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## One-year prevalence and the association between SARS-CoV-2 cycle threshold, comorbidity and outcomes in population of Babol, North of Iran (2020-2021)

### Abstract

**Background:** The present study aimed to investigate the one-year prevalence of SARS-CoV-2, common comorbidities and demographic information among negative- and positive rRT-PCR in health care workers (HCW), hospitalized and outpatients. Also, the association between SARS-CoV-2 cycle threshold (Ct) and the outcomes of patients were analyzed in Babol, northern Iran.

**Methods:** This large retrospective cross-sectional study was performed between March 2020 and March 2021. The records of 19232 hospitalized, outpatients and HCW suspected to COVID-19 were collected from teaching hospitals in the North of Iran.

**Results:** Out of the 19232 suspected to COVID-19 patients, 7251 (37.7%) had a positive rRT-PCR result; 652 (9%), 4599 (63.4%) and 2000 (27.6%) of those were categorized as HCW, hospitalized and outpatients, respectively. Moreover, between the hospitalized and the outpatient group, 10.2 and 0.8% cases died, whereas no death cases were reported in the HCW. Furthermore, it seems that death rate was significantly different between the three groups of Ct value, the highest mortality in those with Ct between 21 and 30 (group B=7.6%) and the lowest in the group with the highest Ct (between 31 and 40 = 5.5%) ( $p<0.001$ ).

**Conclusion:** In summary, 37.7% of cases were positive for SARS-CoV-2; of which, 63.4, 27.6 and 9% were hospitalized, outpatients and HCW, respectively. With regard to the mortality rate in hospitalized patients and the significant association with Ct under 20 and 30, it seems that the early detection and the initial quantification of SARS-CoV-2 in the first week of the conflict and therapeutic considerations to reduce the relative load can reduce the mortality rate.

**Keywords:** COVID-19, Hospitalized, Health care worker, Outpatient, Cycle threshold (Ct)

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The World Health Organization (WHO) was notified in December 2019 of a pneumonia outbreak in Wuhan, Hubei Province, China, with unknown etiology(1). The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic was declared a public health emergency of international concern by WHO on January 30, 2020 (2). COVID-19 is transmitted from person to person by droplets, feces-oral, and direct touch, and has a 2–14-day incubation period. The global mortality rate is varying in different places, countries, and patient categories (3). The United States, India, and Brazil are the three countries in the world with the highest total number of confirmed cases. Iran is one of the nations afflicted by the COVID-19 outbreak, with a large number of confirmed cases and deaths associated with the disease(4). A total of 6.69M people were infected with the virus and 133,000 people died until February 9, 2022.



Babol is as an overgrown city located in the North of Iran. This city experienced six waves of the disease epidemic until February 2022(5). Older patients with medical comorbidities are at higher risk of severe COVID-19 (6). Large number of hospitalized patients, particularly patients that are eventually in the ICU either lost their lives, experienced comorbidities, including cardiovascular disease (CVD), diabetes, cancer and so on (7). With increasing mortality, hospitalization of COVID -19 patients as well as outpatients has become a serious problem in the community but, health care workers (HCWs) are at an elevated risk of contracting infectious diseases because of their job exposure (8). This could be even more problematic. Given COVID-19's rapid expansion, the following scenario has become a global challenge: health-care systems are overburdened in terms of organizational, clinical, and ethical elements, with a large number of weary, unwell health-care personnel, culminating in a high number of deaths (9). The importance of nosocomial transmission of SARS-CoV-2 is becoming more apparent. Importantly, studies reveal that nosocomial transmission may have a higher severity and mortality risk than community-acquired COVID-19 (10). This pneumonia has a significant mortality rate in specific populations, such as the elderly and those with diabetes, hypertension, and other comorbidities, and it is rapidly and sustainably expanding throughout the community. Severe instances can result in death, and the mortality rate for hospitalized patients is currently between 2% and 3% (11, 12).

