DOI: https://doi.org/10.53350/pjmhs22163289

ORIGINAL ARTICLE

Comparison of Clinical and Laboratory Features in RT-PCR Positive and RT-PCR Negative Covid-19 Patients Admitted in High Dependency Unit in a Tertiary Care Hospital, SGRH, Lahore

KHADIJA MUNEER[1], SAIMA AYUB[2], NAUMAN ZAFAR[3], NOMA SARWAR[4], ADNAN HASHAM[5], SHAZIA SIDDIQUE[6]
[1]MBBS, FCPS (Medicine), MRCP (UK), FRCP (Edin) Senior Registrar (Medicine), SHL
[2]MBBS, MPH, M. Phil. Associate Professor Community Medicine, IPH
[3]MBBS, FCPS (Medicine) Senior Registrar (Medicine), SHL
[4]MBBS, FCPS (Medicine) Senior Registrar (Medicine), SGRH
[5]MBBS, FCPS (Medicine), FCPS (Endocrinology), MRCP (UK) Medical Officer (Medicine), SHL
[6]MBBS, MRCP (UK) Assistant Professor (Medicine), FJMU
Correspondence to: Dr. Khadija Muneer, Email: khadija.was@gmail.com, Cell: +92-322-4711973

ABSTRACT

Introduction: Corona virus disease 2019 (COVID-19) is currently diagnosed mainly using reverse transcriptase polymerase chain reaction (RT-PCR). Yet a significant proportion of patients have negative RT-PCR result. A comparative study of RT-PCR negative patients with RT-PCR positive patients will help understand clinical characteristic and differences of this diseased population.

Objective: To compare the clinical and laboratory features of RT-PCR Positive and RT-PCR negative patients admitted in high dependency unit.

Patients and methods: In this retrospective cohort study, the data of 128 patients (59 patients with RT-PCR positive result and 69 patients with RT-PCR negative results) was obtained. These patients had been admitted in high dependency unit of a community hospital. Demographics, clinical characteristics and laboratory abnormalities were noted and a comparison was done using statistical analysis.

Results: In our study-total 128 patients were enrolled out of which 68 (53.1%) were males and 60 (46.9%) were females. 59 (46.1%) patients were RT-PCR positive and 69 (53.9%) patients were RT-PCR negative. Median age was 55.34 years (18 to 95). No significant difference was noted in most of clinical symptoms (fever, sputum production, rhinorrhea, dyspnea, myalgia, nasal congestion, vomiting, diarrhea, urinary symptoms, altered level of consciousness), comorbidities (diabetes mellitus, hypertension, prior lung disease, prior ischemic heart disease, prior kidney disease), laboratory abnormalities (elevated creatinine, elevated liver enzymes, elevated ferritin, elevated C-reactive protein, elevated d-dimers, elevated procalcitonin, abnormal electrocardiogram). Cough was significantly found to be more prevalent in RT-PCR positive patients (p=0.042) and severe disease was also more prevalent in these patients significantly (p=0.000).

Conclusion: Our study shows that patients admitted and diagnosed to be suffering from COVID-19 infection had remarkable similarities in clinical features and laboratory parameters regardless of RT-PCR status, however RT-PCR positive patients suffered from more severe pneumonia as compared to RT-PCR negative patients.

Keywords: COVID-19, RT-PCR positive, RT-PCR negative

INTRODUCTION

In Wuhan, China an increasing number of pneumonia cases were observed since December 2019. As the disease started to spread, the studies carried out held Corona virus infection responsible for this sudden rise. This disease was termed as a novel Corona Virus Infection/Disease by the World Health Organization on 31 December 2019 and was named Corona Virus Disease 2019 (COVID-19) in February 2019[1]. WHO declared it as a pandemic on 11th march 2020. Coronavirus has affected global economies, and the developing countries have been hit hard [3]. Since Pakistan is a developing country, it became more important for the local clinicians to identify cases clinically and take measures to decrease the burden of disease locally.

Various new studies and articles are coming up daily to understand the pathophysiology of the disease in order to improve the treatment and outcomes. One study, Liu et al [4]compared the clinical features of the elderly with middle age and young patients of COVID-1919. These studies showed that the elderly patients had higher mortality and are more vulnerable to this disease. This study was on a very small number, and just targeted confirmed pneumonia patients. Much data is being collected in deciding the best possible way for early detection of the disease in order to prevent the spread.

