Original Article

DOI: 10.7860/JCDR/2022/51204.16102

Role of Modified RALES and Brixia Scores in Predicting the COVID-19 Positivity among the Suspected Patients: A Cross-sectional Observational Study

Internal Medicine Section

NITIN SINHA[1], DIVESH JALAN[2], PRINCI JAIN[3]

ABSTRACT

Introduction: Computed Tomography (CT) chest plays an important role in triaging and managing patients of suspected COVID-19, especially in those where Coronavirus Disease 2019 (COVID-19) report is pending but CT chest has constraints of availability and cost. Chest X-ray (CXR) is a readily available investigation and is cheaper than a CT chest. Hence, any scoring on CXR which proves to be helpful in triaging and managing suspected COVID-19 patients will alleviate the dependency on CT chest. Modified Radiographic Assessment of Lung Edema Score (mRALES) and Brixia scores have been used to assess severity of disease and prognosis in COVID-19 confirmed cases. However, these two scores have never been used as a method to predict the confirmed COVID-19 pateints among the the suspected COVID-19 cases.

Aim: To evaluate the role of mRALES and Brixia score along with clinical and laboratory parameters in predicting confirmed positive cases among suspected COVID-19 patients.

Materials and Methods: This retrospective cross-sectional, observational study was conducted in Department of Medicine at Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) and Dr. Ram Manohar Lohia Hospital, New Delhi, India, from 1st December 2020 to 15th December 2020. Case records of patients admitted with severe acute respiratory illness (suspected COVID-19) were accessed and used to fill up a proforma where clinical and laboratory parameters were recorded. Chest radiographs (posteroanterior and anteroposterior) of the patients were evaluated to calculate mRALES and Brixia scores. Sensitivity, specificity, positive preditive value and negative predictive value were calculated. The p-value <0.05 was considered as statistically significant.

Results: Out of the 113 patients, 62 were males and 51 females. The COVID-19 positivity rate was 15.04% (n=17). Mean age of patients was 52.64±15.63 years. Overall, the mean mRALES and Brixia scores were not statistically different between negative (mRALES=3.94±2.51, Brixia=7.29±4.642), and confirmed COVID-19 (mRALES=4.25±2.56, Brixia=7.73±4.84) patients. However, in the subgroup of patients with history of obstructive airway disease, Brixia score was significantly higher among COVID-19 positive patients (7.09±4.70) as compared to COVID-19 suspected patients (0.53±4.31). Presence of low TLC {<9550/mm^3 with sensitivity of 70.62%, specificity of 67.3%, Positive Predictive Value (PPV) of 26.7% and Negative Predictive Value (NPV) of 92.4%} and low ANC (<7580/mm^3 with sensitivity of 64.7%, specificity of 63.2%, PPV of 22.9% and NPV of 90.5%) significantly predicted the COVID-19 positivity among the suspected COVID-19 patients.

Conclusion: mRALES and Brixia scores on CXR are not significantly different between suspected and confirmed COVID-19 patients and hence, cannot be used to judge who among suspected COVID-19 patients will turn out to be COVID-19 positive later. However, a TLC of less than 9550/ mm^3 and an ANC of less than 7580/mm^3 can predict COVID-19 positivity among suspected patients.

Keywords: Absolute neutrophil count, Chest X-ray scores, Coronavirus disease 2019, Obstructive airway disease, Radiographic assessment of lung edema score, Total leucocyte count

INTRODUCTION

Along with Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) [1] imaging has turned out to be a valuable tool in "ruling in" and "ruling out" suspected COVID-19 patients [2,3]. The choice between imaging modalities like Computed Tomography (CT) chest and Chest X-ray (CXR) depends on local resources and expertise available at the site. In United States of America, CXR has been extensively used in the triage of patients with COVID-19 infection [4]. But, this triaging was to differentiate between those patients who would require critical care and those who would not. These two scores have never been used to predict who among the suspected COVID-19 will turn out to be positive. The most frequent radiographic findings are airspace opacities described as consolidation with bilateral, peripheral, and lower zone predominant distribution. The radiological picture on CXR also consists of atypical pneumonia or organising pneumonia [5,6].

In most of the hospitals including the present study hospital, patients of suspected COVID-19 are placed in a common ward till the time their RT-PCR report is available. A distinction between those who have high likelihood of being COVID-19 positive from those who have a less likelihood can help in placing them in isolation wards at the outset. This can reduce transmission of infection.

Radiographic Assessment of Lung Edema Score (RALES) was initially, used for the assessment of pulmonary oedema and Acute respiratory distress syndrome (ARDS) [7]. Due to its heavy handed calculations and observer bias, it is used in a simplified and convenient form called modified RALES (mRALES) in confirmed COVID-19 patients [8].

