





## Age and clinical signs as predictors of COVID-19 symptoms and cycle threshold value

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### ABSTRACT

Many COVID-19 infected people remain asymptomatic, and hence the diagnosis at first presentation remains a challenge. Assessment at a presentation in primary care settings is usually done by visual triaging and basic clinical examination. This retrospective study involved investigating the medical e-records of COVID-19 positive patients who presented to a COVID-19 centre in Qatar for July 2020. The presence (symptomatic group) or the absence (asymptomatic group) of symptoms along with objective vital examination (*ie*; heart-rate (HR), temperature, haemoglobin saturation (SpO<sub>2</sub>)) were analysed and linked to the viral load (*ie*; cycle threshold (Ct)) of COVID-19 positive patients. Four hundred eighty-one symptomatic (230 males) and 216 asymptomatic (101 males) patients were included. Compared to the asymptomatic male group, the symptomatic male group was older, had lower Ct value and SpO<sub>2</sub>, and higher temperature and HR. Compared to the females asymptomatic group, the symptomatic females group had lower Ct value, and higher temperature. Compared to the asymptomatic group, the symptomatic group had lower Ct value and SpO<sub>2</sub>, and higher temperature and HR. Compared to the asymptomatic group, the symptomatic group had lower Ct values (age groups [21–30], [31–40], [41–50] and [51–60]), higher temperature (age groups [21–30] and [31–40], Ct ranges [20.01–25.00] and [25.01–30.00]), higher HR (age groups [21–30] and [31–40], Ct range [15.01–20.00]); and lower SpO<sub>2</sub> (age groups [41–50] and [51–60], Ct ranges [15.01–20.00] and [35.01–40.00]). Compared with asymptomatic patients, symptomatic patients with COVID-19 are most likely to be febrile, tachycardic, hypoxic and having higher viral load. Higher viral load was associated with higher HR, higher temperature, lower SpO<sub>2</sub>, but there was no relation between viral load and age.

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## 1. Introduction

Since the first report of the unusual cases of types of pneumonia attributed to Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) in December 2019 at Wuhan, China; COVID-19, cases have surged across the world causing considerable strain on the healthcare systems and unprecedented financial recession across the globe [1,2]. As of the 12<sup>th</sup> of November 2021, the reported cases in the World were 252,976,252, and the total deaths reported was at 5,099,860 [3]. The mortality rate varies from country to country and 'seems' low in countries with efficient public health and primary healthcare systems [4]. Qatar has one of the largest numbers of reported COVID-19 positive patients per population, but one of the lowest mortality rates [5,6]. As of the 12<sup>th</sup> of November 2021, the reported cases in Qatar were 240,828, and the total deaths reported was at 611 [3]. The SARS-CoV-2 virus spreads mostly through respiratory droplets during close face-to-face contact,

with an average time from exposure to symptom onset is five days [7]. Initial reports from China showed a high prevalence of symptoms, which were mainly fever in 98%, cough in 77%, and myalgia in 44% of patients examined [8]. However, a richer semiology is starting to be reported in the literature [9–16]. In addition to the cardinal signs of COVID-19 (*i.e.*; fever (88–100%), cough (68–85%), and sputum (23–41%)), several other signs were reported [9–16]: anorexia (84%), asthenia (70–80%), headache (52–55%), ageusia (43%), anosmia (37%), abdominal pain (25%), neuromuscular involvement (19%), dyspnoea (18–85%), odynophagia (19–20%), myalgia (15–48%), confusion (15%), chest pain (6–20%), stroke (6%), rhinitis (5%), nausea/vomiting (4–5%), diarrhoea (4–15%), and haemoptysis (0–5%). Later studies indicated that most of the infected individuals remain asymptomatic or mildly symptomatic [17]. In this context, a Cochrane review analysed 16 studies published between January and April 2020 based on symptoms and

signs of COVID-19 patients [18]. It 'appears' there haven't been any primary care-based studies as per literature review so far [18]. When patients are suspected to have possible COVID-19 symptoms, they are investigated for the same by various testing methods such as reverse transcriptase-polymerase chain reaction (RT-PCR) of nasal and oropharyngeal swabs, saliva-based testing, rapid antigen tests, antibody tests, and high-resolution computed tomography scan of the chest. The most widely used diagnostic tool for the SARS-CoV-2 virus is sampling respiratory secretions using RT-PCR testing of the viral RNA [19–21]. However, the sensitivity of testing varies depending on the adequacy of the specimen, collection technique, time from exposure, and the specimen source [22]. RT-PCR test are reported with cycle threshold (Ct) values. This represents the number of amplification cycles required for the target gene to exceed a threshold level [23]. The Ct values are therefore inversely related to viral load and can provide an indirect method of quantifying the copy number of viral RNA in the sample [23].

