

DEMOGRAPHIC AND CLINICAL OUTCOMES IN COVID-19 PATIENTS WITH POSITIVE AND NEGATIVE RT-PCR TEST

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ABSTRACT:

BACKGROUND: During the COVID 19 pandemic, many patients had respiratory symptoms such as cough, fever, shortness of breath etc. suggestive of SARS virus, but had a negative by nasal swab RTPCR. This study is carried to compare the clinical features, inflammatory markers, HRCT thorax and prognosis between RT-PCR positive and negative patients. **MATERIAL AND METHODS:** This is a retrospective study of RTPCR positive patients and patients with clinical diagnosis of COVID-19 [Suspects] i.e., RTPCR negative. We compared the clinical findings and outcomes of PCR-positive patients with those of PCR-negative patients. A total of 56 RTPCR positive and 28 RTPCR negative patients were taken for the study. **RESULTS:** The RTPCR negative group were younger (52.1 ± 12.2 vs 58.5 ± 15.3 , $p=0.03$) but were similar to RTPCR positive patients in terms of demographics, comorbidities, and presenting symptoms. RTPCR negative had higher lymphocyte counts (1819 ± 868 Vs 1331 ± 737 , $p=0.01$) and less severe elevation of serum CRP values (48mg/dl) (28.57% vs 50% , $p=0.03$). HRCT severity were also less severe in RTPCR negative group (10.7% vs 28.57% $p=0.006$). Also clinical outcomes regarding ICU admission (25% vs 46.42% $p=0.02$), Invasive ventilator support (21.4% vs 39.65% $p=0.03$) and length of hospital stay were also less (9 ± 4 vs 14 ± 9 $p < 0.001$) as compared to RTPCR positive patients. **CONCLUSION:** This study finds that one third of COVID 19 patients were RTPCR negative and were diagnosed based on clinical and radiological findings. These patients had a more favorable clinical course, shorter hospital stay and less frequent admission to the intensive care unit.

KEYWORDS: SARS-CoV-2; RT-PCR; COVID-19; Respiratory infection; hospital mortality; Clinical symptoms.

INTRODUCTION:

Patients with COVID-19 typically exhibit respiratory and systemic symptoms, including fever, cough and shortness of breath. [1] Diagnosis is mainly established by a positive nasal swab RT-PCR. Other diagnostics modalities include high resolution CT chest and elevated blood inflammatory markers. However none of these indicators are distinctive for COVID-19, hence a diagnosis can only be made when the SARS-CoV-2 virus is found in the airways. [2] However Nasopharyngeal swab RT-PCR, has a low Diagnostic

yield of 63 % are compared to bronchoalveolar lavage specimens. [3] There is a subset of population which presents with typical clinical and radiological features of Covid-19 but with a negative nasal swab RT-PCR. Depending on the prevalence of COVID-19 is, the accuracy of RT-PCR test's diagnosis may alter. A meta-analysis recently showed that when the prevalence of COVID-19 was 50%, 20% and 5%, the post-test probability was 96%, 86% and 55% respectively. [4] The other major reason for a negative RT-PCR are as follows. A number of pre-analytical factors include

disease's incubation period, viral mutations that avoid detection and a lack of standards in specimen collection, transport and storage. Other analytical factors include use of non-validated assays, sample contamination, inadequate viral load. [5] The added reason for negative RT-PCR are other viral infections presenting with similar clinical features as that of RT PCR positive patients must be borne in mind. Most of the illnesses in this category are viral respiratory infections followed by infections of the gastrointestinal, urogenital, neurological etc. [6] However, it is unknown if a person with a presumed diagnosis of COVID-19 develop in a manner comparable to RT-PCR test positive patient. Very few studies are there to assess the outcomes between RT-PCR test positive and negative patient. Thus this study, aims to determine whether RTPCR-negative patients have similar clinical features to RTPCR-positive patients and to compare the clinical outcomes of these two groups of patients.