The most sensitive and specific technique is the real-time reverse transcription polymerase chain reaction (rRT-PCR), which was used to identify viral RNA from a throat nose self-swab (13). However, rRT-PCR does not distinguish between infectious and non-infectious virus. A number of amplification cycles necessary for the target gene to exceed a threshold level are represented by rRT-PCR cycle threshold (Ct) values(14). As a result, Ct values are inversely related to viral load and can be used to estimate the number of copies of viral RNA in a sample(15). Though, as highlighted by recent studies, since numerous aspects such as sample type, sampling time, assay design, and report interpretation cannot be directly influenced, Ct data must be regarded with caution (16). Moreover, COVID-19 viral load may be linked to infectivity, disease phenotype, morbidity, and mortality (17). To date, there is not sufficient information in Babol, northern Iran, of this disease and many angles remain unclear, therefore the investigation of this emerging infection is an essential issue.

Thus, the present study aimed to investigate the one-year prevalence of SARS-CoV-2, common comorbidities and demographic information among negative- and positive rRT-PCR in HCW, the hospitalized and the outpatients. Also, the association between Ct value and the outcomes of patients were analyzed in Babol, northern Iran.

## Methods

**Patients and study design:** From March 2020 to March 2021, the records of 19772 hospitalized, outpatient and HCW suspected to COVID-19 who were referred to teaching hospitals (Ayatollah Rohani, Shahid Beheshti, Shahid Yahyanejad and Amirkola Children Hospital) affiliated to Babol University of Medical Sciences (MUBABOL) were collected in the North of Iran. This study was approved by the Research Ethics Committee of Babol University of Medical Sciences, Babol, Iran with ethics code IR.MUBABOL.REC.1400.012.

**Data collection:** Demographic data, underlying disorders, and clinical outcomes were collected at the hospital centers using electronic medical records. For each participant, we additionally gathered the Ct values characteristics from molecular detection lab. Patients with missing oropharyngeal and nasopharyngeal swab samples, unclear rRT-PCR results, samples evaluated on a different diagnostic platform or at a different institution were also eliminated. Therefore, of these, 536 cases were excluded from the study and 19232 cases were enrolled to our study.

**Viral nucleic acid extraction and rRT-PCR reaction for SARS-CoV-2 detection:** After viral RNA extraction of oropharyngeal and nasopharyngeal swab samples according to the manufacturer's instructions, rRT-PCR was performed to determine the presence of SARS-CoV2 RNA. Ct value was used to determine the relative virus load of their swab samples based on ABI One Step rRT-PCR results. Patients were divided into three groups based on diagnostic Ct values: Ct: 10 to 20 as group A, Ct: 21 to 30 as group B, and Ct: 31 to 40 as a group C (18, 19).  
**Statistical analysis:** SPSS software, (Version 16) was used for data analysis .Chi-square and Fisher's exact tests were used to perform intergroup and categorical comparisons as appropriate. Also, to analyze the difference between proportions, two-sample z-test formula was used.  $P < 0.05$  were considered statistically significant. Besides, multiple logistic regression ("enter" method) was used to predict case-fatality based on sex, age, Ct value and type of sample.

## Results

Out of the 19232 suspected COVID-19 patients, 7251 (37.7%) had a positive rRT-PCR result; 652 (9%), 4599 (63.4%) and 2000 (27.6%) were categorized as HCW, the hospitalized and the outpatients, respectively. According to the sex distribution, 435 (66.7%), 2346 (51%) and 1048 (52.4%) of HCW, hospitalized and outpatient were males. Moreover, among the hospitalized and the outpatient group, 10.2 and 0.8% cases died, whereas no death cases were reported in the HCW. Based on age distribution, the highest and the lowest positive cases belong to the group 45-64 years (37.2%) and the group 1-14 years (1.6%), respectively.

Statistical analysis of age distribution showed that the occurrence of positive rRT-PCR among the group of 45-64

and the age group  $\geq 65$  years was significantly high compared to the cases with negative rRT-PCR, shown in table 1.

Based on sex distribution, most cases were males (3829; 52.8%) followed by female (3422; 47.2%) patients. Statistical analysis of sex distribution revealed that the occurrence of positive rRT-PCR was significantly more in male than female cases ( $p < 0.001$ ). As seen in table 1, among the positive rRT-PCR cases, the most frequent comorbidities were CVD (24.9%), followed by diabetes (22.4%) and hypertension (12.7%), which are significantly higher than the negative rRT-PCR cases. Moreover, 31.2% of positive rRT-PCR cases had at least one comorbidity. The details of positive and negative rRT-PCR results based on gender and age distribution and comorbidity are presented in table 1.

