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Effects of Comorbidities on Hospitalization Costs of COVID-19 in Türkiye

Türkiye'de Komorbiditelerin COVID-19 Hastane Yatış Maliyetleri Üzerine Etkileri

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Abstract

Introduction: In December 2019, pneumonia associated with the 2019 novel Coronavirus or Severe acute respiratory syndrome-Coronavirus-2 emerged in Wuhan, China. Its effects on national and global economies have been tremendous. There is limited evidence regarding treatment costs for hospitals and the effects of comorbidities on treatment costs. These factors are crucial inputs for health policymakers. The main objective of this study was to retrospectively determine the direct healthcare costs of hospitalized Coronavirus disease-2019 (COVID-19) patients in Türkiye and estimate the effect of comorbidities on these costs.

Materials and Methods: This study was conducted at two prominent research and training hospitals in İzmir, Türkiye, during the first year of the COVID-19 pandemic. General Linear Models were employed for the calculation of cost figures. The hospitalization costs of 2,067 patients with COVID-19 were analyzed, and the effects of comorbidities on the treatment costs of 532 patients with COVID-19 were estimated.

Results: Our analysis based on the entire sample of 2,067 patients revealed that the mean hospitalization cost was $1,432.3 [purchasing power parity (PPP) $4,994.7]. The mean treatment cost is higher for male patients and increases with age and intensive care unit admissions. The mean length of hospitalization was 10.6 days [standard deviation (SD) ±8.5] and the mean length of intensive care unit hospitalization was 9.9 (SD ±9.6). The mean daily hospitalization cost was $135.25 (PPP $471.63) for 2,067 patients. Hospitalization costs for COVID-19 patients significantly increased due to factors, such as gender, age, intensive care unit hospitalization, and comorbidities, including myocardial infarction, cerebrovascular and transient ischemic attacks, chronic obstructive pulmonary disease, and chronic kidney disease, according to the analysis.

Conclusion: COVID-19 is a novel pandemic that caused morbidity and mortality at considerable levels. A holistic approach to fighting the pandemic requires unraveling not only medical efforts but also financial aspects.

Keywords: Comorbidities, COVID-19, hospitalization cost, treatment cost, Türkiye

Öz

Giriş: Aralık 2019'da, Çin'in Wuhan kentinde Akut solunum sendromu Koronavirüs-2 ile ilişkili pnömoni ortaya çıkmıştır. Pandeminin ulusal ve küresel ekonomiler üzerindeki etkileri çok büyük olmuştur. Hastanelerin tedavi maliyetleri ve komorbiditelerin tedavi maliyetleri üzerindeki etkileri hakkında sınırlı kanıt bulunmaktadır ve bu bilgiler sağlık politikası yapıcıları için önemli girdilerdir. Bu çalışmanın temel amacı, Türkiye'de hastanede yatan Koronavirüs hastalığı-2019 (COVID-19) hastalarının doğrudan sağlık hizmeti maliyetlerini retrospektif olarak belirlemek ve komorbiditelerin bu maliyetler üzerindeki etkisinin belirlenmesidir.

Gereç ve Yöntem: Bu çalışma, COVID-19 salgınının ilk yılında İzmir'de hasta takibi en fazla olan iki eğitim ve araştırma hastanesinde yapılmıştır. Maliyet rakamlarının hesaplanması için General Linear Models kullanılmıştır. Sırasıyla, 2.067 COVID-19 hastasının hastaneye yatış maliyetleri analiz edilmiş ve komorbid hastalığı olan 532 COVID-19 hastasının tedavi maliyetleri üzerindeki etkileri belirlenmiştir.

Bulgular: 22.067 hasta örneklemine dayanan analiz sonuçları, ortalama hastanede yatış maliyetinin 1.432,3 $ [satın alma gücü paritesi (PPP) 4.994,7 $] olduğunu göstermiştir. Ortalama tedavi maliyeti erkek hastalar için daha yüksektir ve yaş ve yoğun bakım ünitesine yatışla birlikte artmaktadır.

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Ortalama hastanede yatış süresi 10,6 gün [standart deviasyon (SD) ±8,5] ve ortalama yoğun bakımda yatış süresi 9,9 (SD ±9,6) gündür. Ortalama günlük hastanede yatış maliyeti 2.067 hasta için 135,25 $'dir (PPP 471,63 $). Analizler, cinsiyet, yaş, yoğun bakım ünitesinde yatış ve miyokard enfarktüsü, serebrovasküler ve geçici iskemik ataklar, kronik obstrüktif akciğer hastalığı ve kronik böbrek hastalığı gibi komorbiditelerin COVID-19 hastalarının hastanede yatış maliyetlerini önemli ölçüde artırdığını göstermiştir.

