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Original Article

Can the cycle threshold (Ct) value of RT-PCR test for SARS CoV2 predict infectivity among close contacts?



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ABSTRACT

Background: COVID-19 global pandemic is an unprecedented health emergency. Rapid identification and isolation of infected individuals is crucial. Qatar's National Health Strategic Command Group adopted a cut off 30 for Ct value of RT-PCR result of a positive case to decide on duration of isolation and quarantine period for their close contacts.

Aim: To test if Ct value cut off 30 reflects on the infectivity potential among close contacts.

Methodology: All positive cases reported during July 2020 whose contacts had been traced and swabbed were extracted from database after removing personal identifiers. Close-contact was defined as anybody who has been within 2 m distance of a confirmed positive case for 15 min or more, without any personal protection equipment. Descriptive analysis was done and test of significance of difference in positivity among the contacts of those with $ct < 30$ and > 30 was done.

Results: 2308 COVID-19 positive cases were followed up. More than three-quarters had a Ct value < 30 , with a mean Ct value of 24.05 (+6.48). On an average 6 contacts were swabbed per case. More than half the positive cases followed up had at least one secondary case, with median positivity rate 12.5%. A significant relation was noted between Ct value cut-off 30 and secondary transmission (1.5 times more risk among those with Ct value < 30). A significant difference was noted in median positivity rate between close contacts of positive cases with Ct value > 30 or < 30 .

Conclusion: Further studies combining PCR assays, culture studies and contact tracing are needed to define which factors can be used to reliably predict the infectious status of patients with COVID-19.

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Introduction

The COVID-19 global pandemic is an unprecedented health emergency. Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) spread rapidly across multiple countries in early 2020 [1–3]. A stable public health control measure for early con-

tainment of an emerging outbreak of directly transmitted infections involves early detection and isolation of infected persons as well as tracing, testing and quarantining of their contacts [2]. Diagnosis is made using clinical, laboratory and radiological features. As symptoms and radiological findings of COVID-19 are non-specific, a positive test enables the clinicians and public health professionals to quickly isolate the patient and prevent spread of the disease. Real-time reverse transcriptase polymerase chain reaction (r RT-PCR) has been the main diagnostic tool for SARS-CoV-2 infection since the early stages of the COVID-19 pandemic and the presence of viral RNA confirms SARS CoV2. There is a fluorescence signal in the test which increases proportional to the amount of amplified nucleic acid enabling accurate quantification of RNA in the sample. The cycle threshold or Ct value of a RT-PCR reaction is the number of cycles at which fluorescence of the PCR product is detectable over and above the background signal. Many PCR assays use 40 as cut off for Ct value to consider the test positive, allowing detection

Abbreviations: COVID-19, coronavirus disease 2019; MOPH, Ministry of Public Health; HP-CDC, Health Protection and Communicable Disease Control.

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of even very few starting RNA molecules [4]. Theoretically, the Ct value is inversely proportional to the amount of genetic material (RNA) in the starting sample and lower Ct values generally correlate with high viral load.⁴ The Ct value is inversely related to the viral load and about every 3.3 increase in Ct value reflects a 10-fold reduction in starting RNA molecules.

A positive PCR result or detection of viral RNA does not necessarily mean that a person is infectious and able to transmit the virus to another person. Factors that determine transmission risk include whether a virus is still replication competent, whether the infected person has symptoms like cough which can spread infectious droplets as well as the behavioral and environmental factors associated with the infected individual. Some researchers/clinicians assume that high viral load directly correlates with increased infectiousness and severity of disease [5,6]. There are no reliable studies to definitively prove a direct correlation between disease severity/infectiousness and Ct values. There are limited studies demonstrating correlation between viral load in respiratory samples and infectivity. The ability of the virus to replicate in cultured cells can serve as surrogate marker of infectivity but may not be as sensitive as PCR [7–9]. Bullard et al. assessed the correlation of real time PCR cycle threshold value (ct) with the growth of SARS CoV2 in cell culture. The data suggest that SARS CoV 2 infectivity was reduced when the Ct value was >24 and that for every single unit increase in Ct value the odds ratio for recovering the virus in cell culture decreased by 32% [8]. La Scola et al. assessed this correlation between isolation of SARS CoV 2 in cell culture with real time PCR Ct values and found significant relationship between Ct values and culture positivity rate. Samples with Ct values between 13–17 all led to positive culture. A PCR Ct value >24 showed a strong correlation with reduced recovery of the virus in cell culture. The culture positivity declined with increasing PCR Ct values to reach 12% at Ct value 33 and SARS CoV-2 could not be isolated from any sample with PCR Ct value >34. Based on this they deduced that patients with Ct values > 34 do not excrete infectious viral particles [9].