**Table 1. Demographic, outcome and comorbidities information of suspected patients with COVID-19 in North of Iran.**

Variable	Total (n=19232) Number (%)	PCR negative (n=11981) Number (%)	PCR positive (n=7251) Number (%)	p-value
<b>Age</b>				
Mean $\pm$ SD	49.7 $\pm$ 21.5	47.7 $\pm$ 22.6	53 $\pm$ 19	<0.001
<1	232 (1.2)	194 (1.6)	38 (5)	
1-14	860 (4.5)	743 (6.2)	117(1.6)	
15-24	1107 (5.8)	877 (7.3)	230 (3.2)	
25-44	5675 (29.5)	3595 (30)	2080 (28.7)	<0.001
45-64	6131 (31.9)	3437 (28.7)	2694 (37.2)	
$\geq 65$	5209 (27.1)	3122 (26.1)	2087 (28.8)	
<b>Sex</b>				
Male	9699 (50.4)	5870 (49)	3829 (52.8)	<0.001
Female	9533 (49.6)	6111 (51)	3422 (47.2)	
<b>Outcome</b>				
Discharge	18370 (95.5)	11602 (96.8)	6768 (93.3)	<0.001
Death	862 (4.2)	379 (3.2)	483 (6.7)	
<b>Comorbidity</b>				
Cardiovascular disease	4470 (23.2)	2666 (22.3)	1804 (24.9)	<0.001
Diabetes	3521 (18.3)	1898 (15.8)	1623 (22.4)	<0.001
Hypertension	1955 (10.2)	1036 (8.6)	919 (12.7)	<0.001
Brain and neurologic disorder	851 (4.4)	604 (5)	247 (3.4)	<0.001
Kidney diseases	724 (3.8)	518 (4.3)	206 (2.8)	<0.001
Malignancy	760 (4)	594 (5)	166 (2.3)	0.42
Respiratory disorder	827 (4.3)	526 (4.4)	301 (4.2)	<0.001
GI diseases	114 (0.6)	87 (0.7)	27 (0.4)	<0.001
Blood disorder	181 (0.9)	135 (1.1)	46 (0.6)	<0.001
Liver disease	147 (0.8)	102 (0.9)	45 (0.6)	0.027
Pregnancy	309 (1.6)	167 (1.4)	142 (2)	<0.001
No-Comorbidity	9698 (50.4)	6252 (52.2)	3446 (47.5)	
Comorbidity	5734 (29.8)	3469 (29)	2265 (31.2)	<0.001
Comorbidity 1 $\leq$	3800 (19.8)	2260 (18.9)	1540 (21.2)	

According to two-sample z-test formula, among the hospitalized patients, CVD (33.9%), diabetes (26.5%), brain and neurologic disorder (BND) (4.8%) and kidney diseases (3.8%) were the most common comorbidities, which are significantly higher than the HCW and the outpatients ( $p < 0.001$ ) (table 2). While, hypertension (15.9%), respiratory disorder (6.6%) and blood disorder (0.9%) had higher rates in the outpatient vs. other cases ( $p < 0.001$ ) (table 2).

Based on the distribution of the Ct values, 1196 (16.5%) of patients had Ct between 10 and 20 (group A), 3260 (45.1%) of patients had Ct between 21 and 30 (group B), 2779 (38.4%) of patients had Ct between 31 and 40 (group C). The overall median Ct value of an individual's first positive test was  $27.6 \pm 6.6$ . Accordingly, among the HCW and the hospitalized cases, the majority cases (39.4% and 50%) belonged to group

B, while, among outpatient, the majority cases (36.6%) belonged to group C.

In all cases, it seems that death rate was significantly different between the three groups of Ct value, the highest mortality is in those with Ct between 20 and 30 (group B = 7.6%) and the lowest in the group C (group C = 5.5%) ( $p < 0.001$ ). Moreover, it seems that having one or more underlying conditions were not significantly different between the three groups, the highest comorbidities are in those with Ct between (group A) ( $P = 0.072$ ). The details of demographic and comorbidities information among positive SARS-CoV-2 rRT-PCR based on Ct value are presented in tables 3 and 4. Adjusted odds ratio revealed that the mortality rate of patients who had Ct value in the range of 21 to 30 is 2.3 times higher than the people with Ct in the range of 10 to 20 (table 5).

