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## Predictive Ability of Factors in diagnosing COVID-19: Experiences from Qatar's Primary Care Settings

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### ABSTRACT

**Objective:** The aim of this paper is to establish the predictive ability of demographic and clinical factors in diagnosing Coronavirus Disease 2019 (COVID-19) in Qatar's publicly funded primary care settings.

**Methods:** Reverse transcription polymerase chain reaction (rt-PCR) test and COVID-19 screening data (COVID-19 related factors) were extracted from electronic medical records for all individuals who visited a primary health care centre in Qatar between 15th March to 15th June 2020. Data analysis was undertaken to assess the validity of individual factors in predicting a positive rt-PCR test.

**Results:** Fever/history of fever [N= 1471 (54.7%); OR 4.6 (95% CI 4.16 - 5.08)], followed by cough [N=1020 (37.9%); OR 1.82 (95% CI 1.65 - 2)] and headache [N=372 (13.8%); OR 1.45 (95% CI 1.27 - 1.67)] were the most frequently reported clinical symptoms amongst individuals who tested positive for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) infection by rt-PCR. Only five factors, fever/history of fever, cough, working/living in an area reporting local transmission, gender and headache (ranked according to predictive power), were found to be statistically significant. Fever/history of fever alone had a specificity of 79.2% and it gradually increased to 99.9% in combination with runny nose, cough, male gender and age  $\geq$  50.

**Conclusions:** The study identified predictive ability of factors in diagnosing COVID-19, individually and in combination. It proposes a scoring system for use in publicly funded primary care settings in Qatar without an rt-PCR test, thus enabling early isolation and treatment where necessary. Further similar studies are needed as newer variations of SARS-CoV2 are continuously emerging to ensure its accuracy.

### Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) is a novel infectious virus which causes Coronavirus Disease 2019 (COVID-19). It has spread to nearly every corner of the world and impacted societies significantly (Kevadiya et al 2021). Since it was declared a Public Health Emergency of International Concern (PHEIC) on the 30<sup>th</sup> January 2020, it continues to be a global public health emergency (BBC 2022). As of 8<sup>th</sup> March 2022, 443 895 905 cases and 5 993 901 deaths were reported globally (World Health Organisation 2022). As new variants of the virus emerge, further waves are anticipated.

Primary care provides infrastructure and plays a variety of key roles such as disease surveillance, diagnosis and treatment, prevention, patient education etc. (Clarke 2015). As the patient's first point of contact is with the health system, challenges are faced by primary care arising from the COVID-19 pandemic (Majeed et al 2020). Additional visits

to primary care are expected (Pandemic Influenza Preparedness Team 2008). Early diagnosis is essential to reduce spread of infection.

Reverse transcription polymerase chain reaction (rt-PCR) is a method that detects the virus using a laboratory technique combining reverse transcription of RNA into DNA (in this context called complementary DNA or cDNA) and amplification of specific DNA targets using polymerase chain reaction (Freeman et al 1999). It is considered the gold standard in diagnosing SARS-CoV2 infection Centers for Disease Control and Prevention (Centers for Disease Control and Prevention 2022). However, it had also been reported that rt-PCR has imperfect sensitivity (Yang et al. 2020a, Arevalo-Rodriguez et al. 2020, Zhao et al 2020). Furthermore, availability of testing supplies and laboratory workforce may prevent its application in some clinical settings (Duffy et al 2020).

SARS-Cov2 is most infectious in the early stages (Woelfel et al 2020, Yang et al 2020b). Therefore, screening people with compatible symptoms is fundamental to determining who should be quarantined and tested (Gostic et al 2020). Targeted screening guided by a structured

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questionnaire based on clinical symptoms is a potentially feasible and valid alternative. The aim of this paper is to establish the predictive ability of demographic and clinical factors in diagnosing COVID-19 in Qatar's publicly funded primary care settings.