Brixia score was exclusively developed for the COVID-19 disease severity assessment by Borghesi and Maroldi R in Italy [9]. In a study on 302 Caucasian patients with COVID-19, only Brixia score, patient age, and conditions that induced immunosuppression were the significant predictive factors for in-hospital mortality. On receiver operating characteristic curve analyses, the optimal cut-off values for Brixia score and patient age were 8 points and 71 years, respectively [10]. A retrospective study including 130 patients in India used Brixia CXR scoring system found that, Brixia score more than 12 was associated with increased mortality (p-value=0.03). The mean Brixia CXR score was calculated to be 12.13±2.50 among dead patients and 11.18±2.30 in patients who were discharged [11].

In this study, two CXR scores (mRALES score and Brixia score) were studied among suspected COVID-19 patients and their role along with other clinical and laboratory parameters in predicting confirmed COVID-19 disease among suspected COVID-19 patients was evaluated.

MATERIALS AND METHODS

This retrospective cross-sectional, observational study was conducted in Department of Medicine at Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) and Dr. Ram Manohar Lohia Hospital, New Delhi, India, from 1st December 2020 to 15th December 2020. An approval of the Ethical Committee of the institute was taken {vide letter no. 485(21/2021)IEC/ABVIMS/RMLH/513}.

Inclusion and Exclusion criteria: All the suspected COVID-19 patients admitted in the designated ward between 1st and 15th December 2020 were included in the study. All patients lacking with appropriate records/data required were excluded from the study.

Methodology: Case records were accessed and a proforma was filled that recorded the demographic details, detailed history (presenting symptoms like fever, cough, sore throat, loss of taste or smell, diarrhoea, constipation, nausea, vomiting, body ache, running nose, headache, altered sensorium, pain abdomen, skin rash, chest pain, medical history regarding any co-morbidities like diabetes, hypertension, bronchial asthma, chronic obstructive airway disease, tuberculosis, interstitial lung disease, coronary artery disease, peripheral vascular disease, cerebro-vascular accident, chronic kidney disease, chronic liver disease, malignancy, immunosuppressive drugs or steroids intake, organ transplant, thyroid disorders, seizure disorder), examination (complete general physical and systemic examination) findings of the patient. The investigations recorded were haemogram with Erythrocyte Sedimentation Rate (ESR), Total Leucocyte Count (TLC), Absolute Neutrophil Count (ANC), Neutrophil Lymphocyte Ratio (NLR), Platelet Lymphocyte Ratio (PLR), C-reactive Protein (CRP), Serum Lactate Dehydrogenase (LDH), liver function tests, kidney function tests, arterial blood gas analysis, Chest X-ray posteroanterior and anteroposterior (CXR PA/AP) view and12 lead electrocardiogram.

Ministry of Health and Family Welfare, Government of India (MOHFW, GOI) clinical classification of COVID-19 infection was used in this study [12]. According to this classification, suspected COVID-19 is defined as:

A. A patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath), AND a history of travel to or residence in a location reporting community transmission of COVID-19 disease during the 14 days prior to symptom onset

OR

B. A patient with any acute respiratory illness AND having been in contact with a confirmed or probable COVID-19 case in the last 14 days prior to symptom onset

OR

C. A patient with severe acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath; AND requiring hospitalisation) AND in the absence of an alternative diagnosis that fully explains the clinical presentation.

Further grading of patients was done as follows as mentioned in [Table/Fig-1]:

COVID-19 was confirmed, if the nasopharyngeal/oropharyngeal sample was positive for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Ribonucleic Acid (RNA) using RT-PCR method. However, COVID-19 was considered negative if two reports, done at least 48 hours apart, did not detect SARS-CoV-2 RNA. RT-PCR was done using the GENES2ME kit by PCR amplification and fluorescence channel settling techniques. It uses the Cycle Threshold value (CT value) of 37 as a cut-off to differentiate the positive or negative results.

Clinical severity	Clinical parameters
Mild	Without evidence of breathlessness or Hypoxia (normal saturation).
Moderate	Adult with presence of clinical features of dyspnea and or hypoxia, fever, cough, including SpO_2 <94% (range 90-94%) on room air, respiratory rate ≥24/min.
Severe	Adult with clinical signs of Pneumonia plus one of the following; respiratory rate >30 breaths/min, severe respiratory distress, SpO_2 <90% on room air. **Acute respiratory distress syndrome (ARDS)** Oxygenation impairment in adults: 1. Mild ARDS: 200 mmHg <PaO_2/FiO_2 ≤300 mmHg (with PEEP or CPAP ≥5 cm H_2O) 2. Moderate ARDS: 100 mmHg <PaO_2/FiO_2 ≤200 mmHg with PEEP ≥5 cm H_2O) 3. Severe ARDS: PaO_2/FiO_2 ≤100 mmHg with PEEP ≥5 cm H_2O) When PaO_2 is not available, SpO_2/FiO_2 ≤315 suggests ARDS.

