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Research Article

Evaluation of Prolonged Rt-Pcr Positivity and Viral Load in COVID-19 Patients

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Abstract

Aim: Real-time reverse transcription polymerase chain reaction (RT-PCR) test is used in the diagnosis of COVID-19. It was aimed to evaluate the factors affecting the viral conversion time, to examine the relationship between viral load, and to determine other factors that may be associated with viral load.

Material and Methods: Patients were hospitalized between 15.03.2020-01.08.2020, and viral conversion detected were evaluated retrospectively. Patients were divided into two according to viral conversion time (0-14 days vs >14 days).

Results: 349 patients were included in the study (284 vs 65 patients). The age and gender characteristics were similar. Prolonged PCR positivity group had more death (p=0.036) and lower cycle-threshold (CT) value (p=0.017). In the examination of CT values of 246 patients, 228 patients with viral conversion and 18 patients without viral conversion due to death, the CT value was found to be lower, therefore the viral load was higher in patients over 60 years of age (p=0.006), in the presence of cardiovascular system disease (p<0.001) and in patients who died (p<0.001).

Conclusion: Prolonged PCR positivity may indicate excess viral load and adverse outcomes. An evaluation including the patient's age, CT value, comorbid conditions, and viral conversion time can give an idea about the prognosis.

Keywords: Clearance, cycle threshold (CT) value, negative conversion, SARS-CoV-2, viral load

INTRODUCTION

Coronavirus Disease 2019 (COVID-19), which is caused by a new virus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), first appeared in China in late 2019 and spread all over the world in a short time, causing a global pandemic (1,2). Although serological diagnoses are possible, real-time reverse transcription polymerase chain reaction (RT-PCR) testing is mainly used for the diagnosis of COVID-19, and it is recommended to evaluate combined swab samples taken from the nasopharynx and oropharynx (3,4). RT-PCR also allows the detection of the cycle threshold (CT) value as well as the diagnosis of the disease. The CT value is defined as the number of amplification cycles required for the target gene to exceed a certain threshold and can be used indirectly to measure viral load (5).

Various studies have been conducted to correlate virus shedding time with disease prognosis, viral load, or other factors. In these studies, it was reported that virus excretion takes a long time in advanced age, in patients with underlying disease or in severe cases (6-8). Despite these data in the literature, viral dynamics related to the disease have not been clarified yet.

In this study, it was aimed to evaluate the factors affecting the viral clearance time, to examine the relationship between viral load and viral clearance time, and to determine other factors that may be associated with viral load.

MATERIAL AND METHOD

This study was planned retrospectively in our center. Ethics committee approval was obtained from the Kirikkale University and the Non-Interventional Studies Ethics Committe with number and date of 2021.03.28

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and 25.03.2021. The patients were informed and a signed consent form was obtained from each patient for inclusion in the study. Patients aged 18 years and older were hospitalized in our center between 15.03.2020 and 01.08.2020, with positive SARS-CoV-2 RT-PCR test and viral conversion detected during follow-up were included in the study. Patients were divided into two groups according to viral conversion time; 0-14 days and >14 days (prolonged polymerase chain reaction -PCR- positivity). The data of the patients were determined from the hospital system and archive files. The age, gender and comorbid conditions of the patients were noted. Complete blood count, creatinine, electrolytes, aspartate aminotransferase (AST), alanine aminotransferase (ALT), C-reactive protein (CRP), ferritin were evaluated at the time of admission to the hospital. Thorax computed tomography images of the patients were categorized according to the COVID-19 Reporting and Data System (CO-RADS) classification evolved by The Radiological Society of the Netherlands (NVvR) and classified between CO-RADS 1-5 (9). Antiviral and antibacterial treatments given to the patients during the hospitalization period were examined from the patient files. Treatment outcomes of the patients were noted as discharge or death. Symptom duration was not included in the study because the information provided was not clear and the data could not be evaluated optimally.

Evaluation of samples and determination of conversion time

Evaluated swabs were taken from both the nasopharynx and oropharynx of the patients in a combined manner. The swabs taken were tested with the RT-PCR method. Bioeksen Bio-Speedy® SARS-CoV-2 Double Gene RT-qPCR Kit and its versions were used for RT-PCR. All of the kits were run on the Biorad CFX96 Touch Real-Time PCR Detection System device. All of the study was completed with the same kit and device.

