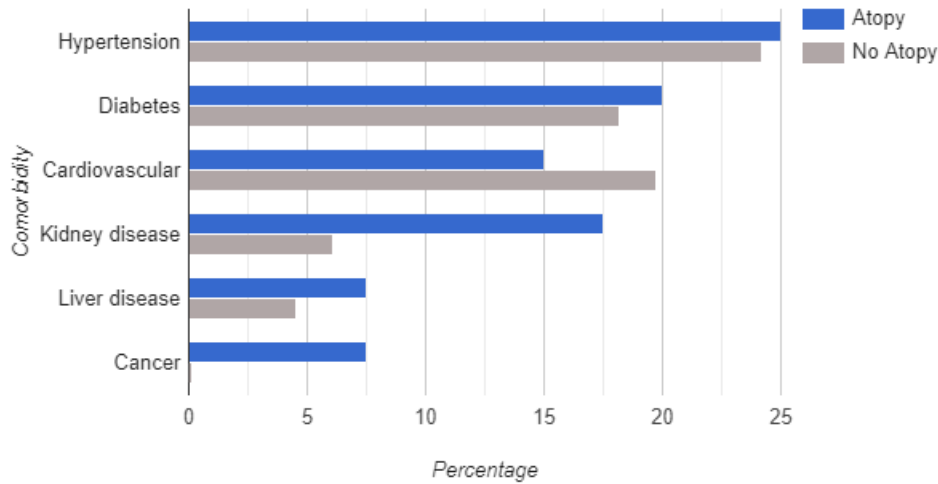


Figure 1. Comorbidity Prevalence in Atopic and Non-atopic Patients Hospitalized with COVID-19.

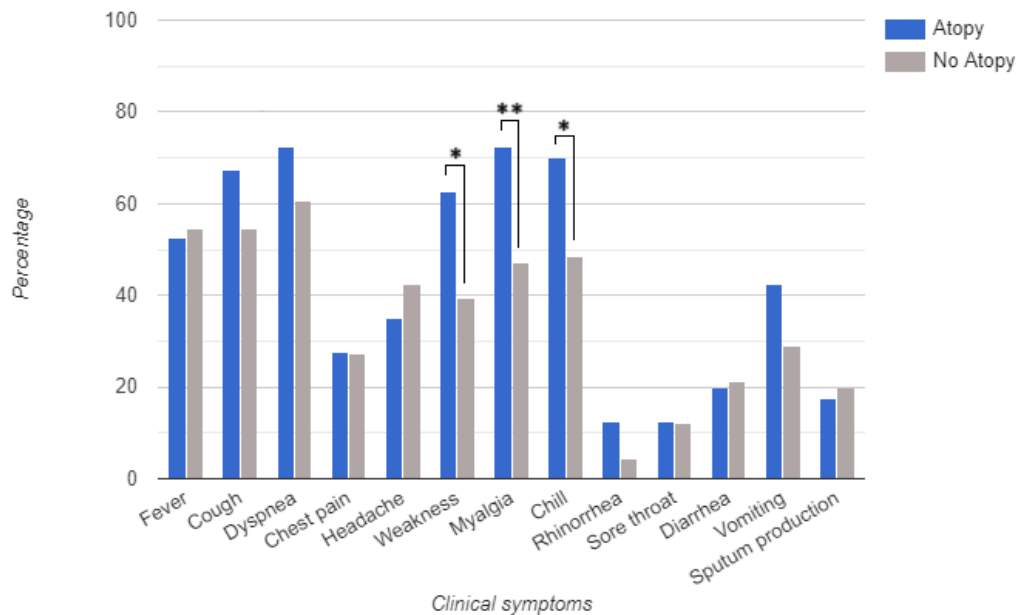


Figure 2. Clinical Symptoms in Atopic and Non-atopic Patients Hospitalized with COVID-19.