Hypothesis

Based on the revised cut off for Ct value 30 adopted by the NHSCG there should be difference in the individual level transmission of infection to his/her close contacts from a positive case whose Ct value is above or below 30.

Significance for public health/ Rationale of study

A stable public health control measure for early containment of an emerging outbreak of directly transmitted infections involves early detection and isolation of infected persons as well as tracing, testing and quarantining of their contacts. The National laboratory in Qatar under Hamad Medical Corporation (HMC), considering significant local and international evidence has adopted a cut off value of Ct 30 for reporting RT-PCR results in addition to the currently reported positive result. The latest guidelines by the National Health Strategic Command Group (NHSCG) dated 19th June 2020 state that any person who is positive for COVID 19 on RT-PCR is considered infectious if the Ct value is <30 and will be admitted to an isolation facility and needs to be quarantined for 14 days [10]. Whereas for those asymptomatic positive cases who have a Ct value >30 are considered non-infectious and will only be home isolated for 7 days after which they are considered fit to rejoin the work and interact with the general community assuming that there is no risk of transmission from them. If this cut off value is used for deciding the isolation criteria, fitness to rejoin work and resume normal social activities, then it should reflect in the infec-

tivity potential (the number of contacts who contract the infection from the positive case) too.

Impact of the study

If found to be significant, the contact tracing criteria may be revised ie do contact tracing only for those with Ct value < 30.

Study objective

To study the individual level transmission of infection from COVID 19 positive case to his/ her close contacts (positivity rate among the contacts) with PCR ct < 30 and >30 and assess if this difference is significant.

Methodology

Study design

Descriptive cross-sectional study.

Study setting

Swabs taken from upper and lower respiratory samples are tested at the national laboratory under Hamad Medical Corporation (HMC) using RT-PCR. The PCR assays used during the time of study were Roche cobas[®] 6800 system using the cobas[®] SARS-CoV-2 Test (Roche, Switzerland), Xpert[®] Xpress SARS-CoV-2 (Cepheid, USA); and TaqPath[™] PCR COVID-19 Combo Kit (Thermo Fisher Scientific, USA) performed on ABI 7500 thermal cyclers (Thermo Fisher Scientific, USA) following sample extraction using EZ1 (QIAGEN, USA) and QIASymphony (QIAGEN, USA); which were sensitive enough to pick up the COVID 19 variants of concern (VOC) circulating those days (**B.1 B.1.428 B1.1.75**).

The COVID-19 track and trace team under HP-CDC in MOPH, then traces, tests and isolates the close contacts of the COVID-19 positive cases.

Study population

All COVID 19 positive persons residing in Qatar irrespective of their nationality or gender or age or possessing residence permit or not, detected during July 2020 and the contacts of whom were traced and swabbed by the COVID-19 track and trace team.

Inclusion/ exclusion criteria

All the positive cases reported during the month of July and residing in Qatar were included; since the national testing laboratory started publishing the Ct values along with the positive results from 14th June 2020 and only a single Ct value from 28th June 2020 [11].

Operational definition of close contact

Anybody who has been within 2 m of distance of a confirmed positive case for 15 or more minutes, without any personal protection equipment, within two weeks of identification of the positive case, has been used for defining a close contact by the COVID-19 track and trace team in Qatar.