[Table/Fig-1]: Grading of severity in suspected COVID-19 patients.
CPAP: Continuous positive airway pressure; PEEP: Positive end expiratory pressure; PaO_2: Arterial oxygen partial pressure; FiO_2: Fractional inspired oxygen

Chest X-ray

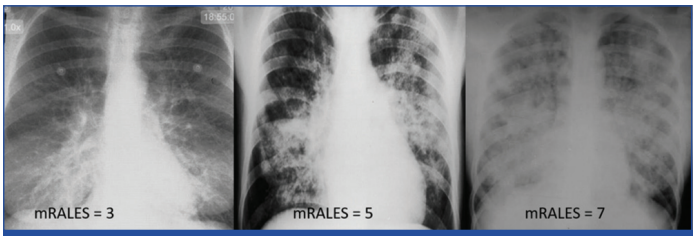
CXR of the patients were evaluated by the authors when they treated the patients to calculate mRALES and Brixia scores.

1. **Modified Radiographic Assessment of Lung Edema Score (mRALES):** Calculated by as follows [8]:

- 0 is no involvement;
- 1 is <25% of lung involved;
- 2 is 25-50% of lung involved;
- 3 is >50-75% lung involved;
- 4 is >75% of lung involved

Score for each lung is calculated and scores of both lungs are added to get the final mRALES [Table/Fig-2]. Severity based on mRALES is defined as follows [13,14]:

- Mild: 0-2,
- Moderate: 3-5,
- Severe: 6-8



[Table/Fig-2]: mRALES scoring on chest x-rays.

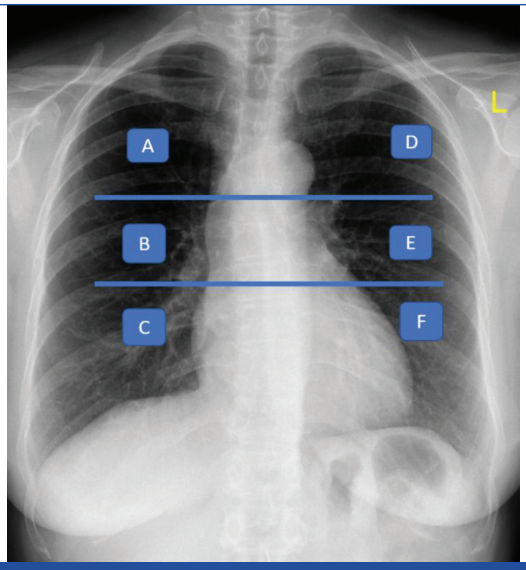
2. Brixia score: In Brixia scoring format, designed exclusively for COVID-19 confirmed patients, the lungs are divided into six zones on AP/PA view as shown in [Table/Fig-3].

- Upper zones (A and D): above the inferior wall of the aortic arch;
- Middle zones (B and E): below the inferior wall of the aortic arch and above the inferior; wall of the right inferior pulmonary vein (i.e., the hilar structures).
- Lower zones (C and F): below the inferior wall of the right inferior pulmonary vein.

A score (from 0 to 3) is assigned to each zone based on the lung abnormalities detected:

- Score 0- No lung abnormalities;
- Score 1- Interstitial infiltrates;
- Score 2- Interstitial and alveolar infiltrates (interstitial predominance);
- Score 3- Interstitial and alveolar infiltrates (alveolar predominance).

The scores of the six lung zones are then added to obtain an overall "CXR score" ranging from 0 to18 [9].



[Table/Fig-3]: Brixia scoring on chest X-ray.

STATISTICAL ANALYSIS

All the details from the filled proforma were recorded on Statistical Package for Social Sciences (SPSS) software (version 16. IBM Inc., Chicago). The qualitative variables are expressed as percentages and all quantitative variables were recorded as Mean±SD. mRALES and Brixia scores were compared between different severity grades of COVID-19 using Kruskal-Wallis H test. These scores were also compared between COVID-19 patients who tested positive by RT-PCR and those who tested negative. This comparison was done using Mann-Whitney U test. To identify factors that predicted COVID-19 positivity, univariate analysis for each factor was done. Sensitivity, Specificity, PPV and NPV of the factors that were found to be significantly different between the two groups on univariate analysis were calculated. The p-value <0.05 was considered as statistically significant.

RESULTS

Between 1st and 15th December 2020, 113 patients who got admitted in suspected COVID-19 wards and whose case records were complete were included in this study. Mean age of the patients was 52.64±15.63 years. There were 62 males and 51 females, and the mean duration of symptoms was 6.6±6.3 days. The symptoms at presentation and presence of various co-morbidities of all the suspected COVID-19 patients are detailed in [Table/Fig-4].