Diagnosis of COVID-19 depends upon confirmation by specific tests. One tool is RT-PCR test; however, the probability of a false negative COVID-19 test is 100% on Day 1 of the infection and remains as high as 67% on Day 4[5]. Thus test result does not always decide about the presence or absence of disease. A suggestive history, radiological and biochemical investigations are very important in suspecting and labelling COVID-19 infection.

This study was conducted to compare and determine symptoms, signs, radiological and laboratory features in both RT-PCR positive and negative cases for earlier detection and management of the patient and reducing the morbidity and mortality of the disease. It will help clinicians in understanding whether or not the admitted patients were correctly identified and will help in relying more confidently on clinical features and laboratory findings and not just on RT-PCR status of the patient for detection and labelling the disease.

Objective: To assess and compare the clinical and laboratory features of RT-PCR Positive and RT-PCR negative patients admitted in high dependency unit.

Operational definitions

Moderate COVID-19: According to the guidelines by the ministry of health Pakistan [6]

Hypoxia (Oxygen saturation <94% but >90%)
Chest X-ray with infiltrates involving <50% of the lung fields
No complications and manifestations related to severe condition

Severe COVID-19: According to the guidelines by the ministry of health Pakistan [6]

In adults, clinical signs of pneumonia (fever/ cough) plus, any of the following:

Respiratory rate > 30
Severe respiratory distress;
SpO2 ≤ 90% on room air.
Chest X-ray involving >50% of lung fields

RT-PCR: This test comprises taking nasal and throat swab by the qualified personnel. The test has been carried out free of cost by the laboratory designated by NIH of Pakistan as advised by ministry of health.[6]

Radiological Criteria: The Chest X-ray or CT Chest findings are airspace opacities, consolidation and ground glass opacity. The distribution is most often bilateral, peripheral, and lower zone predominant. [7,8]

PATIENTS AND METHODS

Study Design: This retrospective cohort study was performed in high dependency unit of Sir Ganga Ram hospital Lahore, Pakistan. Data of 128 patients was collected from charts. Patients older than 16 years, both males and non-pregnant females were included in this study. Study population included patients suffering from moderate and severe COVID-19 infected patients as per operational definition. Demographic, clinical, laboratory, and radiological characteristics were noted. All of this information was collected through a specially designed pro forma. All ethical issues were addressed e.g. confidentiality.

Data Analysis Procedure: Data was collected and compiled in the computer and analysed using SPSS version 23 for Windows. The variables included age and gender, and clinical and radiological findings. Data was divided into continuous and categorical variables. Continuous variables as mean and ranges and categorical variables as numbers percentages were expressed. A correlation was calculated in categorical data and P values in continuous variables were determined through ANOVA Test using SPSS 23.0 for analysis and P values <0.05 were considered significant.

RESULTS

In our study-total 128 patients were enrolled out of which 68 (53.1%) were males and 60 (46.9%) were females. 59 (46.1%) Patients were RT-PCR positive and 69 (53.9%) patients were RT-PCR negative. Median age was 55.34 years (18 to 95). Among RT-PCR positive patients mean age was 57.8 years (range 18 to 80 years), 34 (26.5%) were males and 25 (19.5%) females. Among RT-PCR negative patient's man age was 53.25 years (range 21 to 91 years), 34 (26.5%) were male and 35 (27.3%) were females.

Among quantitative variables mean hemoglobin level was 12.01 ± 2.47(range 6.6 to 16.9) in RT-PCR positive patients and 12.00 ± 2.38(3.4 to 16.9) in RT-PCR negative patient. White blood cell count was 10.81 ± 4.94(2.6 to 22.4) in RT-PCR positive patients while it was 14.01 ± 8.46(3.4 to 40.4) in RT-PCR negative patients. Neutrophil percentage was 77.56 ± 15.60(8.8 to 95.4) in RT-PCR positive patients and 67.83 ± 24.94(1.0 to 96.0) in RT-PCR negative patients. Lymphocyte percentage in blood was 13.05 ± 9.44(0.9 To 35.0) in RT-PCR positive patients and 13.632 ± 9.40(1.1 to 34.4) in RT-PCR negative patients. Platelet count was 237000 ± 99500(40000 to 470000) in RT-PCR positive patients and 235690 ± 140000(7000 to 720000) in RT-PCR negative patients.