SARS-CoV-2 specific N and ORF1ab gene regions were targeted during PCR method. The recommended threshold level in the kit insert for calculating the number of cycles was 200 RFU for Biorad CFX96 instruments. The shape of the amplification curves was examined according to the kit package insert, and sigmoidal curves with assigned CT value and CT value ≤ 33 in the Fam channel were considered positive. If a sample was assigned a CT value but the curve was not sigmoidal, the result was recorded as negative. During the determination of these CT values, attention was paid to the evaluation of all samples by the same person. CT values were evaluated at diagnosis, regardless of patient outcome. Therefore, the CT values of the cases that resulted as dead were also determined.

Internal control (IC) was used in line with the kit recommendations while working the samples. However, due to the retrospective nature of the study, no correction was made according to the internal control value during the analysis of the data. For all that, according to the sampling method of the test, all samples were taken by a predetermined and trained team to prevent false negative results and to ensure that the samples were of similar quality.

When calculating the viral conversion time; the day on the virus was detected by the RT-PCR method was determined as the first day. Viral conversion was defined as two consecutive negative RT-PCR results evaluated at least 24 hours apart. The first day of consecutive tests with a negative result was recorded as the day when viral shedding ended. The control RT-PCR test was taken on the 5th day at the earliest. If the result was positive, control RT-PCR tests were repeated every day or every other day.

Statistical analysis

IBM SPSS for Windows (version 23.0; SPSS Inc., Chicago, IL, USA) program was used for data analysis. Shapiro Wilk test was used for normality assessment. For non-normally distributed continuous variables, Mann-Whitney U and Kruskal Wallis tests were used to compare the two groups. Chi-square test was used to evaluate categorical data. A p value less than 0.05 was considered statistically significant.

RESULTS

349 patients who were hospitalized in our center between 15.03.2020 and 01.08.2020 with the diagnosis of COVID-19 and were found to have viral conversion during the follow-up were included in the study. It was determined that there were 284 and 65 patients in the groups with a viral conversion period of 0-14 days and >14 days, respectively, and the age and gender characteristics of the two groups were similar. CT values of 185 patients in the group with viral conversion duration of 0-14 days and 43 patients in the group with >14 days were evaluated. Since the study was retrospective, the ct value of 121 patients with viral conversion could not be reached. CT value was found to be significantly lower in the group with prolonged PCR positivity compared to the other (28.31 (17.89- 38.38) vs 26.16 (18.77- 34.55) days respectively, p=0.017). The comparison of demographic characteristics, comorbid conditions, radiological images and treatments used according to the viral conversion time of the patients is given in Table I.

AST and lymphocyte levels were found to be lower and sodium levels were higher in those with prolonged PCR positivity in the blood tests. The difference in AST and sodium values was statistically significant, but was not considered clinically significant. Detailed analysis of the blood values of the two groups is given in Table II.

In order to examine the relationship of CT values with age, gender, comorbid conditions, radiological involvement, and clinical outcome, an analysis consisting of 246 patients was performed (Table III). When analyzing the factors related to the CT value; The data of 228 patients with known ct value in the group with viral conversion were analyzed. In addition, the data of 18 patients whose

Table 1. Comparison of demographic characteristics, comorbid conditions, radiological images and treatments used according to viral conversion time