Symptoms and Co-morbidities	Proportion observed (%)
Cough	58 (51.32)
Fever	113 (100)
Breathlessness	96 (84.95)
Sore throat	9 (7.96)
Diarrhoea	6 (5.30)
Nausea	6 (5.30)
Vomiting	13 (11.50)
Bodyache	6 (5.30)
Running nose	2 (1.76)
Anosmia	1 (0.8)
Ageusia	3 (2.65)
Headache	3 (2.65)
Altered sensorium	8 (7.07)
Chest pain	14 (12.38)
Diabetes mellitus	38 (33.62)
Hypertension	37 (32.74)
History of tuberclosis	12 (10.61)
Coronary artery disease	18 (15.92)
Cerebrovascular accident	10 (8.84)
Chronic obstructive airway disease/Bronchial asthma	19 (16.81)
Chronic kidney disease	9 (7.96)
Chronic liver disease	3 (2.65)
Malignancy	1 (0.8)
Human immunodeficiency virus infection	1 (0.8)

[Table/Fig-4]: Symptoms at presentation and Co-morbid illnesses among all suspected COVID-19 patients.

mRALES and Brixia scores among males were 4.50±2.56 and 8.08±2.50, respectively and among females were 3.84±2.50 and 7.16±4.53, respectively. Both the scores were not significantly different between the two genders (p-value=0.15 and p-value=0.30 for mRALES and Brixia score, respectively). mRALES and Brixia CXR scores comparison between the mild, moderate and severe suspected COVID- 19 patients is shown in [Table/Fig-5]. The scores were not significantly different between the three groups.

Scores	Mild (N=31)	Moderate (N=41)	Severe (N=41)	p-value (Kruksal Wallis H test)
mRALES	4.10±2.59	3.61±2.51	4.88±2.44	0.80
Brixia	7.13±4.84	6.58±4.94	8.86±4.47	0.106

[Table/Fig-5]: Comparison of mRALES and Brixia CXR scores in different categories of severity as per Ministry of Health and Family Welfare, Government of India (MOHFW, GOI) guidelines among suspected COVID-19 patients.

The COVID-19 positivity rate was 15.04%, 17 patients positive out of 113. Comparison of mRALES and Brixia scores between the two groups (COVID-19 positive and negative) is described in [Table/Fig-6]. Both the scores had no significant difference between the two groups.

Scores	COVID-19 positive patients (17)	COVID-19 negative patients (96)	p-value (Mann-Whitney U test)
mRALES	4.25±2.56	3.94±2.51	0.571
Brixia	7.73±4.84	7.29±4.642	0.702

[Table/Fig-6]: Comparison of mRALES and Brixia scores between COVID-19 positive and negative patients.

Comparison of mRALES and Brixia scores between the patients having co-morbidities and those without any co-morbidities is depicted in [Table/Fig-7]. The patients with history of airway disease, had significantly lower Brixia score in COVID-19 positive patients as compared to COVID-19 negative patients (p-value=0.003).

Co-morbidities	mRALES			Brixia		
	COVID-19 positive patients	COVID-19 negative patients	p-value	COVID-19 positive patients	COVID-19 negative patients	p-value
Diabetes mellitus	4.16±2.29	4.23±2.68	0.83	7.16±4.53	7.87±5.08	0.52
Hypertension	3.25±2.59	4.33±2.53	0.38	7.27±4.87	7.86±4.78	0.48
Coronary artery disease	4.17±2.33	4.21±2.60	0.96	7.44±4.13	7.71±4.93	0.84
Cerebrovascular accident	3.50±3.17	4.27±2.49	0.45	6.20±5.86	7.81±4.69	0.27
Chronic kidney disease	5.44±2.69	4.10±2.52	0.12	10.00±5.95	7.46±4.65	0.15
Chronic liver disease	5.33±2.30	4.17±2.15	0.44	13.00±4.35	7.53±4.74	0.56
History of pulmonary tuberclosis	4.50±2.90	4.77±2.51	0.57	7.33±4.79	7.7±4.82	0.83
Bronchial asthma/Chronic obstructive pulmonary disease	5.21±2.34	4.00±2.55	0.052	0.53±4.31	7.09±4.70	0.003

[Table/Fig-7]: mRALES and Brixia scores comparison among patients who have co-morbidities and those who don't have co-morbidities.
p-value <0.05 was considered statistically significant; calculated by Mann-Whitney U test

The comparison of mRALES and Brixia scores according to duration of symptoms showed that scores did not differ significantly with increasing duration of symptoms [Table/Fig-8].

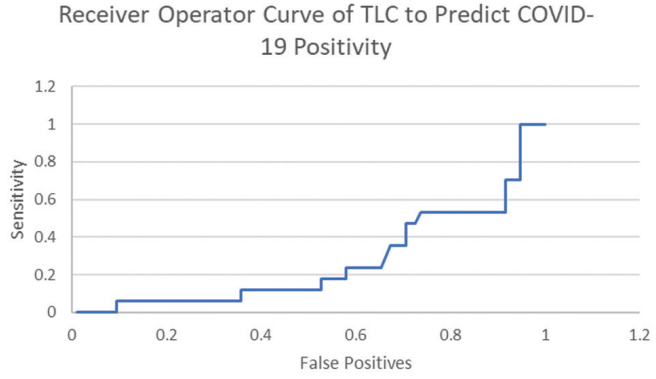
Scores	Duration of symptoms			
	0-4 Days (n=55)	5-8 Days (n=30)	≥9 Days (n=28)	p-value
mRALES	4.27±2.5	4.17±2.78	4.11±2.47	0.932
Brixia	7.67±4.88	7.80±5.02	7.5±4.52	0.963