MATERIAL AND METHODS:

This retrospective study was conducted at Sri Venkateshwaraa Medical college hospital, Puducherry between May 01, 2021 and June 30, 2021. The case sheets of RT-PCR positive patients and RT-PCR negative patient, i.e. cases as those who presented with clinical suspicion of covid-19 or had symptoms compatible with covid-19, and had nasopharyngeal swab performed, were assessed for relevant data. RT-PCR negative patient are those who had clinical features and radiological findings similar to RT-PCR positive patients but with a RT-PCR negative test. The data collected included the demographics, clinical features, laboratory findings and prognosis of the RT-PCR positive and RT-PCR negative patient. A total of 289 patients were analyzed, of which 179 (62%) were RTPCR positive and 110(38%) patients were RTPCR negative. Of the 179 RTPCR positive, 123 patients of mild category were excluded and finally 56 patients were taken up for the study. Of the 110 RTPCR negative, 28 patients with positive findings of HRCT were taken up for the study. The primary endpoint was admission to the intensive care unit. The secondary endpoints were in-hospital mortality and the length of hospital stay. Demographic data collected, includes age, gender and comorbidities. Clinical data collected, includes fever, cough, shortness of breath and SpO₂ requirements. Laboratory data collected, includes C- reactive protein levels [CRP] and lymphocyte counts. Patient prognosis data collected, includes the use of face mask, non invasive ventilation

[NIV], invasive mechanical ventilation [IMV], ICU admission, duration of hospitalization and mortality. The study is been duly approved by the institute ethics committee and the reference number of the same is as follows [No: 13/SVMCH/IEC-Cert/Mar22] Data collected were entered in Microsoft Excel and was analyzed by SPSS version 28.0. Qualitative variables like gender positivity rate extra will be expressed in proportion and percentage. Quantitative variables like duration of hospital stay will be expressed in mean and standard deviation.

RESULTS:

The average age of RT PCR positive patients was 58.5 ± 15.3 and the mean age of RT PCR negative patients was 52.1 ± 12.2 . RT PCR negative patients were relatively young compared to that of RT PCR positive patients. [Figure 1] Among the RT PCR positive, 48.21% [n=27] and 51.78% [n=29] were males and females respectively. In the RT PCR negative group 53.57% [n=15] and 46.42% [n=13] were males and females respectively. Thus in both groups majority were male patients. [Figure 2] In the study population around 64.28% [n=36] of RT PCR positive patients and 53.57% [n=27] RT PCR negative patients had associated comorbidities. Fever was the most common clinical presentation among RT PCR positive that is around 62.5% [n=35]. But cough was the most common clinical presentation among RT PCR negative patients that is 64.28%. Second most common clinical presentation in both RT PCR positive patients and RT PCR negative patients was shortness of breath. Third common clinical presentation was cough in RT PCR positive and fever in RT PCR negative patients. The average SpO₂ levels in in RT PCR positive and RT PCR negative patients were 87 ± 8 and 89 ± 8 respectively. However the above mentioned clinical findings are not statistically significant because of higher P value. [Figure 3] Laboratory findings such as CRP [>48 mcg/dl] levels was seen in more than fifty percentage of RT PCR positive patients [n=28] and in RT-PCR negative patients [n=8]. The average lymphocyte count was 1819 ± 868 in RT PCR negative patients which was higher than the average value seen in RT PCR positive patients that is 1331 ± 737 with a *p* value of 0.01. [Table 1] The HRCT severity score was assessed in RT PCR positive and RT-PCR patients. Around 48.2% of RT PCR positive patients have a moderate score followed by 28.85% having a serious score and the rest 23.2% having a mild score. Around 57.14% of RT PCR

negative patient had a moderate score and 32.1% had a mild score. On comparing the HRCT severity score among RT-PCR and RT-PCR negative patients the p value was statistical significant, p value < 0.05 . [Table 2] On the prognosis of the RT PCR positive patients 41.07% needed face mask and 17.85% needed non-invasive ventilation. Among RT-PCR negative patients 35.71% required face mask and 14.2 required noninvasive ventilation. Patients requiring invasive mechanical ventilation [IMV] and ICU admissions were 39.65% and 46.42% respectively in RT PCR positive

patients. In RT PCR negative patients around 25% patients needed ICU admission while only 21% required invasive mechanical ventilation. The average stay in the hospital was higher in the RT PCR positive patients that is 14 ± 9 days and comparatively lesser duration in RT PCR negative patients that is 9 ± 4 days. Relationship between duration of hospitalization between the study groups was statistical significant, p value < 0.05 . [Table 3] The mortality was higher in RT PCR positive patients that is 26.78% while the mortality was comparatively lesser 21.42% in RT PCR negative patients. [Figure 4]