		All patients (n= 349)	Viral conversion time		p value
			0-14 days (n=284)	>14 days (n=65)	
Median (min- max)					
Age (years)		42 (18-87)	42 (18-85)	43 (21-87)	0.708
Viral conversion time (days)		9 (5-21)	8 (5-14)	16 (15- 21)	<0.001
Hospital stay (days)		9 (5-36)	9 (5-19)	16 (6-36)	<0.001
Intensive Care Unit stay (days)		0 (0- 13)	0 (0-13)	0 (0-3)	0.934
CT value		27.95 (17.89-38.38)	28.31 (17.89-38.38)	26.16 (18.77-34.55)	0.017
n (%)					
Sex (male)		173 (49.5%)	143 (50.3%)	30 (46.1%)	0.541
Smoking		68 (19.4%)	56 (19.7%)	12 (18.5%)	0.739
Pregnancy		3 (0.8%)	3 (1.1%)	0 (0%)	0.405
Comorbid condition (≥1 comorbidity)		126 (36.1%)	103 (36.2%)	23 (35.4%)	0.894
Cardiovascular diseases	Hypertension	51 (14.6%)	43 (15.1%)	8 (12.3%)	0.842
	Coronary artery disease	41 (11.7%)	33 (11.6%)	8 (12.3%)	
Respiratory diseases	Chronic obstructive pulmonary disease	14 (4%)	12 (4.2%)	2 (3%)	0.881
	Asthma	9 (2.5%)	7 (2.5%)	2 (3%)	
Diabetes mellitus		35 (10%)	29 (10.2%)	6 (9.2%)	0.812
Chronic kidney disease		3 (0.8%)	1 (0.3%)	2 (3%)	**0.032**
Neurological diseases		16 (4.5%)	14 (4.9%)	2 (3%)	0.519
Malignancy		3 (0.8%)	3 (1.1%)	0 (0%)	0.405
Radiological findings (Computed tomography)	None	12 (3.4%)	7 (2.5%)	5 (7.7%)	0.087
	CO-RADS 1	207 (59.3%)	167 (58.8%)	40 (61.5%)	
	CO-RADS 2	0 (0%)	0 (0%)	0 (0%)	
	CO-RADS 3	24 (6.8%)	19 (6.7%)	5 (7.7%)	
	CO-RADS 4	9 (2.5%)	6 (2.1%)	3 (4.6%)	
	CO-RADS 5	97 (27.8%)	85 (29.9%)	12 (18.5%)	
Medical treatment	Hydroxychloroquine	339 (97.1%)	275 (96.8%)	64 (98.4%)	0.477
	Favipiravir	17 (4.9%)	10 (3.5%)	7 (10.8%)	**0.014**
	Lopinavir/ritonavir	3 (0.8%)	2 (0.7%)	1 (1.5%)	0.511
	Azithromycin	132 (37.8%)	115 (40.5%)	17 (26.1%)	**0.032**
	Moxifloxacin	8 (2.3%)	6 (2.1%)	2 (3%)	0.639
	Oseltamivir	46 (13.2%)	39 (13.7%)	7 (10.8%)	0.524
Clinical outcome (death)		1 (0.3%)	0 (0%)	1 (1.5%)	**0.036**

Chi-square and Mann Whitney U test was used
CT: Cycle Threshold

Table 2. Comparison of blood tests according to viral conversion time

Laboratory tests Median (min- max)	All patients (n= 349)	Viral conversion time		p value
		0-14 days (n=284)	>14 days (n=65)	
AST (U/L)	25 (12- 331)	25 (12- 331)	21 (13- 98)	0.046
ALT (U/L)	19 (5- 266)	19 (5- 266)	19 (6- 153)	0.884
Creatinine (mg/dL)	0.7 (0.3- 2.1)	0.7 (0.4- 1.9)	0.7 (0.3- 2.1)	0.794
Sodium (mmol/L)	136 (128- 143)	136 (128- 143)	137 (132- 142)	0.045
Potassium (mmol/L)	4.0 (3- 6.2)	4.0 (3.2- 6.2)	4.1 (3- 5.4)	0.981
CRP (mg/dL)	0.5 (0.01- 16.3)	0.5 (0.01- 16.3)	0.5 (0.02- 13.80)	0.177
White blood cell (10^9/L)	5.7 (1.6- 18.8)	5.7 (1.6- 18.8)	6.2 (2.7- 10.7)	0.249
Lymphocyte (10^3/uL)	1.7 (0.35- 6)	1.7 (0.46- 6)	1.36 (0.35- 4)	0.024
Hæmoglobin (g/dL)	14 (6.8- 18.2)	14.1 (6.8- 18.2)	13.7 (7.6- 17.3)	0.379
Platelet (10^9/L)	216 (54- 446)	211 (54- 446)	218 (99- 419)	0.759
Ferritin (µg/L)	84 (0.5- 1002)	86 (0.5- 1002)	71 (9- 849)	0.162

