Section: Microbiology

Original Research Article

ROLE OF CHEST RADIOGRAPH IN ASSISTING RT-PCR FOR THE DIAGNOSIS OF COVID -19 IN A TERTIARY CARE CENTRE IN NORTH KERALA

Rejitha Kurukkanari[1], Neha Mohan[2], Nisar Karekadavath[3], Gomathy Subramaniam[4], Praseeda Chandran[5]

[1]Assistant Professor, Department of Microbiology, Government Medical College, Kozhikode, Kerala, India
[2]Assistant Professor, Department of Radiodiagnosis, Government Medical College, Kozhikode, Kerala, India
[3]Assistant Professor, Department of General Medicine, Government Medical College, Manjeri, Kerala, India
[4]Professor and HOD, Department of Radiodiagnosis, Malabar Medical College, Kozhikode, Kerala, India
[5]Assistant Professor, Department of Community Medicine, Government Medical College, Kannur, Kerala, India

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Corresponding Author:
Dr. Neha Mohan,
Email: drnehamohan@gmail.com

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Abstract

Background: COVID – 19 pandemic caused by severe acute respiratory syndrome Corona virus 2 (SARS – CoV-2) is associated with significant morbidity. Early detection, isolation and treatment is of prime importance to curb the spread of the pandemic. The utility of additional corroborative evidence from an easily available modality like a chest radiograph in supplementing the microbiological tests like RT-PCR, which is likely to have false negative results, for making a clinical diagnosis of COVID -19 is not well studied. The aim is to assess the role of chest radiograph as an add on evidence to RT-PCR in making a clinical diagnosis of COVID – 19 in symptomatic suspects. **Materials and Methods:** A retrospective record based descriptive study of symptomatic COVID 19 suspects, who had two RT-PCR tests done 48 hours apart, with first RT-PCR result negative and who had a chest radiograph taken at time of initial RT-PCR was done. The chest radiographs were interpreted by an independent radiologist blinded to all other patient parameters. Agreement between initial chest radiograph findings and second RT-PCR results were done using Kappa analysis. **Result:** We had 153 patients out of which, second RT-PCR test was positive in 51 patients. Of total 153 chest radiographs examined, 20% (n = 30) had abnormal findings with 9% (n = 13) showing classic COVID - 19 findings. In the RT-PCR positive group, 45.1 % (n = 23) had findings suggestive of probable COVID -19 infection and in the RT-PCR negative group, only 6.9% (n = 7) showed abnormal findings. Agreement between initial chest X - ray findings and results of second RT-PCR showed a kappa value of 0.43 (p <.0.001) indicating moderate agreement. **Conclusion:** Chest radiograph has a key role in assisting the diagnosis of COVID- 19 infection especially when there is dilemma in confirming the diagnosis in case of 1st RT-PCR negative symptomatic cases. It can be used as additional corroborative evidence in supplementing the microbiological tests like RT-PCR, helping in identifying the patients with a likelihood of COVID – 19 and to triage them appropriately regarding isolation, containment and treatment.

INTRODUCTION

COVID – 19 is a highly infectious disease caused by severe acute respiratory syndrome Corona virus 2 (SARS – CoV-2). After the report of first case from Wuhan district in China, the disease spread rapidly resulting in WHO declaring it as a pandemic on March 11, 2020.[1] The characteristic that enabled the large-scale spread were high transmissibility, spread via droplet and contact and asymptomatic occurrence of the disease.[2,3]

Corona viruses are enveloped, single-stranded RNA viruses that belong to the order Nidovirales in the subfamily Coronavirinae and is divided into four genera: alpha (α), beta (β), gamma (γ), and delta (δ).[3,4] Alpha and beta coronaviruses infect

mammals, while gamma and delta primarily infect birds.[5]COVID-19 is primarily considered a viral respiratory illness as its causative agent, SARS-CoV-2, predominantly targets the respiratory system and mainlycausepneumonitis which is best explained by two stages, an early and a late phase. The early phase is characterized by viral replication resulting in direct virus-mediated tissue damage, followed by a late phase when the infected host cells trigger an immune response which releases cytokines. In severe COVID-19, the immune system's overactivation results in a 'cytokine storm' resulting in local and systemic inflammatory response.[6,7]Being an illness with high morbidity, with no effective antiviral drugs against COVID-19, it of prime importance that cases have to be detected early to limit further spread. Nucleic acid based approaches are a rapid and reliable technology for viral detection, especially the polymerase chain reaction (PCR) which is considered as the gold standard for the detection of viruses.[8] Sensitivity and specificity of currently available RT-PCR ranges from 91.4% to 94.00% and 92.29 to 99.73% respectively, and can result in large number of false negatives that may adversely affect early diagnosis and disease control measures.[9,10]Here comes the importance of an additional test that can supplement RT-PCR in diagnosing COVID -19.

