

COVID-19 related hospitalization costs; assessment of influencing factors

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Abstract: **Objective:** Our aim is to assess the effective factors on hospitalization costs of COVID-19 patients. **Methods:** Data related to clinical characteristics and cost of hospitalized COVID-19 patients from February 2020 until July 2020, in a public teaching hospital in Tehran, Iran was gathered in a retrospective cohort study. The corresponding factors influencing the diagnostic and therapeutic costs were evaluated, using a generalized linear model. **Results:** The median COVID-19 related diagnostic and therapeutic costs in a public teaching hospital in Iran, for one hospitalized COVID-19 patient was equal to 271.1 US dollars (USD). In patients who were discharged alive from the hospital, the costs increased with patients' pregnancy ($P<0.001$), loss of consciousness during hospitalization ($P<0.001$), a history of drug abuse ($P=0.006$), history of chronic renal disease ($P<0.001$), end stage renal disease ($P=0.002$), history of brain surgery ($P=0.001$), history of migraine ($P=0.001$), cardiomegaly ($P=0.033$) and occurrence of myocardial infarction during hospitalization ($P<0.001$). In deceased patients, low age ($P<0.001$), history of congenital disease ($P=0.024$) and development of cardiac dysrhythmias during hospitalization ($P=0.044$) were related to increase in therapeutic costs. **Conclusion:** Median diagnostic and therapeutic costs in COVID-19 patients, hospitalized in a public teaching hospital in Iran were 271.1 USD. Hoteling and medications made up most of the costs. History of cardiovascular disease and new onset episodes of such complications during hospitalization were the most important factors contributing to the increase of therapeutic costs. Moreover, pregnancy, loss of consciousness, and renal diseases are of other independent factors affecting hospitalization costs in COVID-19 patients. **Keywords:** Cardiovascular Diseases; COVID-19; Effective Factors; Hospitalization Costs

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1. Introduction

With daily increase in the number of infected people with SARS-CoV-2 worldwide, health care systems across the globe have been under immense pressure and have faced a shortage of hospital beds (1, 2). Most of medical procedures have been delayed due to the risk of infection in hospitals and also to provide more hospital beds for COVID-19 patients (3). In these troubling times, the sources of hospitals have been limited, their costs for providing personal protective equipment (PPE) have increased and they have faced problems

in salary payments for healthcare workers (4). On the other hand, the costs forced on the patients, their families and also the healthcare system have increased. Taking into consideration the various reports showing COVID-19 serious complications, e.g., neurological, cardiovascular, renal and gastrointestinal involvement (5-7), hospitalization period has been prolonged in patients with underlying diseases and these groups of patients have needed more measures in hospitals, and thus faced increase in their hospitalization costs (8, 9). There are currently a small number of studies evaluating the

hospitalization costs of COVID-19 patients and it is not yet clear which underlying and clinical factors have the most impact on patients' expenditure. Whereas, the knowledge of healthcare decision makers about costly medical diagnostic and therapeutic procedures, can lead to a more effective patient management and better allocation of resources for hospitals and healthcare centers for treatment of COVID-19. Since there are no comprehensive studies regarding the matter, our aim is to assess the factors responsible for hospitalization costs, especially underlying conditions.

2. Methods

2.1. Study design

In order to gather the data needed for this cross-sectional study, medical files of COVID-19 patients who were hospitalized from 18th of February until 20th of July 2020, in Imam Hossein Hospital Center, Tehran, Iran, were gathered from the hospital registry system. Imam Hossein Hospital is a teaching public hospital, in which patients' medical costs are based on governmental tariffs. This study was approved by Shahid Beheshti university of medical sciences ethic committee (Code: IR.SBMU.RETECH.REC.1399.683).

2.2. Study sample

The hospitalization costs of COVID-19 patients, whose disease was proved by a positive RT-PCR, were included. Patient files which didn't have the variables of this study or had incomplete data about hospitalization costs were excluded from the study.

2.3. Variables

The evaluated data were patients' demographic information, history of cardiovascular disease, history of other concomitant disease, symptoms at the time of admission, laboratory and radiological findings, previous medications, development of cardiovascular complications and hospital costs. Total hospitalization costs were recorded as Iranian Rials, and by using the exchange rate during the period of this study, were presented as US dollar (USD). Using Iranian Central Bank data, the mean exchange rate of USD to Iranian Rials during study period was 169814 Iranian Rials. Therefore, we divided total hospitalization cost by 169814, to report the data as USD.

The costs are split into 6 groups in this study. These costs include hoteling and nursing, drug, physician services, laboratory services and imaging services' costs. The sum of all costs during hospital stay was also recorded.