Sonuç: COVID-19 ciddi hastalık ve ölüm oranlarına yol açan bir salgına sebep oldu. Salgınla mücadele sadece tıbbi açıdan değil salgının finansal sonuçları da göz önünde bulundurularak bütüncül bir yaklaşımla yapılmalıdır.

Anahtar Kelimeler: Komorbiditeler, COVID-19, yatış maliyeti, tedavi maliyetleri, Türkiye

Introduction

The Coronavirus disease-2019 (COVID-19) pandemic first broke out in China and quickly spread worldwide, affecting every country. It has been reported that the number of confirmed cases and deaths was above 772 million and 6.9 million, respectively[1]. Several measures, such as travel restrictions, border shutdowns, and quarantine, were taken by the international community in an attempt to flatten the epidemic curve. These actions, in turn, have had severe effects on global socioeconomic development[2]. According to estimates, the current COVID-19 outbreak resulted in a loss of at least 1 trillion US dollars to the world economy in 2020, surpassing the impact of the 2008 global financial crisis[3]. In addition, the COVID-19 pandemic caused significant health system challenges and increased health resource consumption. Coronavirus disease-2019 cases have depleted a significant portion of healthcare resources and infected numerous healthcare workers. To estimate the direct costs of COVID-19 and develop treatment strategies, it is crucial to understand the hospitalization costs of COVID-19 cases and related comorbidities[4]. This study was conducted in Türkiye, where, as of February 13, 2022, 12.7 million individuals were reported to be infected with COVID-19, resulting in approximately 90,000 deaths linked to the virus[1]. This study aimed to investigate the hospitalization costs of patients with COVID-19 and examine the effects of comorbidities on treatment costs for hospitalized COVID-19 patients.

Materials and Methods

The study had a multicenter design based on cost estimation. The study used cost and clinical data from two prominent research and training hospitals in the western part of Türkiye, İzmir: Bozyaka Training and Research Hospital and İzmir Tepecik Training and Research Hospital. Due to their staff, bed structures, and location in the İzmir city center, these two hospitals were the most active during the COVID-19 pandemic. We collected data from two different hospitals to mitigate biases arising from institution-specific practices and sampling errors, aiming to analyze a larger number of patients. Since every patient in the cohort of this study was receiving treatment based on the common guidelines issued by the Republic of Türkiye Ministry of Health, and all cost items were reflected in the insurance of the patients according to the Social Security Institution Communiqué on Healthcare Practices, the two hospitals where this research was conducted were both similar-sized research and training hospitals, making their cost figures comparable.

Cost data for patients were retrieved from the Probel Hospital Information Management System, which was used by both hospitals. Clinical data for patients were collected by practitioners from patient records. Cost figures in Turkish Lira (TL) were converted to US dollars using the monthly average TL/USD parity announced by the Central Bank of the Republic of Türkiye. Furthermore, these were converted to purchasing power parity (PPP) dollars using the 2020 PPP conversion factor (2.128,511 TL per international $) as specified by the Organization for Economic Co-operation and Development.

Inclusion criteria: Patients aged ≥18 years, diagnosed with U 07.3, indicative of novel Coronavirus or Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) polymerase chain reaction positivity, and hospitalized in one of the study hospitals between March 18, 2020, and March 23, 2021, were included in the study.

To examine the relationship between comorbidities and hospitalization costs, we explored the linear model: COST=AGE + SEX + ICU + MI + PVD + CVA + DEMENTIA + COPD + LIVER + DM + HEMIP + CKD + SOLID + LEUKEMIA. Here; the dependent variable, "COST," represents the hospitalization cost for each patient during treatment, and "AGE" is a continuous variable indicating each patient's age. SEX, ICU, MI, PVD, CVA, DEMENTIA, COPD, LIVER, DM, HEMIP, CKD, SOLID, and LEUKEMIA are dummy variables representing male sex, intensive care unit (ICU) stay during COVID-19 treatment, myocardial infarction (MI) history, peripheral vascular disease (PVD) diagnosis, cerebrovascular accident (CVA) history with minor or no residual and transient ischemic attacks, chronic cognitive deficit diagnosis, chronic obstructive pulmonary disease (COPD) diagnosis, liver disease diagnosis, diabetes mellitus (DM) diagnosis, hemiplegia history, chronic kidney disease (CKD) diagnosis, presence of a solid tumor, and leukemia history, respectively. The value of 1 was taken if the corresponding condition was present for the patient.