**Table 2: Demographic, outcome and comorbidities information of patients with positive SARS-CoV-2 rRT-PCR based on type of patients in North of Iran.**

Variable	HCW (n=652) Number (%)	Hospitalized (n=4599) Number (%)	Outpatient (n=2000) Number (%)	p-value
<b>Age</b>				
Mean±SD	36.8±9.7	54.5±23.3	45.6±17.8	<0.001
<1	0 (0)	28 (0.6)	9 (0.5)	
1-14	0 (0)	104 (2.3)	12 (0.6)	
15-24	36 (5.5)	83 (1.8)	113 (5.7)	
25-44	472 (72.4)	918 (20)	690 (34.5)	<0.001
45-64	142 (21.8)	1793 (39)	759 (38)	
≥65	2 (0.3)	1669 (36.3)	416 (20.8)	
<b>Sex</b>				
Female	435 (66.7)	2346 (51)	1048 (52.4)	<0.001
Male	217 (33.3)	2253 (49)	952 (47.6)	
<b>Outcome</b>				
Discharge	652 (100)	4131 (89.8)	1985 (99.3)	<0.001
Death	0 (0)	468 (10.2)	15 (0.8)	
<b>Comorbidity</b>				
Cardiovascular disease	10 (1.5)	1558 (33.9)	236 (11.8)	<0.001
Diabetes	15 (2.3)	1219 (26.5)	389 (19.5)	<0.001
Hypertension	9 (1.4)	593 (12.9)	317 (15.9)	<0.001
Brain and neurologic disorder	4 (0.6)	221 (4.8)	22 (1.1)	<0.001
Kidney diseases	1 (0.2)	176 (3.8)	29 (1.5)	<0.001
Malignancy	1 (0.2)	126 (2.7)	39 (2)	<0.001
Respiratory disorder	7 (1.1)	162 (3.5)	132 (6.6)	0.42
GI diseases	0 (0)	13 (0.3)	14 (0.7)	0.002
Blood disorder	0 (0)	28 (0.6)	18 (0.9)	<0.001
Liver disease	2 (0.3)	34 (0.7)	9 (0.5)	0.07
Pregnancy	1 (0.2)	42 (0.9)	99 (5)	0.003
No-Comorbidity	596 (91.4)	1971 (42.9)	879 (44)	

Comorbidity	52 (8)	1363 (29.6)	850 (42.5)	<0.001
Comorbidity 1≤	4 (0.6)	1265 (27.5)	271 (13.6)	

**Table 3: Demographic and comorbidities information of patients with positive SARS-CoV-2 rRT-PCR based on cycle threshold value (Ct) in Babol County, North of Iran.**

Variable	A (Ct: 10-20) 1196 (16.5%)	B (Ct: 21-30) 3260 (45.1%)	C (Ct: 31-40) 2779 (38.4%)	p-value
<b>Type of admission</b>				
HCW	197 (30.4)	256 (39.4)	196 (30.2)	
Hospitalized	445 (9.7)	2299 (50)	1855(40.3)	<0.001
Outpatient	554 (27.9)	705 (35.5)	728 (36.6)	
<b>Age</b>				
<1	7 (0.6)	14 (0.4)	17 (0.6)	
1-14	20 (1.7)	31 (1)	66 (2.4)	
15-24	50 (4.2)	84 (2.6)	95 (3.4)	
25-44	411 (34.4)	889 (27.3)	773 (27.8)	<0.001
45-64	406 (33.9)	1276 (39.2)	1009 (36.3)	
≥65	302 (25.3)	962 (29.5)	818 (29.4)	
<b>Sex</b>				
Male	654 (54.7)	1692 (51.9)	1473 (53)	0.24
Female	542 (45.3)	1568 (48.1)	1306 (47)	
<b>Outcome</b>				
Discharge	1115 (93.2)	3011 (92.4)	2627 (94.5)	0.003
Death	81 (6.8)	249 (7.6)	152 (5.5)	
<b>Comorbidity</b>				
No-Comorbidity	538 (45)	1556 (47.7)	1342 (48.3)	0.072
Comorbidity	415 (34.7)	992 (30.4)	854 (30.7)	
Comorbidity 1≤	243 (20.3)	712 (21.8)	583 (21)	

**Table 4: The details of patients with positive SARS-CoV-2 rRT-PCR based on cycle threshold value (Ct) in North of Iran.**

