

# Estimate and determinants of SARS-CoV-2 RNA clearance time among non-severe COVID-19 patients

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## ABSTRACT

**Objectives:** To estimate SARS-CoV-2 RNA clearance time among non-severe COVID-19 patients and explore factors associated with delayed negative conversion. **Methods:** A retrospective cohort study was conducted at the COVID-19 unit of a tertiary care center in the Western region of Saudi Arabia. Reverse transcriptase-polymerase chain reaction (RT-PCR) confirmed COVID-19 patients diagnosed between April 1 and June 30, 2020, were considered. The primary outcome was the time (days) from disease onset to first negative RT-PCR, which was analyzed using Kaplan-Meier and Cox regression survival methods. Demographic data, clinical history, baseline clinical, radiological and laboratory findings and management, and outcome data were collected and analyzed as factors associated with the viral RNA clearance time. **Results:** One hundred and forty-four patients were included. The mean (standard deviation [SD]) age was 36.93 (14.41) years, 50.7% were females, and 45.1% were healthcare workers. COVID-19 was asymptomatic, mild and moderate in 11.1%, 71.5% and 17.4% of the participants, respectively. Fever (59.4%) and cough (58.0%) were the dominant onset symptoms. The mean viral RNA clearance time was 22.9 days (SD = 8.6; 95% confidence interval [CI] = 21.5–24.3 days). Extended clearance time was associated with older age (mean = 24.0 vs. 22.0 days; log-rank = 0.037), married status (23.2 vs. 22.6 days; log-rank = 0.021), working in health sector (24.2 vs. 21.8 days; log-rank = 0.006), and having a chronic disease (24.8 vs. 21.9 days; log-rank = 0.028), compared to their counterparts, respectively. In the adjusted model, the job sector was the only factor that was independently associated with clearance time. Non-healthcare sector showed hazard ratio 1.8 (95% CI = 1.3–2.7; log-rank = 0.002) with reference to healthcare sector. **Conclusion:** SARS-CoV-2 RNA clearance time is likely to be longer in non-severe COVID-19 patients, representing an additional risk for the virus dissemination among the community and calling for higher caution among the population.

**Keywords:** Clearance, COVID-19, healthcare, negative, RNA, RT-PCR, SARS-CoV-2

## Introduction

Towards the end of 2019 and the start of 2020, the outbreak of a novel airborne viral pandemic, namely COVID-19 (coronavirus disease 2019), was identified from Wuhan, Hubei Province, China.<sup>[1]</sup> The massive impact of this pandemic on the world and the global economy is unprecedented due to the

constant increase of deaths, the continuous panic, adverse effects of lockdown, and social-distancing measures imposed to control the spread of the pandemic.<sup>[2-5]</sup>

Saudi Arabia was one of the countries that implemented early preventive measures against the introduction and local spread of SARS-CoV-2 before the first case was declared in the country on March 2, 2020. Since then, control measures were revised regularly to adapt to the changes of the pandemic and mitigate its socioeconomic impact.<sup>[6,7]</sup>

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The critical issue is to have a strategic plan to return to regular life after several months of the economic shutdown and the social activity.<sup>[8]</sup> As the cases are increasing, it is crucial to have a deeper insight into the infectiousness of convalescent individuals to plan their safe return to workplaces and classrooms. This helps in preventing the secondary spread of the virus along with alleviating staff shortages.

Therefore, understanding the natural history of the viral life cycle in the infected individual is of paramount importance. It is generally reported that the highest RNA titers are reached within 7 to 10 days of symptoms onset, during which the samples should be collected for molecular testing methods for best sensitivity to detect the infection.<sup>[9]</sup> Additionally, several studies have estimated the time between disease onset and negative conversion of Sars-CoV-2 RNA detection in molecular diagnostic methods, as a reflection of the infectiveness time, and analyzed the factors associated with prolonged viral RNA shedding.<sup>[10-15]</sup> However, due to discrepancies in the findings across these studies, it is necessary to obtain the local figures, notably among the individuals with asymptomatic and non-severe forms of the disease. These are the individuals who are at high risk of being undiagnosed or inadequately isolated representing the major vector of the virus dissemination.