Details of quantitative variables is provided in Table 1. Cough was present in significantly more RT-PCR positive patients compared to RT-PCR negative patients (p=0.042). No significant association was found on comparison of fever(p = 0.190), sputum production(p = 0.747),rhinorrhea(p = 0.892), headache(p = 0.201), dyspnea(p = 0.365), myalgia (p = 0.225), nasal congestion(p = 0.810),vomiting(p = 0.827), diarrhea(p = 0.685), urinary symptoms(p = 0.420), altered conscious level(p = 0.389), prevalence o diabetes mellitus(p = 0.589), hypertension(p = 0.101), lung disease(p = 0.953), ischemic heart disease(p = 0.185), prior kidney disease(p =0.106), deranged creatinine(p = 0.699), deranged liver functions(p = 0.963), increased ferritin(p = 0.262), increased C-reactive protein(p = 0.643), increased D-dimers(p = 0.843), procalcitonin(p = 0.427), abnormal ECG(p = 0.173). Also no significant difference was noted in disease outcome (p = 0.439) and gender prediction (p = 0.345). RT-PCR positive patients were significantly more likely to have severe disease as compared to RT-PCR negative patients(p=0.000).

Table 1:

Parameter		RT-PCR		Total(n)	P value
		Positive	Negative		
Gender	Male	34 (26.5%)	34 (26.5%)	68 (53.1%)	0.345
	Female	25 (19.5%)	35 (27.3%)	60 (46.9%)	
	Total	59 (46.1%)	69 (53.9%)	128 (100%)	
Severity	Moderate	20 (17.1%)	46 (39.3%)	51 (43.6%)	0.000
	Severe	32 (27.4%)	19 (16.2%)	66 (56.4%)	
	Total	52 (44.4%)	65 (55.5%)	117 (100%)	
Outcome	Expire	8 (6.2%)	8 (6.2%)	16 (12.5%)	0.439
	Lama	5 (3.9%)	11 (8.6%)	16 (12.5%)	
	Discharge	46 (35.9%)	50 (39.1%)	96 (75%)	
	Total	59 (46.1%)	69 (53.9%)	128 (100%)	
Fever	Yes	49 (38.9%)	51 (40.5%)	100 (79.4%)	0.190
	No	9 (7.1%)	17 (13.5%)	26 (20.6%)	
	Total	58 (46.0%)	68 (54.0%)	126 (100%)	
Cough	Yes	42 (32.8%)	37 (28.9%)	79 (61.7%)	0.042
	No	17 (13.3%)	17 (13.3%)	49 (38.3%)	
	Total	59 (46.1%)	69 (53.9%)	128 (100%)	
Sputum production	Yes	11 (8.8%)	12 (9.6%)	23 (18.4)	0.747
	No	45 (36.0%)	57 (45.6%)	102 (79.7)	
	Total	56 (44.8%)	69 (55.2%)	125 (100%)	
Rhinorrhea	Yes	1 (0.8%)	1 (0.8%)	2 (1.6%)	0.892
	No	56 (44.4%)	68 (53.1%)	124 (98.4%)	
	Total	57 (45.2%)	89 (54.8%)	126 (100%)	
Headache	Yes	3 (2.4%)	8 (6.4%)	11 (8.8%)	0.201
	No	54 (43.2%)	60 (48.0%)	114 (91.2%)	
	Total	57 (45.6%)	68 (54.4%)	125 (100%)	
Dyspnea	Yes	51 (39.8%)	57 (44.5%)	108(84.4%)	0.365
	No	8 (6.2%)	12 (9.4%)	20(15.6%)	
	Total	59 (46.1%)	69 (53.9%)	128 (100%)	
Myalgia	Yes	22 (17.6%)	20 (16.0%)	42(33.6%)	0.225
	No	34 (27.2%)	49 (39.2%)	83 (66.4%)	
	Total	56 (44.8%)	69 (55.2%)	125 (100%)	
Nasal congestion	Yes	3 (2.4%)	3 (2.4%)	6(4.8%)	0.810
	No	54 (42.8%)	66 (52.4%)	120 (95.2%)	
	Total	57 (45.2%)	69 (54.8%)	126 (100%)	
Vomiting	Yes	6 (4.8%)	8 (6.4%)	14 (11.2%)	0.827
	No	51 (40.8%)	60 (48.0%)	111 (88.8%)	
	Total	57 (44.5%)	68 (54.4%)	125 (100%)	
Diarrhea	Yes	9 (7.2%)	9 (7.2%)	18 (14.4%)	0.685
	No	48 (38.4%)	59 (46.1%)	107 (85.6%)	
	Total	57 (45.6%)	68 (54.4%)	125 (100%)	
Urinary symptoms	Yes	2 (1.6%)	4 (3.2%)	6 (4.8%)	0.420
	No	55 (44.4%)	63 (50.8%)	118 (95.2%)	
	Total	57 (46.0%)	67 (54.0%)	124 (100%)	
Altered level of consciousness	Yes	13 (10.5%)	12 (9.7%)	25 (20.2%)	0.389