Upon patient admission, the laboratory findings showed an increase in Erythrocyte Sedimentation Rate (ESR), Aspartate Aminotransferase (AST), Lactate Dehydrogenase (LDH), and C-Reactive Protein (CRP) in both atopic and non-atopic groups, but neutrophil count was above the normal range only in the matched controls. Neutrophil count (68.74 ± 9.73 vs. 73.54 ± 11.99% of leukocytes;

P = 0.041), ESR (32.03 ± 17.06 vs. 47.00 ± 22.05 mm/h; P = 0.001), and CRP (16.53 ± 12.31 vs. 24.92 ± 16.99 mg/L; P = 0.015) were significantly lower in the atopic group compared to the non-atopic one. It is worth mentioning that the other laboratory findings were in the normal range (Table 2).

Most of the patients suffered from pneumonia on

admission (Table 3). In both the atopic and non-atopic groups, radiological manifestations correspondingly revealed that bilateral lung involvement (87.5% vs. 100%; $P = 0.006$), bilateral pneumonia (85.0% vs. 100%; $P = 0.002$), and Ground-Glass Opacity (GGO) (87.5% vs. 98.5%; $P = 0.028$) were significantly less frequent in the atopic group. Moreover, admission oxygen saturation was not significantly different between the patients

with and without atopy (89.78 ± 6.26 vs. 89.86 ± 8.84 ; $P = 0.958$).

As depicted in Table 4, no significant difference was observed regarding hospital discharge (97.5% vs. 95.5%; $P = 0.592$), length of stay (6.4 ± 4.2 vs. 5.8 ± 3.8 days; $P = 0.476$), Intensive Care Unit (ICU) admission (15.0% vs. 18.2%; $P = 0.672$), or death (2.5% vs. 4.5%; $P = 1.00$) between the atopic and non-atopic groups.

Table 2. Laboratory Characteristics in Atopic and Non-atopic Patients Hospitalized with COVID-19

Laboratory results	Normal range	Atopic (n = 40)	Non-atopic (n = 66)	P value
White blood cell count, $\times 10^3/\mu\text{l}$	3.7-9.5	5.94 ± 2.60	6.65 ± 2.86	0.206
Red blood cell count, $\times 10^6/\mu\text{l}$	4.3-5.7	4.81 ± 0.74	4.83 ± 0.76	0.900
Hemoglobin, g/dl	13.3-16.9	14.18 ± 2.17	13.94 ± 1.70	0.528
Hematocrit, %	39-51	42.02 ± 8.18	40.79 ± 4.11	0.306
MCV, fL	80-98	86.19 ± 6.46	86.17 ± 8.79	0.989
MCH, pg	27-35	29.58 ± 2.76	29.49 ± 3.85	0.898
MCHC, g/dl	31-36	34.28 ± 1.27	34.13 ± 1.55	0.611
RDW-CV, %	11.5-15.5	13.95 ± 5.12	13.46 ± 1.87	0.483
MPV, fL	6-13.5	9.81 ± 1.18	9.91 ± 0.88	0.610
Platelet count, $\times 10^3/\mu\text{l}$	145-420	192.47 ± 75.99	200.75 ± 69.59	0.572
Neutrophil count, % of leukocytes	50-70	68.74 ± 9.73	73.54 ± 11.99	0.041
Lymphocyte count, % of leukocytes	11-49	24.18 ± 9.04	21.45 ± 11.72	0.215
BUN, mg/dl	7-19	13.32 ± 5.91	13.25 ± 5.47	0.948
ESR, mm/hour	Up to 15	32.03 ± 17.06	47.00 ± 22.05	0.001
AST, U/L	< 35	36.38 ± 15.31	39.19 ± 21.94	0.576
ALT, U/L	< 45	36.79 ± 25.04	32.19 ± 22.35	0.431
ALP, U/L	Up to 270	186.17 ± 92.65	211.1 ± 164.91	0.504
LDH, U/L	207-414	680.86 ± 238.67	693.6 ± 252.84	0.831
CRP, mg/L	Up to 5	16.53 ± 12.31	24.92 ± 16.99	0.015
Sodium, mEq/L	136-145	136.05 ± 3.59	136.23 ± 2.86	0.786
Potassium, mEq/L	3.5-5	4.06 ± 0.40	4.18 ± 0.43	0.165

MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; RDW: red blood cell distribution width; MPV: mean platelet volume; BUN: blood urea nitrogen; ESR: erythrocyte sedimentation rate; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; LDH: lactate dehydrogenase; CRP: C-reactive protein. P values indicate differences between atopic and non-atopic patients. $P < 0.05$ was considered as statistically significant difference.

Table 3. Oxygen Saturation and Radiology Findings in Atopic and Non-atopic Patients Hospitalized with COVID-19

Characteristic	Atopic (n = 40)	Non-Atopic (n = 66)	P value
Oxygen saturation, %	89.78 ± 6.26	89.86 ± 8.84	0.958
Bilateral lung involvement	35 (87.5%)	66 (100%)	0.006
Unilateral pneumonia	1 (2.5%)	0 (0.0%)	0.377
Bilateral pneumonia	34 (85%)	66 (100%)	0.002
Ground Glass Opacity	35 (87.5%)	65 (98.5%)	0.028

P values indicate differences between atopic and non-atopic patients. $P < 0.05$ was considered as statistically significant difference.

Table 4. Final Outcomes in Atopic and Non-atopic Patients Hospitalized with COVID-19

Outcome	Atopic (n = 40)	Non-atopic (n = 66)	P value
Hospital discharge	39 (97.5%)	63 (95.5%)	0.592
Hospital stay, mean \pm SD, day	6.4 ± 4.2	5.8 ± 3.8	0.476
ICU admission	6 (15.0%)	12 (18.2%)	0.672
Death	1 (2.5%)	3 (4.5%)	0.999

SD: standard deviation; ICU: intensive care unit. P values indicate differences between atopic and non-atopic patients. $P < 0.05$ was considered as statistically significant difference.

5. Discussion

There are contradictory reports on the correlation between COVID-19 and atopy. Therefore, more reports are needed to understand their mutual relationship. The present study aimed to investigate COVID-19 clinical features in patients with and without atopy upon admission and then compare the results between the two groups.

In the atopic group, the male to female ratio was 1:1. Although several studies have shown the increased severity of COVID-19 in male patients,¹⁴ there are reports in which the male proportion of hospitalized COVID-19

patients has not been significantly different from that of females.¹⁵⁻¹⁸ No differences by gender can be considered since it was not a risk factor within this small sample. In a study by Statsenko Y et al., there was no statistical association between the severity of COVID-19 in terms of the percentage of lung involvement and sex. Furthermore, the association of male sex with severe disease was very weak.¹⁹

Research has established that the age over 50 years can be a predictor of increased COVID-19 severity,⁸ and being 60 years or older can even multiply death

probabilities.^{20,21} In addition, Zhang JJ et al. demonstrated that older age and smoking history were independent risk factors for mortality in severe patients.¹⁷ Moreover, Mehra et al. showed that being a current smoker can increase the death rate for in-hospital patients.²² In this study, the mean age of the patients was over 50 years, which was one of the major reasons for intensified COVID-19 severity in these patients. However, the mean age was below 60 years, and smoking prevalence was low among the patients (2.5% and 3% in the atopic and non-atopic groups, respectively), which could result in a low mortality rate in the patients.