2.4. Statistical analysis

All analyses were done with STATA 14.0 analytical program. Quantitative data are reported as median and interquartile range (IQR), and qualitative data are reported as frequency and percentage. Since data distribution was not normal, the analyses were done using generalized linear model (GLM)

with a gamma distribution and log link function. GLM with a gamma distribution is a common method in analysis of disease related cost (10, 11). Firstly, the possible factors effective on hospitalization costs were determined using univariate GLM analysis. Then, the variables with a P-value less than 0.1 in univariate analysis, were entered into a stepwise multivariate GLM model in order to determine the independent factors effecting the hospitalization costs. The results are reported as coefficient and 95% confidence interval (95% CI). The significance level was considered to be $P < 0.05$.

3. Results

3.1. Patients' characteristics

From February until July 2020, data related to 991 COVID-19 patients were extracted from Imam Hossein Hospital's registry system. 54.9% of patients were male and 46.7% were over 65 years of age. In this time period, 256 patients (25.8%) passed away. The median and IQR of total therapeutic costs in alive and deceased patients were 254.5 (165.2-428.0) and 380.8 (194.6-765.0) USD, respectively. The median total cost was estimated to be 271.1 (170.7-489.6) USD.

3.2. Hospitalization costs in alive COVID-19 patients

A review of therapeutically costs of 735 patients, who were discharged from the hospital, showed that the most of the patients' costs were related to hoteling and nursing services (median=109.5; IQR: 64.4-17.5 USD) and after that drug related costs (median=33.9; IQR: 17.5-77.6 USD), laboratory services (median=52.6; IQR: 39.1-76.1 USD), medical services (median=40.2; IQR: 25.2-70.7 USD), and imaging services (median=7.0; IQR: 4.2-12.9 USD) had the highest hospitalization costs (Figure 1).

Table 1 shows the therapeutic costs (as median and IQR) stratified by underlying and clinical variables. The highest cost was observed in patients between 10-24 years of age (309 [203.2-468.2]) and patients with body mass index greater or equal to 40 kg/m² (321.6 [165.2-454.9]). The hospitalization costs of pregnant patients or patients who developed loss of consciousness during hospital stay was higher than other patients (382.4 [282.4-786.7] and 458.3 [198.4-789.3], respectively). Hospitalization costs of patients who had previous history of COVID-19 (467.5 [224.7-716.5]), drug (616.7 [201.6-764.7]) and alcohol abuse (373.3 [223-942.4]), history of deep vein thrombosis (1296.7 [574.8-2018.5]), history of coronary artery bypass graft (334.2 [175.3-727.6]), history of asthma (303.7 [177.5-538.2]), history of pulmonary emboli (432.8 [248.9-439.7]), history of tuberculosis (391 [286-496]), history of respiratory allergies (342.6 [216.1-469.2]), history of cerebrovascular attack (333 [201-655.5]), history of brain surgery (522.7 [297.9-1617.8]), history of migraine (1116.7 [1116.7-1116.7]) and Alzheimer (356.7 [235.9-641.4]) and history of renal disease (479.4 [204-846.9]) in chronic kidney disease, 503.8 [175.3-685.1] in end-stage renal disease,

Table 1 Total cost of hospitalization in COVID-19 patients (USD)