Mann Whitney U test was used. AST: Aspartate Aminotransferase. ALT: Alanine Aminotransferase. CRP. C-reactive Protein

Table 3. Comparison of CT values according to age, gender, radiological involvement, comorbid conditions, and clinical outcome

All patients (n= 246)		CT value (Median (min-max)	p value
Age	≤ 60 years (n=193)	27.94 (18.75-38.38)	**0.006**
	>60 years (n=53)	25.15 (14.40-35.74)	
Sex	Male (n=129)	27.64 (14.40-36.62)	0.642
	Female (n=117)	27.68 (16.22-38.38)	
Radiological findings	CO-RADS 1 (n=145)	27.68 (18.77-38.38)	0.570
	CO-RADS 5 (n=70)	27.61 (14.40-37.50)	
Comorbid condition	No (n=147)	28.22 (18.83-38.38)	**0.020**
	≥1 comorbidity (n=99)	26.97 (14.40-35.74)	
Cardiovascular diseases	No (n=171)	28.23 (18.77-38.38)	**<0.001**
	Yes (n=75)	25.27 (14.40-35.74)	
Diabetes mellitus	No (n=216)	27.94 (18.71-38.38)	0.408
	Yes (n=30)	27.51 (17.89-35.64)	
Respiratory diseases	No (n=227)	27.94 (17.89-38.38)	0.230
	Yes (n=19)	24.51 (18.77-35.74)	
Chronic kidney disease	No (n=241)	27.95 (17.89-38.38)	0.555
	Yes (n=5)	24.36 (21.51-35.08)	
Neurological diseases	No (n=234)	27.89 (17.89-38.38)	0.947
	Yes (n=12)	27.51 (18.77-34.61)	
Clinical outcome	Discharged (n=227)	28.01 (17.89-38.38)	**<0.001**
	Death (n=19)	21.36 (14.40-35.08)	

Chi-square and Mann Whitney U test was used
CT: Cycle Threshold

CT values were determined but we could not detect viral conversion because they died and we could not include them in the study were also included in the study. CT value was found to be statistically significantly lower in patients over 60 years of age, in the presence of at least 1 comorbid condition, in the presence of cardiovascular system (CVS) disease, and in patients who died.

DISCUSSION

In this study was determined that patients with a viral conversion period longer than 14 days had a longer hospital stay, a lower CT value, and a higher death rate. In addition, it was found that the CT value was lower in cases older than 60 years of age, with at least one comorbid condition, with CVS disease and resulting in death, and this result indirectly suggested that the viral load in these patients was higher.

Viral conversion time is variable, and studies have shown that viral RNA mostly becomes negative after the 7th day. In a study by Hu et al., while the PCR test became negative in 10.2% of patients at the end of the 1st week, this rate was found to be 62.7% and 91.2% at the end of the 2nd and 3rd weeks, respectively (10). In another study, the detection time of virus in respiratory samples was determined as 18 days (13-29 days) (6). In our study, the duration of viral

conversion was 9 days (5-21 days), which was interpreted as shorter than the studies in the literature. This result is thought to be due to the fact that the duration of viral conversion is determined from the date of the first positive RT-PCR, not from the onset of symptoms.

The duration of viral conversion is associated with age, and it has been shown in various studies that this period is prolonged in older age (8,10,11). In a study by Bhattacharya et al., the time from symptom onset to PCR negativity was higher in patients aged 60 years and over (mean 21 days, p=0.004) (8). However, when this time was evaluated from the date of the first positive RT-PCR, no significant difference was observed according to age groups (p=0.18) (8). In our study, the ages were similar in both groups, and no difference was found. This result is considered to be obtained because the viral conversion time was evaluated from the date of the first positive RT-PCR, similar to the study of Bhattacharya et al.

There is an inverse relationship between the CT value and the viral conversion time. In the study of Aranha et al., it was reported that the viral conversion period was longer in those with low CT values (12). While viral conversion was frequently observed in the first week in patients with a CT value of 31 and above, it occurred between 2-4 weeks in 79.2% of those with a CT value of 25 and below (12). Similarly, in our study, the CT values of patients who developed viral conversion after 14 days were found to be significantly lower than the others. It is thought that RT-PCR negativity is delayed due to the high viral load in patients with low CT values.