Sample size and sampling technique

This was the first of its kind research relating Ct value with contact tracing or positivity among contacts, and therefore no formal sample size could be computed. Hence all the positive cases

Table 1
Secondary transmission among the close contacts of positive cases with Ct value < 30 vs >30.

Ct value of RT-PCR of index positive case	Secondary transmission		Total
	No secondary cases	At least one secondary case	
Ct < 30	675	1088	1763
Ct >30	327	218	545
Total	1002	1306	2308

Pearson chi-square = 79.894 ($p < 0.001$); odds ratio = 1.543 (1.383–1.721).

Table 2
Positivity rate among the close contacts of positive cases with Ct value < 30 vs >30.

	Ct value of PCR test of positive case	N	Median	Std. deviation	Std. error mean
	CT < 30	1758	31.06	34.43	0.82

$t = -9.144$; $df 2301$, $p < 0.001$.

Table 3
Secondary transmission among the close contacts of positive cases with/without symptoms.

	Secondary transmission		Total	
	No secondary cases	At least one secondary case		
Symptoms	Yes	725	939	1664
	No	277	367	644
Total		1002	1306	2308

Pearson chi-square = 0.059 ($p 0.809$).

reported between July 1st and July 31st, 2020 who were traced and swabbed by the COVID-19 track and trace team were included in the study.

Data collection and management

All the positive cases reported between July 1st and July 31st, 2020, whose contacts had been traced and swabbed were extracted from the database of the COVID-19 track and trace team after removing the personal identifiers. Socio-demographic details like age, gender of the index case; presence/absence of symptoms at the time of testing; Ct values of the PCR result were collected. The **outcome** assessed was the individual-level transmission from the positive case to his/her close contacts in the different settings (household, work, school, or other), represented as how many contacts became positive per positive case, expressed in terms of positivity rate, irrespective of the co-existence of different control measures across settings.

Data analysis

All Statistical analyses was done using statistical packages SPSS 22.0 (SPSS Inc. Chicago, IL) software. Descriptive analysis of the study population was done and test of significance in difference in the positivity among the contacts between the those with $ct < 30$ and >30 , was done using z test for proportions.

Ethical considerations

This study was conducted after approval from the MOPH-IRB. All data was kept in encrypted password-protected laptops and stored in locked cabinets at the Principal Investigator's office at HP-CDC, MOPH. Only the Principal Investigator and co-investigators had access to the study data. The data set was anonymous and personal identifiers were removed. Moreover, there were no foreseen risk associated with this study. There was no collection of bio-specimens for this study per se. There was no issue of subject withdrawal/ withdrawal of consent as secondary data was used.

Results

A total of 2308 COVID-19 positive cases were followed by the MOPH Track and Trace team and their close contacts were swabbed during the month of July 2020. The mean age of the positive cases followed up was 36.56 years (+13.6) and nearly three quarter (73.8%) were males. Most (72.1%) were symptomatic at the time of being confirmed as positive. More than three-quarters (76.4%) had a Ct value less than 30. The mean Ct value of the study population was found to be 24.05 (+6.48). On an average 6 contacts were swabbed per case, ranging between none being swabbed to a maximum of 98 being swabbed for a positive case.

Among the 19,869 close contacts swabbed, 4608 (23.2%) turned out to be positive for SARS CoV2. More than half (56.6%) of the positive cases followed up had at least one secondary case. The median positivity rate among the close contacts was found to be 12.5% (ranging 0%–100%).

A significant relation was noted between Ct value cut off 30 and secondary transmission ($p < 0.001$) with 1.5 times more risk of secondary transmission among those with Ct value <30 (Table 1). A significant ($p < 0.001$) difference was noted in the median positivity rate among close contacts of positive cases with Ct value <30 (31.1%) and those with >30 (16.4%) (Table 2).

No significant relationship could be seen between symptoms of the positive cases and secondary transmission as shown in Table 3 below. No significant difference could be established in median positivity rates between symptomatic and asymptomatic positive index cases (Table 4).