In the initial stages of the pandemic, many countries struggled to get the COVID-19 test kits [24] and to ensure the appropriate use of diagnostic tests, healthcare organizations across the world were using clinical tools and triage systems to assess the probability of COVID-19. Quite often, this approach leads medical professionals working in high-incidence and low-resource areas to make decision about testing and the need for quarantine, based on their clinical evaluation [4,25]. To tackle the pandemic efficiently and use limited hospital and intensive care resources appropriately, clinicians need to triage and identify potential COVID-19 patients and higher risk groups early [25]. This is particularly relevant to countries where there is inadequate healthcare infrastructure at the secondary and tertiary care level [4].

In order to tackle the extremely high number of suspected COVID-19 patients, there have been a push across healthcare organisations to use more all-based assessment systems. Thus, the goal of this study was to evaluate if there is any association between symptoms status with age, clinical signs (heart-rate (HR), temperature, and haemoglobin saturation (SpO<sub>2</sub>)), and viral load, and to test if the viral load is associated with age and clinical signs.

## 2. Patients and methods

### 2.1. Case definition

This was a retrospective study, which analyses the medical e-records of the studied population. The authors identified anonymized patient electronic medical records by a database search for patients who presented to Rawdat Al Khail Health Centre (RAK-

HC) for COVID-19 testing during July 2020. RAK-HC in Doha (Qatar) was designated as a COVID-19 assessment and testing centre in early March 2020 after a surge of COVID-19 infections. In the exclusive COVID-19 centres, all patients were assessed, investigated, and managed at the primary care level. Asymptomatic patients with a confirmed contact with COVID-19 positive cases were included in the asymptomatic group. Patients with symptoms highly suspicious of COVID-19 with or without a positive contact were included in the symptomatic group.

### 2.2. Data collection and participants

The electronic medical records of this cohort of patients were assessed, and sex and age were noted. The following eight age groups were identified: [0–10], [11–20], [21–30], [31–40], [41–50], [51–60], [60–70], and > 71 years.

At the first presentation to the health centre, a visual triaging questionnaire was used as a tool to record the presenting symptoms, any history of contact with COVID-19 positive patients. This was done by medical professionals trained to recognize patients who looked unwell on the initial visual assessment. All patients assessed had their vital sign assessment done in a designated area with the following measurements done: tympanic temperature, HR, and SpO<sub>2</sub> using a standard finger probe pulse oximeter. Any abnormal findings (e.g.; fever, low SpO<sub>2</sub>) were alerted, and appropriate upscaling of care with closer monitoring and management was initiated for the relevant cases.

### 2.3. Inclusion and exclusion criteria

Only patients who presented to Rawdat Al Khail Health Centre (RAK-HC) for COVID-19 testing during July 2020 were included. Electronic medical records with missing data were excluded from the statistical analysis.

### 2.4. RT-PCR assay

All symptomatic patients and asymptomatic close contacts of COVID-19 positive patients had oropharyngeal and nasopharyngeal samples taken at the RAK-HC. These were then immediately transported and analysed using RT-PCR in the central laboratory of Hamad Hospital, the government-run secondary care organization in Qatar, as per the accepted Centres for Disease Control and Prevention guidelines [26]. The following six Ct ranges were identified: [10.00–15.00], [15.01–20.00], [20.01–25.00], [25.01–30.00], [30.01–35.00], and [35.01–40.00].

## 2.5. Statistical analysis

Categorical and quantitative data were expressed as number (%) and means  $\pm$  standard deviations. The categorical and quantitative data of two groups (*ie*; asymptomatic vs. symptomatic, males vs. females) were compared via the two-sided chi-2 and Student t tests, respectively. Kruskal-Wallis test was used to compare mean data of symptomatic vs. asymptomatic groups according to eight age groups and six Ct ranges. Significance was set at 0.05%. Statistical analyses were performed using Statistical Package for the Social Sciences version 20.0 [SPSS Inc., Chicago, IL, USA].

## 2.6. Ethics statement

The research was approved by the research committee of the Primary Health Care Corporation (PHCC), which is the major government-funded primary healthcare provider in Qatar. The approval reference number is (Ref No. PHCC/DCR/2020/08/091). All the subjects gave informed consent and patient anonymity was preserved.