Statistical Analysis

We began by checking the distribution characteristics of the dependent variable "COST." As seen in the histogram plot in

Figure 1, the distribution of the dependent variable is highly left-skewed (Figure 1).

The "COST" variable, which is our focus of interest, is not normally distributed. Hence, we used non-parametric tests, such as the Mann-Whitney U test and the Kruskal-Wallis test, to make comparisons based on the median.

As "COST" data are inherently positive and continuous but exhibit high skewness, we preferred to estimate our model using one of the General Linear Models (GLMs). General Linear Models can directly accommodate skewness and model heteroskedasticity. The specification of the link function is crucial for the consistency of the parameter estimates of the model. Therefore, rigorous tests were conducted to ensure the accuracy of model specification[5].

We first used a Box-Cox approach, in which the scalar power (δ) of the dependent variable that results in the most symmetric distribution is tested. The estimated coefficient of 0.0581458, which is close to 0, indicated that estimation with log-link would yield more consistent coefficients than the square root transformation or the linear model[5]. Second, we employed the modified Park test to determine the distribution family. The coefficient estimate of 2.152181 on the predicted value indicated the use of the gamma family over the Gaussian, Poisson, or inverse Gaussian families[5]. Thus, we estimated our GLM model by quasi-maximum likelihood (Newton-Raphson) with a log-link function and the gamma distribution family. In case a misspecified choice of the distribution family can lead to any inconsistency in inference statistics, we reported the Huber/White/sandwich estimators ("vce(robust)" option in Stata).

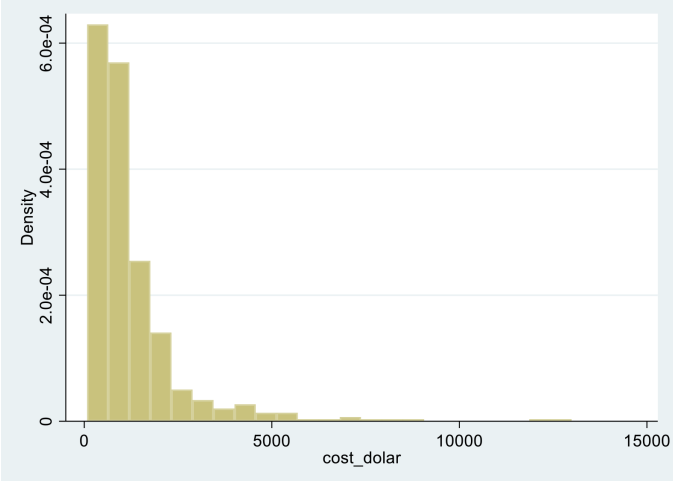

Figure 1. Distribution of the dependent variable

Results

The study was designed to delineate the hospitalization costs of COVID-19 patients and elucidate the impact of comorbidities on hospitalization costs. In the initial phase of the study, data on hospitalization costs were collected for 2,714 patients. We excluded 647 of these patients from the analyses for various reasons. The reasons for the exclusion of patients are summarized in Figure 2. Hospitalization costs and descriptive statistics for the sample of 2,067 patients are demonstrated in Table 1.

A total of 2,067 patients were included in the study, with 974 (47%) being female. The mean age of the patients was 57.6±16.25 (18-96). The mean hospitalization time was 10.6±8.5 days (1-134). Notably, 9.58% (n=198) of the patients required ICU hospitalization. Of the 198 patients hospitalized in the ICU, 91 were female. The mean number of ICU hospitalization days was 9.9±9.6 (0-77). The mean treatment cost of the patients was $1,432.3±2,553.2 (2.8-44, 944.7) and PPP $4,994.7±8,751.5 (8.2-144, 852.6). The mean cost per day was determined through two distinct approaches. In the first approach, the aggregate hospitalization costs ($2,960,653.87 and PPP $10,324,079.49) were divided by the total hospitalization days (21,890 days), resulting in $135.25/day and PPP $471.63/day. The second approach involved averaging the daily mean hospitalization costs for each patient. The mean treatment cost for patients varied between $2.77/day and $2,267.35/day, and the mean of the averages was $112.92/day (PPP $394.32/day).