This study aimed to estimate the time of Sars-CoV-2 RNA clearance among biologically confirmed non-severe COVID-19 patients and explore factors associated with delayed negative conversion.

## Methods

### Design and participants

A retrospective cohort study was conducted in patients who were diagnosed, managed, and followed up for confirmed COVID-19 between April 1, 2020, and June 30, 2020, at the COVID19 Unit of King Abdulaziz University Hospital, Jeddah, Saudi Arabia.

### Case definition and eligibility criteria

Cases were defined as patients diagnosed using molecular methods including real-time reverse transcription-polymerase chain reaction (RT-PCR) analysis for SARS-CoV-2 in nasopharyngeal swabs, which was collected on the day of the patient presentation. Cases were eligible if they had at least two consecutive negative RT-PCR results. Only non-severe cases were included, whereas severe cases that resulted in the intensive care unit (ICU) admission, long-term hospitalization, death, or severe complications were excluded. Further, patients who were swabbed after the day of presentation and those diagnosed using other methods including imaging, serological tests or based on the clinical presentation and epidemiological context only were not included.

### Data collection procedure

Eligible participants were identified using the hospital electronic registry for COVID-19, and the relevant study data were collected from their respective electronic medical

files using a structured data collection sheet. Collected data included 1) demographic and professional data, including age, gender, marital status, professional status, sector (healthcare vs. non-healthcare), residency (cluster vs. outside cluster); 2) pre-COVID-19 health status, including lifestyle (sleep quality, smoking, physical activity, and dietary habits) and comorbidities (hypertension, diabetes, etc.); 3) parameters on presentation, including the date of first positive RT-PCR, onset symptoms, vital signs at the first consultation, symptoms duration before diagnosis, severity level at the worst clinical status (asymptomatic, mild or moderate), lung involvement, lab findings (leukocytes level, liver function, renal function), thrombosis; 4) management and outcome, including hospital admission, oxygen therapy, continuous positive airway pressure, antibiotic therapy, antiviral therapy, and ICU admission, and date of first negative RT-PCR.

### Statistical methods

Data were collected in Microsoft Excel sheets, then coded and transferred to SPSS for statistical analysis, version 21 for Windows (SPSS Inc., Chicago, IL, USA). The primary outcome, viral RNA clearance time, was calculated as the time, in days, from the first positive RT-PCR to the first negative RT-PCR. Descriptive statistical methods were used to present the demographic and clinical parameters of the study population. Kaplan–Meier survival methods were carried out to analyze the factors associated with SARS-CoV-2 RNA clearance time; results were presented as mean (95% confidence interval [CI]) clearance time with the corresponding log-rank level. Multivariate Cox regression was used to analyze the independent factors of clearance time; results are presented as hazard ratio (HR), with 95% CI. A log-rank value <0.05 was considered for statistical significance.

### Ethical clearance

Data were entered anonymously and coded in Excel sheets, and the database was only shared with trusted collaborators. The study was ethically approved by the institutional review board of King Abdulaziz University.

## Results

### Participants' characteristics

One hundred and forty-four patients were included. The mean (standard deviation [SD]) age was 36.93 (14.41) years, 50.7% were females and 45.1% were healthcare workers. The pre-COVID-19 chronic diseases for these patients included hypertension and type 2 diabetes (14.6% each), and asthma and thyroid disease (4.2% each). Other demographic, lifestyle and medical history data are depicted in Table 1.

### COVID-19-related data

In the majority of the participants (71.5%), COVID-19 was mild, and lung involvement was observed in 32.6%, whereas there were no cases of thrombosis diagnosed. Fever (59.4%) and cough (58.0%) were the dominant onset symptoms, followed

by the sore throat (34.3%), headache (21.7%), and shortness of breath (19.6%) [Table 2 and Figure 1].

Laboratory investigations showed anemia in 27.8% of cases, abnormal liver function in 11.1% of cases, and abnormal renal function in 5.6% of cases. More than half of the participants were hospitalized (53.5%), seven (4.9%) required oxygen therapy (average 5 L/min) and one (0.7%) required continuous positive airway pressure. Antibiotic therapy was required for 29.2% of the patients, whereas 20.1% required antiviral therapy [Table 2].

