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ORIGINAL ARTICLE

Investigation of symptoms and mortality in hypertension patients diagnosed with COVID-19: A retrospective case-control study

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Abstract

It was aimed to determine whether there is a difference in mortality and symptoms between patients, aged 60 years or above, with hypertension (HT) and Coronavirus disease 2019 (COVID-19) infection and those without any chronic disease. The population of the study, which was conducted as a retrospective case-control study, consisted of 2747 HT patients diagnosed with COVID-19 and aged 60 years or above. While 170 patients with HT diagnosis formed the case group, 170 patients without any chronic disease formed the control group from the sample. In this study, the time from diagnosis to death was found to be shorter in the presence of HT in COVID-19 patients, while males diagnosed with COVID-19 had higher rates of intensive care unit admittance, intubation and mortality than females irrespective of HT. The presence of HT was determined not to affect symptoms in patients diagnosed with COVID-19. The most common symptoms were fatigue, cough, body ache, fever, headache, and sore throat in HT and control groups and the symptoms were similar in both groups. Further studies are recommended to reveal the relationship between HT, considered one of the most important risk factors for COVID-19, and adverse outcomes related to COVID-19.

Keywords: COVID-19, hypertension, symptom.

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Introduction

Hypertension (HT) is the leading cause of loss of Disability Adjusted Life Years (DALY) among cardiovascular diseases. In 2010, 31.1% of the world's adult population was found to have HT [1, 2]. The Coronavirus 2019 (COVID-19) pandemic began in December 2019 when a group of patients with pneumonia of unknown cause was seen in Wuhan, China. COVID-19, spreading rapidly worldwide, has been officially recognized as a public health emergency by the World Health Organization (WHO). COVID-19 has been the largest pandemic in the last 100 years. It has affected more than 200 countries and millions of people worldwide [3]. The disease pathogen has been named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 caused severe acute respiratory syndrome (SARS) and was associated with intensive care admission and high mortality. HT was among the major comorbidities in cases of death. Some of the study results have shown that patients with severe COVID-19 have a higher prevalence of HT [4-7]. The prevalence of HT in COVID-19 patients ranges from 15-20 % to 30-35 in different studies [6, 8-13]. There are various reasons for these different results. The most important of these is the significantly higher mean age in patients with a high prevalence of HT [6, 8, 9, 11, 14-17]. Angiotensin-converting enzyme 2 (ACE2) is the main active peptide of the renin-angiotensin-aldosterone system (RAAS). ACE2, which targets angiotensin II, is protective in the cardiovascular system and many other organs. It also provides protection against severe acute lung failure caused by severe acute respiratory syndrome (SARS) coronavirus infection. Decreased ACE2 shifts the balance in the RAAS to the angiotensin II (Ang II)/ Angiotensin II receptor type 1 (AT1R) axis, which leads to the progression of heart failure. SARS-CoV-2 binds to ACE2 with high affinity through its spike (S) glycoprotein. COVID-19 infection leads to a further decrease in ACE2, causing RAAS imbalance and aggravation of cardiovascular disease [18-22]. The majorities of COVID-19 patients over 60 years of age has HT and are therefore at higher risk if they are infected with SARS-CoV-2 [23]. In this study, it was aimed to determine whether there is a difference in mortality and symptoms between patients, aged 60 years or above, with HT and COVID-19 infection and those without any chronic disease.

Materials and Methods

The study was conducted as a retrospective case-control study. The study population consisted of 2747 patients, aged 60 years or above, who were diagnosed with COVID-19 in the city of Afyonkarahisar in Türkiye between 01.09.2020 and 30.11.2020. The sample size of 338 was determined using the Power 3.1 program based on the population size. The study's sample size was adjusted to 340 to account for potential data loss. Within this sample, 170 patients diagnosed with hypertension formed the case group, while the control group consisted of 170 patients without any chronic disease. The case and control groups were selected from eligible patients meeting the specified criteria through a simple random sampling method. Patients, who were below 60 years of age, whose records could not be accessed, and who had one or more chronic diseases (diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), cardiovascular disease (CVD), renal failure, cancer) in addition to HT were excluded from the case group. Patients, who were below 60 years of age, whose records could not be accessed, or who had any chronic diseases, were not included in the control group. Our study data were obtained from the records created by the contact tracing teams of Afyonkarahisar Central Community Health Center with the "Data Collection Form" created by the researchers. Ethics committee approval (2021/1) was obtained from the Non-Interventional Clinical Research Ethics Committee of Afyonkarahisar Health Sciences University to conduct the study.