Variable	Alive (n=735)			Dead (n=256)		
	n	Median	IQR	n	Median	IQR
Age (years)						
10-24	12	309.0	(203.2 - 468.2)	0	—	—
25-34	52	228.6	(177.7 - 489.3)	2	2484.3	(505.4 - 4463.1)
35-44	101	237.9	(161.1 - 373.3)	11	305.1	(152.7 - 2568.7)
45-54	146	253.7	(173.3 - 381.1)	20	302.1	(153.0 - 755.9)
55-64	136	250.8	(157.4 - 395.9)	48	368.6	(189.2 - 825.9)
≥ 65	288	267.2	(164.9 - 455.6)	175	396.8	(199.4 - 747.4)
Sex						
Female	347	256.4	(173.3 - 413.3)	100	380.8	(190.1 - 753.4)
Male	388	252.5	(153.3 - 431.3)	156	379.9	(197.6 - 796.8)
Body mass index (kg/m²)						
<18.9	7	266.2	(156.8 - 620.6)	10	353.7	(177.2 - 632.4)
18.9-24.9	223	237.9	(164.8 - 388.4)	85	383.3	(186.1 - 747.4)
25-29.9	330	260.2	(160.5 - 453.9)	102	368.8	(193.6 - 686.8)
30-39.9	153	260.7	(175.3 - 403.3)	55	442.8	(204.9 - 975.6)
≥ 40	22	321.6	(165.2 - 454.9)	4	247.2	(181.9 - 254.2)
Pregnancy						
No	724	252.2	(164.9 - 422.5)	255	378.3	(193.6 - 761.2)
Yes	11	382.4	(282.4 - 786.7)	1	4463.1	(4463.1 - 4463.1)
Loss of consciousness during admission						
No	691	249.1	(164.1 - 403.6)	207	363.3	(193.6 - 747.4)
Yes	44	458.3	(198.4 - 789.3)	49	468.5	(197.0 - 937.2)
Medical history						
Previous COVID-19						
No	731	253.2	(165.2 - 427.6)	255	383.3	(193.6 - 768.8)
Yes	4	467.5	(224.7 - 716.5)	1	239.0	(239.0 - 239.0)
Smoking						
No	660	248.0	(160.8 - 414.2)	223	363.3	(189.9 - 773.7)
Cigarette	62	315.5	(223.0 - 592.6)	32	415.9	(242.8 - 594.7)
Hookah	13	200.5	(142.6 - 483.2)	1	993.7	(993.7 - 993.7)
Substance abuse						
No	701	251.4	(163.4 - 426.7)	241	364.2	(193.6 - 747.4)
Opium	28	277.0	(221.1 - 368.4)	13	529.3	(324.4 - 784.7)
Other drugs	6	616.7	(201.6 - 764.7)	2	710.4	(445.2 - 975.6)
Alcohol use						
No	724	253.0	(165.2 - 422.5)	252	377.2	(191.9 - 760.3)
Yes	11	373.3	(223.0 - 942.4)	4	634.8	(342.8 - 1727.3)
Hypertension						
No	466	235.7	(158.8 - 376.4)	118	410.1	(217.4 - 810.1)
Yes	269	279.0	(175.2 - 488.0)	138	361.1	(184.8 - 736.0)
Hyperlipidemia						
No	694	252.2	(165.2 - 413.3)	234	380.8	(196.6 - 759.4)
Yes	41	280.9	(175.3 - 568.5)	22	369.9	(156.5 - 784.7)
Diabetes mellitus						
No	517	243.6	(158.4 - 406.7)	171	373.3	(186.1 - 768.8)
Yes	218	275.1	(182.6 - 476.2)	85	412.8	(218.0 - 761.2)
Aortic atherosclerosis						
No	651	247.6	(160.4 - 413.3)	211	403.9	(186.1 - 802.3)
Yes	84	297.5	(201.0 - 481.5)	45	316.7	(218.4 - 538.7)
Coronary artery disease						
No	607	247.7	(160.5 - 394.0)	190	377.2	(190.2 - 759.4)
Yes	128	289.7	(183.7 - 666.8)	66	384.9	(199.4 - 784.7)
Cardiomegaly						
No	587	250.9	(160.3 - 426.7)	174	396.8	(193.6 - 772.7)
Yes	147	271.2	(175.3 - 432.8)	82	341.0	(195.6 - 736.0)

Table 1 Total cost of hospitalization in COVID-19 patients (USD) (continued)