[Table/Fig-8]: mRALES and Brixia scores according to duration of symptoms.
p-value <0.05 was considered statistically significant; calculated by Kruskal-Wallis H Test

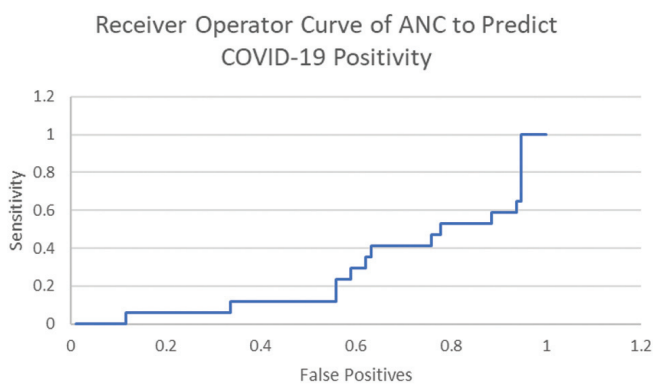
On univariate analysis, it was observed that presence of low TLC (p-value=0.02) and low ANC (p-value=0.016), significantly predicted the COVID-19 positivity among the suspected COVID-19 patients [Table/Fig-9]. With an Area Under the Receiver Operating Characteristics (AUROC) of 0.73 [Table/Fig-10], TLC <9,550/mm^3 had sensitivity of 70.62% and specificity of 67.3% in predicting COVID-19 positivity. AUROC [Table/Fig-11] of ANC <7,580/mm^3 was 0.733 with sensitivity of 64.7% and specificity of 63.2% in predicting COVID-19 positivity [Table/Fig-12].

Demographic parameters	COVID-19 positive patients	COVID-19 negative patients	Unadjusted odds ratio	p-value
Age (in years)	54.88±12.84	52.24±16.1	0.989	0.512
Duration of symptoms (in days)	6.59±4.27	6.6±6.61	1.000	0.992
Chronic obstructive airway disease/Bronchial asthma	1	18	2.609	0.093
Diabetes mellitus	8	30	0.956	0.209
Hypertension	8	31	1.14	0.808
Coronary artery disease	2	16	0.667	0.613
Chronic kidney disease	1	8	0.688	0.732
Cerebrovascular accident	1	9	0.604	0.643
Cough	12	46	0.997	0.919
Nausea	2	4	3.067	0.218
Vomiting	3	10	1.843	0.345
Body ache	3	3	6.643	0.029
Sore throat	3	6	0.324	0.126
Breathlessness	12	84	0.343	0.082
Diarrhoea	2	4	3.067	0.218
Headache	1	2	2.937	0.390
Altered sensorium	1	7	0.795	0.835
Chest pain	1	13	0.394	0.392
Haemoglobin (g/dL)	10.88 (7.73)	10.6 (7.77)	1.033	0.74
TLC (per mm^3)	8482 (4255)	12471.35 (6713.74)	1.00	0.02
Platelet count (per dL)	2.29 (0.69)	2.32 (1.15)	1.025	0.919
ANC (mm^3)	6670 (3577.43)	10394.57 (6100.13)	1.00	0.016
NLR	5.83 (3.64)	7.60 (4.78)	1.113	0.158
PLR	219.41 (27.44)	185.66 (140.77)	0.998	0.358
CRP (mg/dL)	73.42 (64.61)	66.51 (81.35)	0.999	0.753
LDH (IU)	678.27 (290.30)	793.42 (548.3)	1.001	0.430
PCT (pg/dL)	2.53 (3.67)	10.24 (31.98)	1.040	0.486
pH	7.39 (0.04)	7.31 (0.55)	0.387	0.073
$PaCO_2$ (mm of Hg)	34.35 (8.40)	40.49 (18.71)	1.026	0.205
HCO_3	22.53 (5.11)	22.45 (7.44)	0.998	0.96
Urea (mg/dL)	64.24 (46.38)	62.18 (54.09)	0.994	0.758
Creatinine (mg/dL)	1.55 (1.33)	2.87 (10.7)	1.047	0.690
Total Bilirubin (mg/dL)	0.78 (0.66)	1.89 (3.34)	1.281	0.229
Direct bilirubin (mg/dL)	0.39 (0.39)	0.94 (1.75)	1.550	0.256
SGOT (IU)	47.41 (28.36)	91.83 (236)	1.004	0.484
SGPT (IU)	34.00 (33.81)	70.46(185.18)	1.003	0.493
ALP (IU)	105.0 (52.17)	131.24(117.9)	1.005	0.334
Albumin (g/dL)	3.13 (0.62)	3.18 (0.80)	1.114	0.763

[Table/Fig-9]: Univariate analysis of demographic, clinical profile and investigations for predicting the COVID-19 positivity among suspected COVID-19 patients.
Quantitative variables are expressed as mean (SD) and quantitative as proportion (percentages)
TLC: Total leucocyte count; ANC: Absolute neutrophil count; NLR: Neutrophil lymphocyte ratio; PLR: Platelet lymphocyte ratio; LDH: Lactate dehydrogenase; PCT: Procalcitonin; CRP: C-reactive protein, $PaCO_2$: Partial pressure of carbon dioxide in blood; SGOT: Serum glutamic-oxaloacetic transaminase; SGPT: Serum glutamic-pyruvic transaminase; ALP: Alkaline phosphate



[Table/Fig-10]: Receiver operating characteristic curve of TLC to predict COVID-19 positivity.