## 3. Results

During the study period, 6950 patients were presented to the RAK-HC with possible COVID-19, and underwent RT-PCR testing. Amongst this cohort, 1017 (14.6%) patients were tested positive. After analysing these patients medical e-records, some patient files have missing data (Ct value ( $n = 2$ ), temperature ( $n = 254$ ), HR ( $n = 178$ ), SpO<sub>2</sub> ( $n = 125$ )). The aforementioned files were excluded from statistical analysis, and therefore files of 697 patients were included in this study.

Table 1 exposes the distribution of Covid-19 patients according to gender and presence or not of symptoms. There was no significant difference between the distribution frequencies of symptom

**Table 1.** Covid-19 patients' distribution according to gender and presence or not of symptoms.

		Males	Females	Total sample
Asymptomatic group	Count	101	115	216
	% within diagnostic	46.8	53.2	100
	% within gender	30.5	31.4	31.0
	% of total sample	14.5	16.5	31.0
Symptomatic group	Count	230	251	481
	% within diagnostic	47.8	52.2	100
	% within gender	69.5*	68.6*	69.0*
	% of total sample	33.0*	36.0*	69.0*
Total sample	Count	331	366	697
	% within gender	100	100	100
	% of total sample	47.5	52.5	100

\* $p < 0.05$  (two-sided Chi-2): asymptomatic vs. symptomatic (% within diagnostic or % within gender or % of total sample).

prevalence between males and females. Compared to the asymptomatic group, the symptomatic group included higher frequencies of males (30.5 vs. 60.5%, respectively) and females (31.4 vs. 68.6%, respectively).

Table 2 exposes some descriptive statistics (*i.e.*; age, Ct value, temperature, HR, SpO<sub>2</sub>) in relation to gender. The main conclusions of Table 2 were: *i*) Males and females of the asymptomatic and symptomatic groups have similar data; but in the total sample, compared to males, females were younger, and had a higher SpO<sub>2</sub>, *ii*) Compared to males of the asymptomatic group, males of the symptomatic group were older, had lower Ct values and SpO<sub>2</sub>, and higher temperatures and HR; *iii*) Compared to females of the asymptomatic group, females of the symptomatic group had lower Ct values, and higher temperatures; and *iv*) Compared to the asymptomatic total group, the symptomatic total group had lower Ct values and SpO<sub>2</sub>, and higher temperatures and HR (Figure 1).

Table 3 exposes the comparison of vital signs between the symptomatic and asymptomatic groups among eight age groups. Statistical significant differences were noted for Ct, temperature, HR and SpO<sub>2</sub>. Compared to the asymptomatic group, the symptomatic group had *i*) lower Ct values for the age groups [21–30], [31–40], [41–50], and [51–60] years; *ii*) higher temperature values for the age groups [21–30] and [31–40] years; *iii*) higher HR values for the age groups [21–30] and [31–40] years; and *iv*) lower SpO<sub>2</sub> values for the age groups [41–50] and [51–60] years.

Table 4 exposes the comparison of vital signs between the symptomatic and asymptomatic groups among six Ct ranges. Statistical significant differences were noted for temperature, HR and SpO<sub>2</sub>. Compared to the asymptomatic group, the symptomatic group had *i*) higher temperature values for the Ct ranges [20.01–25.00] and [25.01–30.00]; *iii*) higher HR values for the Ct range [15.01–20.00]; and *iv*) lower SpO<sub>2</sub> values for the Ct ranges [15.01–20.00] and [35.01–40.00].

## 4. Discussion

The main results of the present study including 697 COVID-19 patients were that compared to the asymptomatic patients ( $n = 216$ ), the symptomatic patients ( $n = 481$ ) have higher temperature ( $37.07 \pm 0.50$  vs.  $37.30 \pm 0.71^\circ\text{C}$ , respectively) and HR ( $90.74 \pm 16.67$  vs.  $93.91 \pm 15.67$  bpm, respectively), and lower Ct value ( $24.87 \pm 6.06$  vs.  $22.07 \pm 5.22$ , respectively) and SpO<sub>2</sub> ( $98.26 \pm 1.34$  vs.  $98.00 \pm 1.41$ , respectively). In addition, higher viral load was associated with higher HR, higher temperature, and lower SpO<sub>2</sub>, but there was no relation between viral load and age.