### Viral RNA clearance time

The mean viral RNA clearance time was 22.9 days (SD = 8.6; 95% CI = 21.5–24.3 days). Normality testing showed Kolmogorov–Smirnov (statistics = 0.094,  $P = 0.004$ ) and Shapiro–Wilk (0.976,  $P = 0.013$ ), indicating the normal distribution of the variable [Figures 2 and 3].

### Factors associated with extended clearance time

Extended clearance time was significantly associated with age >37 years (mean = 24.0 vs. 22.0 days; log-rank = 0.037), married status (23.9 vs. 20.8 days; log-rank = 0.021), working in health sector (24.2 vs. 21.8 days; log-rank = 0.006), and having a chronic disease (24.8 vs. 21.9 days; log-rank = 0.028), compared to their counterparts, respectively. Additionally, clearance time was longer in patients who received antiviral treatment (mean = 26.6 vs. 22.0 days; log-rank = 0.050) compared

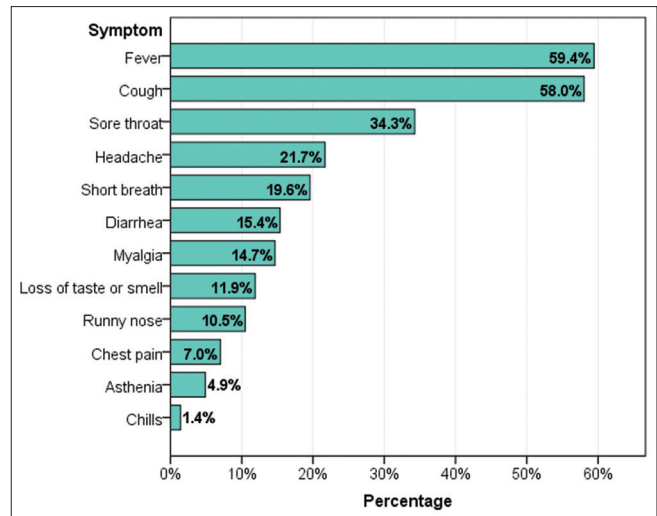


Figure 1: Onset symptoms among COVID-19 patients

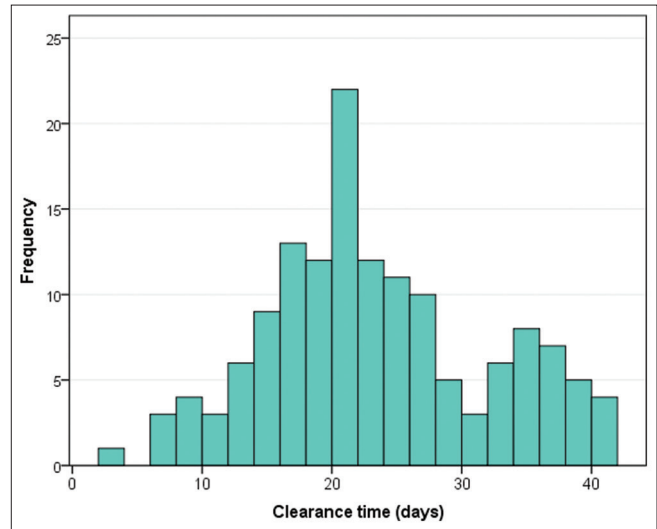


Figure 2: Histogram of COVID-19 PCR clearance time in days among 144 confirmed non-severe cases

Table 1: Participants’ demographics and baseline clinical characteristics (n=144)

Parameter	Category	Frequency	Percentage
Age (y)	Mean, SD (range=1, 77)	36.93	14.41
Gender	Male	71	49.3
	Female	73	50.7
Marital status	Single or separated	49	34.0
	Married	95	66.0
Professional status	Employed	98	68.1
	Non-employed	46	31.9
Job sector	Healthcare	65	45.1
	Non-healthcare	79	54.9
Residency	Cluster	42	29.2
	Outside cluster	102	70.8
Sleep quality	Satisfied	106	73.6
	Unsatisfied	38	26.4
Smoking status	Active smoker	47	32.6
	Non-smoker	97	67.4
Physical activity	Regular	41	28.5
	Irregular	103	71.5
Dietary habits	Healthy	37	25.7
	Unhealthy	107	74.3
Chronic diseases	Hypertension	21	14.6
	Type 2 diabetes	21	14.6
	Thyroid disease	6	4.2
	Asthma	6	4.2
	Heart disease	6	4.2
	Other	12	8.3