Patient	Variable	A (Ct: 10-20) N (%)	B (Ct: 21-30) N (%)	C (Ct: 31-40) N (%)	p-value
HCW	Mean±SD*		25.4 ±7.4		
	<1	0	0	0	
	1-14	0	0	0	
	15-24	13 (6.6)	18 (6.7)	6 (3.1)	0.5
	25-44	142 (72.1)	188 (73.4)	139 (70.9)	
	45-64	42 (21.3)	50 (19.5)	50 (25.5)	
	>65	0	1 (0.4)	1(0.5)	
	Female	126 (64)	176 (68.8)	130 (66.3)	0.56
	Male	71 (36)	80 (31.3)	66 (33.7)	
	Discharge	197 (100)	256 (100)	196 (100)	-
	Death	0	0	0	
	No-Comorbidity	172 (87.3)	239 (93.4)	182 (92.9)	
	Comorbidity	25 (12.7)	15 (5.9)	12 (6.1)	.039
	Comorbidity 1≤	0	2 (0.8)	2 (1)	

	Mean±SD		28.4±5.8		
Hospitalized	<1	2 ( 0.4)	9 (0.4)	17 (0.9)	
	1-14	20 (4.5)	27 (1.2)	57 (3.1)	
	15-24	12 (2.7)	36 (1.6)	35 (1.9)	
	25-44	80 (18)	499 (21.7)	339 (18.3)	<0.001
	45-64	146 (32.8)	932 (40.6)	715 (38.5)	
	>65	185 (41.6)	792 (34.5)	692 (37.3)	
	Female	228 (51.2)	1149 (50)	969 (52.2)	0.34
	Male	217 (48.8)	1150 (50)	886 (47.8)	
	Discharge	368 (82.7)	2054 (89.3)	1709 (92.1)	
	Death	77 (17.3)	245 (10.7)	146 (7.9)	<0.001
	No-Comorbidity	160 (36)	1036 (22.5)	775 (41.8)	
	Comorbidity	125 (28.1)	659 (28.7)	579 (31.2)	<0.001
	Comorbidity 1≤	160 (36)	604 (26.3)	501 (27)	
	Mean±SD		26.5±7.7		
Outpatient	<1	4 (0.7)	5(0.7)	0	<0.001
	1-14	0	3 (0.4)	9 (1.2)	
	15-24	26 (4.7)	32 (4.5)	54 (7.4)	
	25-44	189 (34.1)	202 (28.7)	295 (40.6)	
	45-64	218 (39.4)	294 (41.7)	244 (33.6)	
	>65	117 (21.1)	169 (24)	125 (17.2)	
	Female	300 (54.2)	367 (52.1)	374 (51.4)	0.6
	Male	254 (45.8)	338 (47.9)	354 (48.6)	
	Discharge	550 (99.3)	701 (99.4)	722 (99.2)	
	Death	4 (0.7)	4 (0.6)	6 (0.8)	0.83
	No-Comorbidity	206 (37.2)	281 (39.9)	385 (52.9)	
	Comorbidity	265 (47.8)	318 (45.1)	263 (36.1)	<0.001
	Comorbidity 1≤	83 (15)	106 (15)	80 (11)	

\*Mean(±SD) of Ct value among three group were significant

**Table 5: Summary of Multiple Logistic Regression Results to Predict Mortality**

Variable	B	OR	95% CI	Type of admission	p-value
<b>Ct</b>					
10-20		1	-	-	
21-30	0.843	2.32	1.72-3.13		<0.001
31-40	0.338	1.4	1.13-1.74		0.002
<b>Sample</b>	-2.70	0.067	0.03-0.11		<0.001
<b>Sex(M/F)</b>	0.213	1.23	1.01-1.5		0.032
<b>Age</b>					
<1	-	1	-	-	
1-14	17.8	0.98	0.95-9.6		0.95
15-24	0.12	0.88	0.08-8.87		0.08
25-44	0.45	0.95	0.12-7.25		0.12
45-64	0.87	2.4	0.32-17.9		0.32
>65	1.65	5.3	0.7-38.9		0.7
<b>No-Comorbidity</b>	-	1	-	-	

<b>Comorbidity</b>	0.78	1.08	0.84-1.37	0.52
<b>Comorbidity 1≤</b>	0.48	1.04	0.81-1.34	0.7

## Discussion

To the best of our knowledge, this is the first study from Iran that evaluated the consequences and demographic characteristics in three groups of patients with, COVID-19 infection (hospitalized, outpatient and HCWs) during one year. As depicted in table 1, the incidence of COVID-19 in some age groups (45-64 and  $\geq 65$  years) was significantly high than those with negative SARS-CoV-2. Moreover, based on our results, the mean age of positive cases were 53 years, which were significantly higher than the negative cases. Goshayeshi et al. (2021), in Mashhad (northeast Iran) showed that the most COVID-19 infections happened in the 50–59 and 60–69-year age groups (20).