Radiological evaluation is one way of doing this and the two major modalities are CT scan and chest radiograph.[11-23] CT scan is more sensitive in terms of diagnosis, severity and disease follow up.[11] But routine use of CT scan is not possible as it is expensive, time consuming, has the risk of excessive radiation exposure and may not be readily available. Chest radiographs remain as the first line imaging modality of choice for patients with suspected COVID – 19infections in a developing country like India. COVID - 19 related findings in chest radiograph include ground glass density areas which even in the initial stages can affect both the lungs, particularly the lower lobes especially the posterior segments with a peripheral and sub pleural distribution [Figure 1].[12]Only few studies have been conducted regarding the role of chest radiograph in early diagnosis of COVID - 19 infection.[19-23] This study tries to assess the advantage of using chest radiograph along with RT-PCR in diagnosing COVID- 19.

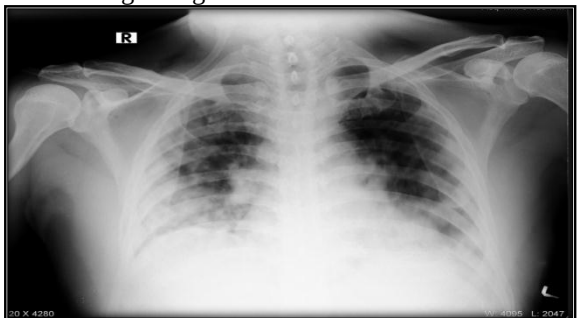

Figure 1: Chest radiograph in a COVID 19 patient showing bilateral ground glass density, predominantly peripheral and basal in distribution.

MATERIALSANDMETHODS

Study Design: Record based descriptive study which was started after getting approval from the Institutional Research Committee (Ref. No: IRC/GMCM/162) and Ethics Committee (Ref No: IEC/GMCM/58).

Study Period: From September 2020 to March 2021.Data collection period was from April 22nd to July 14th of 2020.

Study Settings: Government Medical College, Manjeri.

Sample Size: Sample size was calculated using the

$$n = \frac{4\pi_D(1-\pi_D)Z^2_{1-\alpha/2}}{W^2_D}$$

formula

By keeping the disagreement probability (πD) as 60%, β error (WD) value 20%and α error5% (Z1-α/2 =1.96) a minimum sample size (n) of 92 was obtained.

RT-PCR was started at Govt. Medical College Manjeri, on April 22nd 2020. According to diagnostic protocol followed initially, all symptomatic patients were declared COVIS 19 negative only after 2 consecutive negative RT PCR results, 48 hours apart. This was followed till July 14th 2020. All symptomatic suspect cases who had two RT PCR tests done 48 hours apart, with first RT PCR result negative and had chest radiograph taken at the time of visit to Corona care unit during this time period were included in the study.

Based on this, the number of study participants obtained was 153, out of which 51 had 2nd RT-PCR test result as positive.

Study Subjects: All symptomatic COVID- 19 suspects as per WHO definition,[13] with two RT-PCR tests done 48 hours apart, with initial RT-PCR result negative and a chest radiograph taken at the time of initial RT-PCR which is available.

Exclusion criteria

Patients with current or past history of COPD (chronic obstructive pulmonary disease), Tuberculosis, congenital pulmonary diseases and poor-quality chest radiograph films were excluded from the study.

Methodology

The list of COVID -19 suspected patients with first COVID – 19 RT-PCR test result negative during the period of April 22nd to July 14th of 2020 was obtained from Molecular Diagnostic Lab, Department of Microbiology. Demographic details of these patients and chest radiograph taken at the time of initial RT-PCR were obtained from the Medical Records Library.The chest radiographs were then read and interpreted by an independent radiologist not involved in patient care and blinded to all other patient parameters. Any abnormality in chest radiographs suggestive of a possible lung infection like consolidation, ground glass opacities

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(GGO), effusion, and lymphadenopathy were noted.[14,15] Those patients with characteristic chest radiograph pattern of bilateral ground glass opacities or consolidation in basal and peripheral distribution were taken as classic COVID- 19 findings and those with other patterns of distribution were classified as indeterminate findings. Classic and indeterminate findings were taken as positive chest radiograph findings and the rest were grouped as negative findings [Figure 2].

