RESEARCH NOTE

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Factors predicting readmission in patients with COVID-19



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Abstract

Objective: COVID-19 has been introduced by the World Health Organization as a health emergency worldwide. Up to 9% of the patients with COVID-19 may be readmitted by 2 months after discharge. This study aimed to estimate the readmission rate and identify main risk factors for readmission in these patients. In this prospective study, 416 discharged COVID patients followed up with a minimum 1 month and the readmission rate was recorded. Evaluated characteristics included time of readmission, age and sex, main symptoms of disease, result of computed tomography scan, reverse transcription polymerase chain reaction test and treatment modalities.

Results: Regarding readmission, 51 patients of 416 discharged patients, was readmitted during the study period. The rate of readmission for 30 and 60 days after discharge was 7.6% and 8.1%, respectively. The median age of the readmitted patients was 67 years (IQR: 53–78). About 65% of readmitted patients had underlying disease. The most significant factor in readmission rate was related to the site of lung involvement (OR > 4). Age over 60 years, underlying disease especially diabetes (OR = 3.43), high creatinine level (\geq to 1.2 mg/dl) (OR = 2.15) were the most important predictors of readmission.

Keywords: COVID-19, Readmission, SARS-CoV-2, Iran, Prediction

Introduction

Coronavirus Disease 2019 (COVID-19) was declared by the World Health Organization as a global health emergency on January 30, 2020 [1, 2]. SARS-CoV-2 transmission rate is high but most people recover following COVID-19 like Severe Acute Respiratory Syndrome (SARS), and Middle East Respiratory Syndrome (MERS) [3, 4]. However in 5% of cases, hospitalization is essential to keep on the treatment process [5, 6], in other side the clear guidelines for the management of the patients with COVID-19 and the time of discharge have not yet been

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determined based on clinical evidence [5, 7]. According to the Centers for Disease Control and Prevention (CDC), up to 9% of the patients with COVID-19 may be readmitted within 2 months of discharge [8, 9]. Mostly male, old age and the presence of underlying disease or history of malignancy are associated with poor prognosis and readmission in this group of patients [10-12]. Comorbidities or heart disease were associated with higher odds of readmission in these patients [13–16]. Increment of readmission and ignoring related risk factors could lead to serious form of diseases and mortality based on the experience of previous respiratory pandemics [3, 17–19]. Not only COIVD-19 causes multi-organ failure, but also drugs used to treat COVID-19 cause complications, therefore follow up is essential to complete the treatment course [20-22]. Paying attention to the clinical aspects of readmission in these patients is fundamental to make better decision in follow-up [10, 11,

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23, 24]. This study conducted to estimate the rate of readmission and identify main risk factors for readmission in the patients with COVID-19.

Main text

Methods and materials

Study setting & design

We performed prospective study on patients admitted with a diagnosis of COVID-19 in Vasei hospital, Khorasan Razavi province, Iran, between March 1, 2019 and May 20, 2020. The protocol of study was approved by ethics committee of Sabzevar University of Medical Sciences (IR.MEDSAB.REC.1399.004) and informed consent form was obtained from all patients. The data were analyzed through STATA.

Study population

Study population was a cohort of 506 patients admitted with definite or clinical diagnosis of COVID-19. Diagnosis of COVID-19 was ascertained by a positive result of polymerase chain reaction (PCR) and imaging finding. In this study, 92 patients who died during hospitalization were excluded from the study and 416 patients were discharged and followed up for at least 6 months.

Data collection

Clinical and demographic variables were included age, sex, symptoms, biochemical findings, CT scan and RT-PCR test results and underlying disease, pregnancy, and readmission rate, extracted from health information system (HIS). Comorbidities were measured using ICD-10 and categorized in three main groups diabetes, hypertension and other disease. Main symptoms and clinical variables that assessed in these patients were dry cough, fever and Spo2. Also, we assessed D-dimer (no/ yes) and level of creatinine (mg/dl). Additionally, some of other variable were recorded such as length of stay at hospital and use of mechanical ventilation. Moreover status of ground glass opacity and site of lesions was assessed in patient whit abnormal result through lung CT scans.