[Table/Fig-11]: Receiver operating characteristic curve of ANC to predict COVID-19 positivity.

Parameter	AUROC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
TLC (<9,550/mm^3)	0.73	70.62	67.3	26.7	92.4
ANC (<7,580/mm^3)	0.733	64.70	63.2	22.9	90.5

[Table/Fig-12]: Area Under the Receiver Operating Characteristics (AUROC), sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of Total Leucocyte Count (TLC) and Absolute Neutrophil Count (ANC) to predict COVID-19 positivity.

DISCUSSION

Warren MA et al., used the RALES scoring system initially to assess the extent and severity of pulmonary oedema and ARDS [7]. It was simplified to mRALES by Wong HYF et al, whose study found that at the time of hospital admission, 41% of the patients had mRALES of 1-2 on baseline CXR, while 31% patients had normal radiographs that progressed over time, reaching peak by 10-12 days among COVID-19 positive patients. This study also demonstrated that 91% of patients tested positive for RT-PCR while 59% showed abnormalities on baseline CXR [8]. In the present study, all suspected patients had CXR changes, however only 15.04% were RT-PCR positive. CXR changes among RT-PCR negative patients can be

due to infectious agents other than SARS-CoV-2. Both mRALES and Brixia scores were not significantly different between COVID-19 positive and COVID-19 negative patients in the present study, which further reaffirms that CXR scores show no relation with RT-PCR reports. Hence, these scores cannot be used for demarcating those suspected COVID-19 patients who are likely to come RT-PCR positive from those who are likely to come negative.

A study by Li MD et al., that enrolled 468 confirmed COVID-19 positive patients, showed that the age and mRALES were significantly higher in 134 patients (29%) who were intubated or died within 3 days of hospital admission. Also, mRALES was 9 (5-12.2) in those who were intubated and 3.0 (1.5-5.7) in non intubated with highly significant p-value of <0.001 [15]. Brixia score was exclusively devised for COVID-19 positive patients and was first published by Borghesi A and Maroldi R. The score was significantly higher in patients who died than those discharged from the hospital (p≤0.002) [9]. A study conducted by Maroldi R et al., stated that Brixia score correlated with patient outcome in COVID-19 positive patients and found a prognostic value. A total of 953 patients were included in the study, 677 were discharged and 276 died during hospitalisation. The score was significantly higher in those who died (median: 12; IQR: 9-14) compared to those who got discharged (median: 8; IQR: 5-11) (p-value <0.0001) [16].

In the present study, both the scores were not significantly different between suspected COVID-19 patients with varying degrees of severity of disease at presentation. This could be due to the fact that the severity was assessed based on clinical parameters at the time of presentation. X-ray scores based on changes in X-rays might not be reflective of the severity assessed by clinical parameters. Also, as the study centre is a tertiary care hospital, patients often come after receiving some basic treatment before being referred. This can also influence the X-ray scores. Hence, mRALES and Brixia scores cannot be used to predict severity of disease among suspected COVID-19 patients.

The authors could not find any study where Brixia and mRALES scores have been used to predict COVID-19 positivity among suspected COVID-19 patients. This is probably first study where these scores have been evaluated in suspected COVID-19 patients.

In a cross-sectional observational study done by Agrawal A et al., from 19th March to 15th April 2020 in 102 patients with positive SARS-CoV-2 RT-PCR, 85 (83.33%) patients were asymptomatic (group A) and 17 (16.67%) were symptomatic (group B). Most common symptom was fever, followed by dry cough with haemoptysis being least common. Co-morbidities were seen in 18 patients, six of which were in group B. The most prevalent co-morbid condition was diabetes mellitus followed by hypertension, and Chronic Obstructive Pulmonary Disease (COPD). Haematologically, group B had significantly higher mean total leukocyte count (TLC), neutrophil percentage, NLR, PLR, AST, ALT and LDH values (p-values <0.05). However, lymphocyte count was significantly lower in group B than group A (p-value=0.001) [17].

In the present study, which included both COVID-19 positive and COVID-19 negative patients, most common symptom was fever which was observed in all the patients followed by breathlessness and cough. Haemoptysis was not seen in any case. Most common co-morbidities noticed were diabetes mellitus followed by hypertension and obstructive airway disease.