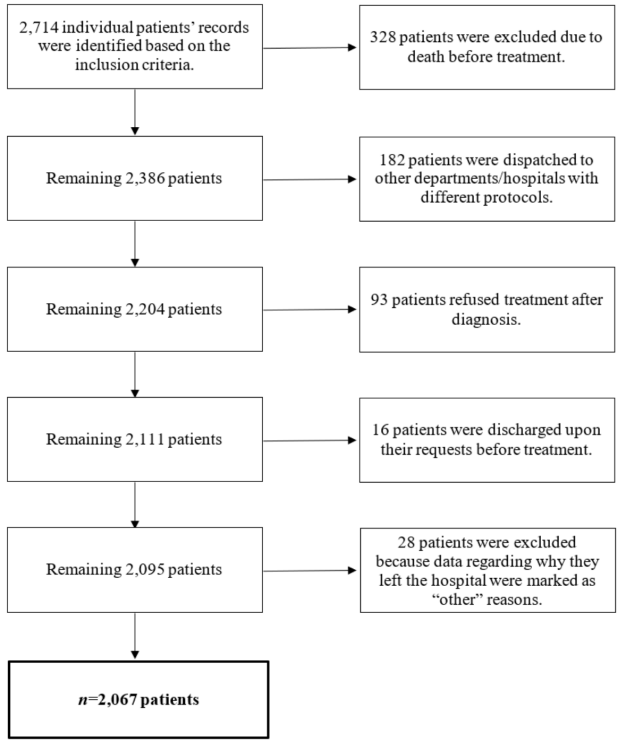

Figure 2. Reasons for excluded patients

Table 1. Descriptive statistics for 2,067 patients

Characteristics		Frequency [n (%)]	Mean cost (USD)	Mean cost (PPP $)
Gender	Female	974 (47.12)	1,356.01	4,715.15
	Male	1,093 (52.88)	1,500.36	5,243.84
Age	18-29	110 (5.32)	757.87	2,573.84
	30-39	211 (10.21)	889.04	3,100.95
	40-49	327 (15.82)	1,415.47	4,834.73
	50-59	416 (20.13)	1,349.57	4,704.05
	60-69	480 (23.22)	1,641.28	5,764.12
	70-79	349 (16.88)	1,753.03	6,176.19
	80-	174 (8.42)	1,527.59	5,324.99
Intensive care unit	No	1,869 (90.42)	1,050.55	3,677.34
	Yes	198 (9.58)	5,036.25	17,429.92
Hospitalization days	1-5	465 (22.5)	329.55	1,150.74
	6-10	864 (41.8)	827.15	2,885.42
	11-15	412 (19.93)	1,563.71	5,472.75
	16-	326 (15.77)	4,443.27	15,463.84
	Total	**2,067 (100)**	**1,432.34**	**4,994.72**

The mean hospitalization cost for the entire sample of 2,067 patients was $1,432.34 (PPP $4,994.72). Hospitalization costs differed significantly between male and female patients (p=0.01). Hospitalization costs were also significantly different between age groups (p=0.01), being the lowest observed for patients aged between 18 and 29 years ($757.87; PPP $2,573.84) and the highest for patients aged between 70 and 79 years ($1,753.03; PPP $6,176.19). The cost of hospitalization in the ICU ($5,036.25; PPP $17,429.92) significantly (p=0.01) differs from the cost of hospitalization in the wards ($1,050.55; PPP $3,677.34). Mean hospitalization costs show a progressive increase with the duration of hospitalization days, and the difference between groups is statistically significant (p=0.01). The lowest mean hospitalization cost was observed for patients hospitalized between 1 and 5 days ($329.55; PPP $1,150.74), while the highest mean hospitalization was observed for patients hospitalized for more than 16 days ($4,443.27; PPP $15,463.84).

In the second part of this study, we examined the association between hospitalization costs and comorbidities using the cost and clinical data of 532 patients hospitalized in December 2020, the month with the highest number of patients hospitalized during the study period. Comorbidities of each patient were checked and listed by a practitioner according to the Charlson Comorbidity Index. Descriptive statistics for the characteristics and comorbidities of our sample of 532 patients are presented in Table 2.

In the subsample of 532 patients, 47% (n=250) were female, and the mean age was 61±14.9 (19-93). The mean hospitalization time was 10.7±8 days (2-68), with 9.58% (n=53) of the patients being hospitalized in the ICU. The hospitalization rate in the ICU was 10.6% for male patients and 9.2% for female patients. The mean ICU hospitalization day was 6.3±5 (1-29). The mean treatment cost of patients was $1,250.60±1,389.8 (78.4-12,987.6) and PPP $4,541.7±5,047.4 (284.8-47,166.3).