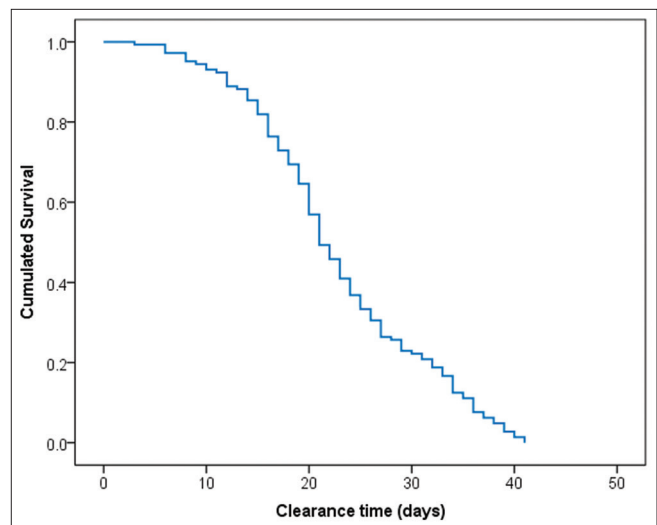


Figure 3: Survival function of COVID-19 PCR clearance among 144 non-severe PCR-confirmed patients

**Table 2: COVID-19 related data: presentation, management and outcomes (n=144)**

Parameter	Category	Frequency	Percentage
<b>Clinical parameters</b>			
Close contact	No	40	27.8
	Yes	104	72.2
Collection site	Nasopharynx	144	100.0
Severity	Asymptomatic	16	11.1
	Mild	103	71.5
	Moderate	25	17.4
Temperature (°C)	Mean, SD (range=36.0, 39.7)	37.2	0.9
Oxygen saturation (%)	Mean, SD (range=90, 100)	98.4	2.0
Pulse (beat/min)	Mean, SD (range=60, 146)	91.8	16.6
Respiratory rate (m/min)	Mean, SD (range=18, 32)	20.8	2.1
Systolic BP (mmHg)	Mean, SD (range=91, 180)	131.0	16.8
Diastolic BP (mmHg)	Mean, SD (range=52, 118)	78.2	12.0
<b>Investigations</b>			
Lung involvement (Radiology)	None	97	67.4
	Yes	47	32.6
Anemia	No	104	72.2
	Yes	40	27.8
Leukocyte	Normal	98	68.1
	Leukocytosis	2	1.4
	Leucopenia	44	30.6
Liver function	Normal	128	88.9
	Abnormal	16	11.1
Renal function	Normal	136	94.4
	Abnormal	8	5.6
Thrombopenia	No	141	97.9
	Yes	3	2.1
Thrombosis	No	143	99.3
	Yes	1	0.7
<b>Management</b>			
Hospital admission	Yes	77	53.5
Oxygen therapy	Yes	7	4.9
CPAP	Yes	1	0.7
Antibiotic therapy	Yes	42	29.2
Antiviral	Yes	29	20.1
Corticosteroids	Yes	0	0.0
ICU admissions	Yes	0	0.0

to those who did not receive. There are other factors worth noting although they did not reach statistical significance. For instance, regular exercise was associated with shorter clearance time (mean = 21.6 vs. 23.6 days; log-rank = 0.076) and moderate severity (27.2 days) versus asymptomatic (22.1 days) and mild (22.1 days) and the comparison approached statistical significance (log-rank = 0.098) [Table 3 and Figure 4].

In the adjusted model, the job sector was the only factor that was independently associated with clearance time as indicated in the non-healthcare sector (hazard ratio [HR] = 1.8, 95% CI = 1.3–2.7; log-rank = 0.002) with reference to healthcare sector [Table 4].