A significant negative correlation was seen between Ct value and positivity rate using non-parametric test for correlation ($r = -0.163$; $p < 0.001$). Using ROC analysis (Fig. 1), the **cut off** was found to be **30.4** for any significant secondary transmission with an area under the curve of **0.590**.

Discussion

Some experts suggest using RT-PCR Ct value or to calculate viral load which can help refine decision-making (shorter isolation

Table 4
Positivity rate among the close contacts of positive cases with or without symptoms.

	Symptoms	N	Mean	Std. deviation	Std. error mean
Positivity rate	Yes	1660	27.5098	33.26353	0.81642
	No	643	27.8108	33.13562	1.30674

$t = -0.195$; $df\ 2301$, $p\ 0.845$.

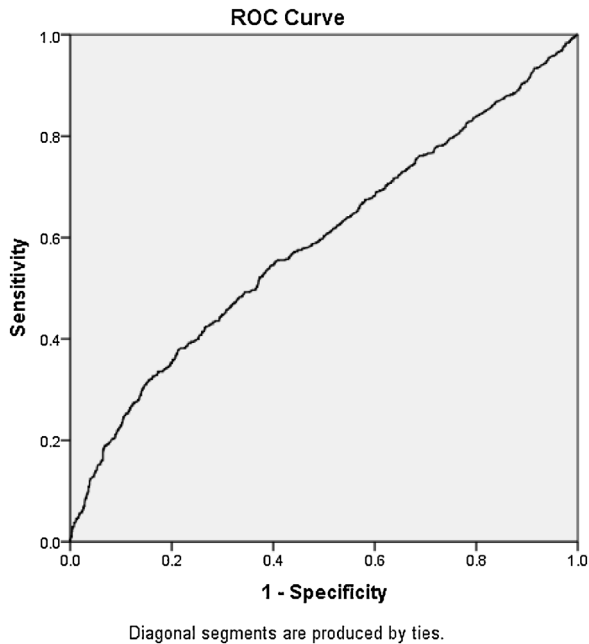


Fig. 1. ROC curve.

etc.) [12]. However, the evidence is not robust enough to definitively support this assumption. Our study showed that there was significant relation between Ct value cut off 30 and secondary transmission.

Recent discussions about guiding the clinical decision-making process based on the Ct values of RT-PCR test reported by laboratories has several limitations.⁵ Comparability of Ct values among different kits is a challenge with different Ct cut-offs, different RNA extraction techniques, primers and probes used for PCR and different gene targets. Other key consideration when interpreting the results should be the temperature at which the samples are stored and transported, systems of sample transport and the time between sample collection and assay. Therefore, Ct value criteria must be established by each testing centers/ laboratories [13].

How the sample has been collected, by technical competence of the person performing the test, calibration of equipment and pipettes and analytical skills of the interpreters, can also adversely impact Ct values. Ct values between nasal and oropharyngeal specimens collected from the same individual may differ. Samples from asymptomatic/mild cases show Ct values like those who develop severe disease. Patients in early symptomatic stage may show a high Ct value which may subsequently change.

During the ongoing coronavirus disease 2019 (COVID-19) pandemic, monitoring patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using viral kinetics or viral loads in various sample types by real-time RT-PCR has become essential. However, understanding whether the RT-PCR test results are interpreted as quantitative, qualitative, or semi-quantitative is important [14]. Unfortunately, several papers on COVID-19 use the naive Ct values from qualitative RT-PCR as a quantitation unit or use the ΔCt values with incorrect quantitation unit [15,16]. Quantitative RT-PCR is entirely different from qualitative RT-PCR. Ct value

itself cannot be directly interpreted as viral load without a standard curve using reference materials. Thorough evaluation of the reliability and robustness of the standard curve is the key to accurately quantify the expected viral copy number. There is wide heterogeneity and inconsistency of the standard curves calculated from studies that provided Ct values from serial dilution samples and the estimated viral loads [15,17,18]. An appropriate standard curve with adequate limit of detection is required for viral load quantification to correctly track the viral titer kinetics. A two-step approach using qualitative RT-PCR (for detection) and quantitative RT-PCR (for viral load quantification) is highly recommended for studies focusing on viral loads, as clearly presented by Lescure and colleagues [19]. Furthermore, using appropriate quantification units according to different sample types—ie, copies per 1000 cells (for respiratory samples), copies per mL (for plasma), and copies per g (for stool)—should be followed by clinicians, as outstandingly shown by Lescure and colleagues [19].