Figure1: Age distribution among RT PCR positive and RT PCR negative patients

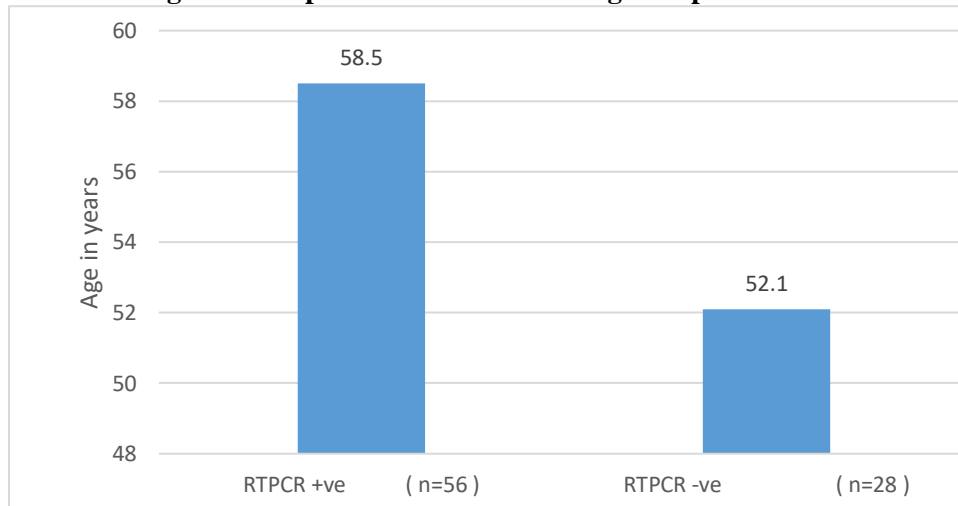


Figure2 : Gender distribution among RT PCR positive and RT PCR negative patients

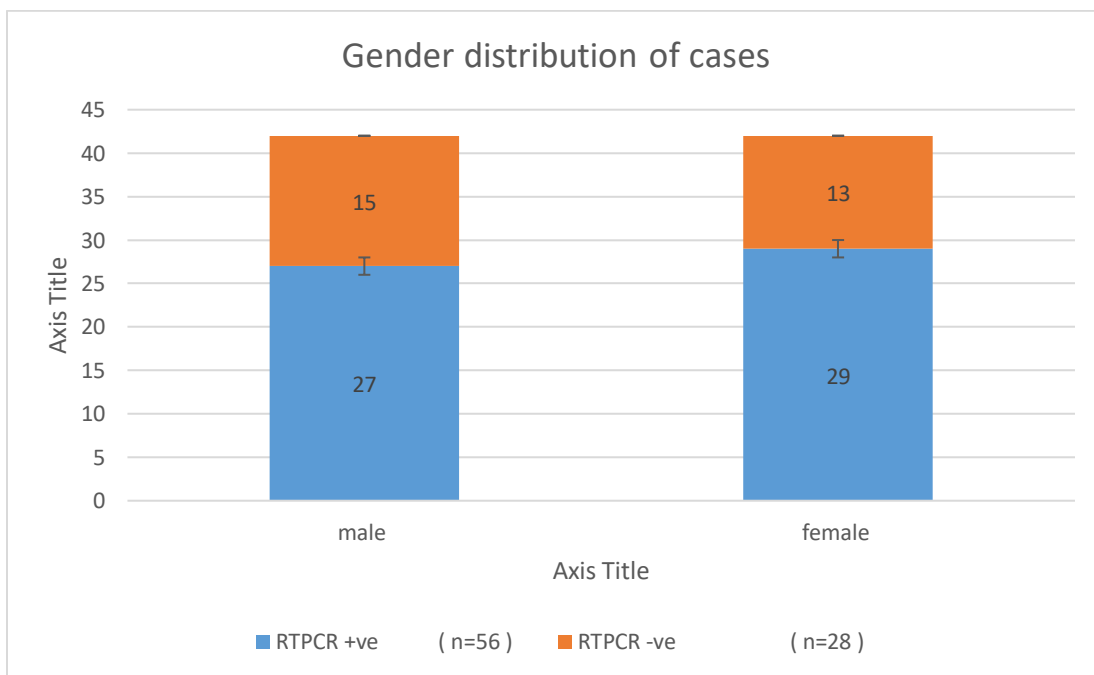


Figure3: clinical presentation among RT PCR positive and RT PCR negative patients