Interestingly, these researchers found that the prevalence of COVID-19 was also notable in the 30–39 and 40–49 years-old groups. The high frequency of the infection in these age groups may be related to the low average age of Iranian population and working-age in these groups.

The age categorizing the patients in our study was from  $<1$  year to  $\geq 65$ , which contradicts the studies directed from China (clustering of cases between 30 and 80 years of age) and India (between 20 and 60 years-old patients). Singla et al. (2021) attributed the higher incidence of COVID-19 in the young Indian population to the geographical distribution of flu-like symptoms (21). In our study, most cases were males (52.8%). In line with other studies, sex distribution in COVID-19 patients were 62%, 54.3%, 60% and 63% in Iran (20), China (22), Italy (23) and United States (24), respectively. According to our results, the most frequent comorbidities were CVD, followed by diabetes, which are significantly higher than negative rRT-PCR cases. Moreover, among the hospitalized patients, two-sample z-test formula for the difference between proportions shows CVD and diabetes were the most common comorbidities, which are significantly higher than the HCW and the outpatients ( $p < 0.001$ ).

In partial agreement with our finding, Solomon et al. (2021) recommended that comorbidities such as hypertension, diabetes, obesity, chronic obstructive pulmonary disease (COPD) and CVD increase the risk of severity and death from COVID-19 (25). Though, there are significant differences in demographic patterns and illness trends between high-income and low- and middle-income countries. On the other hand, age-related diseases such as diabetes and CVD increase the

risk of death from COVID-19 (26-28). In a systematic review and meta-analysis study, the total frequency of comorbidities in the HCWs was 18.4% (95% CI 15.5–21.7), the most prevalent was hypertension 2.5%, CVD 2.4%, COPD 2.4%, and diabetes 1.4% (29).

Khaksar et al. (2021) found that male gender, older age, hyperlipidemia, liver failure, TB, having more than one comorbidity, and elevated inflammatory biomarkers were significantly associated with the risk of severe COVID-19 disease (30). These results are almost consistent with our study. Albadawy et al. (2021) showed that multiple comorbidities in COVID-19 cases are linked to severe clinical symptoms, disease complications, and critical illness progression. So, in concordance with our data, the presence of one or more comorbidities worsened the survival rate of patients (31). Trunfio et al. (2021) stratified patients according to their Ct values as follows: Group A  $\leq 20.0$ ,  $20.0 < \text{group B} \leq 28.0$ , and group C  $> 28.0$ . They showed patients with a Ct  $\leq 28.0$  have a higher viral burden and likely a still replicating virus as testified by viral antigen expression (32). Shah et al. (2021) concluded that the odds of increased disease severity and mortality were less pronounced in patients with Ct values of 25–30 compared with  $> 30$  (33).

In a study by Ramirez-Hinojosa et al. (2021), Ct values obtained by rRT-PCR with clinical and laboratory data from the saliva of 58 inpatients with COVID-19 and 105 asymptomatic health workers (AHW) were examined. The positive rates for inpatients and AHW were 88% and 8%, respectively. The results showed that patients with Ct  $< 38.0$  needed more mechanical ventilation ( $P = 0.013$ ) (34). According to our results the mortality rate of patients who had Ct value in the range of 21 to 30 is 2.3 times higher than those with Ct in the range of 10 to 20. In this regard, Waudby-West et al. showed that a low initial Ct value was associated with increased hazard of mortality compared to a high initial Ct value (19). Moreover, Magleby found that patients admitted to the hospital with high SARS-CoV-2 virus loads, as measured by Ct values, were more likely to be intubated or die during their stay. Even after controlling for age, comorbidities, presenting symptoms, chest radiography results, and the degree of presenting hypoxia, the association remained (35).