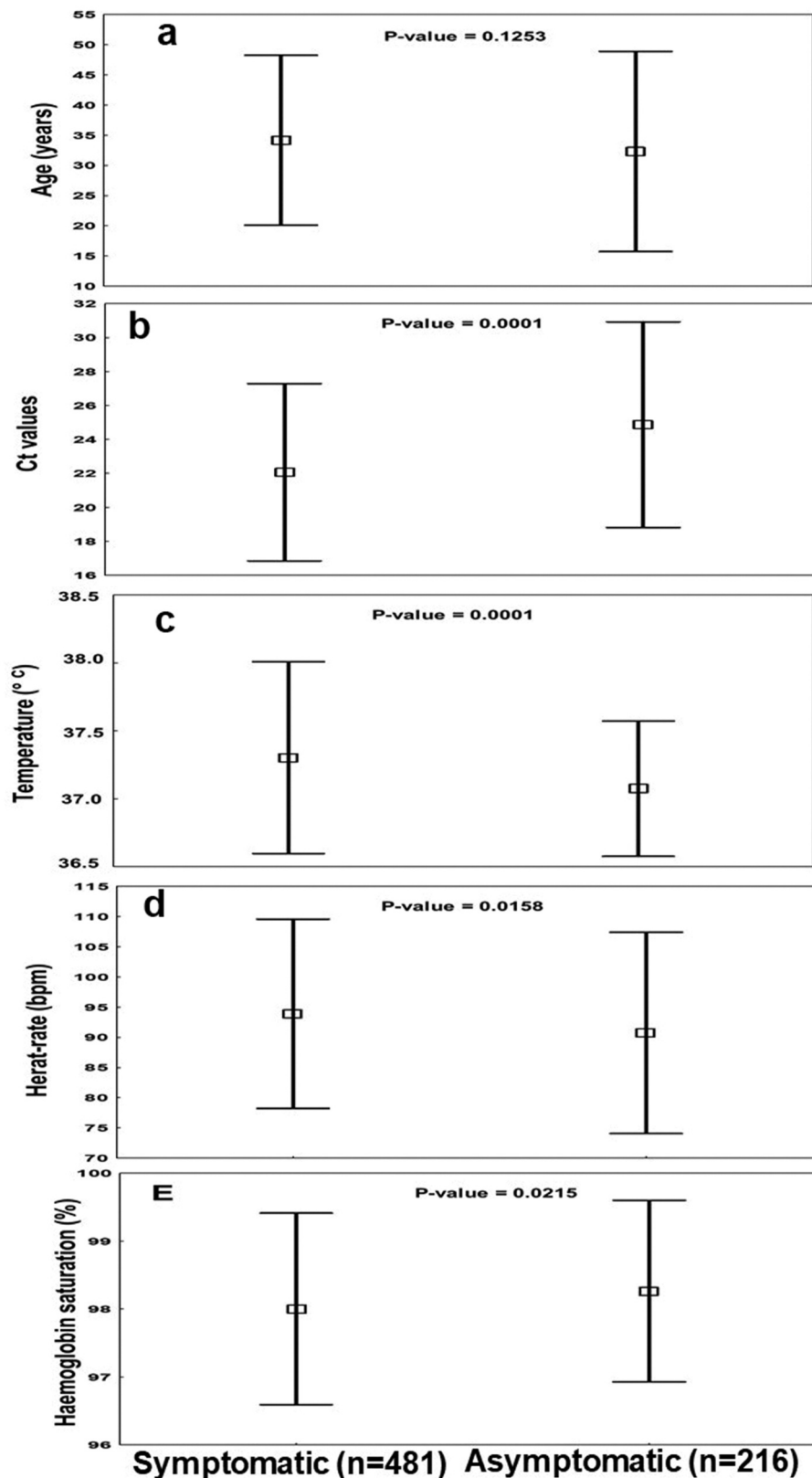
Table 2. Descriptive statistics in relation to gender and sign prevalence.