Guan WJ et al., provided data on the clinical characteristics of 1,099 COVID-19 cases with laboratory confirmation during the first two months of the epidemic in China. Majority of patients had lymphocytopenia (83.2%) on admission. A 36.2% had thrombocytopenia, and 33.7% had leukopenia [18]. Another study by Najim RH and Kadhim SR, found that patients with positive RT-PCR had significant decrease in total White blood cells (3040±1000)/mm^3 count and lymphocytes (23.6) in comparison to those with negative RT-PCR for COVID-19 [19]. In the present study, TLC among COVID-19 positive patients was 8482±4255/mm^3 as compared 12471±6713/mm^3 to COVID-19 negative patients. TLC (<9550/mm^3) was seen to be a significant predictor of COVID-19 positivity among the suspected COVID-19 patients. The higher TLC in COVID-19 negative patients could be due to some other aetiological agent. At the value TLC <9550/mm^3, AUROC was 0.73 to predict COVID-19 positivity with a sensitivity of 70.62% and specificity of 67.3%.

ANC was a significant predictor of COVID-19 positivity among the suspected patients. ANC among COVID-19 positive patients was 6670±3577/mm^3 as compared to 10395±6100/mm^3 in COVID-19 negative patients. At the value ANC <7580/mm^3, AUROC was 0.733, sensitivity was 64.7% and specificity was 63.2% in predicting the COVID-19 positivity. This can be attibuted to the excessive cytokines and chemoattractants circulating in blood due to cytokine storm in COVID-19 [20] and also the hypoxia because of immunothrombosis and ARDS [21].

Neutrophils have been shown to be involved in innate immunity, as well as the state of hyperinflammation seen in COVID-19 patients. The mechanism involves a complex array of receptors and adhesion molecules for various ligands and excessive formation of Neutrophil Extracellular Traps (NETs) [22,23].

In a study from Iran on 200 patients, 70 were COVID-19 RT-PCR positive. White blood cells count among positive patients was 4043±1002/mm^3 as compared to 6894±1982/mm^3 and this difference was statistically significant [24]. This study also shows that TLC was lower in COVID-19 positive patients as compared to COVID-19 negative patients. Other parameters that were found to predict the presence of COVID-19 positivity in the study from Iran were CRP, ALT, AST and LDH. However, none of these were found to be predictive of COVID-19 positivity in the present study.

Limitation(s)

The study sample size was limited. Another limitation was not investigating for other aetiological agents in patients who had CXR changes and were COVID-19 negative by RT-PCR. The possibility, even though minimal, of CXR scores getting modified due to receiving any treatment prior to presenting to our hospital cannot be ruled out completely.

CONCLUSION(S)

Triaging suspected COVID-19 patients who are less likely to have RT-PCR positive from those who are more likely to have RT-PCR positive is the need of the hour as this can prevent cross infections. CXR scores (mRALES and Brixia) that have been used in previous studies to determine prognosis in COVID-19 positive patients were evaluated in this study to determine their role in triaging suspected COVID-19 patients into those who are more likely to come COVID-19 positive. Both these scores were not found to be useful for this purpose. These scores were not statistically different in different severity categories. However, low TLC (<9550/mm^3) and low ANC (<7580/mm^3) were found to predict COVID-19 positivity among suspected COVID-19 patients. More studies to evaluate factors predicting COVID-19 positivity among suspected COVID-19 patients are required.

Author contributions: NS- conception of idea and design of the study, collection of data, data analysis, drafting the article and proof reading, DJ- conception of idea and design of the study, Statistical analysis, interpretation of data for the work, drafting the article and proof reading, PJ- conception of idea and design of the study, collection of data, drafting the article and proof reading.

REFERENCES

[1] Drame M, Teguo MT, Proye E, Hequet F, Hentzien M, Kanagaratnam L, et al. Should RT-PCR be considered a gold standard in the diagnosis of COVID-19? J Med Virol. 2020;92(11):2312-13.
[2] Sverzellati N, Milanese G, Milone F, Balbi M, Ledda RE, Silva M. Integrated radiologic algorithm for COVID-19 pandemic. J Thorac Imaging. 2020;35(4):228-33.