The limitations of the present study include the following: (1) the ambiguity of clinical signs (2) the lack of computed tomography scan (CT scan) of patients and (3) the possible pre-analytical errors. Therefore, it is suggested that the clinical and para-clinical symptoms of patients with Ct value, length of hospitalization, outcomes, and comorbidities over a longer period of time. It is also recommended that sensitivity, specificity, and predictive values (negative and positive) of different laboratory kits be evaluated to determine the loading of different SARS-CoV-2 variants.

In summary, 37.7% of cases were positive for SARS-CoV-2; of which 63.4, 27.6 and 9% were hospitalized, outpatients and HCW, respectively. In this regard, 10.2 and 0.8% of the hospitalized and the outpatients died, whereas no death case was reported in the HCW. Also, the most common comorbidities were CVD, followed by diabetes and hypertension which are significantly higher than negative rRT-PCR cases. Regarding the mortality rate in hospitalized patients and significant association with Ct under 20 and 30, it seems that early detection and initial quantification of SARS-CoV-2 is important to reduce the relative load and can reduce the mortality rate.

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## References

1. She J, Jiang J, Ye L, et al. 2019 novel coronavirus of pneumonia in Wuhan, China: emerging attack and management strategies. *Clin Transl Med* 2020; 9: 19.
2. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *Int J Antimicrob Agents* 2020; 55: 105924.
3. Halaji M, Farahani A, Ranjbar R, Heiat M, Dehkordi FS. Emerging coronaviruses: first SARS, second MERS and third SARS-CoV-2: epidemiological updates of COVID-19. *Infez Med* 2020; 28: 6-17.
4. Rassouli M, Ashrafzadeh H, Shirinabadi Farahani A, Akbari ME. COVID-19 management in Iran as one of the most affected countries in the world: advantages and weaknesses. *Front Public Health* 2020; 8: 510.
5. Worldometers. Total coronavirus cases in Iran. Available at: <https://www.worldometers.info/coronavirus/country/iran/>
6. Asai Y, Nomoto H, Hayakawa K, et al. Comorbidities as risk factors for severe disease in hospitalized elderly COVID-19 patients by different age-groups in Japan. *Gerontology* 2022; 7: 1-11.
7. Caballero AE, Ceriello A, Misra A, et al. COVID-19 in people living with diabetes: An international consensus. *J Diabetes Complications* 2020; 34: 107671.
8. Nguyen LH, Drew DA, Graham MS, et al. Risk of COVID-19 among front-line health-care workers and the general community: a prospective cohort study. *Lancet Public Health* 2020; 5: e475-e83.
9. Demartini K, Konzen VM, Siqueira MO, et al. Care for frontline health care workers in times of COVID-19. *Rev Soc Bras Med Trop* 2020; 53:e20200358.
10. Mo Y, Eyre DW, Lumley SF, et al. Transmission of community- and hospital-acquired SARS-CoV-2 in hospital settings in the UK: A cohort study. *PLoS Med* 2021; 18: e1003816.
11. Simpson S, Kay FU, Abbara S, et al. Radiological society of north America expert consensus statement on reporting chest ct findings related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA- Secondary Publication. *J Thoracic Imaging* 2020; 35: 219-27.
12. Macedo A, Gonçalves N, Febra C. COVID-19 fatality rates in hospitalized patients: systematic review and meta-analysis. *Ann Epidemiol* 2021; 57: 14-21.
13. Sabati H, Mohsenzadeh A. COVID-19 and respiratory tract viral co-infections: Choosing the screening method. *J Curr Biomed Rep* 2021; 2: 1-2.
14. Bonacorsi S, Visseaux B, Bouzid D, et al. Systematic review on the correlation of quantitative PCR cycle threshold values of gastrointestinal pathogens with patient clinical presentation and outcomes. *Front Med* 2021; 8: 711809.
15. Rao SN, Manissero D, Steele VR, Pareja J. A systematic review of the clinical utility of cycle threshold values in the context of COVID-19. *Infect Dis Ther* 2020; 9: 573-86.
16. Rabaan AA, Tirupathi R, Sule AA, et al. Viral dynamics and real-time RT-PCR Ct values correlation with disease severity in COVID-19. *Diagnostics (Basel)* 2021; 11: 1091.