Main measurements

Readmission was evaluated as a primary outcome at a time interval of 3 to 180 days after discharge; secondary outcome was death in readmitted cases.

Results

Readmission time of patients

In this study, 416 discharged patients were followed up, the mean follow-up was 61 ± 11.2 days. Fifty-one of the

patients were readmitted, which 13 patients (25%) 1 week after discharge and 19 patients up to 30 days after discharge and 2 patients up to 60 days after discharge and the rest of the patients (n=17) up to 40 weeks after discharge were readmitted. Readmission rate in 1 week, 30 days, 60 days and up to 40 weeks after discharge were 3.1%, 7.6%, 8.1% and 12.25%, respectively.

Characteristics of the patients

The mean age of the readmitted patients (n=51) 65 ± 15.42 years. The mean age of the recovered patients was 56 ± 18.2 years (p<0.001). The results showed that there was a significant relationship between underlying disease and readmission (p<0.001). Two thirds of readmitted patients had a history of negative PCR results, although 84.3% of the readmitted patients had abnormal chest imaging results in the first hospitalization (Table 1).

However, 84.3% of the readmitted patients had a history of abnormal CT scan presented in detail in Table 2.

Risk factor for readmission

To estimate and predict risk factor, regression models are helpful [25]. Risk of readmission for each of the related factors was estimated using regression model [26]. To find relationship between demographic, clinical, biochemical and therapeutic characteristics and dependent variable (readmission), regression models are used. The distribution of the data was normal checking with Kolmogorov–Smirnov test. After controlling the effect of other variables, the odds ratio of readmission in the patients with abnormal creatinine level and diabetes was 2.15 and 3.43, respectively (Table 3).

Discussion

In this study the rate of readmission with the same interval was consistent with other studies, in which readmission in the first week after discharge was between 2 and 4% [23, 24, 27] and was reported 10% for 2 months after discharge [8]. In the follow-up of 279 discharged patients in Rhode Island of the United States, 30 days after discharge, readmission rate was reported 6.7% [10]. In Turkish study, 7.1% of discharged patients were readmitted [12].The readmission rate 2 months after discharge was 9% in the United States [8]. Donnelly et al. reported readmission rate up to 20% 2 months after discharge in the United States [28]. In another study, 10.3% of the discharged patients were readmitted to hospital 80 days after discharge [29]. However, in different findings in the Korean population, the readmission rate after discharge

Variable	Total number%	Non-readmitted, 365 (87.7)		Readmitted, 51 (12.2)		P-value
		N	%	N	%	
Sex (n=416)						
Male	228 (54.0)	203	55.6	25	49.0	0.78*
Female	188 (45.0)	162	44.4	26	51.0	
PCR (n $=$ 368)						
Negative	227 (61.6)	169	61.2	31	64.6	0.19*
Positive	141 (38.4)	124	38.8	17	35.4	
Comorbidity (n=416)						
No	224 (53.8)	206	56.4	18	35.3	< 0.001**
Diabetes	42 (10.1)	29	8.0	13	25.5	
Hypertension	61 (14.7)	55	15.0	6	11.7	
Others	83 (20.0)	69	18.9	14	27.4	
Pregnancy	6 (01.4)	6	1.64	0	0	
D-dimer (n = 416)						
No	85 (19.7)	78	21.4	7	13.7	0.20*
Yes	331 (80.3)	287	78.6	44	86.3	
Age (year)						
<u>≤</u> 60	226 (54.3)	205	56.2	21	42.1	0.04*
>60	190 (45.7)	160	43.8	30	58.9	
Quantitative variables	Ν	Ν	Mean (CI %95)	Ν	Mean (CI %95)	P value ***
SPO2	407	356	89.3 (88.4, 90.2)	51	88.2 (86.3,90.1)	0.40
Creatinine (mg/dl)	372	326	1.1 (1.1, 1.2)	46	1.5 (1.2, 1.9)	< 0.001
Hospitalization (day)	415	364	5.2 (4.7, 5.7)	51	7.0 (5.5, 8.5)	< 0.001
ICU (day)	52	43	4 (2.75, 5.24)	9	3.4 (0.36, 7.25)	0.72

	Table 1	Characteristics of th	e recovered and	readmitted patient
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* Pearson χ2, ** Fisher's exact, *** t-test

was 4.3% [11] and in Spanish population, the readmission rate was 4.4% up to 3 weeks after discharge [9].