Comorbidities could also play an important role in the higher rate of COVID-19 morbidity and mortality.²³ In this study, the most frequent comorbidities in the atopic group were hypertension, diabetes, cardiovascular disease, and kidney disease (Figure 2), which were in consensus with other reports about the prevalence of comorbidities in COVID-19 patients.^{19,24-26}

Higher ESR, AST, LDH, and CRP in the patients in the present study were also among the laboratory test results observed in both atopic and non-atopic groups on admission, but neutrophil count was augmented only in the group without atopy. In addition, neutrophil count, CRP, and ESR were significantly lower in the atopic group than in the controls. In line with these findings, elevations in CRP, ESR, and LDH have been found to be among the most prevalent laboratory findings in COVID-19 patients.²⁷ Higher neutrophil counts and CRP levels could be correlated with severe pneumonia and composite endpoints caused by COVID-19.²⁸ Besides, in cases with severe COVID-19, higher neutrophil counts and higher levels of C-reactive protein were associated with death, and in comparison with non-severe patients, surviving severe patients had higher neutrophil counts and levels of CRP.¹⁷ Given the findings in previous studies, the study results revealed that the COVID-19 severity in the atopic group was lower than that in the non-atopic one. The fact that the laboratory findings, viz. neutrophil count, ESR, and CRP showed that COVID-19 severity was lower in the group with atopy than in the matched controls, which was consistent with their radiological manifestations.

In this study, most of the patients had bilateral lung involvement, bilateral pneumonia, and GGO upon admission, which have also been reported as the most prevalent characteristics of COVID-19 patients in previous studies.²⁹⁻³² In comparison with the atopic group, the non-atopic group showed less frequent observations of bilateral involvement, bilateral pneumonia and GGO. Sarmin M et al. demonstrated that chest X-ray observation of bilateral X-ray changes on admission was significantly more frequent in patients with severe-critical conditions than in mild-moderate patients.³³ Less severe COVID-19 pneumonia in atopic patients than in that of non-atopic ones could result from the decreased level of ACE2 and increased

Th2 responses associated with the attenuation of Th1-mediated inflammation following virus infection in atopic patients.^{11,13}

The study results also revealed no relationship between atopic conditions and COVID-19-related outcomes, which was in agreement with the findings in previous research.^{34,35}

This study had some limitations. First, its cross-sectional nature did not allow inferring direct causal relationships. In addition, sample size/power analysis was not conducted prior to the study. Furthermore, some biases were expected due to the small number of patients recruited. Finally, the patients were from a single center in the city of Tehran, Iran, so a further multicenter study is needed because the study results could not be generalized to other contexts.

6. Conclusion

In comparison with the patients without a history of atopy, some COVID-19 symptoms were capable of being more frequent in the atopic group. On the other hand, reduced COVID-19 severity was observed with respect to the laboratory findings and radiological manifestations in the atopic patients compared to the group without atopy. Finally, there was no relationship between atopy and COVID-19 outcomes. Reduced severity might have resulted from the decreased level of ACE2 receptor in airway epithelial cells and higher Th2 responses in the patients with atopy.

Research Highlights

What Is Already Known?

There is a contradiction on whether atopy is or is not a risk factor for COVID-19, or even has an attenuating effect on the severity of COVID-19.

What Does This Study Add?

Atopic condition is capable of increasing some COVID-19 symptoms. This is while it can reduce the COVID-19 severity with regards to the laboratory findings and radiological manifestations.

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Author Contributions

MA-D, MA, MA-D conceptualized the study. MA-D and MA-D formulated the methodology. MA, HB, MSH, SHH, MZ, HRJ, RAT and MB carried out the data collection. MA-D extracted and analyzed the data. MA-D drafted the manuscript. EV critically evaluated and revised the manuscript. All authors read and approved the finalized manuscript.

Conflict of Interest Disclosures

All authors declared that they have no conflict of interest.

Ethical Approval

This study was reviewed and approved by the Ethics Committee of Baqiyatallah University of Medical Sciences, Tehran, Iran, with the code no. IR.BMSU.REC.1399.170. It was then performed in accordance with the Declaration of Helsinki guidelines. Verbal consent was also obtained from the patients or their families for the publication of their personal and clinical details.

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