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Association between Upper Respiratory Tract Viral Load and Comorbidities of Patients with COVID-19

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ABSTRACT

Following the emergence and global spread of coronavirus disease 2019 (COVID-19), a pandemic was declared by the World Health Organization on March 11, 2020. Real-time RT-PCR is considered the gold standard confirmatory test for COVID-19. Cycle threshold (Ct) values are being utilized to diagnose or predict SARS-CoV-2 infection. This practice has a significant clinical utility as Ct values can be correlated with the viral load. Ct values play a crucial role in interpreting viral load and disease severity. In this study, we retrospectively reviewed 756 lab confirmed COVID-19 positive patients. The patients were categorized into three groups, those having high (Ct value <25), moderate (Ct value 25-30), or low URT viral load (Ct value >30). Our study showed that patients with high URT viral load were significantly older. Also, patients with high URT viral load had at least one comorbidity compared to patients with moderate or low URT viral load.

Keywords: COVID-19, Viral Load, Co-morbidities, SARS CoV-2

INTRODUCTION

Towards the end of December 2019, a cluster of pneumonia cases, caused by a newly identified β-Coronavirus, occurred in Wuhan, China (1), which was initially named as the 2019- Novel Coronavirus (2019-nCoV) on 12 January 2020 by World Health Organization (WHO). WHO officially named the disease as Coronavirus disease 2019 (COVID-19) and the new coronavirus as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) on 11 February 2020 (2). Furthermore, it was declared as that of a Public Health Emergency of International Concern (PHEIC) (3) and later on as a pandemic on March 11, 2020 (4).

SARS-CoV-2 spreads predominantly by airborne transmission (5). The infection is also transmitted from human to human and through contact with contaminated environmental surfaces (6) and all age groups were found to be susceptible for this infection. (7)

It is estimated that the median incubation period is of 5.1 days and symptoms start to appear after 11.4 days of infection (8). The infectious stage starts from 2.3 days and peaks at 0.7 days before the onset of symptoms. (9)

Most prevalent co-morbidities among COVID-19 positive hospital patients were hypertension, diabetes, cardiovascular disease and respiratory disease. (10)

Rapidly accumulating set of clinical studies revealed atypical symptoms of COVID-19. Cardiac injury is also seen in COVID-19 patients. It is due to direct viral entry through ACE2 receptor and toxicity in host cells, hypoxia related myocyte injury and immune mediated cytokine release synthesis (11). Liver damage – More than one third

of patients admitted to the hospital with SARS-COV-2 infection have abnormal liver function and this is associated with longer hospital stay (12). Patients with severe COVID-19 infections frequently manifest coagulation abnormalities that are associated with respiratory deterioration and death. In addition, many patients with severe COVID-19 infections develop thromboembolic complications, which seem to be related to the coagulopathy. The coagulation changes associated with COVID-19 mimic disseminated intravascular coagulation or thrombotic microangiopathy (13).

Neurologic signs – headache, anosmia, nausea, dysgeusia, damage to respiratory centers and cerebral infarction (14). Apart from all the morbidities COVID -19 is causing, it is having huge impact on the mental health of the world population with massive increase in anxiety and depression. The severe situation is causing mental health problems such as stress, anxiety, depressive symptoms, insomnia, denial, anger (15).

As the pandemic evolved, several studies focused on the critical role of host factors on disease severity in patients with COVID-19. However, there are significant differences between countries in terms of population demographics and prevalence of comorbidities. In addition, recent studies indicate that host responses to SARS-CoV-2 are dependent on viral load and infection time course. In addition, there is a dearth of published information about the association between viral load and comorbidities. Herein, we studied the upper respiratory tract (URT) viral load of patients with symptomatic or asymptomatic SARS-CoV-2 infection and their potential association with age, gender, comorbidities and disease severity in a series of 756 COVID-19 positive patients in a Tertiary care hospital at GMC Jammu, India.

MATERIALS & METHODS

This study was performed in the Viral Research and Diagnostic Laboratory (VRDL), Department of Microbiology, Government Medical College, Jammu.

Sample collection and processing

All sample acquisitions for RT-PCR were carried out by experienced technicians donning the complete personal protective equipment. We obtained swab samples from the nasopharynx. The swabs were inserted through the nostril to a distance equivalent to the outer opening of the ear canal and gently rubbed for several seconds to absorb the secretions. (16). The nasopharyngeal swab was then placed in a single tube containing 300 µL of Viral Transport Medium (VTM) and transported to the VRDL under cold conditions for subsequent RNA extraction and RT-PCR testing.

Study design

In this analytical retrospective study, a total of 756 patients who tested positive for SARS CoV-2 between 1 October 2021 and 31 December 2021 were included.