The mean hospitalization cost for the subsample of 532 patients was $1,250.60 (PPP $4,541.75). Hospitalization costs differed significantly between male and female patients (p=0.01). Hospitalization costs were significantly different among age groups (p=0.01), with the lowest observed for patients aged between 30 and 39 years ($617.70; PPP $2,243.27) and the highest for patients aged between 70 and 79 years ($1,543.37; PPP $5,604.98). The cost of hospitalization in the ICU ($3,604.30; PPP $13,089.55) significantly (p=0.01) differs from the cost of hospitalization in the wards ($990.17; PPP $3,595.96). The most prevalent comorbidities in the subsample were DM (179), MI (93), and COPD (65).

Table 3 illustrates the GLM estimation results along with incremental and marginal values. The predicted mean hospitalization costs from the GLM long link and gamma family, as well as the incremental effects of the covariates, were estimated using the "margins" command in Stata. The predicted mean of hospitalization costs of $1,256.70 (PPP $4,563.89) is slightly (0.49%) higher than the sample mean of $1,250.60 (PPP $4,541.75).

As identified in the earlier univariate analyses, all three control variables, namely sex, age, and ICU, were found to be significant. The results indicate a positive association between male sex and hospitalization costs. Holding other factors constant, the

Table 2. Descriptive statistics for 532 patients

Characteristics		Frequency [n (%)]	Mean cost (USD)	Mean cost (PPP $)
Gender	Female	250 (46.99)	1,146.51	4,163.74
	Male	282 (53.01)	1,342.88	4,876.88
Age	18-29	10 (1.88)	867.17	3,149.26
	30-39	34 (6.39)	617.70	2,243.27
	40-49	82 (15.41)	977.85	3,551.20
	50-59	103 (19.36)	1,166.55	4,236.48
	60-69	143 (26.88)	1,405.07	5,102.70
	70-79	107 (20.11)	1,543.37	5,604.98
	80-	53 (9.96)	1,306.51	4,744.79
Intensive care unit	No	479 (90.04)	990.17	3,595.96
	Yes	53 (9.96)	3,604.30	13,089.55
	Total	**532 (100)**	**1,250.60**	**4,541.75**
Comorbidities	DM	179 (33.65)	1,375.76	4,996.29
	MI	93 (17.48)	1,566.90	5,690.44
	COPD	65 (12.22)	1,499.59	5,445.98
	CKD	44 (8.27)	1,689.20	6,134.57
	CVA	24 (4.51)	2,621.79	9,521.40
	SOLID	18 (3.38)	1,490.46	5,412.81
	DEMENTIA	16 (3.01)	1,741.10	6,323.05
	LEUKEMIA	8 (1.5)	1,417.90	5,149.31
	LIVER	3 (0.56)	867.44	3,150.24
	HEMIP	3 (0.56)	1,546.80	5,617.43
	PVD	1 (0.19)	1,284.79	4,665.91

CKD: Chronic kidney disease dummy, COPD: Chronic obstructive pulmonary disease dummy, CVA: Cerebrovascular accident and transient ischemic attack dummy, DEMENTIA: Chronic cognitive deficit dummy, DM: Diabetes mellitus dummy, LIVER: Liver disease dummy, MI: Myocardial infarction dummy, PVD: peripheral vascular disease dummy, SOLID: Solid tumor dummy, PPP $: Purchasing power parity dollar

Table 3. General linear model results

Variables	Coefficient (z statistic)	95% confidence interval		Incremental effect	
				$	PPP $
SEX	0.180** (2.55)	0.042	0.319	226.76	823.51
AGE	0.011*** (4.58)	0.006	0.016	14.24	51.73
ICU	1.273*** (11.64)	1.059	1.487	1,599.76	5,809.77
MI	0.132* (1.85)	-0.008	0.272	165.72	601.84
PVD	-0.019 (-0.24)	-0.178	0.139	-24.47	-88.86
CVA	0.336** (2.07)	0.019	0.653	422.07	1,532.82
DEMENTIA	-0.126 (-0.69)	-0.483	0.231	-157.96	-573.67
COPD	0.260** (2.48)	0.055	0.466	326.82	1,186.91
LIVER	-0.059 (-0.20)	-0.635	0.516	-74.66	-271.15
DM	0.085 (1.17)	-0.057	0.227	106.43	386.51
HEMIP	-0.107 (-0.29)	-0.826	0.612	-134.26	-487.57
CKD	0.228** (2.50)	0.049	0.406	286.09	1,038.99
SOLID	-0.002 (-0.01)	-0.287	0.283	-2.04	-7.42
LEUKEMIA	-0.062 (-0.24)	-0.568	0.443	-78.53	-285.19
CONSTANT	5.965 (43.63)	5.697	6.233	1,256.70	4,563.89