	No	42 (33.9%)	57 (46.0%)	99 (79.8%)	
	Total	55 (44.4%)	69 (55.6%)	124 (100%)	
Diabetes mellitus	Yes	30 (23.6%)	39 (30.7%)	69 (54.3%)	0.589
	No	28 (22.4%)	30 (23.6%)	58 (45.7%)	
	Total	58 (45.7%)	69 (54.3%)	127 (100%)	
Hypertension	Yes	32 (25.2%)	28 (22.0%)	60(47.2%)	0.101
	No	26 (20.5%)	41 (32.3%)	67(52.8%)	
	Total	58 (45.7%)	69 (54.3%)	127 (100%)	
Prior lung disease	Yes	9 (7.4%)	12 (9.8%)	21(17.2%)	0.953
	No	44 (30.1%)	57 (46.7%)	101(82.8%)	
	Total	53 (43.4%)	69 (56.6%)	122 (100%)	
Prior ischemic heart disease	Yes	15 (12.1%)	12 (9.7%)	27 (21.8%)	0.185
	No	40 (32.2%)	57 (46.0%)	97 (78.2%)	
	Total	55 (44.4%)	69 (55.6%)	124 (100%)	
Prior kidney disease	Yes	10 (8.3%)	6 (5.0%)	16(13.2%)	0.106
	No	43 (35.5%)	62 (51.2%)	105(84.3%)	
	Total	53 (43.8%)	68 (56.2%)	121 (100%)	
Creatinine	Abnormal	14 (12.8%)	13 (11.9%)	27(24.8%)	0.699
	Normal	39 (37.8%)	43 (39.4%)	82(75.2%)	
	Total	53 (48.6%)	56 (51.4%)	109 (100%)	
Liver enzymes	Normal	44 (40.7%)	49 (45.4%)	93(86.1%)	0.963
	Abnormal	7 (6.5%)	8 (7.4%)	15(13.9%)	
	Total	51 (47.2%)	57 (52.8%)	108 (100%)	
Ferritin	Normal	10 (13.0%)	13 (16.9%)	23 (29.9%)	0.262
	Abnormal	31 (40.2%)	23 (29.9%)	54 (70.1%)	
	Total	41 (53.2%)	36 (46.8%)	77 (100%)	
C-reactive protein	Normal	5 (7.7%)	7 (10.8%)	12 (18.5%)	0.643
	Abnormal	26 (40.0%)	27 (41.5%)	53 (81.5%)	
	Total	21 (32.3%)	34 (52.3%)	65 (100%)	
D-dimers	Normal	10 (15.2%)	9 (13.6%)	19 (28.8%)	0.843
	Abnormal	26 (39.4%)	21 (31.8%)	47 (71.2%	
	Total	36 (54.5%)	30 (45.5%)	66 (100%)	
Procalcitonin	Normal	4 (57.1%)	1 (14.3%)	5 (71.4%)	0.427
	Abnormal	1 (14.3%)	1 (14.3%)	2 (28.6%)	
	Total	5 (71.4%)	2 (28.6%)	7 (100%)	
ECG	Normal	11 (15.3%)	7 (9.7%)	18 (25.0%)	0.173
	Abnormal	23 (31.9%)	31 (43.0%)	54 (75%)	
	Total	34 (47.2%)	38 (52.5%)	72 (100%)	

DISCUSSION

This retrospective cohort study was aimed at determining differences in clinical features, laboratory abnormalities, disease severity and outcome between COVID-19 RT-PCR positive and COVID-19 RT-PCR negative patients who were admitted and treated with presumptive diagnosis of COVID-19 infections. As sensitivity of sputum and nasal swabs are described as 72% and 63% by Wang et al[9], at least 30 to 40 percent of patients have to be diagnosed on the basis of clinical history, examination and imaging finding. Concern regarding over-diagnosis and under-diagnosis remains in place for RT-PCR negative patients.