Limitations

The outcome was assessed irrespective of the co-existence of different control measures across settings. Targeted interventions such as contact tracing (the manual tracing of acquaintances whom they have met during a specified period in recent past) needs to consider individual-level variations in transmission. Defining a close contact is challenging. Close contact of a probable or confirmed case includes a person living in the same household as a COVID-19 case; a person having had direct physical contact with a COVID-19 case (e.g. shaking hands); a person having unprotected direct contact with infectious secretions of a COVID-19 case (e.g. being coughed on, touching used paper tissues). Factors to consider when defining close contact include proximity, the duration of exposure (e.g., longer exposure time likely increases exposure risk), and whether the exposure was to a person with symptoms (e.g., coughing likely increases exposure risk). As per Keeling MJ, contact tracing anybody who has been within 2 m of distance of a confirmed positive case for 15 or more minutes within two weeks period by the coronavirus track and trace system should curb the spread of COVID-19 infection [7]. But this will be at the cost of having to trace and test many uninfected people [7]. Guidelines from the Centers for Disease Control and Prevention defines “close contact” as anyone who has been within 6 feet of a person infected with the virus for a “prolonged period of time,” as well as those who have had direct contact with the infected person’s secretions [20]. The effectiveness of contact tracing and the extent of resources required to implement it successfully will also depend on the social interactions within a population, such as, family meals, parties and other gatherings involving close contacts [21].

Moreover, transmission from an infected case to his/her close contacts can be proved conclusively only by doing genomic study.

Conclusion

Our study showed that there was significant relation between Ct value cut off 30 and secondary transmission. Using ROC analysis, the ideal cut off was found to be 30.4 for any significant secondary transmission. Some experts suggest using RT-PCR Ct value or to calculate viral load which can help refine decision-making (shorter

isolation etc). However, the evidence is not robust enough to definitively support this assumption.

Further studies combining testing using PCR assays, culture studies and contact tracing are needed to define which factors can be used to reliably predict the infectious status of patients with COVID 19.

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Competing interests

None declared.

Ethical approval

Ethical clearance was obtained from the IRB, MOPH (ERC-929-3-2020).