Symptomatic patients had one or more symptoms consistent with COVID-19 (cough, fever/chills, shortness of breath, sore throat, abdominal pain, diarrhoea, fatigue, myalgias, loss of taste or smell, headache, congestion/rhinorrhoea, nausea/vomiting, rash, or conjunctivitis) at the time of testing and were tested due to clinical suspicion of COVID-19. Asymptomatic patients had no symptoms of COVID-19 (as defined above) or any clinical suspicion of COVID-19 (other than potential contact status) at the time of testing. Only the first positive test for each patient was included. Data was obtained by telephonic interviews based on an extensive questionnaire.

Comorbidities included chronic cardiovascular disease, hypertension, diabetes mellitus, chronic pulmonary disease, chronic renal disease, chronic neurological disease, chronic hepatic disease, malignancy, immunosuppression, and obesity. Complications included pneumonia, acute respiratory distress syndrome (ARDS), renal failure,

cardiovascular complications, and multi-organ failure.

RNA extraction and real-time polymerase chain reaction

The RNA extraction was performed using Genetix Purifier HT 96 as per manufacture's guidelines using GeneMag Viral DNA/RNA Purification kit. SARS CoV 2 RNA detection was performed using Meril COVID-19 One Step RT-PCR Kit, manufactured by Meril Diagnostics Pvt Ltd, India. It has the sensitivity and specificity of 100% and it detects the Open Reading Frame 1ab (ORF 1ab) and Nucleocapsid (N gene) of the SARS-CoV-2. A Ct value of <35 was used as the cut-off for determining positivity, according to ICMR guidelines.

RESULT

A total of 756 patients which included 405 males (53.6%) and 351 females (46.4%) [Figure1] with SARS-CoV-2 infection were studied amongst which 352 (46.56%) patients had at least one comorbidity; 211 (28%) had an asymptomatic infection and 545 (72%) [Figure 2] developed symptoms of COVID-19.

Of the 756 patients, 342 patients (45.2 %) had high URT viral load, 259 (34.3%) moderate, and 155 (20.5%) low URT viral load [Figure 3]. Patients with high URT viral load were significantly older than patients with moderate or low URT viral load (mean age: 51 years compared to 47 years and 38 years, respectively)

Patients with high URT viral load more often had at least one comorbidity compared to patients with moderate or low URT viral load (48.6% compared to 35.6% and 27.5%, respectively).

Chronic cardiovascular disease, diabetes mellitus, hypertension, chronic pulmonary disease and obesity were the most common co-morbidities among patients with high URT viral load.

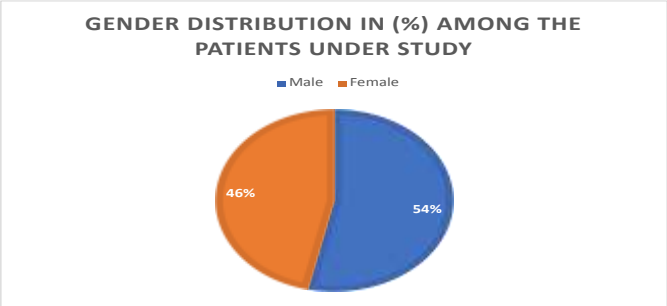

Figure 1: Gender distribution in (%) among the patients under study.

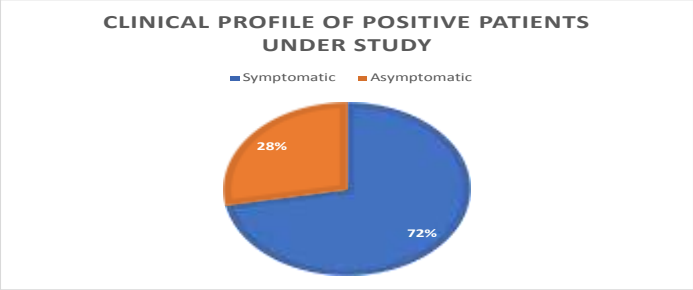

Figure 2: Clinical profile of positive patients under study.

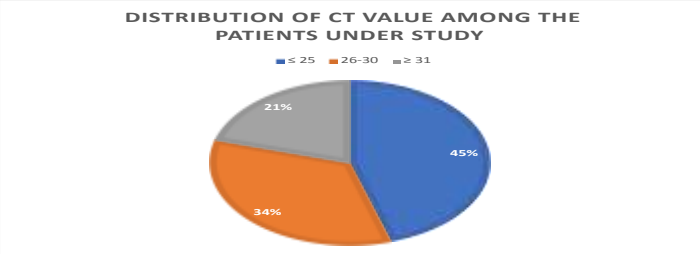

Figure 3: Distribution of Ct value among the patients under study.

