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IMPORTANCE OF COMORBIDITY AND AGE IN THE HOSPITALIZATION DECISION IN COVID-19 PATIENTS

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ABSTRACT

Aim: COVID-19 is an important problem, and comorbidities may worsen the course of the disease. We aimed to investigate the role of comorbidities in COVID-19 patients hospitalized for outpatient treatment failure.

Methods: Hospitalized COVID-19 patients were included in this study between March 1 and May 15, 2020. Those hospitalized due to treatment failure were defined as Group-1, and those hospitalized at first admission were defined as Group-2. Demographic information, comorbidities, laboratory data, and clinical results of the patients were examined.

Results: A total of 514 patients were included in the study; 19.3% (n=99) were patients who worsened despite outpatient treatment (Group-1), and 80.7% (n=415) were hospitalized at first admission (Group-2). Group-1 cases were younger, but comorbidities were as high as the older Group-2 cases. We found that increasing age increases the risk of hospitalization (OR=1.02), bronchiectasis reduces the risk of hospitalization (OR=0,109), and other comorbidities have no impact on the risk of hospitalization. There was no difference between groups according to ICU transfer (Group-1: 6.1%, Group-2: 9.2%, p=0.32), hospital discharge rates (Group-1: 100%, Group-2: 96.6%, p=0,064), and mortality rates (p=0.064). In Group-1, leukocyte, thrombocyte, neutrophil, lymphocyte, eosinophil, monocyte, and basophil values were lower, and urea and D-Dimer values were higher than Group-2.

Conclusions: This study identified age as a factor in increasing hospitalization in COVID-19 patients. On the other hand, the presence of bronchiectasis in patients appears to be a factor in reducing hospitalization. This situation raises a new question about whether the permanent dilation resulting from the damage caused by bronchiectasis in the bronchi could act as a preventive factor for the coronavirus. We believe that well-designed studies involving a large case series could lead the way in exploring this aspect further.

Keywords: COVID-19, comorbidity, hospitalization

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INTRODUCTION

The epidemic, which emerged in China in December 2019 and caused the new Coronavirus 2019 disease (COVID-19), spread all over the world, and the World Health Organization declared a global epidemic (pandemic) on March 11 [1]. Nowadays, 772 million cases and more than 6 million deaths have been reported worldwide [2]. Besides asymptomatic cases in COVID-19, the spectrum of symptomatic infections ranges from mild to critical illness requiring severe intensive care support; most infections are not severe [3, 4].

Critical or fatal disease rates are higher among patients requiring hospitalization [5, 6]. Therefore, hospitalized patients should be evaluated more carefully regarding mortality and morbidity risk. Some cases that are asymptomatic during the disease may be symptomatic in the follow-up; these cases are even defined as presymptomatic [7]. In the follow-up after treatment, some cases may require hospitalization with ongoing symptoms or complications. In the follow-up of COVID-19, managing the delayed recovery process can provide control of the disease and reduce possible complications, mortality, and morbidity related to the disease.

We aimed to investigate possible causes of worsening by comparing patients who needed to be hospitalized after worsening with outpatient treatment and patients hospitalized at first admission. Learning the reasons for admission and the need for hospitalization can help use healthcare resources effectively in managing the pandemic.

METHODS

It was planned as a retrospective case-control study. The files of all COVID-19 patients hospitalized in the tertiary chest diseases hospital between March 1, 2020, and May 15, 2020, were reviewed.

The cases that were hospitalized due to the worsening of the COVID-19 disease despite being given outpatient treatment were defined as Group-1 (case group), and those who were diagnosed with COVID-19 at the first admission and decided to be hospitalized were defined as Group-2 (control group). Patients hospitalized with COVID-19 PCR positivity in nasal/nasopharyngeal swabs or clinically and radiologically compatible with COVID-19 according to the national COVID-19 guidelines were included in the study. Those admitted to the intensive care unit were excluded from the study. All cases were over the age of 18 years.

According to the national guide, those who are over 50 years old, have underlying diseases, severe pneumonia (confusion or tachycardia (>125/min), or respiratory distress or tachypnea (>30/min) or hypotension (<90/60 mmHg or SpO2<92% on room air, or those with bilateral diffuse involvement on lung imaging), sepsis, septic shock, cardiomyopathy, arrhythmia or acute kidney injury, and poor prognostic criteria in blood tests (lymphocyte count<800/µl or serum CRP>40mg/l or ferritin>500ng/ml or D-

Dimer>1000ng/ml, etc.) admission hospitalization was recommended for patients with [8].