## Discussion

### Summary of findings

The appraisal of viral RNA clearance time and the associated factors represent a crucial epidemiological parameter to

understand and control the spread of SARS-CoV-2 infection. This retrospective cohort study used Kaplan–Meier survival analysis to estimate the viral RNA clearance time and characterize its variance among 144 non-severe RT-PCR confirmed COVID-19 patients. Findings suggest that, on average, SARS-CoV-2 RNA remains detectable in the nasopharynx of the patient for 21 to 24 days. Older age and the existence of comorbidities were among the factors associated with prolonged clearance time, whereas non-healthcare professions were independently associated (HR = 1.8).

### Clearance time

Estimated clearance time in this study was relatively high compared with those reported in the literature. A study by Chen *et al.*<sup>[16]</sup> that included 267 hospitalized COVID-19 patients found the median viral RNA clearance time was 12 days. The viral RNA remained detectable until 21 days among approximately 11% of the patients. Another study by Li *et al.*<sup>[10]</sup> showed comparable

**Table 3: Factors associated with COVID-19 clearance time (Kaplan-Meier analysis)**

Factor	Category	Clearance time (days)			Log-rank
		Mean	95% CI		
Age (y)	≤37	22.0	20.2	23.8	0.037*
	>37	24.0	21.7	26.2	
Gender	Male	22.6	20.8	24.3	0.229
	Female	23.2	21.0	25.4	
Marital status	Single	20.8	18.5	23.2	0.021*
	Married	23.9	22.2	25.7	
Profession	Employed	23.3	21.5	25.1	0.172
	Non-employed	22.0	19.8	24.1	
Job sector	Healthcare	24.2	21.7	26.7	0.006*
	Non-healthcare	21.8	20.3	23.3	
Residency	Cluster	20.6	17.9	23.4	0.134
	Outside cluster	23.8	22.2	25.4	
Sleep quality	Satisfactory	23.1	21.4	24.7	0.944
	Unsatisfactory	22.4	19.6	25.2	
Smoking status	Active smoker	22.6	20.5	24.6	0.472
	Non-smoker	23.0	21.2	24.9	
Physical exercise	Regular	21.2	18.8	23.6	0.076
	Irregular	23.6	21.8	25.3	
Dietary habits	Healthy	21.6	18.4	24.8	0.631
	Unhealthy	23.3	21.8	24.9	
Any chronic disease	No	21.9	20.3	23.6	0.028*
	Yes	24.8	22.1	27.5	
No. symptoms	0	21.9	18.3	25.5	0.808
	1-2	23.3	20.7	25.8	
	3	23.0	20.4	25.5	
	4+	23.0	20.0	26.0	
Severity level	Asymptomatic	22.1	17.6	26.5	0.098
	Mild	22.0	20.3	23.6	
	Moderate	27.2	24.4	30.0	
Lung involvement	No	22.6	20.7	24.4	0.887
	Yes	23.6	21.5	25.6	
Anemia	No	23.1	21.4	24.8	0.441
	Yes	22.4	19.9	24.9	
Leukocytes	Normal	22.4	20.6	24.1	0.293
	Leukocytosis	30.5	11.9	49.1	
	Leukopenia	23.7	21.3	26.1	
Antibiotic	No	22.1	20.4	23.9	0.290
	Yes	24.7	22.5	27.0	
Antiviral	No	22.0	20.4	23.5	0.050*
	Yes	26.6	23.9	29.3	

\*Statistically significant result (Log rank <0.05)

results with a median viral RNA clearance time of 11 days. More than half of the patients achieved viral RNA clearance after 11 days.

A study by Ling *et al.*<sup>[11]</sup> that included 66 COVID-19 convalescent patients showed a mean (95% CI) clearance time of 11.0 (9.0–16.0) days, which is shorter compared to the one observed in the present study. Another study that included 684 adult patients of different severity levels reported a clearance time of <14 days in approximately 30% of the patients. The clearance time was between 14 and 28 days in the other 30% and >28 days among 40% (approximately) of the patients, which is relatively consistent

**Table 4: Predictors of COVID-19 clearance time (Cox regression)**

Factor	Category	Clearance time			Log-rank
		HR	95% CI		
Age (y)	≤37	Ref			0.708
	>37	0.9	0.6	1.5	
Marital status	Single	Ref			0.812
	Married	0.9	0.6	1.5	
Job sector	Healthcare	Ref			0.002*
	Non-healthcare	1.8	1.3	2.7	
Any chronic disease	No	Ref			0.242
	Yes	0.8	0.5	1.2	
Antiviral	No	Ref			0.065
	Yes	0.6	0.4	1.0	