DISCUSSION

COVID-19 has been the deadliest disease of the 21st century that has spread rapidly in many parts of the world (17). Most prevalent co-morbidities among COVID-19 positive hospital patients were hypertension, diabetes, cardiovascular disease and respiratory disease. These co-morbidities might have increased the risk of mortality independent of COVID-19 infection (10).

In this study the URT viral load of 756 patients with SARS-CoV-2 infection diagnosed during the last quarter of 2021 at VRDL, Department of Microbiology, GMC, Jammu. The large number of cases allowed us to investigate the association between URT viral loads and specific comorbidities.

It was observed that patients with high SARS-CoV-2 URT viral load tended to be older than patients with moderate or low URT viral load, which is in accordance with a study at the University of Washington Virology Laboratory and demonstrated similar findings (18). A retrospective cohort study of patients hospitalized with COVID-19 at two hospitals in New York City evaluated 678 patients with COVID-19 and observed that higher viral load was associated with an increased age (19). Another study at two hospitals in Hong Kong correlated older age with higher viral load (20). A study on 1,122 COVID-19 positive patients in Greece reported 336 (29.9%) patients with comorbidities. Furthermore, 309 patients (27.5%) had high, 316 (28.2%) moderate, and 497 (44.3%) low viral load. They further observed that patients with high viral load were older with comorbidities, developed symptomatic disease, were intubated and died. In addition, patients with high viral load had longer stay in intensive care unit and longer intubation compared to patients with low viral load (p-values <0.05 for all). (21)

Another finding of the current study is that specific comorbidities significantly correlated with a high SARS-CoV-2 URT viral load at diagnosis. An association between high viral load at admission and specific comorbidities has been also reported from a tertiary care centre in New York City by (22). A study also reported the association of higher SARS-CoV-2 viral load with pre-existing comorbidities. They conducted a study of 678 hospitalized patients with COVID-19 in New York found that patients with high viral load in nasopharyngeal swab samples were more like to get intubated compared to patients with moderate or low viral load (29.1%, 20.8%, and 14.9%, respectively; p-value <0.001) or to die in hospital (35%, 17.6%, and 6.2%, respectively; p-value<0.001) (19).

A similar study conducted in a series of 100 hospitalized patients with hematologic malignancies were admitted to three New York City hospitals. They observed that patients with hematologic malignancies had higher median viral loads (CT = 25.0) than patients without cancer (CT = 29.2; p = 0.0039) (23).

A high SARS-CoV-2 viral load may reflect uncontrolled virus replication in the upper respiratory tract and thus an inefficient immune response in the context of immune dysfunction in patients with specific comorbidities as observed by (24).

Epidemiological studies depict that diabetes contributes to an increase in hospitalisation, admission to critical care and mortality due to COVID-19. In U.S. among 122,653 COVID-19 cases reported to CDC (March 28, 2020) 7,162 (5.8%) patients had data available pertaining to underlying health conditions or potential risk factors. Among these patients, higher percentages of patients with underlying conditions were admitted to the hospital and to an ICU than patients without reported underlying conditions (25). It was reviewed in a study that Chronic Obstructive Pulmonary Disease (COPD) patients are more prone to suffer a severe COVID-19 clinical course (26). A recent meta-analysis has reported that COPD is associated with a significant, over five-fold risk of severe COVID-19 infection (27). A recent review indicated that immunocompromised patients and patients with severe-to-critical illness shed infectious virus for longer (28). The pathogenic mechanism for this correlation may vary by comorbidity and needs further investigation.

In conclusion, the current study provides an insight into the association between URT viral load, host characteristics, clinical severity and outcome in patients with SARS-CoV-2 infection. In our population, higher URT viral load has been detected in symptomatic patients and could be used as a marker of infectivity for infection control purposes. Higher URT viral load was also found in patients with specific comorbidities. Our findings could be used to identify those patients at higher risk for severe morbidity or a fatal outcome and therefore to guide therapeutic interventions. Further, more studies are needed to explore the underlying pathogenetic mechanisms of disease severity and fatal outcome at the host level, including the association between high URT viral load and comorbidities.

CONCLUSION

Our study showed that patients with high URT viral load were significantly older than patients with moderate or low URT viral load. Also, patients with high URT viral load more often had at least one comorbidity compared to patients with moderate or low URT viral load.