Variable	Alive (n=735)			Dead (n=256)		
	n	Median	IQR	n	Median	IQR
Deep vein thrombosis						
No	733	253.2	(165.2 - 426.7)	254	383.5	(195.6 - 768.8)
Yes	2	1296.7	(574.8 - 2018.5)	2	195.1	(78.3 - 311.8)
Coronary revascularization						
No	659	248.9	(164.2 - 409.3)	215	396.8	(189.2 - 768.8)
CABG	38	334.2	(175.3 - 727.6)	19	304.0	(218.0 - 442.8)
Angioplasty	35	280.9	(195.0 - 592.6)	20	331.6	(198.2 - 946.1)
Family history of cardiovascular disease						
No	658	250.8	(164.8 - 427.6)	237	376.1	(190.2 - 768.8)
Yes	77	273.5	(179.8 - 469.2)	19	420.1	(301.9 - 747.4)
Respiratory disorders						
No	677	252.0	(164.9 - 409.3)	227	383.6	(190.2 - 773.7)
Asthma	49	303.7	(177.5 - 538.2)	24	427.5	(242.2 - 637.0)
Pulmonary emboli	3	432.8	(248.9 - 439.7)	1	177.2	(177.2 - 177.2)
Pneumonia	2	168.7	(122.7 - 214.7)	2	187.1	(141.6 - 232.5)
Tuberculosis	2	391.0	(286.0 - 496.0)	2	104.7	(56.7 - 152.8)
Allergy	2	342.6	(216.1 - 469.2)	0	—	—
CNS disorders						
No	673	250.9	(164.2 - 413.3)	211	364.2	(186.1 - 796.9)
Cerebral vascular accident	38	333.0	(201.0 - 655.5)	32	419.0	(199.0 - 605.3)
Seizure	7	194.4	(111.3 - 627.4)	4	384.6	(197.5 - 715.0)
Parkinson	3	100.5	(96.5 - 179.8)	3	442.8	(396.8 - 506.1)
Brain surgery	3	522.7	(297.9 - 1617.8)	2	271.4	(254.2 - 288.6)
Multiple sclerosis	10	223.9	(171.4 - 309.1)	2	279.4	(129.3 - 429.5)
Migraine	1	1116.7	(1116.7 - 1116.7)	1	650.2	(650.2 - 650.2)
Alzheimer disease						
No	719	252.3	(165.0 - 418.3)	239	383.6	(193.6 - 772.7)
Yes	16	356.7	(235.9 - 641.4)	17	343.1	(235.2 - 589.6)
Kidney disease						
No	672	248.0	(165.0 - 399.2)	226	385.0	(195.6 - 772.6)
Chronic kidney disease	36	479.4	(204.0 - 846.9)	27	324.4	(177.2 - 736.0)
End-stage renal disorders	15	503.8	(175.3 - 685.1)	3	641.3	(190.2 - 2514.0)
Kidney transplantation	3	373.5	(184.0 - 1025.5)	0	—	—
Nephrotic syndrome	2	787.0	(39.0 - 1535.0)	0	—	—
Nephrectomy	7	271.6	(121.9 - 832.1)	0	—	—
Cancer						
No	706	253.8	(165.3 - 427.6)	243	373.3	(193.6 - 761.2)
Yes	29	262.7	(143.0 - 429.6)	13	599.9	(231.5 - 927.1)
Thyroid disorders						
No	684	254.5	(164.8 - 428.2)	240	368.8	(190.1 - 765.0)
Hypothyroidism	7	312.4	(175.9 - 714.5)	3	132.1	(123.5 - 196.1)
Hyperthyroidism	44	250.6	(200.0 - 393.7)	12	625.0	(384.9 - 742.3)
Immunosuppressive disorder						
No	710	251.7	(164.9 - 426.7)	244	377.2	(190.1 - 773.2)
Yes	25	306.7	(225.5 - 474.7)	12	401.9	(290.3 - 510.2)
Congenital disorders						
No	720	255.4	(165.3 - 427.2)	250	377.2	(193.6 - 759.4)
Yes	15	249.1	(142.9 - 771.6)	6	614.8	(342.5 - 936.8)
In-hospital cardiac complication						
No	688	247.8	(164.2 - 398.8)	216	368.8	(187.7 - 693.5)
Myocardial infarction	27	561.9	(289.3 - 1151.8)	12	791.4	(298.8 - 920.7)
Cardiogenic shock	2	204.8	(141.7 - 267.9)	3	1050.6	(808.9 - 1715.4)
Heart failure	15	396.6	(207.0 - 657.9)	17	363.3	(217.1 - 904.5)
Sudden cardiac death	—	—	—	8	351.8	(200.9 - 608.5)
Pericarditis	2	442.1	(352.7 - 531.5)	0	—	—
Cardiac dysrhythmia						
No	331	236.5	(156.5 - 382.4)	63	364.2	(218.0 - 569.7)
Yes	311	276.7	(177.8 - 486.2)	160	411.3	(196.4 - 833.3)

IQR: Interquartile range; CNS: Central nervous system

Table 2 Associations of patient and hospital characteristics with hospitalization costs for COVID-19

Characteristics	Alive		Dead	
	Unadjusted Coef. (95% CI)	P	Unadjusted Coef. (95% CI)	P
Age (years)				
10-24	Reference			-
25-34	0.21 (-0.57 - 0.99)	0.594	Reference	
35-44	0.05 (-0.71 - 0.82)	0.890	1.48 (1.04 - 1.92)	0.000
45-54	0.03 (-0.73 - 0.78)	0.944	0.71 (0.30 - 1.12)	0.001
55-64	0.22 (-0.52 - 0.97)	0.559	0.24 (-0.23 - 0.71)	0.315
≥ 65	0.05 (-0.69 - 0.79)	0.891	0.03 (-0.36 - 0.42)	0.883
Sex				
Female	Reference		Reference	
Male	0.11 (-0.06 - 0.28)	0.193	0.06 (-0.24 - 0.37)	0.683
Body mass index (kg/m²)				
<18.9	Reference		Reference	
18.9-24.9	-0.22 (-1.03 - 0.58)	0.586	0.14 (-0.74 - 1.03)	0.753
25-29.9	-0.04 (-0.84 - 0.75)	0.912	-0.01 (-0.90 - 0.88)	0.983
30-39.9	-0.06 (-0.87 - 0.75)	0.883	0.45 (-0.42 - 1.33)	0.312
≥ 40	0.01 (-0.89 - 0.91)	0.982	-0.90 (-4.30 - 2.50)	0.604
Pregnancy*				
No	Reference		—	
Yes	0.88 (0.58 - 1.18)	<0.001	—	—
Loss of consciousness during admission				
No	Reference		Reference	
Yes	0.65 (0.44 - 0.86)	<0.001	0.23 (-0.09 - 0.55)	0.165
Medical history				
Previous COVID-19				
No	Reference		Reference	
Yes	0.18 (-0.77 - 1.14)	0.706	-0.96 (-7.02 - 5.10)	0.757
Smoking				
No	Reference		Reference	
Cigarette	0.21 (-0.04 - 0.47)	0.102	-0.31 (-0.88 - 0.25)	0.279
Hookah	-0.02 (-0.69 - 0.65)	0.954	0.44 (-1.03 - 1.90)	0.559
Substance abuse				
No	Reference		Reference	
Opium	0.26 (-0.09 - 0.61)	0.149	0.10 (-0.51 - 0.71)	0.755
Other drugs	0.55 (0.00 - 1.11)	0.051	0.14 (-1.31 - 1.59)	0.851
Alcohol abuse				
No	Reference		Reference	
Yes	0.60 (0.21 - 0.99)	0.003	0.52 (-0.19 - 1.23)	0.153
Hypertension				
No	Reference		Reference	
Yes	0.18 (0.01 - 0.35)	0.040	-0.16 (-0.45 - 0.13)	0.293
Hyperlipidaemia				
No	Reference		Reference	
Yes	0.04 (-0.32 - 0.39)	0.834	0.10 (-0.38 - 0.58)	0.686
Diabetes mellitus				
No	Reference		Reference	
Yes	0.14 (-0.04 - 0.32)	0.119	-0.08 (-0.40 - 0.24)	0.612
Aortic atherosclerosis				
No	Reference		Reference	
Yes	0.20 (-0.03 - 0.43)	0.091	-0.21 (-0.66 - 0.23)	0.345
Coronary artery disease				
No	Reference		Reference	
Yes	0.39 (0.21 - 0.56)	<0.001	-0.21 (-0.58 - 0.16)	0.268
Cardiomegaly				
No	Reference		Reference	
Yes	0.25 (0.07 - 0.43)	0.008	-0.07 (-0.39 - 0.25)	0.655
Coronary revascularization				
No	Reference		Reference	
CABG	0.44 (0.18 - 0.71)	0.001	-0.42 (-1.22 - 0.38)	0.302
Angioplasty	0.36 (0.06 - 0.65)	0.019	-0.20 (-0.83 - 0.43)	0.540