HR: hazard ratio; \*statistically significant result (Log-rank <0.05)

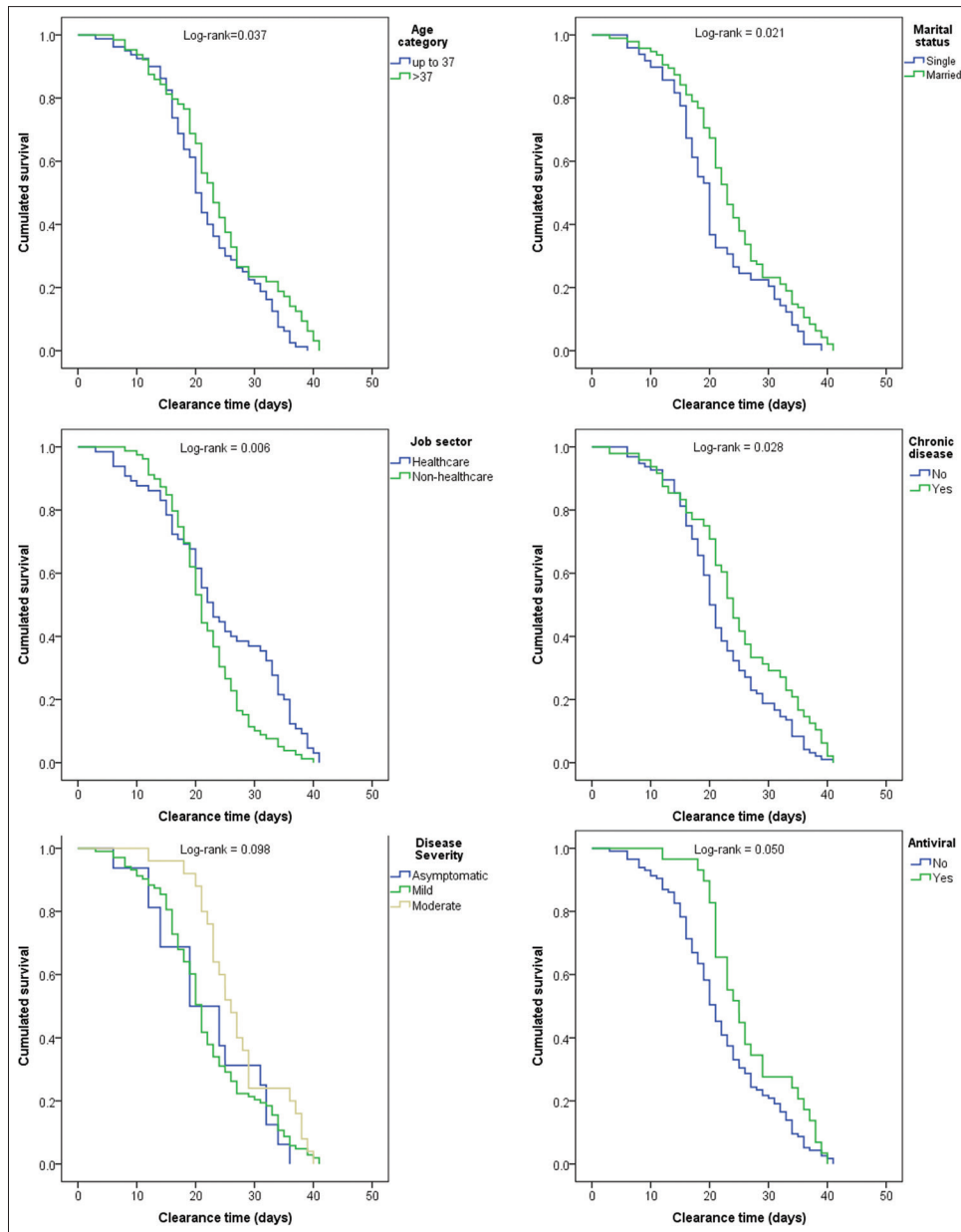
with our findings.<sup>[17]</sup> Another study by Hu *et al.*<sup>[12]</sup> studied the negative conversion rate among 59 cases with different severity levels. They found that only 10.2% achieved negative conversion 7 days after the infection, 62.7% at 14 days and 91.2% at 21 days. Similar to our findings, Fu *et al.*<sup>[13]</sup> reported a median viral RNA clearance time of 19 days in throat-swab specimens of 410 confirmed COVID-19 patients.