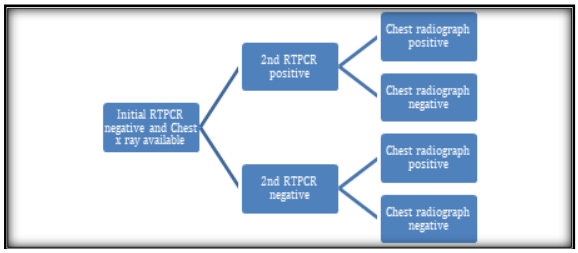

Figure 2:Flowchart showing methodology of study

Statistical analysis

Quantitative variables were expressed as mean and standard deviation and qualitative variables were expressed as percentage. Agreement between the two variables (initial Chest radiograph findings and result of second RT-PCR) was done using Kappa Statistics in whichvalues ≤ 0 is interpreted asno agreement, 0.01–0.20 as none to slight agreement, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.[15]

RESULTS

We had 153 patients who satisfied the inclusion criteria. Out of this, second RT-PCR test was positive in 51 patients. Mean age of the study participants were 36 years in the second RT-PCR positive group and 42 years in the second RT-PCR negative group. There were 70.6% (n = 36) males and 29.4% (n = 15) females in the positive group and 72.6% (n = 74) males and 27.4% (n=28) females in the negative group [Table1].

Of the total 153 chest radiographs examined, 20% (n = 30) had abnormal findings with 9% (n = 13) showing classic COVID - 19 findings [Table 2, Figure 3].

Table 1: General characteristics of study participants.

Characteristics		Second RT-PCR positive (51)	Second RT-PCR negative (102)
Age (mean) in years		36	42
Gender n (%)	Male	36 (70.6%)	74 (72.55%)
	Female	15 (29.4%)	28 (27.45%)

Table 2: Radiographic findings of study participants

Chest radiograph findings	Second RT-PCR positive patients (n = 51)	Second RT-PCR negative patients (n = 102)
Normal	28 (54.9%)	95 (93.1%)
Abnormal	23 (45.1%)	7 (6.9%)
Classic/Probable Covid – 19 (Bilateral consolidation/ Ground glass density in peripheral, basal distribution)	12 (23.5%)	1 (0.98%)
Indeterminate for Covid – 19 (other patterns of consolidation/ effusion/ lymphadenopathy)	11 (21.57%)	6 (5.9%)

In the RT-PCR positive group, 45.1 % (n = 23) had findings suggestive of probable COVID -19 infection and in the RT-PCR negative group, only 6.9% (n = 7) showed abnormal findings. This difference was found to be statistically significant with Chi-square value, $\chi 2$ (1, n = 153) = 31.1,p < 0.05.

Interrater Reliability

The interrater reliability for the tests was found to be Kappa = 0.43 (p <0.001), 95% CI (0.28, 0.58) indicating moderate agreement.

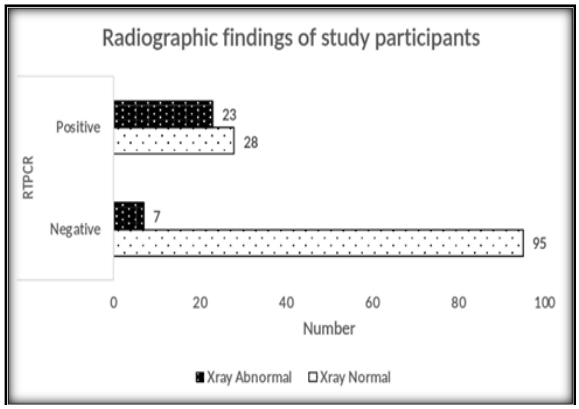

Figure 3: Bar chart showing distribution of radiographic findings in study participants

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DISCUSSION

COVID- 19 is a disease that spreads rapidly, has no specific treatment and has the potential to overburden the system to the verge of collapse. Early diagnosis, isolation and initiation of supportive management is necessary to control the situation effectively. Though RT-PCR, a gold standard investigation, is available, it is limited by cost, sampling issues, availability, delay in obtaining results and reduced sensitivity in actual clinical practice, especially in resource limited settings.[16-18] This imposes problems in making early diagnosis, treatment and proper isolation of symptomatic COVID – 19 suspects especially when initial RT-PCR result is negative.

