ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 10 | October - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CLINICAL PROFILE OF RT-PCR POSITIVE COVID-19 PATIENTS AND ITS CORRELATION WITH CYCLE THRESHOLD (Ct) VALUES AT A TERTIARY CARE HOSPITAL IN CENTRAL INDIA

Virology

Dr Shiva Shankari L* MBBS, MD MICROBIOLOGY, Senior Resident, Department of Microbiology, Co Principal Investigator, Viral Research and Diagnostic Laboratory (VRDL) Government Medical College Gondia, Maharashtra, India. *Corresponding Author

Dr Gedam D MBBS, MD MICROBIOLOGY, Professor and Head, Department of Microbiology, Principal Investigator, Viral Research and Diagnostic Laboratory (VRDL), Government Medical College Gondia, Maharashtra, India

ABSTRACT

Background: Real-time RT-PCR is considered the gold standard confirmatory test for detection of SARS CoV-2 (COVID-19) viral infection. Cycle threshold (Ct) values are being utilized to diagnose or predict SARS-CoV-2 infection. Viral load of SARS CoV-2 loosely correlates with ΔCt value of RT-PCR assay. The ΔCt value can thus be useful in predicting the outcome of a patient in presence of co-morbid conditions. **Material and Methods:** The present Observational Cross-sectional study was conducted at Viral Research and Diagnostic Laboratory (VRDL), Government medical college Gondia where nasopharyngeal swabs from suspected COVID-19 patients were tested for presence of SARS CoV-2 RNA using RT-PCR. The ΔCt values of RT-PCR positive samples were analysed with respect to the demographic details and pre-existing co-morbid conditions. **Results:** Among total 12298 tested samples, 1705 were RT-PCR positive over period of six months from September 2021 to February 2022. Male Female ratio was 1.27: 1 and 74.90% patients had no pre-existing co-morbid conditions. Case fatality rate was 24.63%. One-way ANOVA test showed that the variation of ΔCt value in different age groups and number of co-morbidities were significant among the two outcome groups. **Conclusion:** ΔCt value can be utilized as a marker for predicting outcome in COVID-19-positive patients with pre-existing co-morbid conditions. This is particularly useful in resource-constrained settings for early intervention and mitigation of poor outcomes.

KEYWORDS

SARS CoV-2, RT-PCR, ICMR, VRDL, Ct values.

INTRODUCTION:

In December 2019, a series of pneumonia cases of unknown cause emerged in Wuhan, Hubei, China with clinical presentations greatly resembling viral pneumonia[1]. On 11th February 2020, World Health Organization (WHO) announced official name for disease as the coronavirus disease 2019 (COVID-19), while the International Committee on Taxonomy of Viruses (ICTV) officially named it as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), owing to genetic likeliness to the coronavirus responsible for SARS outbreak of 2003[2,3]. Being a novel disease, clinical course was unknown, initially engendering various theories predicting the outcome. A consistent correlation was found between high viral load of SARS-CoV-2 and poor prognosis[4]. Presence of chronic co-morbidities is a clinical risk factor for severe or fatal outcome associated with COVID-19[5]. The diagnosis of COVID-19 is made using Reverse-transcription Polymerase Chain Reaction (RT-PCR)[6]. The viral load of SARS-CoV-2 is a marker of disease severity and predicts the risk of death[7]. The cycle threshold (Ct) values of PCR reaction correlate inversely with viral load; low Ct values indicate high viral loads and vice versa[8]. Cycle threshold (ΔCt) value which is readily calculable with RTPCR acts as a coarse marker of viral load in any given sample[9]. As many laboratories carrying out RTPCR especially in remote locations lack the ability to estimate viral load, ΔCt values of RT-PCR results can be used as a coarse marker for viral load. The present study was undertaken with an objective of studying the correlation between ΔCt value and outcome of a patient with presence of co-morbid conditions.

MATERIAL AND METHODS:

The present study Retrospective Cross-sectional Observational study carried out at Government Medical College Gondia, Maharashtra, a Dedicated COVID-19 Hospital (DCH). The patients were tested for presence of SARS COV-2 RNA using Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) over period of Six months commencing from September 2021. The nasopharyngeal samples collected were transported in cold chain and triple-layer packaging to Viral Research and Diagnostic Laboratory (VRDL), Department of Microbiology, GMC Gondia, a Indian Council of Medical Research (ICMR) approved Medical college level COVID-19 testing laboratory. Ribonucleic Acid (RNA) Extraction was done by automated technique with extraction control. The extracted RNA was then subjected to real time RT-PCR with amplification of extraction control determining validity of reaction[10]. Various kits approved for use by ICMR were used for RT-PCR according to current government guidelines. The targets for amplification were E-gene or S-gene for screening and RdRP gene, OFR1b gene, or N-gene for confirmatory according to kit used. The Cycle Threshold for positivity was determined as per kit literatures. Inconclusive results, samples sent for repeat testing and Patients whose pre existing co-morbid conditions could not be traced were excluded from study. Demographic details of SARS CoV-2 RT-PCR positive patients along with pre-existing co-morbid conditions were obtained from institutional medical records section. The data obtained were compiled using Microsoft® Excel for Mac. Statistical tests of significance one-way ANOVA was used to analyze the data in IBM SPSS v26 software.