## Methods

### Study settings

Primary Health Care Corporation (PHCC) is a publicly funded primary care provider in Qatar. It has 27 health centres across the country which use an integrated electronic medical record (EMR) system. Citizens and resident of Qatar are eligible to register with a PHCC health centre and utilise its services for a nominal annual fee. A majority of the country's population is registered with PHCC.

### Study population and design

The study population comprised all PHCC registered individuals who presented to a PHCC health centre with a suspected SARS-CoV2 infection, completed a COVID-19 screening questionnaire and undertook an rt-PCR test between 15<sup>th</sup> March to 15<sup>th</sup> June 2020. A case-control study design was employed – individuals with a positive rt-PCR test (cases) were compared to individuals with a negative test result (controls).

### Data collection

rt-PCR test and COVID-19 screening data (COVID-19 related factors) required for the study was extracted from PHCC's EMR system. COVID-19 screening data included:

- Demographic information
  - Age
  - Gender
  - Working/living in an area reporting local transmission
  - Contact with a suspected or confirmed case
- Clinical symptoms of SARS-CoV2 infection
  - Fever/history of fever, arthralgia, cough, headache, runny nose, shortness of breath, sore throat, and diarrhoea
- Health Status
  - Diagnosis of diabetes mellitus, hypertension, cardiac disease, asthma/chronic obstructive pulmonary disease (COPD), chronic kidney disease and dyslipidaemia

### Data analysis

Data extracted from PHCC's EMR was reviewed and cleaned. Statistical Package for Social Sciences (IBM SPSS, USA ver. 23) was used for statistical analysis of data. Frequency distributions for selected variables were done to measure the strength of association between 2 categorical variables and report as odds ratio (OR). The statistical significance of these associations was assessed using Chi-square test of independence at  $P < 0.05$  level of statistical significance.

Receiver operating characteristic (ROC) analysis was undertaken to assess the validity of individual factors in predicting a positive rt-PCR test. The positive predictive value was calculated for four pre-test probabilities. The 25% pre-test probability was the positivity rate of an rt-PCR test in the current study sample. The 50% pre-test probability was undertaken for study participants with clinical symptoms, while the 90% pre-test probability was undertaken for study participants with clinical symptoms and contact history. A pre-test probability of 90% was not applicable for a negative predictive value and therefore was not undertaken. Parallel combinations of factors were identified to increase the specificity and positive predictive value compared to individual factors. Combinations were considered positive only if each individual factor was positive.

Demographic information, clinical symptoms and health status of having at least one health condition were factors tested for their ability to predict a positive COVID-19 test result in a multivariate model using discriminant analysis. The unstandardized canonical discriminant function coefficients were used to calculate a prediction score for each statistically significant factor identified by the discriminant model. The score was calculated by summing scores of individual factors when present in a specific tested individual.

### Ethical considerations

The study presented a minimal risk of harm to its subjects, and the data collected for it were anonymised. None of the subjects' personal information was available to the research team. Overall, the study was conducted with integrity according to generally accepted ethical principles and was approved by the PHCC's Research Sub-Committee (PHCC/DCR/2020/06/059).

## Results

### Overview

A total of 8,335 individuals presented at a PHCC health centre with a suspected SARS-CoV2 infection, completed a COVID-19 screening questionnaire and undertook an rt-PCR test during the study period. Of those, 2688 (32.24 %) individuals had a positive rt-PCR test result.

### rt-PCR results by demographics

There were no differences in adults 30-39 (OR 1.43; 95% CI 1.26 - 1.62), 40-49 (OR 1.75; 95% CI 1.51 - 2.01) and  $\geq 50$  age (OR 1.59; 95% CI 1.36 - 1.86) groups by positive rt-PCR test results compared to adults 18-29. Males had a higher positivity rate (OR 1.61; 95% CI 1.47 - 1.78). Individuals working or living in an area of local transmission were also found to have a higher positivity rate (OR 1.83; 95% CI 1.66 - 2.02). Similarly, individuals reporting contact with a suspected or confirmed COVID-19 case had a lower positivity rate (OR 0.72; 95% CI 0.65 - 0.79) (Table S1 - See supplementary file).

