Chest Radiography in COVID-19 Pregnancy and Its Clinicobiochemical Correlation: A Retrospective Single-center Study

Rakhee Sharma¹, Ritu Sharma², Shikha Seth³, Neema S Agarwal⁴, Ruchi Pandey⁵

ABSTRACT

Aim: We have witnessed diverse presentations of coronavirus disease-2019 (COVID-19) in pregnant females during first and second waves. The aim of this study was to evaluate the usefulness of chest X-ray and its correlation of severity scoring with clinical, laboratory parameters and maternal-fetal outcome during management of COVID-19 pregnant women in low resource settings.

Methodology: This was a retrospective observational study conducted at the Government Institute of Medical Sciences, Greater Noida, from May 2020 to May 2021. The study included 185 pregnant women in second and third trimesters with reverse transcription-polymerase chain reaction (RT-PCR)-confirmed COVID-19 disease. The chest radiographs of all patients were analyzed and severity scoring was done using modified radiographic assessment of lung edema (RALE) criteria. The correlation of severity index with clinical and biochemical profile of patients with normal and abnormal X-ray findings was compared. Two-tailed *p*-value of <0.05 was considered significant in our study.

Results: Out of 185 patients, 38 had abnormal X-ray findings, whereas 147 had normal X-ray. A significant difference was observed in mean values of lactate dehydrogenase (LDH), ferritin, C-reactive protein (CRP), D-dimer, total leukocyte count (TLC), and interleukin 6 (IL-6) levels across both X-ray groups. The proportion of pregnant mothers with live birth, high-risk pregnancy, steroid treatment, oxygen supplementation, invasive ventilation, and number of presenting symptoms varied statistically across both the X-ray groups (*p*-value <0.05). Receiver-operating characteristic (ROC) analysis revealed that an X-ray score of "5.5" has the best prognostic significance of maternal death with sensitivity of 87.5 and 96.6% specificity.

Conclusion: Chest radiography for the assessment of disease status in COVID-19 pregnancies is an effective and affordable alternative to CT scan in low resource settings.

Keywords: COVID-19 pregnancy, Modified RALE score, X-ray.

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INTRODUCTION

The World Health Organization (WHO) declared the novel coronavirus disease-2019, outbreak as global pandemic on March 11, 2020, after reporting cohort of unusual pneumonia in Wuhan, the capital city of Hubei in China.¹ Highly contagious new coronaviridae, affects lungs initially and later multisystem involvement due to hyperimmune response with clinical features ranging from asymptomatic to adult respiratory distress syndrome (ARDS).^{2,3} Because of its predilection to respiratory system, CT scan has been suggested as modality of choice for screening of COVID-19 by a few with or without laboratory confirmation even in pregnancy. However, it is difficult to have CT imaging as well as costly inflammatory markers serially, especially in low resource setting that too in pandemic lockdown; therefore, we planned to find out clinico-biochemical correlation of the chest radiography in reverse transcription-polymerase chain reaction confirmed COVID-19 pregnancies retrogradely. X-ray although less sensitive but has minimal radiation exposure compared to CT scan and widely available low-cost test can be done bedside in isolation settings. Till date, existing data are very limited on role of chest X-ray in management of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-positive pregnant women.

MATERIALS AND METHODS

This was a retrospective study conducted in the Department of Obstetrics from May 2020 to May 2021 at the Government Institute of Medical Sciences (GIMS), Greater Noida, a dedicated COVID center ^{1–3}Department of Obstetrics and Gynaecology, Government Institute of Medical Sciences, Greater Noida, Uttar Pradesh, India

⁴Department of Radio-diagnosis, Government Institute of Medical Sciences, Greater Noida, Uttar Pradesh, India

⁵Department of Community Medicine, Government Institute of Medical Sciences, Greater Noida, Uttar Pradesh, India

Corresponding Author: Rakhee Sharma, Department of Obstetrics and Gynaecology, Government Institute of Medical Sciences, Greater Noida, Uttar Pradesh, India, Phone: +91 9695043030, e-mail: rakhee1789@gmail.com

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of Gautam Buddha Nagar, UP. The study was approved by the Ethical Committee of Institute (GIMS/IEC/HR/2021/24).

Inclusion Criteria

All the RT-PCR-confirmed COVID-19-positive second- and third-trimester pregnancy cases.

Exclusion Criteria

First-trimester pregnancies, cases without RT-PCR confirmation, women with incomplete records, and preexisting respiratory and cardiac diseases were excluded from the study.