***Significant at 1%, **significant at 5%, *significant at 10%.

SEX: Gender dummy that takes the value of 1 for males, ICU: Intensive care unit dummy, CKD: Chronic kidney disease dummy, COPD: Chronic obstructive pulmonary disease dummy, CVA: Cerebrovascular accident and transient ischemic attack dummy, DEMENTIA: Chronic cognitive deficit dummy, DM: Diabetes mellitus dummy, LIVER: Liver disease dummy, MI: Myocardial infarction dummy, PVD: Peripheral vascular disease dummy, SOLID: Solid tumor dummy, PPP $: Purchasing power parity dollar

hospitalization costs of male patients were, on a mean, $226.76 (PPP $823.51) higher than those of the female patients. Additionally, with each 1-year increase in a patient's age, the mean hospitalization cost for that patient increased by $14.24 (PPP $51.73). The ICU variable had the strongest effect among all variables. If a COVID-19 patient was admitted to the ICU during treatment, the mean hospitalization cost for that patient increased by $1,599.76 (PPP $5,809.77).

All comorbidities were anticipated to exhibit a positive association with hospitalization costs. However, only four of our variables were found to be significantly associated with these costs. The MI variable was positively associated with hospitalization costs. The hospitalization cost of patients with a history of MI was $165.72 (PPP $601.84) higher. The second comorbidity variable, which has a significantly positive association with hospitalization cost is "CVA." Patients with a history of a CVA with minor or no residual effects and transient ischemic attacks required an additional $422.07 (PPP $1,532.82) for their treatments. In line with the expectations, COPD was also found to have a positive effect on hospitalization costs. The treatment of hospitalized patients with COPD costs $326.82 (PPP $1,186.91). Chronic kidney disease is another comorbidity found to have a positive association with hospitalization costs. Patients with CKD require $286.09 (PPP $ 1,038.99) higher than the mean hospitalization cost.

While rigorous tests were conducted to determine the distribution family and link function for GLM estimation, we present results for alternative model specifications to assess the robustness of our estimated model. The results of the alternative models, along with our main model, are displayed in Table 4. The results of GLM estimations using different distribution families and link functions, along with ordinary least squares estimation of log-transformed-dependent variables, validate our findings. "Sex," "Age," "ICU," "COPD," and "CKD" variables were statistically significant in all models, whereas the "MI" variable exhibited statistical significance in four out of five models.

Discussion

COVID-19, currently a devastating pandemic, is caused by SARS-CoV-2. Despite the negative socioeconomic effects of lockdown and social distancing as preventive measures for such contagious diseases[6,7], approximately half of the world has been under lockdowns because of COVID-19. It is highly crucial to explain the epidemiology and determinants of disease morbidity, mortality, and spread, and to conduct cost-benefit analyses to address this issue[8].

This study aimed to determine the hospitalization costs of COVID-19 patients and investigate the association of comorbidities with the treatment costs of COVID-19. The study estimated the direct cost of COVID-19 treatment at

Table 4. Robustness check results

	Gamma log	Gamma identity	Gamma power 0.5	Poisson log	Log-transformed DV OLS
	Coefficient (z statistic)	Coefficient (z statistic)	Coefficient (z statistic)	Coefficient (z statistic)	Coefficient (t statistic)
SEX	0.180** (2.55)	144.368** (2.06)	2.669** (2.34)	0.172** (2.18)	0.213*** (3.35)
AGE	0.011*** (4.58)	10.012*** (4.14)	0.177*** (4.31)	0.010*** (4.38)	0.009*** (4.27)
ICU	1.273*** (11.64)	2,519.378*** (7.07)	27.794*** (9.17)	1.252*** (11.99)	1.257*** (11.03)
MI	0.132* (1.85)	180.730** (2.16)	2.555** (2.08)	0.050 (0.61)	0.176** (2.13)
PVD	-0.019 (-0.24)	-23.645 (-0.27)	-0.588 (-0.44)	0.092 (0.91)	0.151* (1.74)
CVA	0.336** (2.07)	443.908 (1.33)	6.105 (1.64)	0.479*** (2.64)	0.235 (1.21)
DEMENTIA	-0.126 (-0.69)	-72.661 (-0.32)	-1.535 (-0.46)	-0.167 (-0.96)	-0.026 (-0.16)
COPD	0.260** (2.48)	296.213** (2.05)	4.433** (2.29)	0.234** (2.27)	0.263*** (2.59)
LIVER	-0.059 (-0.2)	58.337 (0.35)	0.348 (0.1)	-0.394 (-0.84)	-0.064 (-0.15)
DM	0.085 (1.17)	88.884 (1.19)	1.419 (1.18)	0.041 (0.54)	0.130** (1.96)
HEMIP	-0.107 (-0.29)	-216.510 (-0.42)	-2.562 (-0.36)	-0.084 (-0.24)	0.000 (0)
CKD	0.228** (2.5)	255.236** (2.12)	3.897** (2.3)	0.241*** (2.83)	0.307*** (3.22)
SOLID	-0.002 (-0.01)	-25.193 (-0.14)	-0.256 (-0.1)	-0.010 (-0.07)	0.078 (0.53)
LEUKEMIA	-0.062 (-0.24)	0.119 (0.01)	-0.641 (-0.14)	-0.041 (-0.17)	-0.081 (-0.27)
CONSTANT	5.965 (43.63)	173.603 (1.69)	17.050 (8.44)	6.090 (43.83)	5.811 (44.32)