Table 2 Associations of patient and hospital characteristics with hospitalization costs for COVID-19 (continued)

Characteristics	Alive		Dead	
	Unadjusted Coef. (95% CI)	P	Unadjusted Coef. (95% CI)	P
Deep vein thrombosis				
No	Reference		Reference	
Yes	1.20 (0.71 - 1.70)	<0.001	-1.16 (-6.41 - 4.08)	0.664
Family history of cardiovascular disease				
No	Reference		Reference	
Yes	0.22 (-0.01 - 0.46)	0.061	-0.20 (-0.86 - 0.46)	0.554
Respiratory disorders				
No	Reference		Reference	
Asthma	0.14 (-0.16 - 0.44)	0.373	-0.10 (-0.64 - 0.43)	0.706
Pulmonary emboli	-0.04 (-1.43 - 1.35)	0.956	-1.28 (-9.47 - 6.91)	0.759
Pneumonia	-0.83 (-4.61 - 2.94)	0.664	-1.23 (-6.71 - 4.26)	0.662
Tuberculosis	0.01 (-1.62 - 1.63)	0.995	-1.81 (-11.60 - 7.99)	0.718
Allergy	-0.13 (-1.98 - 1.73)	0.894	—	—
CNS disorders				
No	Reference		Reference	
Cerebral vascular accident	0.25 (-0.06 - 0.55)	0.115	0.08 (-0.34 - 0.49)	0.719
Seizure	-0.18 (-1.23 - 0.87)	0.742	-0.32 (-1.93 - 1.29)	0.699
Parkinson	-1.12 (-5.24 - 3.00)	0.593	-0.33 (-2.22 - 1.55)	0.729
Brain surgery	0.74 (0.10 - 1.39)	0.023	-0.84 (-4.65 - 2.98)	0.667
Multiple sclerosis	-0.19 (-1.08 - 0.70)	0.674	-0.81 (-4.51 - 2.90)	0.669
Migraine	1.06 (0.26 - 1.87)	0.010	0.04 (-2.22 - 2.29)	0.975
Alzheimer disease				
No	Reference		Reference	
Yes	0.35 (-0.06 - 0.77)	0.097	-0.17 (-0.84 - 0.51)	0.632
Kidney disease				
No	Reference		Reference	
Chronic kidney disease	0.62 (0.38 - 0.85)	<0.001	-0.20 (-0.76 - 0.36)	0.484
End-stage renal disorders	0.64 (0.29 - 0.98)	<0.001	0.57 (-0.19 - 1.34)	0.141
Kidney transplantation	0.37 (-0.61 - 1.34)	0.464	—	—
Nephrotic syndrome	0.76 (-0.04 - 1.57)	0.062	—	—
Nephrectomy	0.26 (-0.45 - 0.97)	0.471	—	—
Cancer				
No	Reference		Reference	
Yes	-0.07 (-0.53 - 0.39)	0.765	-0.05 (-0.75 - 0.64)	0.879
Thyroid disorders				
No	Reference		Reference	
Hypothyroidism	0.04 (-0.79 - 0.87)	0.923	-1.43 (-7.00 - 4.14)	0.615
Hyperthyroidism	-0.14 (-0.54 - 0.26)	0.497	-0.07 (-0.80 - 0.66)	0.847
Immunosuppressive disorder				
No	Reference		Reference	
Yes	-0.02 (-0.49 - 0.46)	0.943	-0.27 (-1.15 - 0.61)	0.548
Congenital disorders				
No	Reference		Reference	
Yes	0.10 (-0.44 - 0.64)	0.720	0.60 (0.05 - 1.15)	0.033
In-hospital cardiac complication				
No	Reference		Reference	
Myocardial infarction	0.76 (0.52 - 0.99)	0.000	0.25 (-0.31 - 0.80)	0.381
Cardiogenic shock	-0.60 (-3.65 - 2.44)	0.698	0.66 (-0.06 - 1.38)	0.073
Heart failure	0.08 (-0.50 - 0.65)	0.796	-0.19 (-0.90 - 0.52)	0.600
Sudden cardiac death	—	—	-0.14 (-1.11 - 0.83)	0.775
Pericarditis	0.17 (-1.25 - 1.58)	0.817	—	—
Cardiac dysrhythmia				
No	Reference		Reference	
Yes	0.27 (0.09 - 0.46)	0.003	0.40 (-0.03 - 0.83)	0.067

