ORIGINAL ARTICLE - PUBLIC HEALTH

RT-PCR CYCLE THRESHOLD VALUES MAY NOT BE USEFUL FOR PRIORITIZATION OF CONTACT TRACING IN THE CONTEXT OF SARS-COV-2 INFECTION

B.Baranidharan[(1)], Suganya Barani [(1)], Tarun Bhatnagarb[(2)], TS Selvavinayagam[(1),]

(1) - Directorate of Public Health and Preventive Medicine, Tamil Nadu, India

(2) - ICMR School of Public Health, ICMR-National Institute of Epidemiology, Chennai, India

Abstract

BACKGROUND: Viral load is an important factor determining the likelihood of transmission of COVID-19. Assuming that Cycle threshold (Ct) values of the diagnostic RT-PCR assay are a surrogate marker of viral load, we wanted to determine whether Ct values can be used to estimate the infectivity in terms of secondary attack rate among COVID-19 positive individuals so as to inform public health surveillance.

METHODS: We conducted a cross sectional study to compare cycle threshold values by secondary attack rates, age, gender, symptom status and comorbidity of COVID-19 individuals. We extracted data of Ct values from the sample referral form of all 485 COVID-19 positive individuals from three districts, tested in the state public health laboratory in three days. We extracted patient details like symptom status, number of contacts who tested positive for COVID-19 from the district surveillance records. We report median with interquartile range of Ct values and tested between groups using Mann-Whitney test.

RESULTS: There was no statistically significant difference in median Ct values across sub groups of secondary attack rate. COVID-19 positive individuals with symptoms had lower Ct value in all three genes with statistically significant difference in E gene (21.8; IQR 18.5-24.6) vs 23; IQR 19.7-26.1, p<0.02) and RDRP gene (21.4; IQR 18.5-25) vs 22.7; IQR 19.3-26, p<0.03). There was no significant difference in median Ct values between individuals with and without comorbidity.

CONCLUSION: We could not identify a relationship between Ct values and secondary attack rate. Symptomatic COVID-19 positive individuals have a significant lower Ct values corroborating with a higher viral load among them. Our findings indicate that Ct values of RT-PCR assay cannot be used in public health surveillance to predict transmission of COVID-19.

KEY WORDS: Contact Tracing, Covid-19, Cycle Threshold Value, Sars-Cov-2, Secondary Attack Rate, Surveillance.

INTRODUCTION

Viral load is an important factor determining the likelihood of transmission of COVID-19.1 Aggressive contact tracing and isolation will aid in quick isolation of high viral shedders who may play a critical role in transmission of infection among their contacts.[2] Resource constrained settings warrant measures that will save time and efforts in identification of individuals who need to be prioritised and isolated. The cycle threshold values generated during RT-PCR have an inverse correlation with the viral load of the person who is infected. Positive association is reported between sputum viral load and disease severity, risk of intubation, disease progression and death.3,4 With an underlying assumption that cycle threshold (Ct) values of the diagnostic RT-PCR assay are a surrogate marker of viral load of the individual, we did a cross-sectional study to determine whether Ct values could be used to estimate the infectivity in terms of secondary attack rate and association with age, gender, symptom status and comorbidity among COVID-19 positive individuals in order to inform public health surveillance.

METHODOLOGY

We extracted data of 485 COVID-19 positive individuals and their contacts from state public health laboratory. We extracted details about the symptom status, comorbidity, and number of contacts who tested positive for COVID-19 available with the district surveillance records. We calculated the secondary attack rate of COVID-19 for positive individuals. We divided them into four subgroups with secondary attack rate <25%, 25-50%, 50-75% and >75%. We calculated the median with interquartile range of Ct values and tested between groups using Mann-Whitney test.

RESULTS AND DISCUSSION

The difference in median Ct values of all three genes was not statistically significant across subgroups of age. Females had a significantly lower Ct value in RDRP gene compared to males. There was no statistically significant difference of

Please Scan this QR Code to
View this Article Online
Article ID: 2021:01:02:02
Corresponding Author : B.Baranidharan
e-mail: baraniddhs@gmail.com

median CT values across sub groups of secondary attack rate. COVID-19 positive individuals with symptoms had lower Ct value in all three genes with statistically significant difference in E gene and RDRP gene. There was no significant difference in median Ct values between individuals with and without comorbidity. (Table 1)