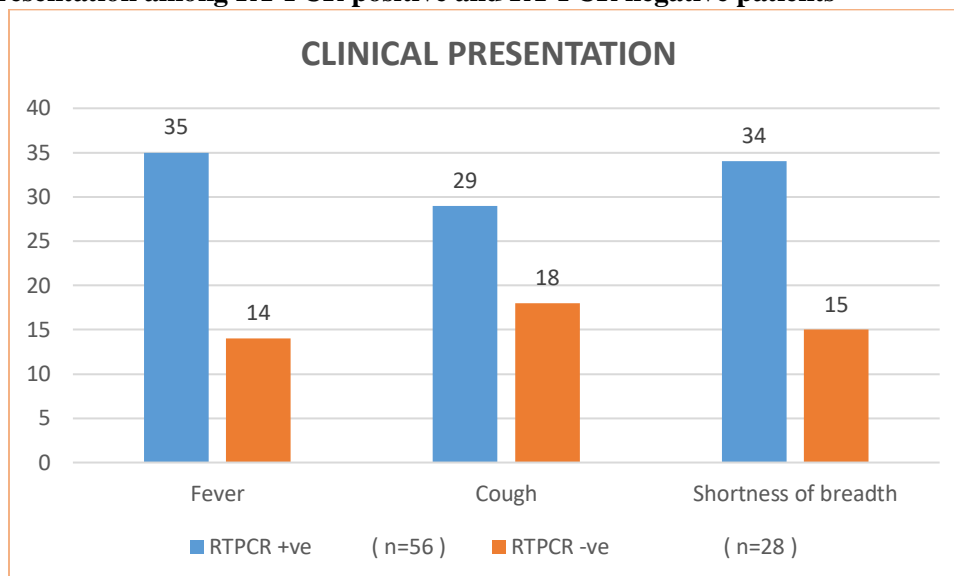


Table 1: Laboratory tests among RT PCR positive and RT PCR negative patients

Inflammatory markers	RTPCR +ve (n=56)	RTPCR -ve (n=28)
CRP : >48mcg/dl, avg	28(50)	8(28.57)
Lymphocyte count/mm ³ ,avg	1331+/-737	1819+/-868

Table 2: HRCT SEVERITY score in RT PCR positive and RT PCR negative patients

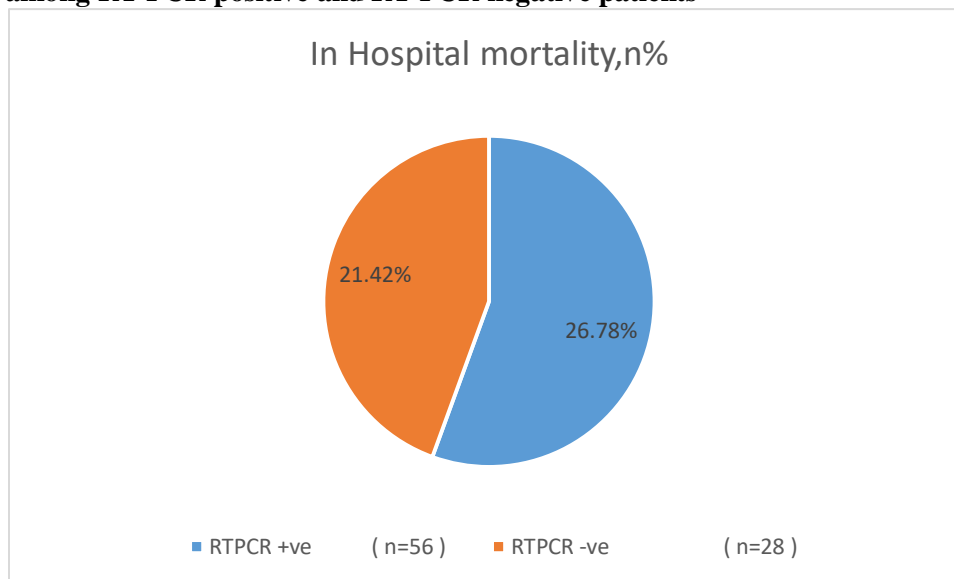
HRCT SEVERITY	RTPCR +ve (n=56)	RTPCR -ve (n=28)	p value
Mild score <8/25 ,n%	13(23.21)	9(32.14)	0.38
Moderate 9-25,n%	27(48.25)	16(57.14)	0.42
Severe >15/25,n%	16(28.57)	3(10.71)	0.006

Table 3: Prognosis of RT PCR positive and RT PCR negative patients

IN HOSPITAL COURSE	RTPCR +ve (n=56)	RTPCR -ve (n=28)
Face mask, n(%)	23(41.07)	10(35.71)
NIV, n(%)	10(17.85)	4(14.28)
IMV, n(%)	23(39.65)	6(21.4)

ICU admission, n(%)	26(46.42)	7(25)
Duration of hospitalization. [in days]	14±9	9±4