RESULTS:

Among 12298 patients admitted in various wards of a Dedicated COVID19 Hospital (DCH), 1705 (13.86%) patients tested positive by RT-PCR. Positivity rate was higher in males (n = 954; 55.95%) than females (n = 751; 44.05%) [Table 1]. Majority of patients were in 18-59-year age group (n = 1175; 68.91%) [Table 2].

Table 1: Gender Distribution Of Patients

Co-Morbidities	None	One	Two	Three	>Four	Total
Male	711	156	65	15	7	954
	41.70%	9.15%	3.81%	0.88%	0.41%	55.95%
Female	566	103	62	17	3	751
	33.20%	6.04%	3.64%	1%	0.18%	44.05%

Table 2: Age Distribution Of Patients

Co-Morbidities	None	One	Two	Three	>Four	Total
1-17 years	41	3	0	0	0	44
	2.40%	0.18%	0%	0%	0%	2.58%
18-59 years	960	141	53	16	5	1175
	56.30%	8.27%	3.11%	0.94%	0.29%	68.91%
>60 years	276	115	74	16	5	486
	16.19%	6.74%	4.34%	0.94%	0.29%	28.50%

Pre-existing co-morbid conditions were numerically noted for each patient [Table 3]. 74.90% of the patients did not have any pre-existing co-morbid conditions (n = 1127). 15.19% had one co-morbid condition (n = 259), 25.10% of patients had multiple co-morbid conditions.53.85% patients succumbed when the ΔCt value was less than 10, whereas 81.63% recovered when it was over 30. [Table 4]. Patients succumbing to COVID-19 showed a steady rise in the number of pre-existing co-morbid conditions. Conversely, most of recovered patients had ≤1 pre-existing co-morbid condition (n = 1213; 71.14%).

Table 3. Pre-existing Co-morbid Conditions Among COVID-19 Positive Patients.

Pre existing Co-morbid conditions	None	One	Two	Three	Four	Five	TOTAL
Succumbed	189	134	68	21	7	1	420
	14.80 %	51.74 %	53.54 %	65.63 %	77.78 %	100%	24.63%
Recovered	1088	125	59	11	2	0	1285
	85.20 %	48.26 %	46.46 %	34.38 %	22.22 %	0%	75.37%
Total	1277	259	127	32	9	1	1705
	100%	100%	100%	100%	100%	100%	100%

Table 4. ΔCt Value Among COVID-19 Positive Patients

ΔCt Value	≤10	11 to 20	21 to 30	>30	TOTAL
Succumbed	7	104	239	70	420
	53.85%	31.90%	24.26%	18.37%	24.63%
Recovered	6	222	746	311	1285
	46.15%	68.10%	75.74%	81.63%	75.37%
Total	13	326	985	381	1705
	100%	100%	100%	100%	100%

One-way ANOVA test was applied to study the variation among ΔCt values, different age groups, and number of co-morbidities between the two outcomes that is, recovery and death.There was statistically significant difference ($p < 0.05$) between groups and within groups as shown in Table 5.

Table 5. One way Analysis of Variance (ANOVA)

		Sum of Squares	Df	Mean Square	F	Significance
ΔCt Value	Between groups	715.27	1	715.27	21.471	0
	Within groups	56731.871	1703	33.313		
	Total	57447.141	1704			
Age	Between groups	70870.029	1	70870.029	254.18	0
	Within groups	467856.423	1678	278.818		
	Total	538726.452	1679			
Co-morbidities	Between groups	133.91	1	133.91	270.748	0
	Within groups	842.29	1703	0.495		
	Total	976.199	1704			

DISCUSSION:

Out of 12298 patients, 1705 patients tested positive by RT-PCR with percent positivity = 13.86% over Six months of study period. 954 were male (55.95%) and 751 were female (44.05%) attributing to Male:Female ratio1.27: 1 and majority of patients belonged to 18-59-year age group (n = 1175; 68.91%). Similar findings were obtained in an initial study in Wuhan, Hubei, China by Xiao et al where 63.5% patients were below 65 years and positivity showed male preponderance[11]. Studies conducted in Jaipur, Rajasthan by Bhandari et al showed similar findings where 80.9% of patients were below 60 years of age with male preponderance[12].Most of the patients did not have any pre-existing co-morbid conditions (n=1127; 74.90%). The mortality rate of COVID-19 was 3.42% (n = 420 of 12298). Similar findings were obtained in a study in China by Baud et al with mortality rate of 3.6%[13]. The global mortality rate is found to be 4.7%[14]. The present study substantiated the findings of Jain et al, who reported mortality in India to be lower than that in western world[15].