By examining the case files from the hospital electronic database, demographic information, comorbid diseases, the reason for hospitalization, symptoms, vital signs, blood count, biochemical values, inflammatory markers, D-Dimer, lung radiology, received treatments, and clinical results of the cases were recorded. The recorded data were analyzed by comparing the two defined groups.

Local ethics committee approval was obtained for the study (approval date/No:14.05.2020/084), and it was performed according to the ethical principles stated in the Declaration of Helsinki. The diagnosis was based on the Republic of Turkey Ministry of Health COVID-19 (SARS-CoV-2 Infection) Guide 2020 [8].

The study analysis used the SPSS-22 package program (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). The study findings of categorical variables (gender, presence of comorbidities) were summarized in number (n) and percentage (%). The continuous variables (age, hemogram, biochemistry values, length of hospital stay) were defined as mean and standard deviation (SD) when normally distributed; the median and interquartile range (IQR, 25%-75%) were used if non-normally distributed. The distribution of the data was assessed using the Shapiro-Wilk test.

Two study groups were compared to the Student T test for normally distributed continuous variables. Mann-Whitney U Test was used if continuous variables were non-normally distributed. The chi-square test was used for categorical variables. The type I error was set at 5%. The impact of factors influencing the risk of hospitalization was examined through Multivariate Binary Logistic Regression Analysis.

RESULTS

In this study, 592 COVID-19 patients who were hospitalized were included, with those hospitalized in intensive care (n=78) excluded from the study. The cases receiving outpatient treatment and hospitalized with treatment failure were defined as Group-1 (n=99, 19.3%).

COVID-19 cases (n=415, 80.7%) hospitalized at the first admission were defined as Group-2. Gender distribution was similar between groups (p=0.35). Group-1 cases were younger when comparing the mean ages. Age distributions are shown in Table-1. There was no statistical difference between groups according to ICU transfer (p=0.32), hospital discharge rates (p=0,064), and mortality rates (p=0.064).

Table1. Gender and age distribution of the study groups

	Group				
	Group-1 (Home treatment failure) n=99		Group-2 (Baseline hospital admission) n=415		
	n	%	n	%	p
Male	60	60.6	230	55.4	**0.35**
Age above 65 years	15	15.2	114	27.5	**0.011**
Age above 50 years	44	44.4	240	57.8	**0.016**

Dichotomous variables were summarized number (n) and percentage (%). The continuous variables were defined as mean and standard deviation (SD) when normally distributed; the median and interquartile range (IQR, 52%-75%) was used if non-normally distributed. The distribution of the data was assessed using the Shapiro-Wilk test.

The presence and frequency of comorbidity were similar between the two groups (p=0.087). The frequency of comorbidities is shown in Table-2.

Table-2: Comorbidity distribution in the study groups

	Group				
	Group-1 (Home treatment failure) n=99		Group-2 (Baseline hospital admission) n=415		
	n	**%**	**n**	**%**	**p-value**
Hypertension	23	23.2	102	24.6	0.78
Diabetes	9	9.1	66	15.9	0.084
CAD	6	6.1	39	9.4	0.29
CHF	2	2.0	11	2.7	>0.99
COPD	5	5.1	44	10.6	0.13
Asthma	11	11.1	35	8.4	0.40
Malignancy	1	1.0	24	5.8	0.064
Bronchiectasis	4	4.0	5	1,2	0.074
CAD: coronary artery disease; CHF: congestive heart failure; COPD: chronic obstructive pulmonary diseases					

Dichotomous variables were summarized in number (n) and percent (%).

According to the Multivariate Binary Logistic Regression Analysis, an increase in age was found to increase the risk of hospitalization by 1.02 times (CI: 1.003-1.038). Additionally, the presence of bronchiectasis was found to significantly decrease the risk of hospitalization at a statistically significant level (OR=0.109, CI: 0.020-0.593). Furthermore, it was found that other coexisting diseases and gender did not significantly increase the risk of hospitalization (p>0.05) (Table-3).