Viral conversion time is associated with disease severity, and it has been found that this period increases in severe disease (6). Although the severity of the disease was not directly evaluated in our study, it was found that mortality was higher in cases whose conversion period exceeded 2 weeks. From a radiological point of view, no relationship was found between radiological involvement and viral conversion time, and a similar result was obtained in our study (10).

When the patients followed up with the diagnosis of COVID-19 were analyzed in terms of blood tests, low lymphocyte levels were found to be associated with severe illness and the need for intensive care (13). In addition, we determined that patients with prolonged PCR positivity had significantly lower lymphocyte counts. In our study, the low lymphocyte count in patients with a longer viral conversion period suggests that viral load is higher in this patient group and adverse outcomes may be more.

Factors associated with CT value

Although the CT value is not directly related to age, it has been shown in various studies that the viral conversion period is longer in elderly patients (8,10,11). In addition, when we look at the literature, it is seen that patients with a long conversion period have low CT values and high viral loads (12,14). In our study, the CT values of patients over 60 years of age were found to be significantly lower, and the viral load is thought to be high in these patients. In our study, the age of the patients was found to be associated with the CT value but not with the conversion time. Because data of 18 patients whose viral conversion could not be detected due to death were included in the analyzes related to the CT value. Therefore, the thought that patients who died had a lower CT value and a higher viral load could explain this finding.

Although it has been reported in various case series that the CT value decreases as the lung damage increases, no significant relationship was found between the presence of pneumonia and the CT value in a study conducted in our country (15,16). Similarly, in our study, no correlation was found between the CT values of the group whose computed tomography findings were classified as CO-RADS 1 (normal or noninfectious findings) and the groups classified as CO-RADS 5 (typical COVID-19 findings).

There is an interaction between viral load, mortality and CVS diseases in the course of COVID-19 (17-19). In a study by Huang et al.; myocardial enzymes were found to be higher in patients with high viral load (17). In another study, it was reported that troponin and CT values showed a negative correlation (18). Evaluation of these enzymes at the time of diagnosis strengthens the possibility of underlying CVS disease rather than CVS involvement due to COVID-19. Similar to these studies, we found a correlation between the presence of underlying CVS disease and the CT value and viral load.

There is an inverse relationship between the CT value and the severity of the disease. Studies have reported that the CT value is lower in cases with severe disease (18,20). Considering the relationship between CT value and mortality, in a study conducted by Huang et al., was reported that the CT value of the cases resulting in mortality was lower than the survivors (p<0.001) (17,21). In our study, the CT value of the cases that resulted in death was found to be significantly lower, and it is thought that these patients have higher viral loads and therefore result in severe disease and mortality.

The strengths of our study are that it considers the CT value and indirectly the viral load as well as viral conversion, and the evaluation of a large population in terms of number of patients. In addition, the definition of viral conversion as the detection of two consecutive negative RT-PCR results in samples taken at least 24 hours apart prevented false-negative results and increased the reliability of the study results. The weakness is that the conversion time is evaluated from the date of the first positive RT-PCR and does not include the symptoms of the patients.

Although it was determined in our study that there was a relationship between CT value and advanced age, presence of comorbid conditions, presence of CVS disease and mortality, in the RT-PCR test performed with different samples taken from the same patient, there may be a difference in the internal control CT values of the samples, which indicates the virus load. It should be noted that it may

affect the CT value. Since our study was retrospectively designed, no correction was made according to the IC value, but all of the samples were taken by a team who had previously been trained in this subject in order to ensure that the samples were similar. In addition, when the studies in the literature were examined, it was determined that no correction was made according to the IC value (17-21).

The strengths of our study are that it considers the CT value and indirectly the viral load as well as viral conversion, and the evaluation of a large population in terms of number of patients. In addition, the definition of viral conversion as the detection of two consecutive negative RT-PCR results in samples taken at least 24 hours apart prevented false-negative results and increased the reliability of the study results. The weakness is that the conversion time is evaluated from the date of the first positive RT-PCR and does not include the symptoms of the patients. In addition, the fact that there is no correction according to the IC value can be considered as another weakness.