The CFR turned out to be 24.63% (n = 420 of 1705) and recovery rate was 75.37% (n = 1285 of 1705). The variation among ΔCt values, different age groups and number of co-morbidities between the two outcomes, recovery, and death, was determined using One-way ANOVA test. The test showed significant within and between group variation and This was followed by positive linear correlation between number of pre-existing co-morbid conditions in a COVID—19 positive patient and outcome. These findings indicate that a COVID-19 positive patient is more likely to succumb as the ΔCt value decreases, and also as the number of pre-existing co-morbid conditions increase. It can therefore be inferred that a low ΔCt value in a patient with more pre-existing co-morbid conditions is more likely to succumb, while a high ΔCt value in the presence of fewer or no pre-existing comorbid condition is likely to survive.

CONCLUSION

The ΔCt value of RT-PCR positive patients can be utilized as a marker for predicting the outcome in COVID-19-positive patients with pre-existing co-morbid conditions. This is particularly useful in resource constrained settings, where facilities and consumables for determination of viral load are scant. As these findings are available to the clinician along with the positive RT-PCR report itself. An early intervention can be instituted in such cases to mitigate a poor outcome.

Funding: Nil

Conflict of Interest: None declared

REFERENCES:

[1]. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P. A novel coronavirus from patients with pneumonia in China, 2019. New England Journal of Medicine. 2020 Jan 24.
[2]. Coronavirus Disease 2019 (COVID-19), Centers for Disease Control and Prevention, 01 September2020.https://www.cdc.gov/coronavirus/2019ncov/cdcresponse/aboutCOVID19.html#:~:text=On%20February%2011%2C%202020%2C%20the,and%20'D'%20for%20disdise.
[3]. Naming the coronavirus disease (COVID-19) and the virus that causes it; World Health Organization, 11 February 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirusdisease-(covid-2019)-and-the-virus-that-causesit#:~:text=ICTV%20announced%20%E2%80%9Csevere%20acute%20respiratory,the%20SARS%20outbreak%20of%202003.
[4]. Liu Y, Yan LM, Wan L, Xiang TX, Le A, Liu JM, Peiris M, Poon LL, Zhang W. Viral dynamics in mild and severe cases of COVID-19. The Lancet Infectious Diseases. 2020 Mar 19.
[5]. Zhou Y, Yang Q, Chi J, Dong B, Lv W, Shen L, Wang Y. Comorbidities and the risk of severe or fatal outcomes associated with coronavirus disease 2019: A systematic review and meta-analysis. International Journal of Infectious Diseases. 2020 Jul 25.
[6]. Bullard J, Dust K, Funk D, Strong JE, Alexander D, Garnett L, Boodman C, Bello A, Hedley A, Schiffman Z, Doan K. Predicting infectious SARS-CoV-2 from diagnostic samples. Clinical Infectious Diseases. 2020 May 22.
[7]. Fajnzylber J, Regan J, Coxen K, Corry H, Wong C, Rosenthal A, Worrall D, Giguel F, Piechocka-Trocha A, Atyeo C, Fischinger S. SARS-CoV-2 viral load is associated with increased disease severity and mortality. Nature communications. 2020 Oct 30;11(1):1-9.
[8]. Yu F., Yan L., Wang N. Quantitative detection and viral load analysis of SARS-CoV-2 in infected patients. Clin Infect Dis. 2020 Pg.345
[9]. Rhoads D, Peaper DR, She RC, Nolte FS, Wojewoda CM, Anderson NW, Pritt BS. College of American Pathologists (CAP) microbiology committee perspective: caution must be used in interpreting the cycle threshold (Ct) value. Clinical Infectious Diseases. 2020 Aug 12.
[10]. Magleby R, Westblade LF, Trzebucki A, Simon MS, Rajan M, Park J, Goyal P, Safford MM, Satlin MJ. 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.
[11]. Xiao AT, Tong YX, Gao C, Zhu L, Zhang YJ, Zhang S. Dynamic profile of RT-PCR findings from 301 COVID-19 patients in Wuhan, China: a descriptive study. Journal of Clinical Virology. 2020 Jun 1;127: 104346.
[12]. Bhandari S, Bhargava A, Sharma S, Keshwani P, Sharma R, Banerjee S. Clinical profile of covid-19 infected patients admitted in a tertiary care hospital in north India. J Assoc Phys India. 2020 May 1;68: 13-7.
[13]. Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, Favre G. Real estimates of mortality following COVID-19 infection. The Lancet infectious diseases. 2020 Jul 1;20(7):773.
[14]. Omer SB, Malani P, Del Rio C. The COVID-19 pandemic in the US: a clinical update. JAMA. 2020 May 12;323(18):1767-8.
[15]. Jain VK, Iyengar K, Vaish A, Vaishya R. Differential mortality in COVID-19 patients from India and western countries. Diabetes & Metabolic Syndrome : Clinical Research & Reviews. 2020 Sep 1;14(5):1037-41.