Table-3: Factors influencing the risk of hospitalization

	B	S.E.	Wald	df	p	Odds Ratio	95% CI	
							LL	UL
Age	0,020	0,009	5,250	1	**0,022**	1,020	1,003	1,038
Gender (Female)	0,367	0,245	2,251	1	0,133	1,444	0,894	2,333
Hypertension	-0,629	0,333	3,560	1	0,059	0,533	0,277	1,025
Diabetes	0,766	0,423	3,280	1	0,070	2,152	0,939	4,932
CAD	-0,079	0,506	0,025	1	0,875	0,924	0,342	2,492
CHF	-0,298	0,838	0,127	1	0,722	0,742	0,144	3,834
COPD	0,720	0,581	1,536	1	0,215	2,054	0,658	6,412
Asthma	-0,500	0,396	1,588	1	0,208	0,607	0,279	1,320
Malignancy	1,915	1,077	3,166	1	0,075	6,790	0,823	56,005
Bronchiectasis	-2,218	0,864	6,580	1	**0,010**	0,109	0,020	0,593

CAD: coronary artery disease; CHF: congestive heart failure; COPD: chronic obstructive pulmonary diseases

The impact of factors influencing the risk of hospitalization was examined through Multivariate Binary Logistic Regression Analysis. Multivariate Binary Logistic Regression Analysis, Nagelkerke R2=0.08 and p=0.003.

In the comparative analysis of laboratory parameters in Group-1 cases, lower leukocyte count (p=0.037), platelet count (p=0.006), neutrophil percentage (p=0.017), lymphocyte count (p=0.001), eosinophil percentage and count (p<0.001), monocyte count (p=0.001), basophil percentage (p=0.011) were detected respectively. Urea (p=0.021) and D-Dimer (p=0.015) values were found to be higher in Group-1 cases compared to Group-2 (Table-4).

Table-4: Comparison of Group-1 and Group-2 data

	Group-1 (Home treatment failure) (n= 99)	**Group-2 (Baseline hospital admission) (n= 415)**	
	value	**value**	**p value**
Age, year *	47 (37-56)	54 (40-65)	0.004
Leucocyte cell count/L 10^9**	6.2 (4.8-8)	6.9 (5.2-8.6)	0.037
Platelet cell count/ L 10^9*	255 (204-331)	299 (224-395)	0.006
Neutrophil % **	68 ± 12	71 ± 12	0.017
Neutrophil cell count/L 10^9 *	4.29 (3.08-5.42)	4.53 (3.34-6.69)	0.045
Lymphocyte cell count/L 10^9 *	1.36 (0.98-1.87)	1.59 (1.24-2.05)	0.001
Eosinophil % *	0.95 (0.15-2.46)	2.02 (0.97-3.15)	<0.001
Eosinophil cell count/L 10^9 *	0.06 (0.01-0.17)	0.12 (0.05-0.21)	<0.001
Monocyte cell count/ L 10^9 *	0.48 (0.36-0.69)	0.59 (0.44-0.75)	0.001
Monocyte % *	7.95 (6.13-9.58)	8.68 (7.51-9.6)	0.012
Basophil % *	0.48 (0.34-0.90)	0.59 (0.41-1.07)	0.011
Urea (BUN) mg/dl *	2.4 (1.3- 4.5)	2.3 (0-5.8)	0.021
D-Dimer mg/L*	0.55 (0.28-1.12)	0.38 (0-5.8)	0.015
*Median (25%-75%), **Mean± SD			

Two study groups were compared Student T test for normally distributed continuous variables. Mann-Whitney U Test was used if continuous variables were non-normally distributed. Chi-square test was used for dichotomous variables.

DISCUSSION

Our study compares patients who needed to be hospitalized after worsening with outpatient treatment and patients hospitalized at first admission. We aimed to investigate possible causes of second readmission and worsening with outpatient treatment. Learning the reasons for admission and the need for hospitalization can help use healthcare resources effectively in managing the pandemic.

In this study, age was found to increase the risk of hospitalization. Additionally, the presence of bronchiectasis was found to decrease the risk of hospitalization at a statistically significant level. In the literature, comorbidities in the advanced age group are reported as a risk factor for hospitalization [9-11]. Our study found that an increase in age elevated the risk of hospitalization by a factor of 1.02.

In our study, the presence of comorbidities and the number of comorbidities in the young age group who failed outpatient treatment and required hospitalization were high, like those in the elderly patient group. Although the average age differed between the two groups, the frequency of comorbidities was similar. However, the frequency of comorbidities is expected to be less in the younger group than in the older group. The fact that Group-1 cases had as much comorbidity as Group-2 cases, despite their younger age, suggested that comorbidities, like other aggravating factors, may be important in re-admission to the hospital. In the United Kingdom, patients discharged following COVID-19 had higher rates of chronic respiratory disease, diabetes, and cardiovascular disease compared to patients discharged with non-COVID diagnoses [12]. Hypertension, diabetes, COPD, cardiovascular disease, and cerebrovascular disease have been identified as major risk factors for patients with COVID-19 [13]. The presence of comorbidity has also been associated with poor clinical outcomes for COVID-19 [14]. In this study, even younger patients need to be hospitalized, and since the comorbidities in this group are at least as high as the elderly, the clinical course of the disease may be worse, and hospitalization may be required. This situation made us think that comorbidities should also be considered when deciding on hospitalization.