	Gender	Age (years)	Ct value	Temperature (° C)	Heart-rate (bpm)	SpO <sub>2</sub> (%)
Asymptomatic	Male (n = 101)	31.38 ± 14.980	25.37 ± 6.07	37.05 ± 0.51	88.24 ± 16.13	98.13 ± 1.46
	Female (n = 115)	33.14 ± 17.88	24.43 ± 6.04	37.10 ± 0.49	92.94 ± 16.90	98.38 ± 1.21
	Total (n = 216)	32.31 ± 16.57	24.87 ± 6.06	37.07 ± 0.50	90.74 ± 16.67	98.26 ± 1.34
Symptomatic	Male (n = 230)	36.35 ± 14.12*	21.84 ± 5.13*	37.33 ± 0.75*	93.41 ± 15.81*	97.68 ± 1.34*
	Female (n = 251)	32.20 ± 13.77	22.28 ± 5.31*	37.28 ± 0.67*	94.36 ± 15.57	98.30 ± 1.41
	Total (n = 481)	34.19 ± 14.08	22.07 ± 5.22*	37.30 ± 0.71*	93.91 ± 15.67*	98.00 ± 1.41*
Total	Male (n = 331)	34.84 ± 14.55	22.92 ± 5.66	37.24 ± 0.69	91.83 ± 16.06	97.82 ± 1.39
	Female (n = 366)	32.50 ± 15.16 <sup>#</sup>	22.95 ± 5.63	37.22 ± 0.62	93.91 ± 15.99	98.33 ± 1.35 <sup>#</sup>
	Total (n = 697)	33.6 ± 14.9	22.94 ± 5.64	37.2 ± 0.7	93.00 ± 16.00	98.00 ± 1.00

Data were mean ± SD. **Ct**: cycle threshold. **SD**: standard deviation. **SpO<sub>2</sub>**: haemoglobin saturation.

\*p < 0.05 (T Student test): Asymptomatic vs. Symptomatic (male vs. male, female vs. female, total vs. total).

<sup>#</sup>p < 0.05 (T Student test): male vs. female .



**Figure 1.** Descriptive statistics in relation to sign prevalence (n = 697).

(a). Age. (b). Cycle threshold (Ct). (c). Temperature. (d). Heart-rate. (e). Haemoglobin saturation (SpO<sub>2</sub>). Data were mean (□), standard deviation (I). \*p-value (T Student test): Asymptomatic vs. Symptomatic.

The present study revealed that the symptomatic and asymptomatic groups have similar ages, but symptomatic males were five years older than asymptomatic males (Table 2). Old age is a high-

risk factor for serious outcomes in COVID-19 patients [27]. A study done by Jin et al. [28] identified that males and females have a similar prevalence of COVID-19, but males were found to be

**Table 3.** Symptom prevalence, cycle threshold (Ct), temperature (T), heart-rate (HR), and haemoglobin saturation (SpO<sub>2</sub>) among different age groups.