* the analysis did not perform in dead people since there is only 1 observation

Coef.: Regression coefficient; CNS: Central nervous system

373.5[184-1025.5] in kidney transplant patients, 787[39-1535] in nephrotic syndrome and 271.6[121.9-832.1] in nephrectomy patients) was higher than other patients. It's also worth noting that hospitalization costs increased with development of cardiovascular complications during hospital stay (561.9[289.3-1151.8] in myocardial infarction, 204.8[141.7-267.9] in cardiogenic shock, 396.6[207-657.9] in heart failure and 442.1[352.7-531.5] in pericarditis) (Table 1).

According to the conducted univariate analysis, pregnancy ($P<0.001$), loss of consciousness ($P<0.001$), alcohol use ($P=0.003$), hypertension ($P=0.04$), history of coronary artery disease ($P<0.001$), history of cardiomegaly ($P<0.001$), history of coronary artery bypass surgery ($P=0.001$), history of angioplasty ($P=0.019$), history of deep vein thrombosis ($P<0.001$), history of brain surgery ($P=0.023$), history of migraine ($P=0.01$), history of end-stage renal disease ($P<0.001$) and history of chronic kidney disease ($P<0.001$) have possible effecting factors of hospitalization costs. Regarding the complications during hospitalization, it was shown that development of myocardial infarction ($P<0.001$), sudden cardiac death ($P<0.001$) and cardiac dysrhythmias ($P=0.003$) were related to an increase in hospitalization costs (Table 2).

Multivariate analysis showed that in living discharged patients, pregnancy (adjusted coefficient=1.05; 95% CI: 0.74, 1.36; $P<0.001$), loss of consciousness during hospitalization (adjusted coefficient=0.53; 95% CI: 0.34, 0.73; $P<0.001$), history of substance abuse (adjusted coefficient=0.78; 95% CI: 0.22, 1.34); $P=0.006$), history of renal disease (adjusted coefficient=0.68; 95% CI: 0.46, 0.90; $P<0.001$), end-stage renal disease (adjusted coefficient=0.56; 95% CI: 0.21, 0.91; $P=0.002$), history of brain surgery (adjusted coefficient=0.95; 95% CI: 0.41, 1.49; $P=0.001$), history of migraine (adjusted coefficient=1.29; 95% CI: 0.52, 2.06; $P=0.001$), and cardiomegaly (adjusted coefficient=0.19; 95% CI: 0.01, 0.36; $P=0.033$) were significantly related to hospitalization costs (Table 3).

3.3. Hospitalization costs in deceased COVID-19 patients

Evaluation of hospitalization costs of 256 deceased COVID-19 patients showed that the greatest expenditure was for hoteling and nursing services (median=109.4; IQR: 51.5-271.1 USD), followed by drug (median=85.0; IQR: 37.8-175.6 USD), physician services (median=72.0; IQR: 47.7-106.2 USD), laboratory (median=71.5; IQR: 46.8-106.2 USD), and imaging services (median=11.0; IQR: 7.0-23.5 USD) (Figure 1).

