



AN EPIDEMIOLOGY-CLINICAL CORRELATION OF VIRAL LOAD AS MEASURED BY CYCLE THRESHOLD VALUE BY RT-PCR IN COVID-19

General Medicine

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KEYWORDS

INTRODUCTION :

The 2019 novel coronavirus [severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)] was first documented in December 2019 in Wuhan, China, and spread across the globe resulting in significant global morbidity and mortality^[1].

Diagnosis of COVID-19 is mainly done by nasopharyngeal and oropharyngeal swab RT-PCR (Reverse transcriptase - polymerase chain reaction). Real time RT-PCR is of great interest today for detection of SARS- CoV-2 due to its benefits as a specific assay.

Cycle threshold (Ct) values of Real-time RT-PCR represent the number of amplification cycles required for the target gene to exceed a threshold level. 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^[2].

Some studies suggest that there is a correlation between viral load and disease severity in SARS-CoV-2^[3]. Hence, it is important to predict the likely prognosis and infectiousness of the patient at the time of diagnosis which would help in the management of the patient.

Studies done during the SARS-CoV-1 outbreak suggested that the viral load of the patient is associated with the disease severity and mortality^[4,5].

In our study, We observed the cycle threshold values of E, RDRP and ORF1 genes on the day of admission and on day 10 detected by RT-PCR and its correlation with the clinical severity of COVID-19.

OBJECTIVES:

- To study the correlation of clinical severity with Ct Values in COVID-19.

METHODOLOGY:

- This is single centered RETROSPECTIVE STUDY.
- Patients tested positive for COVID 19 by RT-PCR at SVP hospital between 10/04/2020 and 10/05/2020 were included in the study.
- Patient's demographic, clinical history, detailed past history, clinical variable and drug treatment were recorded.
- Analysis was as per appropriate statistical methods.
- The study was approved by the Institutional Review Board.
- Patients were classified into mild, moderate and severe according to MoHFW guidelines^[6].

Mild case :

Patient with mild symptoms of URTI but no breathlessness or hypoxia.

Moderate case :

Patient with dyspnea and hypoxia with SpO₂ <94% (range 90-94%) on room air and Respiratory rate more or equal to 24 per minute.

Severe case :

Patient with dyspnea and hypoxia with SpO₂ <90% on room air and

Respiratory rate more or equal to 30 per minute, patient with new or worsening respiratory symptoms within one week of known clinical insult with CXR s/o ARDS or patient with Acute life-threatening organ dysfunction caused by a dys-regulated host response to suspected or proven infection.

- Total number of patients - 430 (Male - 257)
- Number of patients with comorbidity - 151
- Total number of patients in different clinical stages on admission according to MoHFW guidelines (Mild - 351, Moderate - 49, Severe - 30)

STUDY SITE:

- Department of General Medicine, Sardar Vallabhbhai Patel Institute of Medical Sciences and Research, Ahmedabad.

ELIGIBILITY CRITERIA:

All patients tested positive for COVID 19 by RT-PCR patients at SVP hospital between 10/04/2020 and 10/05/2020 were included in the study. COVID positive patients who were admitted at our hospital but were already tested COVID positive in a different hospital or laboratory were excluded from the study. Pediatric and pregnant patients were excluded.

RESULTS :

Comparison of Ct value with different parameters	Number of patients	p value
1. Comorbidity	Patients with comorbidity (n = 151)	p = 0.052
2. Symptom onset	0-3 days (n = 182) 4-7 days (n = 170) >7days (n = 55) Asymptomatic (n = 23)	p = <0.001
3. Clinical severity on admission	Mild (n = 351) Moderate (n = 49) Severe (n = 30)	p = 0.131
4. Clinical severity on day 10	Mild (n = 150) Moderate (n = 28) Severe (n = 20)	p = 0.019

DISCUSSION :

In our study we have recorded different drug treatment given to the patients. Out of 430 patients, all patients received SOC (standard of care - Azithromycin), 163 patients received HCQ, 111 patients received injectable steroids and 211 patients received LMWH injection. Out of 430 patients 232 patients were tested negative for Covid 19 on day 10 by RT-PCR swab which is approximately 54% of total sample size.

One study conducted in China including 96 patients suggested that patients with severe disease had significantly low Ct values than patients with mild disease (p = 0.03). Another study conducted in

China including 92 patients suggested that Ct value is not correlated with clinical severity at admission while lower Ct values were observed in patients who became severely ill during hospitalisation than those who did not ($p=0.008$), this results were similar to our study in which clinical severity at admission is not related to Ct value but there is significant correlation of Ct value with clinical severity on day 10 ($p=0.019$). This can be due to active viral replication in the host. We have seen that many patients worsen during the second week of their illness. This worsening can be due to an increase in the viral load in the host which can be reflected by the low Ct values. So that from this observation these values can aid in the early administration of the treatment to prevent the worsening of the patients. Early treatment can lead to negative RT PCR by day 10 and also prevent the worsening of the patient.

Many other studies have found the similar results that Ct value have no correlation with the clinical severity at admission^[7,8]. This can be due to the reason that patients with mild disease can have lower Ct value if tested earlier and patients with severe disease can have higher Ct value if tested later.

One study conducted with 90 patients found that Ct values are lower in patients who presented soon after symptom onset and are significantly correlated with the time elapsed since onset ($p < 0.001$)^[9]. Our study demonstrate similar results with lower Ct values in patients who present earlier to the hospital ($p < 0.001$).

We have found that comorbidity of the patient does not affect the viral load when the patient presents to the hospital ($p = 0.052$).

Our study has several strengths. It includes a large sample size with 430 patients with a wide range of patients of varying ages, comorbidities and clinical severity. The results of our study are similar to several other studies conducted at different regions.

The limitation of our study is that the Ct value to reflect the viral load is questionable. There is a difference of Ct values between different kits and different techniques (including target genes, primers and threshold fluorescence values)^[10]. The Ct value also depends on the method of collection of the sample and hence there may be variation in Ct values between two different samples obtained from the same person on the same day and run on the same kit. The Ct values also depend on the timing of sample collection in relation to onset of symptoms; samples collected earlier in the illness will have lower Ct values than those collected later in the illness^[11]. Some other studies found that viral load was not a critical factor for hospitalization and mortality^[12]. The Ct value of the sample may not be the true reflection of the viral load in the host but it can be helpful to understand the clinical course of the patient and offer benefit in making clinical decisions. However, the results of this study can not be generalised to the population.

CONCLUSION :

Our study demonstrates that Ct value has no association with comorbidity and clinical severity on admission but it is related to the clinical severity on day 10. Further studies over a large and more varied population are needed for further evaluation of correlation of Ct value with clinical severity.

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CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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The study protocol was approved by the Institutional Review Board and the Ethics Committee.

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