The median length of stay at hospitals for the first time was 4 days similar to the findings of previous studies in Iran [30, 31]. A review of 52 studies estimated the median length of stay at hospitals up to 5 days [32] similar to the median length of stay in New York performed on 5700 patients [23]. Length of stay was very different in Korean hospitals (17 days) [11]. Also, in the present study, the median length of stay for readmitted and non-readmitted patients was 5 days (IQR: 3–9) and 4 days (IQR: 3–6), respectively, while in the Turkish study, the median length of stay was 4 days and 3 days, respectively [12].

The median length of stay in the Spanish readmitted patients with COVID-19 was lower than other patients (6 days vs. 9 days) [9]. Hospitalization of the patients has some conditions which include the capacity of the medical system, the quality of care and the demand for hospital beds in the pandemic period [12, 17, 33]. Different quality of post-discharge care can also have main role in the completion of the treatment process [24, 29].

Wu and McGoogan [34] and Richardson et al. [23] revealed that the odds ratio of readmission in elderly patients was higher than in other age groups. Underlying diseases, especially hypertension and diabetes, have also been confirmed in other COVID-19 studies [9, 10, 12, 24]. Aging reduces the response of immune cells to SARS-CoV-2; consequently the virus may be able to stay in the body longer. Complications in readmitted COVID-19 patients are more in elderly people [35], however these two factors may be strong predictors for readmission in the hospitalized patients [36]. High creatinine level in the hospitalized patients was another predictor for readmission in COVID-19 patients, so that the odds ratio of readmission for a creatinine level greater than 1.2 mg/dl was 2.15. Findings of the previous studies on other diseases also consider creatinine level as an effective factor for readmission of COVID-19 patients [37-39].

Variable	Total n%	tal n% Readmission						Log rank test
		3–7 days		8–30 days		31–60 days		
		N	Failure function	N	Failure function	N	Failure function	
History of CT result (n	=51)							
Normal	8 (15.7)	1	0.12	2	0.25	3	0.37	P = 0.04
Abnormal	43 (84.3)	12	0.27	30	0.69	31	0.72	
Ground Glass Opacity	r(n = 43)							
No	6 (13.95)	2	0.33	3	0.50	3	0.50	P = 0.65
Yes	37 (86.05)	10	0.27	27	0.72	28	0.75	
Site of lesions (n = 43))							
Multiple lobes	4 (9.30)	3	0.75	4	1.0			P = 0.04
Peripheral	20 (46.51)	6	0.30	15	0.75	16	0.80	
Lung bases	14 (32.56)	3	0.21	10	0.71	10	0.71	
Peribronchovascular distribution	2 (4.65)	-	-	-	-	-	-	
Central	3 (6.96)	0	0	1	0.33	1	0.33	
Bilateral								
No	12 (27.91)	4	0.33	4	0.33	4	0.33	P = 0.002
Yes	31 (72.09)	8	0.25	26	0.83	27	0.87	
Pleural effusion								
No	39 (90.7)	10	0.25	26	0.66	27	0.69	P=0.38
Yes	4 (9.3)	2	0.50	4	1.0			

Table 2 Comparison of readmission time of patients based on CT scan

This finding was consistent with the findings of previous studies that introduced abnormal chest imaging results as a predictor of readmission [11, 40], so chest imaging is a suitable tool for managing COVID-19 patients after discharge [41–43]. Also, the possibility of a false negative result in PCR test was reported in previous studies [41]. At the end, the key point to indirectly avoid readmission is fully vaccination of the patients after recovery from the COVID-19 through approved vaccine as soon as possible [44, 45].