***Significant at 1%, **significant at 5%, *significant at 10%.

SEX: Gender dummy that takes the value of 1 for males, ICU: Intensive care unit dummy, CKD: Chronic kidney disease dummy, COPD: Chronic obstructive pulmonary disease dummy, CVA: Cerebrovascular accident and transient ischemic attack dummy, DEMENTIA: Chronic cognitive deficit dummy, DM: Diabetes mellitus dummy, LIVER: Liver disease dummy, MI: Myocardial infarction dummy, PVD: Peripheral vascular disease dummy, SOLID: Solid tumor dummy, DV OLS: Stands for dependent variable ordinary least squares

two training and research hospitals in İzmir from March 2020 to March 2021. To the best of our knowledge, this is the first study regarding the association between comorbidities and hospitalization costs in COVID-19 patients. Our study, conducted on a comprehensive sample of 2,067 patients, revealed that the average hospitalization cost was $1,432.3 (adjusted for PPP, $4,994.7). Treatment expenses were notably higher for male patients and exhibited an upward trend with increasing age and the number of ICU admissions. The average duration of hospitalization was 10.6 days, whereas the mean length of ICU hospitalization was 9.9 days. The average daily cost of hospitalization for the entire cohort was $135.25 (PPP $471.63). Notably, comorbidities, including MI, CVS along with transient ischemic attacks, COPD, and CKD, significantly contributed to the increased hospitalization costs for COVID-19 patients.

One of the main findings is that the mean direct cost of COVID-19 hospitalization is lower than that of some developed countries, with costs of $6,827 in China[9], $14,366 in the US[10], and $10,000 in Canada[11]. In contrast, hospitalization costs in Türkiye are higher than those of €408 in Spain[12] and $1,384 in Arabia[13]. Certain cost drivers, such as examination and consultation costs, polyclinic costs, and hospitalization costs, are significantly lower in Türkiye. Moreover, less developed countries have lower medication costs[14].

The study conducted by Gedik[15] in a training and research hospital in İstanbul between March 17 and May 11, 2020, found that the mean cost per hospitalized patient was $881.75, which was lower than our observed costs for patients. Our study, with a larger population size than the one in Gedik's[15] study, is less susceptible to deviations in treatment cost that may arise from smaller sample sizes. His study period reflected the first wave of the pandemic. The treatment procedures changed over time, and depreciation in TL may have affected the findings. Over the course of 1 year, our study, encompassed various treatment procedures, taking into account the depreciation in TL. Oksuz et al.[16] found that the mean cost of COVID-19 episodes per patient was PPP $5,557.9, which is about 10% higher than our mean cost of PPP $4,994.72. We posit that deviations in treatment costs in a country like Türkiye, where all state-owned hospitals follow the same protocols in costing, arise from differences in sample sizes. If the sample sizes from previously studied hospitals were sufficiently large, the mean costs would likely converge.

Our finding, indicating higher mean costs in male patients compared to female patients, aligns with previous studies[4]. It has been shown that male COVID-19 patients have a higher prevalence of comorbidities[17], leading to an increased risk of more severe clinical conditions and mortality compared to female patients[17-21]. Moreover, female patients may be protected against clinical aggregation due to sex hormones and the X chromosome, which play a crucial role in adaptive and innate immunity[22].

We observed significantly different treatment costs among age categories, with costs increasing as age advances. However, it should be noted that the mean cost for patients over 80 years old deviates from this pattern. This could be attributed to higher death rates among patients over 80 years. Since patients who died during their treatment were excluded from our sample, the cost data for age groups may have been influenced differently by this exclusion. The higher cost in older patients was associated with an elevated risk of infection, aggregation, morbidity, and mortality[4,13,17,18,23,24]. Comorbidities, including cardiovascular disease, DM, and hypertension among older cases, coupled with the body's declined immunity, make them more susceptible to developing critical illnesses or even facing mortality. This, in turn, increases their hospitalization costs[25].