### rt-PCR results by clinical symptoms

Fever/history of fever (N=1471; 54.7%), followed by cough (N=1020; 37.9%) and headache (N=372; 13.8%) were the most frequently reported clinical symptom amongst individuals who tested positive for SARS-CoV2 infection by rt-PCR (Table S2 - see supplementary file). Symptoms most strongly associated with a positive rt-PCR test were fever (OR 4.6; 95% CI 4.16 - 5.08) followed by arthralgia (OR 1.92; 95% CI 1.33 - 2.76), cough (OR 1.82; 95% CI 1.65 - 2), headache (OR 1.45; 95% CI 1.27 - 1.67) and runny nose (OR 1.4; 95% CI 1.19 - 1.65). Sore throat was negatively associated with a positive rt-PCR test result (OR 0.79; 95% CI 0.71 - 0.87). All symptoms except shortness of breath and diarrhoea had a statistically significant association with a positive rt-PCR test result (Table S2 - See supplementary file).

### rt-PCR results by health status

Of all health conditions considered in the study, only diabetes mellitus was positively associated with a SARS-CoV2 infection (OR 1.19; 95% 1.04 - 1.36). All other conditions were inversely associated with a SARS-CoV2 infection. Asthma/COPD was the strongest predictor for the absence of an infection. The absence of asthma/COPD as a diagnosis significantly increased the likelihood of a positive rt-PCR test result by 90 % (Table S3 - See supplementary file).

**Table 1**  
Predictive ability of individual factors

	Area Under Curve	P
Fever/history fever	0.67	<0.001
Cough	0.56	<0.001
Working/living in an area reporting local transmission	0.56	<0.001
Male gender	0.56	<0.001
Headache	0.52	0.004
Runny nose	0.51	0.06[NS]
≥ 50 age	0.51	0.09[NS]
Arthralgia	0.50	0.47[NS]
Shortness of breath	0.50	0.83[NS]
Diarrhea	0.50	0.64[NS]
Absence of a contact with an individual suspected/confirmed with SARS-CoV2 infection*	0.537	<0.001
Absence of sore throat*	0.527	0.031
Absence of any of the health conditions listed*	0.515	<0.001

\* Validity parameters not presented for absence of a factor

**Table 2**  
Overall predictive accuracy of a positive rt-PCR test result

	Unstandardized Canonical Discriminant Function Coefficients	Score
Fever or History Fever	1.931	9
Sore Throat	-0.623	-3
Diarrhoea	-0.593	-3
Runny Nose	0.559	3
Male gender	0.506	2
Cough	0.475	2
≥ 50 age	0.329	2
Working/living in an area reporting local transmission	0.277	1
Headache	0.267	1
Diagnosis of at least one health condition	-0.209	-1
Constant	-0.945	0.209

Wilks' Lambda=0.855

P=<0.001

Predictive accuracy for positive cases = 45.3%

Predictive accuracy for negative controls = 87.1%

Overall predictive accuracy = 73.6%

#### Predictive ability of individual factors

All factors were tested for their ability to predict a positive rt-PCR test result. Only five factors, fever/history of fever, cough, working/living in an area reporting local transmission, gender and headache (ranked according to predictive power), were found to have statistically significant predictive ability in univariate modelling (Table 1).

#### Overall predictive accuracy of a positive rt-PCR test result

Ten factors were retained in the multivariate modelling analysis (See Table 2). The model was statistically significant with an overall predictive accuracy of 73.6%. The unstandardized canonical discriminant function coefficients were used to calculate prediction scores for each of the nine factors (Fever/history fever = 9; runny nose = 3; male gender, cough and age >50 = 2; working/living in area of transmission and headache = 1; sore throat and diarrhoea = -3; having at least one health condition = -1).