[3] Rubin GD, Ryerson CJ, Haramati LB, Sverzellati N, Kanne JP, Raoof S, et al. The role of chest imaging in patient management during the COVID-19 pandemic: A multinational consensus statement from the fleischner society. Chest. 2020;158(1):106-16.
[4] Kim HW, Capaccione KM, Li G, Luk L, Widemon RS, Rahman O, et al. The role of initial chest X-ray in triaging patients with suspected COVID-19 during the pandemic. Emerg Radiol. 2020;27(6):617-21.
[5] 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):323-25.
[6] Kooraki S, Hosseiny M, Myers L, Gholamrezanezhad A. Coronavirus (COVID-19) outbreak: What the department of radiology should know. J Am Coll Radiol. 2020;17(4):447-51.
[7] Warren MA, Zhao Z, Koyama T, Bastarache JA, Shaver CM, Semler MW, et al. Severity scoring of lung oedema on the chest radiograph is associated with clinical outcomes in ARDS. Thorax. 2018;73(9):840-46.
[8] Wong HYF, Lam HYS, Fong AH, Leung ST, Chin TW, Lo CSY, et al. Frequency and distribution of chest radiographic findings in patients positive for COVID-19. Radiology. 2020;296(2):E72-78.
[9] Borghesi A, Maroldi R. COVID-19 outbreak in Italy: Experimental chest X-ray scoring system for quantifying and monitoring disease progression. Radiol Med. 2020;125(5):509-13.
[10] Borghesi A, Zigliani A, Golemi S, Carapella N, Maculotti P, Farina D, et al. Chest X-ray severity index as a predictor of in-hospital mortality in coronavirus disease 2019: A study of 302 patients from Italy. Int J Infect Dis. 2020;96:291-93.
[11] Agrawal N, Chougale SD, Jedge P, Iyer S, Dsouza J. Brixia chest X-ray scoring system in critically Ill patients with COVID-19 pneumonia for determining outcomes. Journal of Clinical and Diagnostic Research. 2021;15(8):OC15-17.
[12] Clinical Management protocol for COVID-19. https://www.mohfw.gov.in/pdf/ClinicalManagementProtocolforCOVID19dated27062020.pdf. Accessed on 04.03.2022.
[13] Yasin R, Gauda W. Chest X ray findings monitoring COVID-19 disease course and severity. Egypt J Radiol Nucl Med. 2020;51:193.
[14] Colman J, Zamfir G, Sheehan F, Berrill M, Saikia S, Saltissi F. Chest radiograph characteristics in COVID-19 infection and their association with survival. Eur J Radiol Open. 2021;8:100360. Doi: 10.1016/j.ejro.2021.100360.
[15] Li MD, Arun NT, Gidwani M, Chang K, Deng F, Little BP, et al. Automated assessment of COVID-19 pulmonary disease severity on chest radiographs using convolutional Siamese neural networks. medRxiv [Preprint]. 2020 May 26:2020.05.20.20108159. Doi: 10.1101/2020.05.20.20108159.
[16] Maroldi R, Rondi P, Agazzi GM, Ravanelli M, Borghesi A, Farina D. Which role for chest x-ray score in predicting the outcome in COVID-19 pneumonia? Eur Radiol. 2020;31(6):4016-22.
[17] Agrawal A, Tyagi P, Mahavar S, Banerjee S, Sharma R, Bhandhari S, et al. Study of hematological and biochemical parameters in a cohort of Indian COVID-19 patients admitted in a tertiary care centre. International Journal of Advances in Medicine. 2020;7(12):1840-45.
[18] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. China medical treatment expert group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708-20.
[19] Najim RH, Kadhim SR. Biochemical and hematological parameters as a predictor for COVID-19 infection in 65 patients diagnosed by real time- PCR in Kirkuk city. Sys Rev Pharm. 2020;11(5):797-99.
[20] Borges L, Pithon-Curi TC, Curi R, Hatanaka E. COVID-19 and neutrophils: The relationship between hyperinflammation and neutrophil extracellular traps. Mediators Inflamm. 2020;2020:8829674. Doi: 10.1155/2020/8829674.
[21] Reusch N, De Domenico E, Bonaguro L, Schulte-Schrepping J, Baßler K, Schultze JL, et al. Neutrophils in COVID-19. Front Immunol. 2021;12:652470. Doi: 10.3389/fimmu.2021.652470.
[22] Saffarzadeh M, Juenemann C, Queisser MA, Lochnit G, Barreto G, Galuska SP, et al. Neutrophil extracellular traps directly induce epithelial and endothelial cell death: A predominant role of histones. PLoS One. 2012;7(2):e32366. Doi: 10.1371/journal.pone.0032366.
[23] Villanueva E, Yalavarthi S, Berthier CC, Hodgin JB, Khandpur R, Lin AM, et al. Netting neutrophils induce endothelial damage, infiltrate tissues, and expose immunostimulatory molecules in systemic lupus erythematosus. J Immunol. 2011;187(1):538-52.
[24] Mardani R, Ahmadi Vasmehjani A, Zali F, Gholami A, Mousavi Nasab SD, Kaghazian H, et al. Laboratory parameters in detection of COVID-19 patients with positive RT-PCR; a diagnostic accuracy study. Arch Acad Emerg Med. 2020;8(1):e43.

PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Internal Medicine, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) and Dr. Ram Manohar Lohia Hospital, New Delhi, India.
2. Assistant Professor, Department of Orthopaedics, Vardhman Mahavir Medical College and Safdarjang Hospital, New Delhi, India.
3. Associate Professor, Department of Internal Medicine, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) and Dr. Ram Manohar Lohia Hospital, New Delhi, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Princi Jain,
Associate Professor, Department of Medicine, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) and Dr. Ram Manohar Lohia Hospital, New Delhi, India.
E-mail: princija@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jul 09, 2021
- Manual Googling: Dec 27, 2021
- iThenticate Software: Jan 01, 2022 (17%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jul 08, 2021**
Date of Peer Review: **Nov 22, 2021**
Date of Acceptance: **Jan 03, 2022**
Date of Publishing: **Mar 01, 2022**