	Age groups	n	% within diagnostic	% within age groups	% of total	Age	Ct	T	HR	SpO <sub>2</sub>	
Asymptomatic	[0–10]	27	12.5	46.6	3.9	5.37 ± 2.31	25.36 ± 6.80	37.22 ± 0.49	102.59 ± 16.93	98.48 ± 1.09	
	[11–20]	19	8.8	30.2	2.7	14.89 ± 3.20	23.46 ± 5.63	37.24 ± 0.61	100.63 ± 17.81	97.63 ± 1.30	
	[21–30]	55	25.5	35.3	7.9	26.36 ± 2.56	24.29 ± 6.05	37.05 ± 0.46	87.07 ± 16.35	98.44 ± 1.26	
	[31–40]	52	24.1	24.2	7.5	34.79 ± 2.85	25.49 ± 5.55	37.08 ± 0.43	86.08 ± 12.52	98.25 ± 1.62	
	[41–50]	29	13.4	25.9	4.2	44.97 ± 2.82	26.22 ± 6.35	37.03 ± 0.53	89.00 ± 14.91	98.41 ± 1.09	
	[51–60]	24	11.1	35.8	3.4	54.42 ± 3.03	25.08 ± 6.41	36.95 ± 0.52	94.08 ± 18.14	98.46 ± 1.10	
	[61–70]	7	3.2	33.3	1.0	63.57 ± 3.15	20.30 ± 5.8	36.97 ± 0.59	79.14 ± 15.46	96.86 ± 1.57	
	≥ 71	3	1.4	60.0	0.4	79.33 ± 1.15	25.07 ± 4.69	36.40 ± 0.10	86.67 ± 6.11	97.67 ± 0.58	
Total	216	100	31.0	31.0	32.31 ± 16.57	24.87 ± 6.06	37.07 ± 0.50	90.74 ± 16.67	98.26 ± 1.34		
Symptomatic	[0–10]	31	6.4	53.4	4.4	5.74 ± 2.84	24.06 ± 4.70	37.35 ± 0.74	104.94 ± 16.25	98.74 ± 1.18	
	[11–20]	44	9.1	69.8	6.3	15.45 ± 2.65	22.56 ± 5.27	37.22 ± 0.45	96.36 ± 18.43	98.16 ± 1.27	
	[21–30]	101	21.0	64.7	14.5	26.99 ± 2.48	21.61 ± 5.07	37.29 ± 0.76	92.69 ± 15.79	98.10 ± 1.40	
	[31–40]	163	33.9	75.8	23.4	35.12 ± 2.77	21.86 ± 5.56	37.40 ± 0.74	93.33 ± 14.87	98.17 ± 1.23	
	[41–50]	83	17.3	74.1	11.9	44.58 ± 2.84	22.54 ± 5.08	37.23 ± 0.65	92.64 ± 14.42	97.61 ± 1.76	
	[51–60]	43	8.9	64.2	6.2	54.79 ± 2.56	21.20 ± 4.34	37.25 ± 0.68	94.35 ± 14.89	97.49 ± 1.14	
	[61–70]	14	2.9	66.7	2.0	65.07 ± 3.52	21.79 ± 6.28	36.95 ± 0.79	84.86 ± 13.33	97.14 ± 1.61	
	≥ 71	2	0.4	40.0	0.3	84.00 ± 14.14	21.16 ± 3.61	37.80 ± 0.28	84.00 ± 14.14	97.50 ± 0.71	
Total	481	100	69.0	69.0	34.19 ± 14.08	22.07 ± 5.22	37.30 ± 0.71	93.91 ± 15.67	98.00 ± 1.41		
Total sample	[0–10]	58	8.3	100	8.3	5.57 ± 2.59	24.67 ± 5.76	37.29 ± 0.64	103.84 ± 16.47	98.62 ± 1.14	
	[11–20]	63	9.0	100	9.0	15.29 ± 2.81	22.84 ± 5.35	37.23 ± 0.50	97.65 ± 18.21	98.00 ± 1.30	
	[21–30]	156	22.4	100	22.4	26.77 ± 2.52	22.55 ± 5.57	37.20 ± 0.68	90.71 ± 16.17	98.22 ± 1.36	
	[31–40]	215	30.8	100	30.8	35.04 ± 2.79	22.74 ± 5.76	37.32 ± 0.69	91.57 ± 14.65	98.19 ± 1.33	
	[41–50]	112	16.1	100	16.1	44.68 ± 2.83	23.49 ± 5.65	37.19 ± 0.62	91.70 ± 14.57	97.82 ± 1.65	
	[51–60]	67	9.6	100	9.6	54.66 ± 2.72	22.59 ± 5.46	37.14 ± 0.64	94.25 ± 15.99	97.84 ± 1.21	
	[61–70]	21	3.0	100	3.0	64.57 ± 3.40	21.29 ± 5.84	36.96 ± 0.71	82.95 ± 13.96	97.05 ± 1.56	
	≥ 71	5	0.7	100	0.7	81.20 ± 7.56	23.50 ± 4.34	36.96 ± 0.78	85.60 ± 8.41	97.60 ± 0.55	
Total	697	100	100	100	33.61 ± 14.91	22.94 ± 5.64	37.23 ± 0.66	92.93 ± 16.04	98.08 ± 1.39		
Asymptomatic vs. symptomatic according to age groups						Kruskal-Wallis test	3.4747	32.4745	13.1635	7.3849	6.4115
						p-value	0.062	0.001 <sup>abcd</sup>	0.0003 <sup>ab</sup>	0.006 <sup>ab</sup>	0.011 <sup>cd</sup>

Data were % and mean ± SD for categorical and quantitative data, respectively.

Age in years, HR in bpm, SpO<sub>2</sub> in %, and T in ° C.

\*p-value (Kruskal–Wallis test) < 0.05: asymptomatic vs. symptomatic for age groups: <sup>a</sup> [21–30]; <sup>b</sup> [31–40]; <sup>c</sup> [41–50]; <sup>d</sup> [51–60].

more at risk for worse outcomes and death, independent of age. However, no studies were found comparing symptomatology between the genders or age groups.

As compared to symptomatic patients, asymptomatic patients had significantly lower mean body temperature (~0.25, ~0.18, ~0.32°C, respectively, for the total group, females, and males) (Table 2). A 2020 meta-analysis of studies conducted in China indicated that fever was the most prevalent symptom in 80.4% of COVID-19 patients [29], while the large case series of hospitalized COVID-19 positive patients in New York reported 30.7% to be febrile at triage [30].

In comparison to asymptomatic patients, the mean HRs for symptomatic patients were significantly higher by ~ 3 bpm for the total group, and by ~ 5 bpm for the male group (Table 2). Tachycardia (in comparison to fever) was not found to be a strong predictor of COVID-19 in the studies conducted in Singapore [31], but there is a need for further comparative studies correlating HRs with symptom prevalence.