17. Abed HM, Dizaji PP, Hekmatnezhad H, et al. A mini-review of the validity, quality and efficacy of candidate vaccines in controlling the COVID-19. *J Curr Biomed Rep* 2021; 2: 3-7.
18. Karahasan Yagci A, Sarinoglu RC, Bilgin H, et al. Relationship of the cycle threshold values of SARS-CoV-2 polymerase chain reaction and total severity score of computerized tomography in patients with COVID 19. *J Infect Dis* 2020; 101: 160-6.
19. Waudby-West R, Parcell BJ, Palmer CNA, et al. The association between SARS-CoV-2 RT-PCR cycle threshold and mortality in a community cohort. *Eur Respir J* 2021; 58:2100360.
20. Goshayeshi L, Rad MA, Bergquist R, et al. Demographic and clinical characteristics of the severe Covid-19 infections: first report from Mashhad University of Medical Sciences, Iran. *Cold Spring Harbor Laboratory* 2020. Available at: <https://www.medrxiv.org/content/10.1101/2020.05.20.20108068v2.full-text>
21. Singla N, Gowda R, Mohindra R, et al. Clinical spectrum and outcome of patients visiting coronavirus screening centre in North India and clinical predictors for COVID-19. *Fam Med Prim Care Rev* 2021; 10: 454-61.
22. Shi S, Qin M, Shen B, et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. *JAMA Cardiol* 2020; 5: 802-61.
23. Grasselli G, Pesenti A, Cecconi M. Critical care utilization for the COVID-19 outbreak in Lombardy, Italy. *JAMA* 2020; 323: 1545-6.
24. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in critically ill patients in the Seattle Region- Case Series. *N Engl J Med* 2020; 382: 2012-22.
25. Solomon S, Hochman S, Sheikh R, et al. The impact of age, sex, and race on the association of risk factors and mortality in covid-19 patients. *J Infect Dis Epidemiol* 2021; 7: 215.
26. Kang SJ, Jung SI. Age-related morbidity and mortality among patients with covid-19. *Infect Chemother* 2020; 52: 154-64.
27. Rastad H, Karim H, Ejtahed H-S, et al. Risk and predictors of in-hospital mortality from COVID-19 in patients with diabetes and cardiovascular disease. *Diabetol Metab Syndr* 2020; 12: 57.
28. Romero Starke K, Petereit-Haack G, Schubert M, et al. The age-related risk of severe outcomes due to COVID-19 infection: a rapid review, meta-analysis, and meta-regression. *Int J Environ Res* 2020; 17: 5974.
29. Gholami M, Fawad I, Shadan S, et al. COVID-19 and healthcare workers: A systematic review and meta-analysis. *Int J Infect Dis* 2021; 104: 335-46.
30. Khaksar MA, Zanganeh Yousefabadi E, Taleb Zadeh R, et al. Prevalence of comorbidities and its impacts in Hospitalized patients with COVID-19. *J Contemp Med Sci* 2021; 7: 295-302.
31. Albadawy RM, Jadoon BA, Mogahed MM, et al. The Impact of Comorbidities on the Outcomes of Egyptian COVID-19 Patients: A Follow-Up Study. *J Environ Public Health* 2021; 2021: 6662476.
32. Trunfio M, Venuti F, Alladio F, et al. Diagnostic SARS-CoV-2 Cycle threshold value predicts disease severity, survival, and six-month sequelae in COVID-19 symptomatic patients. *Viruses* 2021; 13: 281.
33. Shah VP, Farah WH, Hill JC, et al. Association Between SARS-CoV-2 Cycle Threshold Values and Clinical Outcomes in Patients With COVID-19: A Systematic Review and Meta-analysis. *Open Forum Infect Dis* 2021; 8: ofab453.
34. Ramirez-Hinojosa JP, Rodriguez-Sanchez Y, Romero-Gonzalez AK, et al. Association between cycle threshold (Ct) values and clinical and laboratory data in inpatients with COVID-19 and asymptomatic health workers. *J Med Virol* 2021; 93: 5969-76.
35. Magleby R, Westblade LF, Trzebucki A, et al. Impact of severe acute respiratory syndrome coronavirus 2 viral load on risk of intubation and mortality among hospitalized patients with coronavirus disease 2019. *Clin Infect Dis* 2021; 73: e4197-e205.