Table 1 summarizes the median and IQR of treatment costs separated by the baseline and clinical variables of deceased patients. Highest hospitalization costs were seen in the age group of 25-34 (2484.3 [505.4-4463.1]). Also, in the group of patients with history of cigarette smoking costs were considerably higher (415.9[242.8-594.7]). Alcohol (634.8[342.8-1727.3]) and substance abuse (710.4 [445.2-975.6]), history of migraine (650.2 [650.2-650.2]), end-stage renal disease (641.3 [190.2-2514]), history of cancer (599.9 [231.5-927.1]),

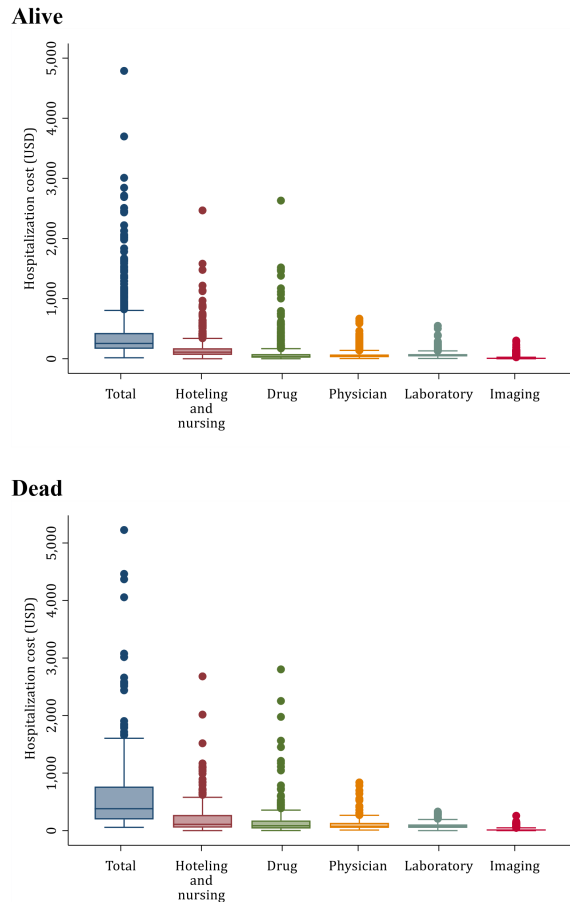


Figure 1 Hospitalization costs for COVID-19 according to type of cost and stratified by patients' outcome

history of thyroid disease (132.1[123.5-196.1] in hypothyroidism and 625[384.9-742.3] in hyperthyroidism) and congenital diseases (614.8 [342.5-936.8]) were other factors that were related to higher treatment costs. It is worth noting that along with the incidence of cardiovascular complications during hospitalization, treatment costs increased (791.4[298.8-920.7] in myocardial infarction, 1050.6[808.9-1715.4] in cardiogenic shock and 363.3 [217.1-904.5] in heart failure).

Univariate analysis showed that age ($P<0.001$), congenital diseases ($P=0.033$) as well as occurrence of cardiogenic shock ($P=0.073$), and cardiac dysrhythmia ($P=0.067$) during hospitalization were related to higher treatment costs in deceased patients (Table 2). Based on multivariate analysis, hospitalization costs were higher in lower age (adjusted coefficient= -0.02; 95% CI: -0.03, -0.009; $P<0.001$) and showed direct relationship with history of congenital diseases (adjusted coefficient=0.53; 95% CI: 0.07, 0.98; $P=0.024$). Finally, occurrence of cardiac dysrhythmia (adjusted coefficient=0.45; 95% CI: 0.01, 0.90; $P=0.044$) during hospitalization was associated with higher costs in deceased patients (Table 4).

Table 3 Multivariate analysis for assessment of independent factors associated with hospitalization cost in alive COVID-19 patients

Characteristics	Adjusted Coef. (95% CI)	P-value
Pregnancy		
No	Reference	
Yes	1.05 (0.74, 1.36)	<0.001
Loss of consciousness during admission		
No	Reference	
Yes	0.53 (0.34, 0.73)	<0.001
History of substance abuse		
No	Reference	
Opium	0.30 (-0.01, 0.60)	0.053
Other drugs	0.78 (0.22, 1.34)	0.006
History of kidney disease		
No	Reference	
Chronic kidney disease	0.68 (0.46, 0.90)	<0.001
End-stage renal disorders	0.56 (0.21, 0.91)	0.002
History of CNS disorders		
No	Reference	
Brain surgery	0.95 (0.41, 1.49)	0.001
Migraine	1.29 (0.52, 2.06)	0.001
Cardiomegaly		
No	Reference	
Yes	0.19 (0.01, 0.36)	0.033
History of coronary revascularization		
No	Reference	
Yes	0.23 (-0.02, 0.47)	0.072
In-hospital cardiac complication		
No	Reference	
Myocardial infarction	0.71 (0.48, 0.93)	<0.001
Cardiac dysrhythmia during hospitalization		
No	Reference	
Yes	0.16 (-0.02, 0.47)	0.067
Alcohol abuse		
No	Reference	
Yes	0.45 (-0.03, 0.94)	0.069
Diabetes mellitus		
No	Reference	
Yes	0.14 (-0.02, 0.32)	0.096

Coef.: Regression coefficient; CNS: Central nervous system

Table 4 Multivariate analysis for assessment of independent factors associated with hospitalization cost in dead COVID-19 patients