As expected, compared with non-ICU units, the mean treatment cost in the ICU was higher. A considerable relationship exists between ICU severity scores and health costs[26]. In a retrospective study conducted over approximately six months in Türkiye, Ekingen and Yildiz[27] reported that the mean cost for patients in the general ward (service) was $518.41, while the mean cost for ICU patients was $1,656.78. Patients in the ICU and patients older than 65 years are generally accompanied by malignancy, COPD, DM, CHF, chronic liver disease, and chronic kidney insufficiency, and these comorbid situations increase hospital costs[26,28].

Several studies have stated that the diagnosis and mortality of COVID-19 may be considerably affected by comorbidities, such as cardiovascular disease, DM, hypertension, and respiratory diseases[18,19,29]. For instance, as stated in the findings of a meta-analysis of 13 studies, patients with hypertension had a 1.72 times higher critical/morbid risk than those without hypertension[17]. Hospitalization was directly related to comorbidities and age[30]. As anticipated, our findings revealed incremental cost effects of comorbidities at admission, suggesting that comorbidities at admission may well predict COVID-19 hospitalization costs[4,9]. The mean hospitalization cost of patients with comorbidities was higher than the sample mean for all comorbidities except for liver disease. Due to the small number of patients diagnosed with liver disease (3), hemiplegia (3), and PVD (1), their representation power may be low. Therefore, the results based on these comorbidities should be interpreted cautiously.

DM is one of the most common comorbidities in COVID-19 patients[12,31]. We found that DM increased the treatment cost by $106.43 per patient; however, its effect is statistically not significant. Chan et al.[32] found that the presence of comorbidities, particularly cardiac diseases and DM, was associated with both adverse outcomes and higher mortality in

patients. Individuals with DM and cardiovascular disease have a higher risk of developing severe disease from COVID-19[33]. Our results indicated that MI increased the treatment cost by $165.72 per patient.

Study Limitations

This study has several limitations. First, although the analyses of hospitalized COVID-19 patients were conducted in two prominent hospitals in İzmir, the costs of outpatients were not considered. Additionally, the lack of inclusion of follow-up care after the treatment may have weakened the cost analysis. Second, this study excluded indirect costs, such as lost working days, decreased production, and equity losses. Therefore, the total cost of a nation burdened by COVID-19 is underestimated. Third, the Medical Enforcement Declaration of the Ministry of Health has not been updated since 2007 for most items. Updated cost reimbursement figures would enable decision-makers to estimate more realistic treatment costs in Türkiye[14]. Moreover, the TL has depreciated approximately 20.92% during the study period. We were unable to analyze patients' habits, such as alcohol and smoking use, or the extent of these habits. Another factor that could not be included in the analyses but could influence patients' health status during treatment was their socioeconomic status.

Conclusion

In December 2019, pneumonia associated with the 2019 novel Coronavirus emerged in Wuhan, China, and its effects on national and global economies have been tremendous. There is limited evidence on treatment costs for national health institutions and the effects of comorbidities on treatment costs, which are crucial inputs for health policymakers.

This study aimed to ascertain the direct healthcare costs of hospitalized COVID-19 patients in Türkiye and to analyze the effect of comorbidities on these costs. The findings reveal that the mean hospitalization cost was $1,432.3 (PPP $4,994.7), and some comorbidities significantly increased the hospitalization costs of COVID-19 patients, such as CKD, MI, COPD, and CVA. Treatment cost data presented in this study can be used for cost control, performance evaluation, budget planning, and policy formulation by health authorities, thereby contributing to public health planning. Well-estimated and effectively controlled treatment costs facilitate more efficient decision-making in limited budget allocation. With efficient budget allocation, more patients can receive the same quality of health services within the constraints of the budget. With efficient budget allocation, more patients can receive the same quality of health services with the same budget. Estimation of costs strictly is even more crucial for middle-income countries. Additionally, local cost figures can serve as benchmarks for health authorities in other middle- and high-income countries.

Ethics

Ethics Committee Approval: Ethical approval was granted by the University of Health Sciences Türkiye, İzmir Tepecik Training and Research Hospital Non-invasive Investigation Ethics Committee in September 2020 (approval no: 2020/11-32).

Informed Consent: Retrospective study.

Authorship Contributions

Concept - Design - Data Collection or Processing - Analysis or Interpretation - Literature Search - Writing: N.B., H.Ö., A.A., S.T., B.T., Ş.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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