Table 1: Median CT values by age, gender, secondary attack rate, symptom and comorbidity status in COVID-19 positive individuals, Tamil Nadu, India, August 2020

Characteristics	n	E gene		RDRP gene		ORF-1B gene	
		Median (IQR)	p value	Median (IQR)	p value	Median (IQR)	p value
Age group (years)							
0-17	67	23.8(20.0,25.9)	0.4	24(20.4,26.6)	0.1	22.7(20.2,25.2)	0.2
18-44	260	22.6(19.1,25.6)		22.5(18.7,25.5)		21.9(18.4,25.2)	
45-60	109	21.8(18.8,25.4)		21.5(18.5,25.4)		21.3(18.5,24.6)	
60 & above	46	23.4(19.7,26.0)		23.2(19.5,25.9)		22.9(19.6,24.6)	
Sex							
Male	282	22.8(19.7,30)	0.2	22.8(19.8,25.9)	0.03	21.9(19.3,25.1)	0.5
Female	203	22.1(18.6,22.7)		21.8(18.1,25.5)		21.9(18.2,25.2)	
Secondary attack rate							
<25%	375	23(20,25.9)		22.7(19.4,25.8)		22.1(19.2,25.1)	0.2
25-50%	41	22.8(18.1,26.5)	0.1	22.8(19.3,26.4)	0.2	21.7(17.6,26.6)	
50-75%	17	20.8(17.3,26.5)		21.2(17.8,26.2)		21.7(17.6,26.6)	
75-100%	5	15.6(13.2,18.7)		16.1(14,16.2)		16.1(13.9,19.3)	
Symptomatic							
Yes	126	21.8(18.5,24.6)		21.4(18.5,25)		21.0(18.2,24.6)	
No	350	23(19.7,26.1)	0.02	22.7(19.3,26)	0.03	22.4(19.4,25.2)	0.05
Comorbidity							
Yes	48	24.4(19.7,26.6)	0.1	24.1(19.4,26.5)	0.2	23.7(19.5,25.7)	0.2
No	427	22.4(19.2,25.7)		22.4(18.9,25.6)		21.8(18.9,25.1)	

Ct values were not associated with secondary attack rate for SARS-CoV-2 infection in our setting. However, we have not accounted for the contacts who have not been tested and for unknown confounders with relation to the value of the cycle threshold numbers. Symptomatic COVID-19 positive individuals have a significant lower Ct values corroborating with a higher viral load among them. It may be noted that self-reported symptoms and comorbidity could be a source of information bias. This could have led to misclassification in the subgroup analysis and biased the association. Ct values can vary based on the sample collection, type of sample, workflow, standard curve and interpretation of the assay during confirmation of diagnosis.[5] However we report our findings from a single laboratory and we assume that some operational biases are nullified in the process.

CONCLUSION

Our findings indicate that Ct values may not be of use in public health surveillance to predict transmission of SARS-CoV-2 infection.

CONFLICT OF INTERESTS

None declared

AUTHORS' CONTRIBUTIONS

SB and BB conceived the study; SB and TB designed the study protocol, carried out analysis, interpretation of data and drafted the manuscript; TSS, BB critically reviewed the manuscript for intellectual content. All authors read and approved the final manuscript.

ACKNOWLEDGEMENTS

We acknowledge the contribution of Sivadoss Raju, Deputy Director of State Public Health Laboratory (SPHL) of Department of Public Health and Preventive Medicine, Tamil Nadu.

REFERENCES

1. Rao SN, Manissero D, Steele VR, Pareja J. A Systematic Review of the Clinical Utility of Cycle Threshold Values in the Context of COVID-19. Infect Dis Ther. 2020/07/28 ed. 2020 Sep;9(3):573–86.

2. Do super spreaders generate new super spreaders? A hypothesis to explain the propagation pattern of COVID-19. International Journal of Infectious Diseases. 2020 Jul 1; 96:461–3.

3. Yu X, Sun S, Shi Y et al. SARS-CoV-2 viral load in sputum correlates with risk of COVID-19 progression. Critical Care 2020; 24.

4. Magleby R, Westblade LF, Trzebucki A et al. Impact of SARS-CoV-2 Viral Load on Risk of Intubation and Mortality Among Hospitalized Patients with Coronavirus Disease 2019. Clinical Infectious Diseases 2020 Jun 30

5. Han MS, Byun J-H, Cho Y et al. RT-PCR for SARS-CoV-2: quantitative versus qualitative. Lancet Infect Dis 2020 May 20