Conclusion

According to the results, age over 60 years, underlying disease especially diabetes, high creatinine level, duration of first-time hospitalization and lung involvement were the most important predictors of readmission in the patients with COVID-19. The site of lung involvement was had very crucial role in readmission with odds ratio of 4.5 for peribronchovascular distribution or central involvement and odds ratio of 4.16 for basal lung involvement. The readmission rate was 3.1% for 1 week after discharge, 7.6% for 1 month after discharge, and 8.6% for 2 months after discharge.

Limitation

One of the main limitations in the present study was small sample size which makes it hard to generalize the obtained results.

Table 3 Relationship between characteristics and readmission of COVID-19 patients

Adjusted OR (95% CI)	Crude OR (95% CI)	Variable		
Age				
≥ 60	1	1		
>60	1.83 (1.00, 3.31)*	1.12 (0.52, 2.47)		
Sex				
Male	1	-		
Female	1.30 (0.72, 2.34)	-		
Dry cough				
No	1	-		
Yes	0.68 (0.37, 1.23)	-		
Fever				
No	1	_		
Yes	0.62 (0.34, 1.12)	_		
Comorbidity				
No	1	1		
DM	5.27 (2.34, 11.89)*	3.43 (1.13, 8.37)*		
HTN	1.28 (0.48, 3.39)	0.72 (0.21, 2.47)		
Others	2.38(1.13, 5.05)*	1.24 (0.46, 3.27)		
D-dimer (ng/ml)				
No	1	_		
Yes	1.70 (0.74, 3.94)	_		
PCR				
No	1	_		
Yes	0.86 (0.46, 1.63)	_		
Creatinine, mg/dL				
<1.2	1	1		
≥ 1.2	2.84 (1.48, 5.43)*	2.15 (1.00, 4.59)*		
Duration of hospitalization				
<6	1	1		
≥ 6	1.93 (1.06, 3.51)*	2.00(0.94, 4.27)		
Admission to ICU				
No	1	_		
Yes	1.60(0.73, 3.52)	_		
CT result				
Normal	1	_		
Abnormal	1.48 (0.67, 3.28)	_		
Site of lesion(s)				
Multiple lobes	1	1		
Peripheral	3.36 (1.10, 10.19)*	2.40 (0.75, 7.67)		
Lung bases	4.41 (1.38, 14.05)*	4.16 (1.23, 14.05)*		
Peribronchovascular distribu- tion	4.55 (0.72, 28.4)	4.43 (0.65, 30.51)		
Central	20.5 (3.10, 135.5)*	6.15 (0.66, 56.93)		

Abbreviations

COVID-19: Coronavirus Disease 2019; WHO: World Health Organization; CDC: Centers for Disease Control and Prevention; PCR: Polymerase Chain Reaction; ICUs: Intensive Care Units.

The online version contains supplementary material available at https://doi. org/10.1186/s13104-021-05782-7.

Additional file 1. Raw data for possible analysis and review studies.

Acknowledgements

We would like to express our sincere gratitude to all people participated in the study specially Dr Seyed Alireza Javadinia for his great advice on different steps of work.

Authors' contributions

Conceptualization; DS and MN, SAJ. Data extraction; DS, MN, FA, MN, FR. Funding acquisition; MN. Investigation; MN, DS, FA, MN. Methodology; FA. Project administration; DS and FA. Resources; MN, DS, Software; FA. Supervision; DS. Roles/writing original draft; MN, DS, FA, MN, FR. Writing—review & editing: FA, DS and SAJ. All authors read and approved the final manuscript.

Funding

The work was fully funded by Sabzevar University of Medical Sciences (Grant Number 99007, 2019 to Mohammad Nematshahi).

Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request (Additional file 1).

Declarations

Ethics approval and consent to participate

The protocol of study was approved by Sabzevar University of Medical Sciences (IR.MEDSAB.REC.1399.004) and informed consent form was written and obtained from all patients.

Consent to publish

Not applicable.

Competing interests

There are no financial conflicts of interest to disclose for any authors.

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Received: 4 May 2021 Accepted: 13 September 2021 Published online: 26 September 2021

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