Characteristics	Adjusted Coef. (95% CI)	P-value
Age	-0.02 (-0.03, -0.009)	<0.001
History of congenital disorders		
No	Reference	
Yes	0.53 (0.07, 0.98)	0.024
In-hospital cardiac complication		
No	Reference	
Cardiogenic shock	0.70 (-0.02, 1.42)	0.055
Cardiac dysrhythmia during hospitalization		
No	Reference	
Yes	0.45 (0.01, 0.90)	0.044

Coef.: Regression coefficient; CNS: Central nervous system

4. Discussion

The current retrospective cohort study evaluated the association between factors influencing hospitalization costs. Based on our findings, a history of heart disease and occurrence of cardiovascular complications during hospitalization results in an increased cost of COVID-19 patients. This along with other findings that point to dangerous cardiovascular complications of COVID-19, indicate the importance of paying more attention to cardiovascular complications of COVID-19. Alongside these complications, loss of consciousness during hospitalization, history of brain surgery, history of renal disease, migraine, and pregnancy are other independent factors influencing hospitalization costs.

Underlying diseases predispose patients to develop severe forms of COVID-19, and loss of consciousness and cardiac dysrhythmias demonstrate severe condition of patients with increase potential risk of hospitalization and need for intensive care unit admission (12-15). There is a paucity in studies that have tried to evaluate the relationship of COVID-19 patients' mortality and hospitalization costs; therefore, it is not possible at the moment to conclude whether COVID-19 mortality is associated with higher hospital costs or not. Developing a severe form of COVID-19 on one hand increases mortality rates that can result in reduced duration of hospitalization, while on the other hand can increase the amount of total costs by increasing the need for admission in intensive care units and patient hoteling costs (16, 17).

In this study, analyses were stratified based on patients' discharge status (alive or deceased) in order to remove the effect of outcome. We observed that underlying cardiovascular diseases were associated with higher costs of treatment in living discharged patients, but not in deceased patients.

Our study results appoint equal importance to underlying renal diseases and cardiovascular diseases in increasing hospitalization costs; this finding is in alignment with recent studies on risk factors of severe COVID-19 infection that have concluded history of renal disease is a stronger risk factor than chronic pulmonary diseases and therefore its importance might have been underestimated in previous researches (18).

Based on guidelines of NIH, pregnant women infected with COVID-19 with indications for hospitalization, should be hospitalized in a ward where both mother and the fetus can be monitored and isolated if needed (19, 20). As most studies on COVID-19 have excluded pregnant and breastfeeding women from study population, more studies are needed for evaluating the effects of COVID-19 on this population and its hospitalization costs.

Loss of consciousness can be due to cardiac or brain injuries and poisoning (21). COVID-19 can result in loss of consciousness by causing encephalopathy, pulmonary involvement and hypoxia, and cardiac ischemic diseases (22). According to the guideline of COVID-19 hospitalization, loss of consciousness is an important indication for intensive care unit admission (23); therefore, it is expected that loss of con-

sciousness would increase hospitalization costs dramatically. One of the factors that is directly related to increased hospital costs is the length of hospital stay. Nevertheless, what is important about it is that the length of stay is practically the main part of the cost of hoteling. Therefore, practically the length of hospital stay is a part of the response variable, i.e., hospital costs. The cost of hoteling depends on the length of stay, and the longer the stay, the higher the cost of hoteling. In other words, the length of hospital stay is concealed in total hospital cost and bringing this variable as a separate factor in the model causes bias in the model. Since once the dependent costs (hotelings) are included in the total cost calculations (in the response variable) and once again the length of hospital stay within the model is entered as a possible influential factor (independent variable); accordingly, the effect of hospital stay is falsely overestimated.

5. Limitations

This study had some limitations. In assessing the relationship between some underlying diseases and costs, the number of patients with that special comorbidity has been low, which can potentially decrease the power of our analyses. Also, due to the possibility of bias in self-reporting the history of addiction and alcohol abuse in patients, and also lack of definitive diagnostic tests for confirmation of underlying diseases, there could have been some error in our analyses on that matter; therefore, more comprehensive prospective studies are required for evaluating the effect of underlying disorders on COVID-19 infection and hospitalization costs. Finally, the hospital in which this study was conducted, is a teaching public hospital that has cost rates based on government tariffs; therefore, other study is needed for evaluating costs in private hospitals.

6. Conclusion

The median cost for a COVID-19 patient hospitalized in a teaching public hospital in Tehran, Iran was 271.1 USD. Hoteling services and drug made up the majority of costs. History of cardiovascular diseases and occurrence of new cardiovascular complications during hospitalization were the most important factors influencing costs. Along with these factors, pregnancy, loss of consciousness, history of alcohol abuse, and underlying renal diseases were other independent factors that were associated with higher costs of treatment in COVID-19 patients.

7. Declarations

7.1. Acknowledgment

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7.2. Authors' contribution

Study design: MHA, MY; Collecting and cleaning the data: All authors; Analysis and interpretation of results: MY, AT, AMN; Drafting: MY, AT, AMN; Revising: All authors

7.3. Conflict of interest

Authors declare no conflict of interest.

7.4. Funding

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