#### Predictive ability of combined factors

The COVID-19 score ranged between a minimum of (-4) to a maximum of 17 points. A higher resulting score would increase the probability of testing positive for COVID-19. This score and a combination of single predictors were tested for their ability to predict a positive

COVID-19 test result. The COVID-19 score alone was associated with a reasonably good criterion to predict the COVID-19 status, as the area under ROC curve was higher than 0.7 (Table 3). The optimum cut-off value for a score of ≥3 is 62.0 % sensitive and 71.9% specific in predictive positive COVID-19 status.

Testing negative at the most sensitive cut-off value for the score of -6 (100%) would exclude a possible diagnosis of COVID-19 with 100.0% confidence at any pre-test probability for a symptomatic case (Table 4). Obtaining a COVID-19 score of 15 or higher would predict a positive COVID-19 diagnosis with 100% confidence under any pre-test probability, since the specificity of this cut-off value of the score is 100%.

A report of fever/history of fever alone had a specificity of 79.2% and it gradually increased to 99.9% in combination with runny nose, cough, male gender and age ≥ 50. A combination of five factors (fever/history fever + runny nose + cough + male gender + ≥ 50 age) would predict a positive COVID-19 test result with a confidence level ranging between 53.9%, 77.8% and 96.9% at the 25%, 50% and 90% pre-test probabilities. On the contrary, a sensitivity of 54.7% for fever/history of fever only decreases to 0.2 % for a combination of five factors (fever/history fever + runny nose + cough + male gender + ≥ 50 age) (Table 4).

## Discussion

### Summary

Increases in COVID-19 cases seriously disrupt the health system (Tangcharoensathie et al 2021). The study identified predictive ability of factors in diagnosing COVID-19, individually and in combination. It proposes a scoring system for use in publicly funded primary care settings in Qatar. In developing the scoring system, the study took into consideration demographic data, clinical symptoms and health status. Other published studies evaluating performance of screening questionnaires did not use disease predictors included in this study and their combinations along with a scoring system (Aldobyany et al 2020, Ornaghi et al 2020). Furthermore, they were conducted in tertiary care settings.

### Strengths and limitation

The key strengths of the study are that it included all individuals who presented to any PHCC primary health care centre in Qatar with a suspected SARS-CoV2 infection. The study included data extracted from the EMR which included data on multiple disease predictors collected by trained data collectors who followed a standard data collection protocol. The key limitations of the study are that it included data for a three-month period only and did not include data on the loss of smell and taste. It was also limited to individuals who presented to health centres and not from general screening. Furthermore, the study was conducted before

**Table 3**  
Predictive ability of combined factors

	Area Under Curve	P
COVID-19 score	0.72	<0.001
Fever/history fever	0.67	<0.001
Fever/history fever + runny nose	0.52	0.024
Fever/history fever + runny nose + cough	0.51	0.25[NS]
Fever/history fever + runny nose + cough + male gender + $\geq$ 50 age	0.50	0.92[NS]