### Factors associated with clearance time

Although healthcare workers showed longer clearance time in univariate analysis, the adjusted model revealed an inverse trend where non-healthcare professionals were associated with 1.8 HR for clearance time compared to healthcare professionals. This might be explained due to better awareness of healthcare workers with respect to diagnosis, symptoms, accessibility to testing, etc., This is supported by findings from other studies that showed that longer interval from disease onset to hospital admission was significantly associated with an extended viral RNA clearance.<sup>[14,16]</sup> Further, the present study showed that clearance time was significantly prolonged among older patients and those having comorbidities.

Consistent with our findings, other studies reported age to be significantly associated with RNA viral clearance time in COVID-19. A study by Hu *et al.*<sup>[12]</sup> showed that the conversion rate was lower among patients aged ≥45 years at 14 days (45.2% vs. 82.2%) and 21 days (87.1% vs. 96.5%) compared with their counterparts ( $P = 0.009$ ). In the study by Chen *et al.*<sup>[16]</sup> the median viral RNA clearance time was increased by 2 days in 16 to 49 age category and by 4 days in older categories (>49 years) with reference to <16 years categories where the difference was statistically significant ( $P = 0.018$ ). However, this was not supported by findings from the studies by Ji *et al.* and Xu *et al.*<sup>[14,17]</sup>

The association of SARS-CoV-2 clearance time with baseline clinical and biological parameters explored in other studies showed conflicting findings. For instance, the clearance time was longer in patients with obesity, coronary heart disease, hypertension, diabetes, or hypoalbuminemia, whereas it was shorter in patients with asthma or chronic obstructive pulmonary



**Figure 4:** Factors associated with PCR clearance time among non-severe COVID-19-confirmed patients

disease.<sup>[13,18,19]</sup> The association of cardiovascular diseases with delayed viral RNA clearance was suspected to be associated with a higher expression of angiotensin-converting enzyme 2 (ACE2) in such diseases.<sup>[18]</sup> Another study showed that higher hemoglobin levels were associated with delayed viral RNA clearance. However, this was not reflected in the multivariate analysis.<sup>[10]</sup>

**Other factors associated with clearance time**

In addition to the severity level and presentation symptoms, several other factors associated have been explored by different authors and showed significant association with SARS-CoV-2 clearance time. Although the present study included only non-severe cases, we observed a relatively longer mean clearance time in patients with moderate severity compared with mild or

asymptomatic COVID-19 patients. Additionally, symptomatic forms were associated with extended viral RNA clearance time, irrespective of the number or type of symptoms. This is consistent with findings by Hu *et al.*,<sup>[12]</sup> who reported lower negative conversion rates among severe cases at 2 weeks (44.5% vs. 66.7%) and 3 weeks (81.9% vs. 93.8%) compared to non-severe respectively ( $P = 0.02$ ). Similarly, the study by Ji *et al.*<sup>[17]</sup> found significant positive association of RNA viral clearance time with disease severity ( $P = 0.009$ ). Interestingly, the study by Hu *et al.*<sup>[12]</sup> explored several symptoms separately and found that fatigue and chest tightness were associated with significantly lower negative conversion rates. Other data showed that the presence of diarrhea in the clinical picture was significantly associated with prolonged viral RNA clearance time ( $P = 0.042$ ), and so was muscular pain with a near statistical significance ( $P = 0.085$ ).<sup>[16]</sup> In

contrast, other authors observed that patients with a mild form of COVID-19 had prolonged RNA clearance time compared to those with a severe form of COVID-19. This might be due to the robust immune response in severe forms of the disease, which prompts earlier clearance of the viral RNA.<sup>[15]</sup> This hypothesis might explain the relatively longer clearance time in the present study, where all patients had a mild form of COVID-19. In line with this observation, a study by Antar *et al.*<sup>[19]</sup> demonstrated that the absence of early fever in COVID-19 presentation was associated with delayed viral RNA clearance.