Statistical analyses were performed using the IBM SPSS Statistics 26.0 package program. Descriptive statistics were given as a number, percentage, mean and standard deviation. The visual (histogram and the normal probability plot) and analytical methods (*Kolmogorov-Smirnov*, *Shapiro-Wilk* tests) were used to check whether the variables had a normal distribution. Quantitative variables that did not show normal distribution were analyzed with the Mann-

Whitney U test between the two groups. Chi-square analysis and Fisher's exact test were preferred for comparison of nominal data. Comparisons with a *p*-value below 0.05 were considered statistically significant.

Results

The mean age of the HT groups was 68.79±6.9 years and in both groups, 50% of the participants were female and 50% were male. No significant difference was found between the two groups in terms of age and gender ($p>0.05$) (Table 1).

There was no significant difference between the groups according to the time from diagnosis to recovery, hospitalization status, duration of hospital stay, intensive care admission status, duration of intensive care stay and mortality rates ($p>0.05$). There was a statistically significant difference between the groups according to the time from the diagnosis of the disease to death and this time was shorter in the HT group ($p=0.045$) (Table 2).

In the HT group, the time from diagnosis to recovery was longer in male patients than in female patients ($p=0.012$), whereas in the control group, there was no significant difference in the time from diagnosis to recovery according to gender ($p>0.05$). Furthermore, male patients had more hospitalizations than female patients in the HT group ($p=0.033$), while there was no significant difference between hospitalization and gender in the control group ($p>0.05$). When the groups were reviewed in terms of duration of hospital stay, no statistically significant difference was found in the HT group according to gender ($p>0.05$), whereas in the control group, the duration of hospital stay was longer in male patients ($p=0.045$). Intensive care unit admission ($p=0.001$ and $p=0.007$), intubation ($p=0.003$ and $p=0.005$) and mortality ($p=0.002$ and $p=0.005$) rates were significantly higher in males in both groups. There was no significant difference in the duration of intensive care stay and the time from diagnosis to death according to gender in both groups ($p>0.05$) (Table 3).

The majority of the patients (95.3% in the HT group and 91.2% in the control group) had COVID-19 symptoms. There was no significant difference between the groups according to the presence of symptoms ($p>0.05$). The most common symptoms were fatigue (45.3% and 44.7%), cough (41.8% and 35.3%), body aches (29.4% and 31.8%), fever (22.9% and 22.9%), headache (17.6% and 21.6%), and sore throat (18.8% and 12.9%) in HT and control groups and the symptoms were similar in both groups. Comparison was carried out between the groups for each symptom, however, there was no significant difference between the groups according to any symptom ($p>0.05$). The most common first symptom at the onset of the disease was sore throat ($p=0.001$) in the HT group, while body aches and chills were the most common first symptoms in the control group ($p=0.001$ and $p=0.037$) (Table 4).

Discussion

In our study, patients with comorbidity of HT formed the case group among the patients diagnosed with COVID-19. HT was reported to be the most common comorbidity in COVID-19 patients in meta-analysis studies [24-26]. DM, CVD and COPD were noted as the other most common comorbidities [6, 8-11, 14-16, 25, 27, 28]. Although patient records and follow-up data are limited, HT is more prevalent in COVID-19 patients admitted to the intensive care unit, requiring mechanical ventilation and resulting in death. Therefore, it is important to reveal the determinant effect of HT on mortality in COVID-19 patients [10, 12, 14, 17, 29, 30]. There was a statistically significant difference between the groups according to the time from the diagnosis of the disease to death and the time was shorter in the HT group. In the literature, Ruan et al. [31] reported that mortality was more common in COVID-19 patients with HT, Wu et al. [32] noted that the mortality rate was 2.3% in COVID-19 and increased to 6% with the presence of HT, Zhou et al. [12] highlighted that HT increased the risk of mortality 3.05 times in COVID-19, Barrera et al. [33] determined that HT increased the risk of mortality by 2.39 times in COVID-19 patients, and Yanbin et al. [34] found that patients with HT had a 2.17 times higher risk of mortality due to COVID-19. In the study by Pena et al. [26], the case mortality rate was higher in males (20.2%) than in females (13%). Although all these findings support our study, the fact

Table 1. Demographic data of the patients in the HT group and the control group.

	HT group n=170	Control group n=170	*P* value
Age (years), mean ± SD	68.79±6.9	68.45±6.86	0.606#
Gender, n (%)			
Female	85 (50)	85 (50)	-
Male	85 (50)	85 (50)	

HT: Hypertension; mean ± SD: Mean ± standard deviation; # Analyzed with the Mann-Whitney U Test.

Table 2. Comparison of data on hospitalization, intensive care unit admission and mortality of patients in HT group and control group.