Declaration by Authors

Ethical Approval: Approved

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REFERENCES

1. Guo YR, Cao QD, Hong ZS, et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak- An update on the status. Military Medical Research. 2020;7(1):11.
2. WHO COVID-19 Dashboard. Geneva: World Health Organization, 2020. Available online: https://covid19.who.int/ .
3. Ge H, Wang X, Yuan X, et al. The epidemiology and clinical information about COVID-19. Eur J Clin Microbiol Infect Dis. 2020;39(6):1011-19.
4. Parasher A. COVID-19: Current understanding of its Pathophysiology, Clinical presentation and Treatment. Postgrad Med J. 2021;97(1147):312-20.
5. Greenhalgh T, Jimenez JL, Prather KA, et al Ten scientific reasons in support of airborne transmission of SARS-CoV-2. Lancet. 2021 May 1;397(10285):1603-1605.
6. Pascarella G, Strumia A, Piliego C, et al. COVID-19 diagnosis and management: a comprehensive review. Journal of Internal Medicine. Blackwell Publishing Ltd; 2020;288(2):192-206.
7. Singhal T. A Review of Coronavirus Disease-2019 (COVID-19). Indian J Pediatr. 2020;87(4):281-86.
8. Lauer SA, Grantz KH, Bi Q, et al. The incubation period of coronavirus disease 2019 (CoVID-19) from publicly reported confirmed cases: Estimation and application. Ann Intern Med. 2020;172(9): 577-82.
9. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and

transmissibility of COVID-19. Nat Med. 2020;26(5):672-75.
10. Tandon VR, Meeta M. COVID-19 pandemic – Impact on elderly and is there a gender bias? J Midlife Health. 2020;11(3): 117-19.
11. Zhu H, Rhee JW, Cheng P, et al. Cardiovascular Complications in Patients with COVID-19: Consequences of Viral Toxicities and Host Immune Response. Curr Cardiol Rep. 2020;22(5):36.
12. Fan Z, Chen L, Li J, et al. PANCREAS, BILIARY TRACT, AND LIVER Clinical Features of COVID-19-Related Liver Functional Abnormality. Clin Gastroenterol Hepatol. 2020;18(7):1561-66.
13. Levi M, Thachil J. Coronavirus Disease 2019 Coagulopathy: Disseminated Intravascular Coagulation and Thrombotic Microangiopathy-Either, Neither, or Both. Semin Thromb Hemost. 2020;46(7):781-84.
14. Jarrahi A, Ahluwalia M, Khodadadi H, et al. Neurological consequences of COVID-19: What have we learned and where do we go from here? J Neuroinflammation. 2020; 17(1):1-12.
15. Kang L, Li Y, Hu S, et al. The mental health of medical workers in Wuhan, China dealing with the 2019 novel coronavirus. The Lancet Psychiatry. 2020;7(3):e14.
16. Ra SH, Lim JS, Kim GU, et al. Upper respiratory viral load in asymptomatic individuals and mildly symptomatic patients with SARS-CoV-2 infection. Thorax. 2021;76(1):61-63.
17. Mahallawi WH, Alsamiri AD, Dabbour AF, et al. Association of Viral Load in SARS-CoV-2 Patients with Age and Gender. Front Med. 2021; 8:1-5.
18. Lieberman NAP, Peddu V, Xie H, et al. In vivo antiviral host transcriptional response to SARS-CoV-2 by viral load, sex, and age. PLoS Biol. 2020 Sep 8;18(9): e3000849.
19. Magleby R, Westblade LF, Trzebucki A, et al. Impact of Severe Acute Respiratory Syndrome Coronavirus 2 Viral Load on Risk of Intubation and Mortality Among Hospitalized Patients with Coronavirus Disease 2019. Clin Infect Dis. 2021 Dec 6;73(11): e4197-e4205.
20. To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis. 2020 May;20(5): 565-574.
21. Maltezou HC, Raftopoulos V, Vorou R, et al. Association Between Upper Respiratory Tract Viral Load, Comorbidities, Disease Severity, and Outcome of Patients With SARS-CoV-2 Infection. J Infect Dis. 2021 Apr 8;223(7):1132-1138.
22. Argyropoulos KV, Serrano A, Hu J, et al Association of Initial Viral Load in Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Patients with Outcome and Symptoms. Am J Pathol. 2020 Sep;190(9):1881-1887.
23. Westblade LF, Brar G, Pinheiro LC, et al. SARS-CoV-2 Viral Load Predicts Mortality in Patients with and without Cancer Who Are Hospitalized with COVID-19. Cancer Cell. 2020 Nov 9;38(5):661-671.e2.
24. Vas P, Hopkins D, Feher M, et al. Diabetes, obesity and COVID-19: A complex interplay. Diabetes Obes Metab. 2020 Oct;22(10):1892-1896.
25. CDC COVID-19 Response Team. Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 - United States, February 12-March 28, 2020. MMWR Morb Mortal Wkly Rep. 2020 Apr 3;69(13):382-386.
26. Olloquequi J. COVID-19 Susceptibility in chronic obstructive pulmonary disease Eur J Clin Invest. 2020;50:e13382.
27. Lippi G, Henry BM. Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). Respir Med. 2020 Jun;167:105941
28. Walsh KA, Jordan K, Clyne B, et al. SARS-CoV-2 detection, viral load and infectivity over the course of an infection. J Infect. 2020 Sep;81(3):357-371.

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