In the literature, the rate of severe COVID-19 patients in patients with bronchiectasis was significantly higher than in those without bronchiectasis [15]. Another study indicated that individuals with bronchiectasis experienced fewer attacks during the epidemic than in previous years [16]. Our research found that the presence of bronchiectasis reduced the risk of hospitalization at a statistically significant level. This result can be attributed to those patients with bronchiectasis adhering to physical contact restrictions and lockdown rules during the epidemic. Alternatively, this situation could raise a new question regarding whether the permanent dilation resulting from the damage caused by bronchiectasis in the bronchi could impede the attachment of the coronavirus to the lungs.

The study, which included more than 100,000 COVID-19 patients in the USA, found that 9% of those discharged were re-admitted within two months, and 1.6% were admitted more than once. Being older than 65 years is identified among risk factors for hospitalization [10]. In another study of 1775 COVID-19 patients discharged, 20% were readmitted within 60 days; readmissions have been reported to be associated with advanced age [17]. Our study also found that an increase in age elevated the risk of hospitalization.

Mortality rates are reported to be high in COVID-19 cases re-admitted to the hospital. Donnelly et al. reported that 20% of 1775 cases were readmitted, and 9% of them died [17], while Ayoubkhani et al. reported that in their study of 50.000 patients, 30% were readmitted and 10% died after discharge [12]. In this study, the two groups were similar in terms of mortality rates.

However, it was interesting that there were no deaths in Group-1. This situation can be interpreted as younger Group-1 cases benefiting from healthcare treatment. In a retrospective evaluation cohort of 1409 patients, male gender was found to be a risk factor for readmission [9], but this was not a risk factor in our study.

Leukocytes, neutrophils, eosinophils, and platelets are identified as markers of severe COVID-19. In determining severity, attention is drawn to lymphocyte count, CRP, D-dimer, ferritin, troponin, and IL-6 levels [18]. In our study, leukocyte values were lower in Group-1 compared to Group-2. The literature has reported that leukocyte counts increase the severity of the COVID-19 disease [19]. However, there is no data on re-admissions to the hospital. In our study, leukocyte levels were high, and thrombocyte, lymphocyte, and eosinophil counts were lower in Group-1, which may be a guide in predicting admission to the hospital. The fact that the platelet, lymphocyte, and eosinophil values were lower and the D-Dimer value higher in Group-1 cases during hospitalization suggested that these cases were in the process of going into a cytokine storm. Cytokine storm and macrophage activation syndrome in the course of the disease is the clinical situation that causes the clinician the most concern. It has been emphasized that D-Dimer elevation may be one of the markers of cytokine storm activation [20]. The high presence of D-Dimer can be interpreted as Group-1 cases being hospitalized while at the stage of the cytokine storm.

The first limitation of the study is the retrospective review of patient data. It does not show homogeneity between groups regarding demographic characteristics such as age and gender but reflects real-life data. The second limitation is comparing the data during the first hospital admission of the patients who were admitted to the hospital again, creating a temporal difference in the course of the disease and reducing the power of the study. The third limitation of the study is that our data only reflects the data of a tertiary education and research hospital; it is not a model for the whole society of our Country. These results cannot be generalized on the whole.

In conclusion, the presence of comorbidities in COVID-19 patients should be considered both in the elderly group hospitalized at the first admission and in the younger group who were admitted to the hospital after the decision for outpatient treatment was made. The presence of thrombocytopenia, lymphopenia, eosinopenia, and elevated D-Dimer should also be considered. The presence of comorbidities may contribute to the effective use of health resources when deciding on hospitalization, according to the symptoms, radiological progression of the cases, and inflammatory variables in laboratory parameters.

This study identified age as a factor in increasing hospitalization in COVID-19 patients. On the other hand, the presence of bronchiectasis in patients appears to be a factor in reducing hospitalization. This result can be attributed to

patients with bronchiectasis adhering to physical contact restrictions and lockdown rules during the epidemic. Furthermore, this situation raises a new question about whether the permanent dilation resulting from the damage caused by bronchiectasis in the bronchi could act as a preventive factor for the coronavirus. We believe we can lead to studies that include well-planned large case series on these issues.

Conflicts of interest: The authors have nothing to disclose.