Another factor is the leukocyte level, which showed no significant association with clearance time in the present study. However, Ji *et al.*<sup>[17]</sup> showed a decrease of 40% and 50% in CD4 cells among the patients who had clearance time of 14 to 28 days and >28 days, respectively, compared to those who had shorter clearance time (<14 days). This difference was statistically significant.

Further, a statistically significant decline (50%) in B cells count was observed among patients with prolonged clearance time (>28 days) compared to those with ≤14 days. Similarly, a study by Ling *et al.*<sup>[11]</sup> found that the CD4+ cells count was a significant predictor of viral RNA clearance time, explaining 12% of its variance. Other inflammation markers included in the multivariate model, namely erythrocyte sedimentation rate, C-reactive protein and procalcitonin were not significant predictors. Other authors observed that the clearance of the SARS-CoV-2 among patients with leukopenia was achieved after the restoration of the leukocyte count, notably CD3+, CD4+, and CD8+ T cells and B cells.<sup>[20]</sup>

Gender was one of these factors identified in several studies. For instance, a study by Shastri *et al.*,<sup>[21]</sup> which included 68 patients from the isolation ward found statistically significant prolonged clearance time in males (median = 6 days, range = 1–15 days) compared to females (4 days, 1–10 days). The authors completed these observations by evaluating the expression of mRNA and tissue protein level of ACE2, the plasma membrane-bound receptor that interacts with the SARS-CoV-2 spike protein enabling the virus entry to the host cells. These analyses confirmed the highest ACE2 expression in the testes and testicular proteins, whereas very little expression was observed in the ovarian tissue. Such findings support the prolonged clearance time of the viral RNA in males compared with females and suggest that testicular tissue may serve as a reservoir for the virus. This mechanism may also explain the cases of male gonadal dysfunctions that were observed during the pandemic.<sup>[22]</sup> Another study by Xu *et al.*<sup>[14]</sup> found that male gender was an independent factor associated with the duration of viral RNA detection with a 2.9 odds ratio. However, gender differences observed in the literature are not consistent (e.g., the study by Ji *et al.*<sup>[17]</sup>).

Treatments were also investigated among the factors associated with viral RNA clearance time in COVID-19. The study by Ji *et al.*<sup>[17]</sup> did not show any difference in viral RNA clearance

time in patients who received glucocorticoids compared to those who did not receive in all forms of COVID-19 severity (mild and moderate,  $P = 0.737$ ; severe and critical forms,  $P = 0.471$ ). Conversely, Chen *et al.*<sup>[6]</sup> observed that the viral RNA clearance time was prolonged by 6 days in patients treated with corticosteroids and by 2 days in patients treated with antiviral drugs. Both the treatments remained significant in the multivariate model; however, antibiotic therapy showed no association with RNA clearance time. Another study showed that invasive mechanical ventilation was associated with prolonged duration of viral RNA detection (log-rank < 0.001); however, this was not confirmed in adjusted multivariate analysis ( $P = 0.076$ ).<sup>[14]</sup>

## Limitations

The major limitations of the present study are 1) small sample size impacting the statistical power of the study and 2) retrospective design that might impact the validity of the clearance time measurement, as the monitoring of nasopharynx swabs for RT-PCR was not carried out according to the pre-defined protocol. Additionally, the time between disease onset and first positive RT-PCR may vary between the patients that might have impacted the estimation of the clearance time.

## Conclusion

The SARS-CoV-2 RNA clearance time is likely to be longer in non-severe COVID-19 patients. This represents an additional risk for the virus dissemination among the community alerting for caution. Older age and the presence of comorbidities are likely to prolong the virus clearance time, especially in non-severe forms, symptomatic, and relatively severe forms of COVID-19. With the advent of accurate molecular methods and advances in the understanding of SARS-CoV-2, further studies are warranted to provide updated data for the duration of the infectiveness period and the associated factors, awaiting the achievement of immunization goals.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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