During the initial phase of the disease, the protocol followed in our hospital which was a designated COVID treatment centre, was to do RT-PCR and chest radiograph along with routine blood investigations for symptomatic patients attending the outpatient department of the covid care unit as COVID suspects. In case of RT-PCR negative patients, a repeat RT-PCR was done after 48 hours for confirmation of diagnosis and admissions were based on the severity of symptoms. But when the number of outpatient department increased drastically the protocol was changed and instead of repeat RT-PCR, rapid antigen test was performed for those admitted symptomatic patients before discharge.

As the disease affects mainly the respiratory system we thought of taking initial chest radiograph findings as a supplementary evidence of infection in initial RT PCR negative symptomatic patients. Our study compares the early chest radiograph findings with the second RT-PCR result to find the agreement between the two so as to replace or supplement RT-PCR with a chest radiograph so that false negative RT-PCR patients will not be missed during the initial screening itself.

We had a total 153 patients satisfying the inclusion criteria. Among them, second RT-PCR turned out to be positive for 51 patients and negative for the rest 102. Analysis by the independent radiologist revealed that abnormal chest radiograph findings were present in 23 cases (45.1%) in 1st group (second RT-PCR positive) and in 7 cases (6.9%) in 2nd group (second RT-PCR negative). So an additional 16 cases (15.8%) would have been identified if chest radiograph findings were also considered initially.

Kappa analysis in our study showed the agreement value as 0.43 ($p < .0.001$), indicating moderate agreement between initial chest radiograph and 2nd RT PCR.[15] Thus, chest radiograph may be taken as corroborative evidence to microbiological testing at the time of seeking medical advice and will help in determining patients who needs isolation and containment. This could have an impact in reducing the disease overburden by preventing rapid spread from undiagnosed false negative cases.

Various studies have been conducted about the chest radiographic findings associated with COVID - 19 disease in various stages with sensitivities ranging from 9% (Wong et al) to 89% (Schiaffino et al).[19-23] But only a few studies have described the role of initial chest radiograph in diagnosis of COVID- 19 among symptomatic suspects. Wong et al conducted a study on the time course and severity of findings of COVID- 19 at chest radiograph and correlated these with RT PCRfor SARS CoV – 2 nucleic acid and found that 9% showed abnormalities at initial chest radiography before eventually testing positive for Covid 19 with RT PCR.[19] In the study by Abougazia et al, it was seen that 16.8% showedearly chest radiographic findings along with a positive COVID - 19 diagnosis.[20] HY Yoon et al also confirms that that 8.33% patients had abnormal findings in the initial chest radiograph itself.[21]

Ng et al,[22] reported that CXR was not sensitive in the early stages of pulmonary disease. However, our study is novel in that we assessed the findings in initial chest x ray in RT PCR test negative symptomatic COVID - 19 suspects and compared this with the second RT-PCR result to find the agreement between the two. Chest radiograph findings were analysed according to Fleishner's society glossary of terms for Thoracic Imaging.[14] Classic COVID -19 findings were seen in 23 % of positive patients. Various other studies also support this and moreover, chest radiographic findings can vary according to the different racial, ethnic groups and also based on the immune status of the individuals and time since onset of symptoms.

Clinical significance of this study is that if the RT-PCR result is negative or if it is not available, a chest radiograph may be taken as a part of the screening procedure for suspected COVID- 19 symptomatic cases.As chest radiograph is one of the most readily available and feasible investigation in our urban and rural set up with minimal chances of cross contamination, looking into the initial chest radiograph findings even if the first RT-PCR is negative in symptomatic patients can help the general practitioners and clinicians in finding out the missed out positive cases.

A major limitation of our study was a short study period of around three months because the hospital diagnostic protocol was changed after that. We could however achieve an adequate sample size as calculated due to our huge case load during this period. Another limitation was absence of serial chest radiographs to see progression of disease as very early chest radiograph can be normal in a COVID - 19 patient. Time since onset of symptoms when chest radiograph is taken can be included in future studies for better results.

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CONCLUSION

In COVID- 19 infection chest radiograph has a key role in assisting the diagnosis especially when there is dilemma in confirming the diagnosisin case of 1st RT-PCR negative symptomatic cases with abnormal chest radiograph findings. Hence it can be used as a screening test in identifying the patients with a likelihood of COVID – 19 and to triage them appropriately regarding isolation, containment and treatment.

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