**Table 4**  
Validity parameters for COVID-19 score and clinical symptoms

Positive if $\geq$ cut-off value	Sensitivity	Specificity	Accuracy	PPV at pre-test probability			NPV at pre-test probability	
				25%	50%	90%	25%	50%
<b>COVID-19 score</b>								
-6	100.0	0.1	32.3	25.0	50.0	90.0	100.0	100.0
-5	99.9	0.2	32.4	25.0	50.0	90.0	85.1	65.6
-4	99.4	1.2	32.9	25.1	50.2	90.1	86.8	68.6
-3	98.1	4.6	34.8	25.5	50.7	90.3	88.0	70.9
-2	96.8	8.9	37.2	26.1	51.5	90.5	89.2	73.3
-1	92.5	17.8	41.9	27.3	53.0	91.0	87.7	70.4
0	85.4	33.5	50.2	30.0	56.2	92.0	87.3	69.6
1	79.3	45.5	56.4	32.7	59.3	92.9	86.8	68.7
2	67.6	64.7	65.6	38.9	65.7	94.5	85.7	66.6
<b>3 (Optimum cut-off value)</b>	<b>62.0</b>	<b>71.9</b>	<b>68.7</b>	<b>42.4</b>	<b>68.8</b>	<b>95.2</b>	<b>85.0</b>	<b>65.4</b>
4	58.5	76.0	70.3	44.8	70.9	95.6	84.6	64.7
5	56.2	79.0	71.6	47.1	72.8	96.0	84.4	64.3
6	54.5	80.8	72.3	48.6	73.9	96.2	84.2	64.0
7	52.0	82.6	72.8	49.9	75.0	96.4	83.8	63.3
8	47.5	85.6	73.4	52.5	76.8	96.8	83.0	62.0
9	41.0	88.9	73.4	55.1	78.7	97.1	81.9	60.1
10	34.4	91.6	73.1	57.7	80.4	97.4	80.7	58.3
11	24.5	94.5	71.9	59.9	81.8	97.6	79.0	55.6
12	16.0	97.1	71.0	65.2	84.9	98.1	77.6	53.6
13	9.2	98.6	69.8	68.8	86.9	98.4	76.5	52.1
14	3.4	99.7	68.6	78.2	91.5	99.0	75.6	50.8
15	0.6	100.0	67.9	100.0	100.0	100.0	75.2	50.3
16	0.2	100.0	67.8	100.0	100.0	100.0	75.1	50.1
<b>Clinical factors</b>								
Fever/history fever	54.7	79.2	71.3	46.7	72.5	95.9	84.0	63.6
Fever/history fever + runny nose	4.8	98.3	68.1	48.3	73.7	96.2	75.6	50.8
Fever/history fever + runny nose + cough	2.2	99.3	68.0	51.9	76.4	96.7	75.3	50.4
Fever/history fever + runny nose + cough + male gender + $\geq$ 50 age	0.2	99.9	67.8	53.9	77.8	96.9	75.0	50.0

the emergence of newer variants of concern and prior to the introduction of a vaccination programme.

#### Comparison with existing literature

Grant et al (2020) in a systematic review and meta-analysis reported fever (78 %) and cough (57 %) as the most prevalent symptoms of COVID-19 while headache, arthralgia, runny nose and diarrhoea were found to be less prevalent. These reports are in line with findings of this study. In terms of combinations of symptoms, a study reported the probability of having a positive test increased with the increased number of symptoms (Cadejani et al 2021). However, in our study, the probability was associated with specific combinations of symptoms. Such information is likely to be more useful in real world clinical settings.

#### Implications for research and/or practice

During an outbreak, health systems can be overwhelmed with suspected COVID-19 cases. The findings of the study can help allocate resources efficiently and effectively. Furthermore, they can be incorporated with e-triaging systems.

#### Conclusion

The study identified predictive ability of factors in diagnosing COVID-19, individually and in combination. It proposes a scoring system for use in publicly funded primary care settings in Qatar without an rt-PCR test, thus enabling early isolation and treatment where necessary. Further similar research will be needed as newer variations of SARS-CoV2 are identified.

#### Conflict of interest

All authors declare no conflict of interest.

#### Funding source

Funding for the study was approved by Primary Health Care Corporation's Research Budget Working Group (Ref. No PHCC/DCR/2020/06/059).

#### Ethical approval

The study was conducted with integrity according to generally accepted ethical principles and was approved by the Pri-

mary Health Care Corporation's research-sub committee (Ref. No. PHCC/DCR/2020/06/059). Informed consent was waived due to the retrospective nature of the study.

### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.ijregi.2022.03.018](https://doi.org/10.1016/j.ijregi.2022.03.018).

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