In comparison to asymptomatic patients, the mean SpO<sub>2</sub> for symptomatic patients were significantly lower by ~ 0.26% for the total group, and by ~ 0.45% for the male group (Table 2). An

observational study of adult patients with COVID-19 admitted to one acute hospital trust in the UK showed patients who deteriorated in the hospital experienced rapidly worsening respiratory failure, with low SpO<sub>2</sub>, as compared to minor abnormalities in other vital sign parameters [32]. Hence, this is an important sign to be monitored in COVID-19 patients.

We observed a significant difference between symptomatic and asymptomatic COVID-19 positive individuals to their viral loads as measured by the Ct values (Table 4). Some studies have indicated an inverse correlation of initial viral load with duration and severity of COVID-19 symptoms [33], but a systematic review of 18 studies indicated that lower Ct values are potentially associated with worse outcomes in COVID-19 patients [34]. Earlier studies in China indicated viral shedding (measured by Ct values) in confirmed COVID-19 patients peaked on or before symptom onset, with possible transmission happening before first symptoms in the index case [35]. Further studies are required comparing Ct values with symptomatology and disease outcomes, as the results from past studies are conflicting and the present study could not find a significant correlation.

There was a significant correlation of Ct values to vital sign parameters of temperature, HR, and SpO

**Table 4.** Symptom prevalence, cycle threshold (Ct), temperature (T), heart rate (HR) and haemoglobin saturation (SpO<sub>2</sub>) in different Ct ranges.

	Ct Range	n	% within diagnostic	% within Ct range	% of total	Ct	Age	T	HR	SpO <sub>2</sub>
Asymptomatic	[10.00–15.00]	1	0.5	20.0	0.1	14.73	5	37.4	116	98
	[15.01–20.00]	61	28.2	22.8	8.8	17.71 ± 1.30	31.93 ± 17.93	37.18 ± 0.64	91.16 ± 17.09	98.31 ± 1.42
	[20.01–25.00]	53	24.5	27.6	7.6	22.73 ± 1.33	33.45 ± 16.36	37.05 ± 0.51	90.45 ± 17.17	98.19 ± 1.32
	[25.01–30.00]	51	23.6	40.2	7.3	27.59 ± 1.55	32.49 ± 13.16	36.95 ± 0.37	89.12 ± 16.67	98.25 ± 1.18
	[30.01–35.00]	41	19.0	45.6	5.9	32.65 ± 1.36	31.71 ± 18.93	37.09 ± 0.39	91.54 ± 15.24	98.17 ± 1.53
	[35.01–40.00]	9	4.2	56.3	1.3	36.25 ± 0.93	33.00 ± 15.91	37.09 ± 0.29	92.33 ± 19.04	98.89 ± 0.78
Total		216	100	31.0	31.0	24.87 ± 6.06	32.31 ± 16.57	37.07 ± 0.50	90.74 ± 16.67	98.26 ± 1.34
Symptomatic	[10.00–15.00]	4	0.8	80.0	0.6	14.64 ± 0.11	41.25 ± 16.46	37.30 ± 0.95	104.00 ± 10.42	97.75 ± 0.50
	[15.01–20.00]	206	42.8	77.2	29.6	17.60 ± 1.27	35.28 ± 13.47	37.37 ± 0.72	95.02 ± 15.70	97.97 ± 1.34
	[20.01–25.00]	139	28.9	72.4	19.9	22.05 ± 1.33	33.69 ± 15.07	37.31 ± 0.72	95.20 ± 15.06	98.09 ± 1.25
	[25.01–30.00]	75	15.8	59.8	10.9	26.98 ± 1.38	33.54 ± 14.30	37.25 ± 0.68	92.91 ± 17.12	97.82 ± 1.90
	[30.01–35.00]	49	10.2	54.4	7.0	31.82 ± 1.17	30.86 ± 13.20	37.09 ± 0.59	87.37 ± 14.13	98.27 ± 1.34
	[35.01–40.00]	7	1.5	43.8	1.0	36.56 ± 0.90	38.14 ± 12.39	37.41 ± 0.76	86.14 ± 11.02	97.57 ± 0.79
Total		481	100	69.0	69.0	22.07 ± 5.22	34.19 ± 14.08	37.30 ± 0.71	93.91 ± 15.67	98.00 ± 1.41
Total sample	[10.00–15.00]	5	0.7	100	0.7	14.66 ± 0.11	34.00 ± 21.59	37.32 ± 0.83	106.40 ± 10.50	97.80 ± 0.45
	[15.01–20.00]	267	38.3	100	38.3	17.62 ± 1.27	34.52 ± 14.64	37.32 ± 0.71	94.14 ± 16.07	98.05 ± 1.37
	[20.01–25.00]	192	27.5	100	27.5	22.24 ± 1.36	33.62 ± 15.40	37.24 ± 0.68	93.89 ± 15.77	98.11 ± 1.26
	[25.01–30.00]	127	18.2	100	18.2	27.23 ± 1.47	33.12 ± 13.81	37.13 ± 0.59	91.39 ± 16.98	97.99 ± 1.66
	[30.01–35.00]	90	12.9	100	12.9	32.19 ± 1.32	31.24 ± 15.97	37.09 ± 0.51	89.27 ± 14.71	98.22 ± 1.42
	[35.01–40.00]	16	2.3	100	2.3	36.38 ± 0.90	35.25 ± 14.26	37.23 ± 0.55	89.63 ± 15.87	98.31 ± 1.01
Total		697	100	100	100	22.94 ± 5.64	33.61 ± 14.91	37.23 ± 0.66	92.93 ± 16.04	98.08 ± 1.39
Asymptomatic vs. symptomatic according to Ct ranges					Kruskal-Wallis test	32.4744	3.4748	13.1635	7.3849	6.4115
					p-value	0.001 <sup>bcd</sup>	0.062	0.001 <sup>bc</sup>	0.006 <sup>a</sup>	0.011 <sup>ae</sup>