References

- [1] Cereda D, Tirani M, Rovida F, Demicheli V, Ajelli M, Poletti P, et al. The early phase of the COVID-19 outbreak in Lombardy, Italy. *ArXiv* 2020. DOI: 2003.09320 published online March 20. (preprint).
- [2] Ng Yixiang, Li Zongbin, Chua Yi Xian, Chaw Wei Liang, Zhao Zheng, Er Benjamin, et al. Evaluation of the effectiveness of surveillance and containment measures for the first 100 patients with COVID-19 in Singapore—January 2–February 29, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:307–11.
- [3] Gudbjartsson Daniel F, Helgason Agnar, Jonsson Hakon, Magnusson Olafur T, Melsted Pall, Norddahl Gudmundur L, et al. Spread of SARS-CoV-2 in the Icelandic population. *N Engl J Med* 2020;382:2302–15, <http://dx.doi.org/10.1056/NEJMoa2006100>.
- [4] Corman Victor M, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu Daniel KW, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill* 2020;25(3), <http://dx.doi.org/10.2807/1560-7917.ES.2020.25.3.2000045>, pii=2000045.
- [5] Abbott S, Hellewell J, Thompson RN, et al. Estimating the time-varying reproduction number of SARS-CoV-2 using national and subnational case counts [version 2; peer review: 1 approved with reservations]. *Wellcome Open Res* 2020;5:112, <http://dx.doi.org/10.12688/wellcomeopenres.16006.2>.
- [6] He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med* 2020;26:672–5.
- [7] Keeling MJ, Hollingsworth TD, Read JM. Efficacy of contact tracing for the containment of the 2019 novel coronavirus (COVID-19). *J Epidemiol Community Health* 2020;74(10):861–6, <http://dx.doi.org/10.1136/jech-2020-214051>.
- [8] Bullard J, Dust K, Funk D, et al. Predicting infectious SARS-CoV-2 from diagnostic samples. *Clin Infect Dis* 2020:ciaa638, <http://dx.doi.org/10.1093/cid/ciaa638>.
- [9] La Scola B, Le Bideau M, Andreani J, et al. Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards. *Eur J Clin Microbiol Infect Dis* 2020;39(6):1059–61, <http://dx.doi.org/10.1007/s10096-020-03913-9>.
- [10] Health Strategic Command Group, Qatar. Revised policy on use of PCR test Ct values for admission and discharge from isolation facilities. HMC Reference CI 001190620. Dated 19th June 2020.
- [11] System Wide Incident Command Committee Chair, HMC, Qatar. Memo on COVID-19 Ct values. Peter Coyle. Reference 68/2020/SWICC. Dated 28th June 2020.
- [12] Tom Michael R, Mina Michael J. To interpret the SARS-CoV-2 test, consider the cycle threshold value. *Clin Infect Dis* 2020;71(October (16)):2252–4, <http://dx.doi.org/10.1093/cid/ciaa619>.
- [13] Cheng HW, Jian SW, Liu DP, Ng TC, Huang WT, Lin HH, et al. Contact tracing assessment of COVID-19 transmission dynamics in Taiwan and Risk at different exposure periods before and after symptom onset. *JAMA Intern Med* 2020;180(9):1156–63, <http://dx.doi.org/10.1001/jamainternmed.2020>.
- [14] Han MS, Byun JH, Cho Y, Rim JH. RT-PCR for SARS-CoV-2: quantitative versus qualitative. *Lancet Infect Dis* 2021;21(2):165, [http://dx.doi.org/10.1016/S1473-3099\(20\)30424-2](http://dx.doi.org/10.1016/S1473-3099(20)30424-2).
- [15] Zou L, Ruan F, Huang M, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med* 2020;382:1177–9.
- [16] Shen C, Wang Z, Zhao F, et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. *JAMA* 2020, <http://dx.doi.org/10.1001/jama.2020.4783> (published online March 27).
- [17] Chu DKW, Pan Y, Cheng SMS, et al. Molecular diagnosis of a novel coronavirus (2019-nCoV) causing an outbreak of pneumonia. *Clin Chem* 2020;66:549–55.
- [18] Chan JF, Yip CC, To KK, et al. Improved molecular diagnosis of COVID-19 by the novel, highly sensitive and specific COVID-19-RdRp/HEV real-time reverse transcription-polymerase chain reaction assay validated in vitro and with clinical specimens. *J Clin Microbiol* 2020;58:e00310–20.
- [19] Lescure FX, Bouadma L, Nguyen D, Parisey M, Wicky PH, Behillil S, et al. Clinical and virological data of the first cases of COVID-19 in Europe: a case series. *Lancet Infect Dis* 2020;20(6):697–706, [http://dx.doi.org/10.1016/S1473-3099\(20\)30200-0](http://dx.doi.org/10.1016/S1473-3099(20)30200-0). Epub 2020 Mar 27. Erratum in: *Lancet Infect Dis*. 2020 May 19; Erratum in: *Lancet Infect Dis*. 2020 Jun;20(6):e116. PMID: 32224310; PMCID: PMC7156120.
- [20] National Center for Immunization and Respiratory Diseases (NCIRD), Division of viral diseases. COVID-19. [Accessed 17 December 2020].
- [21] Endo A, Abbott S, Kucharski AJ, Funk S, CMMID COVID-19 Working Group. Estimating the overdispersion in COVID-19 transmission using outbreak sizes outside China. *Wellcome Open Res* 2020;5:67.