	HT group n=170	Control group n=170	P value
Time from diagnosis to recovery (days), mean ± SD	15.52±3.44	15.6±3.12	0.817#
Hospitalization, n (%)			
Yes	42 (24.7)	40 (23.5)	0.800*
No	128 (75.3)	130 (76.5)	
Duration of hospital stay (days), mean ± SD	12.95±7.84	15.9±9.17	0.106#
Intensive care admission, n (%)			
Yes	20 (11.8)	19 (11.2)	0.865#
No	150 (88.2)	151 (88.8)	
Duration of stay in intensive care (days) mean ± SD	8.63±7.04	9.33±6.37	0.737#
Intubation, n (%)			
Yes	15 (8.8)	17 (10)	0.710*
No	155 (91.2)	153 (90)	
Mortality, n (%)			
Yes	16 (9.4)	17 (10)	0.855*
No	154 (90.6)	153 (90)	
Time from diagnosis to death (days), mean ± SD	14.62±10.78	18.64±10.55	**0.045#**

*HT: Hypertension; mean ± SD: Mean ± standard deviation; # Analyzed with the Mann-Whitney U Test; *Analyzed with the Pearson Chi-Square Test; ≠Analyzed with the Fisher's Exact Test.*

that mortality occurs in a shorter time in HT patients suggests that HT may be an accelerating factor for mortality. In our study, the time from diagnosis to recovery in the HT group was longer in male patients than in female patients. This data indicated that the disease lasted longer in male patients with HT, that is, recovery was delayed. Furthermore, hospitalization was higher in male patients in the HT group. In line with these findings, it can be suggested that the combination of HT and male gender is associated with more severity of COVID-19 infection. Also, Pranata et al. [35] showed that HT increased the severity of the disease 2.04-fold in patients with COVID-19 and that the relationship between HT and COVID-19 was stronger with male gender, as in our study. Yanbin et al. [34], stated in their meta-analysis study that caution should be exercised especially in HT patients who are male and >60 years of age, in line with our study. Our findings are in line with the literature findings, as negative outcomes are more common in male patients also in the literature.

If the presence of intensive care admission and intubation in patients is interpreted as an increase in the severity of the disease, no significant difference was found in our study that HT affects the severity of COVID-19. However, there are also studies with different results compared to our study in the literature. Li et al. [10] have shown that HT, CVD and DM increased the severity of disease two to three times more in COVID-19 patients, while HT was reported to increase the severity of COVID-19 disease 2.3 times in the study by Chen Y et al. [36], and HT was noted to increase the severity of disease 3.64 times in COVID-19 patients in the study by Chen C et al. [37].

Table 3. Comparison of data on hospitalization, intensive care unit admission and mortality of patients in the HT group and control group according to gender.

	HT group n=170		Control group n=170	
	Female n=85	Male n=85	Female n=85	Male n=85
Time from diagnosis to recovery (days), mean ± SD	15.09±3.61	15.95±3.22	15.18±2.75	16.01±3.42
P value	0.012#		0.074#	
Hospitalization, n (%)				
Yes	15 (17.6)	27 (31.8)	15 (17.6)	25 (29.4)
No	70 (82.4)	58 (68.2)	70 (82.4)	60 (70.6)
P value	0.033*		0.071*	
Duration of hospital stay (days) mean ± SD	12.80±10.03	13.03±6.53	12.66±6.65	17.84±10.02
P value	0.599#		0.045#	
Intensive care admission, n (%)				
Yes	3 (3.5)	17 (20)	4 (4.7)	15 (17.6)
No	82 (96.5)	68 (80)	81 (95.3)	70 (82.4)
P value	0.001*		0.007*	
Duration of stay in intensive care (days), mean ± SD	11.33±9.29	8.12±6.8	9.5±6.55	9.28±6.56
P value	0.398#		0.957#	
Intubation, n (%)				
Yes	2 (2.4)	13 (15.3)	3 (3.5)	14 (16.5)
No	83 (97.6)	72 (84.7)	82 (96.5)	71 (83.5)
P value	0.003*		0.005*	
Mortality, n (%)				
Yes	2 (2.4)	14 (16.5)	3 (3.5)	14 (16.5)
No	83 (97.6)	71 (83.5)	82 (96.5)	71 (83.5)
P value	0.002*		0.005*	
Time from diagnosis to death (days), mean ± SD	18.5±10.6	14.07±11.08	15±4.35	19.42±11.42
P value	0.200#		0.752#	

*HT: Hypertension; mean ± SD: mean ± standard deviation; # Analyzed with the Mann-Whitney U Test; *Analyzed with the Pearson Chi-Square Test; ≠Analyzed with the Fisher's Exact Test.*

In our study, the most common symptoms were fatigue, cough and sore throat in the HT group and similarly fatigue, cough and body ache in the control group. The comparison was carried out between the groups for each symptom; however, there was no significant difference between the groups according to any symptom. In our study, it was concluded that HT did not affect disease symptoms. Similarly, Shaghee et al. [38] reported that the most common symptom in COVID-19 patients with HT was fever, followed by cough, shortness of breath, and fatigue, and Chengyi et al. [39] stated that the symptoms observed in HT and control groups were fever and cough, and no significant difference was found between the groups. In this respect, our study

Table 4. Comparison of HT group and control group according to presence of symptoms, first symptoms and symptoms seen.