Our study has shown that patients admitted and diagnosed with COVID-19 infection had remarkable similarities in clinical features and laboratory parameters regardless of RT-PCR status. These results are similar to work of Zhang JJ et al [10] which also reported no significant difference in most clinical, laboratory and radiological parameters of initial COVID-19 RT-PCR positive and negative patients. However, RT-PCR positive patents are more likely to progress to severe disease. Another study by Li et al suggested similar results and authors described no significant difference in most of demographic and clinical features of RT-PCR positive and negative COVID-19 infected patients[11].

In our study, cough was found to be more prevalent in COVID-19 RT-PCR positive patients and reached level of significance. Overall prevalence of cough in our patients was 61.7% (n=128) similar to prevalence of 68.6% reported in earlier meta-analysis[12]. Severe COVID-19 pneumonia was found to be more prevalent in RT-PCR positive patients.

CONCLUSION

Our study has shown that patients admitted and diagnosed to be suffering from COVID-19 infection had remarkable similarities in clinical features and laboratory parameters regardless of RT-PCR status, however RT- PCR positive patients suffered from more severe pneumonia as compared to RT-PCR negative patients.

Limitation: Major limitations of our study include small sample size of 128 patients. Another limitation is that the study was carried out on patients requiring high dependency and intensive care management. These can be dealt with, by carrying out studies on patients with less severe disease as well.

REFERENCES

1. WHO Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020 [Internet]. [cited 2020 Jul 2]. Available from: https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020
2. The WHO just declared coronavirus COVID-19 a pandemic [Internet]. Time. [cited 2020 Jul 2]. Available from: https://time.com/5791661/who-coronavirus-pandemic-declaration/
3. Okyere MA, Forson R, Essel-Gaisey F. Positive externalities of an epidemic: The case of the coronavirus (COVID-19) in China. J Med Virol [Internet]. 2020 Apr 10 [cited 2020 Jul 2]; Available from: http://doi.wiley.com/10.1002/jmv.25830
4. Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. Journal of Infection. 2020;80(6):e14–8.
5. Dangers of false negative COVID-19 RT-PCR tests [Internet]. BioTechniques. 2020 [cited 2020 Jul 2]. Available from: https://www.biotechniques.com/coronavirus-news/false-negatives-how-accurate-are-RT-PCR-tests-for-COVID-19/
6. COVID-19 health advisory platform by ministry of national health services regulations and coordination [Internet]. [cited 2020 Jul 2]. Available from: http://COVID-19.gov.pk/guideline
7. Rodrigues JCL, Hare SS, Edey A, Devaraj A, Jacob J, Johnstone A, et al. An update on COVID-19 for the radiologist - A British society of Thoracic Imaging statement. Clin Radiol. 2020;75(5):323–5.
8. Wong HYF, Lam HYS, Fong AH-T, Leung ST, Chin TW-Y, Lo CSY, et al. Frequency and distribution of chest radiographic findings in COVID-19 positive patients. Radiol. 2019;201160.
9. Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. JAMA. 2020 May 12; 323(18): 1843–1844. doi: 10.1001/jama.2020.3786. Epub 2020 Mar 11.
10. Zhang JJ, Cao YY, dong X, Wang BC, Lia MY, Lin j, Yan YQ, et al. Distinct characteristics of COVID-19 patients with initial rRT-PCR-positive and rRT-PCR-negative results for SARS-CoV-2. Allergy. 2020 Jul; 75(7):1809-1812. doi: 10.1111/all.14316. Epub 2020 Apr 27.
11. Li C, Su Q, Liu J, Chen L, Li Y, Tian X, Li W. Comparison of clinical and serological features of RT-PCR positive and negative COVID-19 patients. J Int Med Res. 2021 Feb;49(2):1-11. doi: 10.1177/0300060520972658.
12. Li LQ, Huang Tian, Wang YQ, Wang ZP, Liang Y, Huang TB, et al. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. J Med Virol. 2020 Jun; 92(6):577-583. doi: 10.1002/jmv.25757. Epub 2020 Mar 23