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References

1. World Health Organization (2020) Novel coronavirus (2019-nCoV). Situation Report. 11 March 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-March-2020.
2. World Health Organization. Coronavirus disease (COVID-2019) situation reports November 2023. https://www.who.int/publications/m/item/covid-19-epidemiological-update---24-november-2023.
3. Sakurai, A., Sasaki, T., Kato, S., Hayashi, M., Tsuzuki, S.I., Ishihara,T., … & Doi, Y. (2020). Natural History of Asymptomatic SARS-CoV-2 Infection. *N Engl J Med*. 383(9):885-886.
4. Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., … & Cao, B.(2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 395(10223):497-506.
5. Cummings, M.J., Baldwin, M.R., Abrams, D., Jacobson, S.D., Meyer, B.J., Balough, E.M., … & O'Donnell, M.R. (2020). Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *Lancet.* 395(10239):1763-1770.
6. Petrilli, C.M, Jones, S.A., Yang, J., Rajagopalan, H., O'Donnell, L., Chernyak, Y., … & Horwitz, L.I. (2020). Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ.* 22(369), m1966.
7. He, J., Guo, Y., Mao, R., & Zhang, J..(2021). Proportion of asymptomatic coronavirus disease 2019: A systematic review and meta-analysis. *J Med Virol.* 93(2), 820-830.
8. The Republic of Turkey Ministry of Health Directorate General of Public Health. COVID-19 (SARS-CoV-2 Infection) Guide 2020. https://ohsad.org/wp-content/uploads/2020/04/COVID-19_Rehberi-2.pdf
9. Bowles, K.H., McDonald, M., Barrón, Y., Kennedy, E., O'Connor, M., & Mikkelsen, M. (2021). Surviving COVID-19 After Hospital Discharge: Symptom, Functional, and Adverse Outcomes of Home Health Recipients. *Ann Intern Med.* 174(3), 316-325.
10. Lavery, A.M., Preston, L.E., Ko, J.Y., Chevinsky, J.R., DeSisto, C.L., Pennington, A.F., & Gundlapalli A.V. (2020). Characteristics of Hospitalized COVID-19 Patients Discharged and Experiencing Same-Hospital Readmission - United States, March-August 2020. *MMWR Morb Mortal Wkly Rep.* 69(45), 1695-1699.
11. Subramaniam, A., Lim, Z.J., Ponnapa Reddy, M.,& Shekar, K. (2021). Systematic review and meta-analysis of the characteristics and outcomes of readmitted COVID-19 survivors. *InternMed J.* 51(11), 1773-1780.
12. Ayoubkhan,i D., Khunti, K., Nafilyan, V., Maddox, T., Humberstone, B., Diamond, I., & Banerjee A. (2021). Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study. *BMJ.* 31(372), n693.
13. Wang, B., Li, R., Lu, Z., & Huang, Y. (2020). Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. *Aging (Albany NY).* 12(7), 6049-6057.
14. Guan, W.J., Liang, W.H., Zhao, Y., Liang, H.R., Chen, Z.S., Li, Y.M., & He, J.X.; China Medical Treatment Expert Group for COVID-19. (2020). Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *EurRespir J.* 55(5), 2000547.
15. Choi, H., Lee, H., Lee, S.K., Yang, B., Chung, S.J., Yeo, Y., … & Kim, S.H. (2021). Impact of bronchiectasis on susceptibility to and severity of COVID-19: a nationwide cohort study. *Ther Adv Respir Dis.* 15, 1753466621995043.
16. Seo, C., Kaur, S., & Thornton, C.S. (2024). Bronchiectasis and COVID-19: For Better or for Worse? *Ann Am Thorac Soc.* 21(2):208-210.
17. Donnelly, J.P., Wang, X.Q., Iwashyna, T.J., & Prescott, H.C. (2021). Readmission and Death After Initial Hospital Discharge Among Patients With COVID-19 in a Large Multihospital System. *JAMA.* 325(3), 304-306.
18. Velavan, T.P., & Meyer, C.G. (2020). Mild versus severe COVID-19: Laboratory markers. *Int J Infect Dis.* 95, 304-307.
19. Elshazli, R.M., Toraih, E.A., Elgaml, A., El-Mowafy, M., El-Mesery, M., Amin, M.N., & Kandil, E. (2020). Diagnostic and prognostic value of hematological and immunological markers in COVID-19 infection: A meta-analysis of 6320 patients. *PLoSOne.* 15(8), e0238160.
20. Henderson, L.A., Canna, S.W., Schulert, G.S., Volpi, S., Lee, P.Y., Kernan, K.F., … & Nigrovic, P.A. (2020). On the Alert for Cytokine Storm: Immunopathology in COVID-19. *Arthritis Rheumatol.* 72(7), 1059-1063.