Figure 4: Mortality among RT PCR positive and RT PCR negative patients



DISCUSSION:

The age of our study groups were between 50 to 60 years while in most of the studies mean age was above 60 years, indicating that the our study population were comparatively younger than other study groups in the study by Palmer ET Al on RT PCR negative covid-19, the mean age of their study population [probable] was 53 years, consistent with our study findings. [7] There is no much gender difference compared to other studies as male population more are more commonly affected. Clinical presentation were quite different between the groups of our study. Fever was the most common clinical presentation among RT PCR positive that is around 62.5% [n=35]. But cough was the most common clinical presentation among RT PCR negative patients that is 64.28%. Second most common clinical presentation in both RT PCR positive patients and RT PCR negative patients was shortness of breath followed by cough and fever in RT PCR positive and RT PCR negative patient respectively. Our study findings differ from similar studies on the most common clinical findings because, for shortness of breath which is the common presentation, in those studies. [7,8] However the correlations between clinical presentations and our

study groups were not statistically significant. On the laboratory inflammatory makers, The CRP levels were elevated in more than 50% of the RT PCR positive patient compared to the RT PCR negative patients and is on par with similar studies.[8] Elevated CRP is a defined inflammatory marker in COVID-19.[9] The lymphocyte count was relatively low up in RT PCR positive compared to the RT PCR negative patients. A study by Liu, on the relationship between the lymphocyte counts and the viral load shows that lymphocyte counts are lower when the viral load are high and more often associated with high end organ damage[10] A similar comparative study also showed that in the RT PCR positive groups around 56% of the patients had the lymphocyte count between 1.0 to 0.5.[8] Our study finding with respect to the lymphocyte count between the two groups is somewhat statistically significant and similar to the existing literature In diagnosis by CT chest, sensitivity and specificity is around 60% to 98% and 25% to 53%, respectively. [11] With the increased use of chest CT imaging varied presentation of the virus was identified. According to reports, numerous different infections, most notably viral pneumonia, and non-infectious illnesses, most notably organizing pneumonia, may overlap with the

characteristic chest CT findings of COVID-19 pneumonia.[12] The RSNA[Radiological Society of North America], however, stated that CT was successful in identifying COVID-19 pneumonia and distinguishing from other viral etiology. [13] The other respiratory pathogen with clinical and radiological features of similar to SARS-COVID are metapneumovirus, rhinovirus, adenovirus, RSV , influenza A/B and mycoplasma pneumonia.[14] Unfortunately, due to the pandemic, the microbiology laboratories had to concentrate their efforts on the diagnosis of SARS-CoV-2 infection and had to temporarily stop testing for other respiratory viruses, thus missing the differential diagnosis. Need for oxygen through face mask in RT PCR positive patients was more than 50% and around 35.71% in RT PCR negative patient . The need for face mask, non-invasive ventilation and mechanical ventilation was more in RT PCR positive patients and is consistent with similar studies. [15] Association between the use of face mask, non invasive ventilation and mechanical ventilation between the RT-PCR positive and RT-PCR negative patient was not statistical significant, however the necessity for the above was seen increased in the RT PCR positive group. ICU admission in RT PCR positive patients was at the rate of 46.42%, higher than the RT PCR negative patient and this finding is consistent with the literature. A study by Menezes et al. showed 67.1% of RT-PCR positive patients and 50% RT-PCR negative patient needed ICU admission and this association was statistically significant. [16] The average duration hospital stay was 14 days and 9 days in RT PCR positive and RT PCR patient respectively. The increase Hospital stay among of RT-PCR patients is common and is consistent with the study by Menezes et al. The association between the duration of hospitalization among the two study groups was statistically significant with the *P* value of <0.001. Hospital mortality was higher in the RT PCR positive patients. The reason for higher mortality in the RT PCR positive patients is due to the increased incidence of associated comorbidities in them. Other major reason for increased mortality in RT PCR positive patients is due to the increased viral load [16] [17]. A lower rate of viral replication and a weaker inflammatory response in RT PCR negative patients would result in milder disease with better clinical outcomes.[18]

CONCLUSION:

The study suggests that the parameters such as clinical presentation, hospital course and mortality are better in

the RT PCR negative compared to the RT PCR positive patients. Our Study finding is consistent with similar comparative studies available in the literature and the associations between the duration of stay in our study groups was statistically significant .The mortality and admission rate to ICU among RTPCR negative were low but not statistically significant. The main limitation of our study is due to relatively small sample size and this is the main reason for many parameters to be statically non-significant

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