	HT group n=170 *n (%)*	Control group n=170 *n (%)*	*P* value
Presence of Symptoms	162 (95.3)	155 (91.2)	0.131*
First symptom			
Fatigue	36 (22.2)	34 (21.9)	0.789*
Cough	35 (21.6)	31 (20)	0.538*
Sore throat	24 (14.8)	7 (4.5)	0.001*
Fever	12 (7.4)	15 (9.7)	0.547*
Body ache	7 (4.3)	24 (15.5)	0.001*
Headache	7 (4.3)	10 (6.5)	0.455*
Dyspnea	6 (3.7)	5 (3.2)	0.759*
Loss Of Appetite	5 (3.1)	2 (1.3)	0.448≠
Sweating	5 (3.1)	2 (1.3)	0.448≠
Tremors	4 (2.5)	3 (1.9)	1.000≠
Nausea	4 (2.5)	4 (2.6)	1.000≠
Diarrhea	3 (1.9)	3 (1.9)	1.000≠
Vomiting	3 (1.9)	0 (0.0)	0.248≠
Back pain	3 (1.9)	2 (1.3)	1.000≠
Loss of taste and smell	2 (1.2)	2 (1.3)	1.000≠
Chest pain	2 (1.2)	0 (0.0)	0.499≠
Back pain	2 (1.2)	1 (0.6)	1.000≠
Chills	1 (0.6)	8 (5.3)	0.037≠
Runny nose	1 (0.6)	1 (0.6)	1.000≠
Nasal congestion	0 (0.0)	1 (0.6)	1.000≠
Symptoms			
Fever	39 (22.9)	39 (22.9)	1.000*
Cough	71 (41.8)	60 (35.3)	0.220*
Dyspnea	16 (9.4)	13 (7.6)	0.560*
Tremors	15 (8.8)	20 (11.8)	0.372*
Body ache	50 (29.4)	54 (31.8)	0.638*
Fatigue	77 (45.3)	76 (44.7)	0.913*
Runny nose	11 (6.5)	8 (4.7)	0.479*
Sore throat	32 (18.8)	22 (12.9)	0.138*
Headache	30 (17.6)	35 (20.6)	0.490*
Diarrhea	5 (2.9)	11 (6.5)	0.124*
Nausea	16 (9.4)	18 (10.6)	0.718*
Vomiting	8 (4.7)	6 (3.5)	0.585*
Loss Of Appetite	13 (7.6)	10 (5.9)	0.517*
Dizziness	1 (0.6)	0 (0.0)	1.000≠
Loss of taste and smell	6 (3.5)	6 (3.5)	1.000*
Sweating	10 (5.9)	7 (4.1)	0.455*
Chills	8 (4.7)	8 (4.7)	1.000*
Sneezing	1 (0.6)	0 (0.0)	1.000≠
Back pain	4 (2.4)	5 (2.9)	1.000≠
Chest pain	4 (2.4)	0 (0.0)	0.123≠
Nasal congestion	0 (0.0)	1 (0.6)	1.000≠
Back pain	1 (0.6)	1 (0.6)	1.000≠
Palpitations	0 (0.0)	1 (0.6)	1.000≠
Hemoptysis	0 (0.0)	0 (0.0)	-

**Analyzed with the Pearson Chi-Square Test; ≠Analyzed with the Fisher's Exact Test.*

result shows similarities with the literature. In some studies, there is no clarity on whether HT is an independent risk factor for COVID-19 patients [40-42]. However, in this study, when the time from the diagnosis of COVID-19 to death was analyzed, the presence of HT was determined to be a risk factor. This is thought to have developed due to increased endothelial cell activation, endothelial dysfunction and prothrombotic effect in the case group [20, 43-46]. The limitations of our study are that it was retrospective and conducted in a single center. There is a need for further prospective and multicenter studies.

Conclusion

In this study, the time from diagnosis to death was found to be shorter in the presence of HT in COVID-19 patients, while males diagnosed with COVID-19 had higher rates of intensive care unit admittance, intubation, and mortality than females irrespective of HT. The presence of HT was determined not to affect symptoms in patients diagnosed with COVID-19. Further studies are recommended to reveal the relationship between HT, considered one of the most important risk factors for COVID-19, and adverse outcomes related to COVID-19.

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Conflict of interest

There are no conflicts of interest for the authorship and/or publication of this study.

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