Data were % and mean ± SD for categorical and quantitative data, respectively.

Age in years, HR in bpm, SpO<sub>2</sub> in %, and T in ° C.

\*p-value (Kruskal-Wallis test) < 0.05: asymptomatic vs. symptomatic for Ct ranges:

<sup>a</sup>[15.01–20.00]; <sup>b</sup>[20.01–25.00]; <sup>c</sup>[25.01–30.00]; <sup>d</sup>[35.01–40.00]; <sup>e</sup>[35.01–40.00].

2, but no correlation was found with age. Past studies did indicate that high viral load was associated with hypoxemia and adverse outcomes [27].

In summary, symptomatic COVID-19 patients in the study population had a higher mean body temperature, higher HR, and lower SpO<sub>2</sub> levels as compared to the asymptomatic group of patients. Additionally, Ct values correlated to symptoms measured temperature, HR, and SpO<sub>2</sub>, but no correlation was found between Ct values and age.

The findings of the present study only partly confirm our hypothesis of vital signs predicting viral load. However, the authors believe that this study can pave way for future research on implications of clinical presentation of COVID-19 patients and their relationship with viral load. Using technological innovations to aid diagnosis and management of COVID-19 has been generating considerable interest among healthcare organizations. Developing protocols based on clinical parameters at first presentation and aiding the diagnostic process by developing predictors using artificial intelligence and machine learning techniques could potentially offer a large-scale solution for the control of the COVID-19 pandemic [36].

The present study has three limitations. First, even though the study population encompassed a wide variety of demographics, the population group is comparatively small as this is a single centre-based study. Secondly, this was a retrospective study that does not allow to examine some clinical and laboratory parameters in dynamics. Furthermore, due to the nature of the research, 'follow-up' of patients cannot be realized. In this regard, the results and conclusions

of this study should be interpreted with caution. Thirdly, the lack of data related to the medical profile of patients (*i.e.*; chronic illness, types of the illnesses) is a third limitation. It is possible that there is an association between co-morbidity and viral load.

## 5. Conclusion

To conclude, compared with asymptomatic patients, symptomatic patients with COVID-19 are most likely to be febrile, tachycardic, hypoxic and having higher viral load. Symptomatic and febrile patients may have a higher viral load as measured by the Ct values of the RT-PCR testing, but the clinical validity of measuring Ct values to predict severity and outcomes in COVID-19 patients' needs further research. COVID-19 outcome is effectively predicted by immediate, objective, and culturally generalizable measures available at the time of clinical presentation. These findings may also help inform timely and effective strategies aimed at optimizing healthcare delivery in regions of the world are anticipating additional waves of COVID-19.

## 6. Recommendations

We recommend that monitoring (*eg*; patient being sent home with a monitor) vital signs is pertinent in probable COVID-19 patients presenting to a primary care centre for testing. However, there is a lack of robust evidence in the significance of measuring Ct values of RT-PCR tests depicting viral loads to predict outcomes and hence the suggestion to conduct further studies to identify the value of the same.

Further research is needed to develop protocols that use clinical and diagnostic tools to predict COVID-19 outcomes.

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