CONCLUSION

Patients with a viral conversion duration longer than 14 days have a higher viral load and more adverse outcomes like death. In addition, the viral load is higher in cases older than 60 years of age, with at least one comorbid condition, CVS disease and death. An evaluation including the patient's age, CT value, comorbid conditions, and viral conversion time can give an idea about the prognosis of the disease. Therefore, the development of a scoring system that includes these values may help clinicians in approaching patients. However, further studies are needed for this. We believe that our study will be a guide for future scoring and prediction studies.

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REFERENCES

1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382:727-33.
2. World Health Organization. Director-General's opening remarks at the media briefing on COVID-19- 11 March 2020, https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020.
3. World Health Organization. Laboratory testing for 2019 novel coronavirus (2019-nCoV)in suspected human cases. Interim guidance. Jan 17,2020.
4. Praharaj I, Jain A, Singh M, et al. Pooled testing for COVID-19 diagnosis by real-time RT-PCR: A multi-site comparative evaluation of 5-& 10-sample pooling. Indian J Med Res. 2020;152:88.
5. Bustin SA, Mueller R. Real-time reverse transcription PCR (qRT-PCR) and its potential use in clinical diagnosis. Clin Sci. 2005;109:365-79.
6. Zheng S, Fan J, Yu F, et al. Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study. BMJ. 2020;369.
7. Liu R, Yi S, Zhang J, et al. Viral Load Dynamics in Sputum and Nasopharyngeal Swab in Patients with COVID-19. J Dent Res. 2020;99:1239-44.
8. Bhattacharya B, Kumar R, Meena VP, et al. SARS-CoV-2 RT-PCR profile in 298 Indian COVID-19 patients: a retrospective observational study. Pathog Dis. 2021;79:ftaa064.
9. Prokop M, Van Everdingen W, Van Rees Vellinga T, et al. COVID-19 Standardized Reporting Working Group of the Dutch Radiological Society. CO-RADS: a categorical CT assessment scheme for patients suspected of having COVID-19—definition and evaluation. Radiology. 2020;296:E97-E104.
10. Hu X, Xing Y, Jia J, et al. Factors associated with negative conversion of viral RNA in patients hospitalized with COVID-19. Sci Total Environ. 2020;728:138812.
11. Howard-Jones AR, Maddocks S, Basile K, et al. Prolonged PCR positivity in elderly patients infected with SARS-CoV-2. Pathology. 2021;53:914-6.
12. Aranha C, Patel V, Bhor V, Gogoi D. Cycle threshold values in RT-PCR to determine dynamics of SARS-CoV-2 viral load: An approach to reduce the isolation period for COVID-19 patients. J Med Virol. 2021;93:6794-7.
13. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet. 2020;395: 497-506.
14. Sarinoglu RC, Guneser D, Sengel BE, et al. Evaluation of different respiratory samples and saliva for the detection of SARS-CoV-2 RNA. Marmara Med J. 2021;34:51-6.
15. Liu Y, Yang Y, Zhang C, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. Sci China Life Sci. 2020;63:364-74.
16. Nar R, Caliskan A, Sari T, et al. Evaluation of the relationship between viral load and biochemical parameters in Covid-19 patients. Medicine. 2021;10:469-73.
17. Huang JT, Ran RX, Lv ZH, et al. Chronological changes of viral shedding in adult inpatients with COVID-19 in Wuhan, China. Clin Infect Dis. 2020;71:2158-66.
18. Liu Y, Liao W, Wan L, et al. Correlation between relative nasopharyngeal virus RNA load and lymphocyte count disease severity in patients with COVID-19. Viral immunol. 2021;34:330-5.
19. Abus S, Kapici OB. Investigation of clinical and sociodemographic characteristics of critically patients with COVID-19 admitted to intensive care unit. Med Records. 4:141-7.
20. Yu X, Sun S, Shi Y, et al. SARS-CoV-2 viral load in sputum correlates with risk of COVID-19 progression. Crit care. 2020;24:1-4.
21. 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 and Ther. 2020;9:587.