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All the records of COVID-19 pregnancy admissions were screened. Clinical diagnosis of COVID-19 pneumonia was based on WHO guidelines⁴ and four category classifications such as mild/ asymptomatic, moderate, severe, and critical. Laboratory values of CBC, neutrophil-lymphocyte ratio (NLR), PLR, LFT, KFT, C-reactive protein, lactate dehydrogenase, D-dimer, ferritin, interleukin 6, procalcitonin at time of admission were notified.

Being a new medical college and not having the in-house CT facility, X-ray chest at the time of admission was our institutional protocol for all RT-PCR-confirmed COVID-19 cases. We opted the same for the pregnant women of second and third trimesters with abdominal shield, irrespective of their symptomatology, taking the informed consent. Digital radiography facility was available with mobile units in emergency, isolation wards and intensive care units ICUs which were analyzed by expert radiologist for findings and scoring.

Radiologic features such as ground-glass opacities (GGOs), consolidation pulmonary nodules and reticulations were identified as per the Fleischner Society Glossary of Terms. Distribution of lung parenchymal findings was classified as (i) peripheral or peri-hilar (ii) unilateral (right/left) or bilateral lung involvement, (iii) zonal involvement (described as upper, middle, and lower) zones.⁵

On basis of X-ray, enrolled cases were divided into the following groups:

Group I (score 0)—women who had normal X-ray

Group II (score 1–8)—women with one or more abnormal findings

The extent of lung involvement by disease severity was assessed by using radiographic assessment of lung edema RALE score proposed initially by Warren et al.⁶ and later modified by Wong et al.⁷ in COVID-19 which we followed.

A score of 0–4 was assigned to each lung depending on the extent of involvement by consolidation or alveolar/interstitial infiltrates (0 = no involvement; 1 = <25%; 2 = 25–50%; 3 = 50–75%; and 4 = >75% involvement). The scores for each lung (right + left) were summed to produce the final severity score (range 0–8).⁷ We

opted modified RALE score based on Group II cases that were further divided into two subgroups:

Group IIA—score <4 and Group IIB—score \geq 4.

Scores of both groups and subgroups were correlated with clinical, biochemical, inflammatory parameters and with maternal and fetal outcomes using appropriate statistical tools.

Study protocol is shown in Flowchart 1.

RESULTS

A total of 185 RT-PCR-confirmed COVID-19-positive pregnant women were enrolled with a mean age of 26.9 ± 4.94 years and gestational age of 33 ± 7.52 weeks, respectively. Seventy-six were primigravida and 109 were multigravida. Clinico-demographic profile is demonstrated in Table 1.

The most common presenting symptoms were cough, fever, sore throat, dyspnea, and myalgia. Inflammatory markers (CRP, LDH, Ferritin, D-dimer, and IL-6) were found significantly raised in Group II women with abnormal X-ray findings. None of the patient in Group I required oxygen therapy, while in Group II, 65.7% required oxygen supplementation.

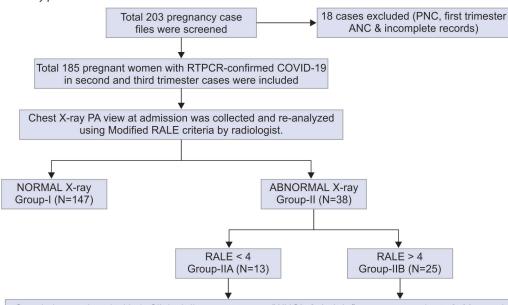
Among the abnormal X-ray Group II cases, "9" required invasive ventilation as compared to only one with normal X-ray (p = 0.0001) and succumbed to death.

Overall 51% women delivered in facility with 53.7% C-section rate notified. C-section rate was high in Group II (64.7%) as compared to Group I (51.3%) although not statistically significant. Neonatal outcome in terms of live birth with better Apgar was noted in Group I as compared to six intrauterine devices (IUD) notified in the Group II (Table 2).

X-ray-finding spectra in pregnancy cases and subgroup distribution based on RALE score are shown in Table 3.

Among 13 pregnant women of Group IIA, 4 (30.7%) were asymptomatic and 9 (69.2%) had mild disease, none had severe and critical disease, while in patients with score \geq 4, all were symptomatic, 7 (28%) had moderate, 10 (40%) severe, and 8 (32%)

Flowchart 1: Study protocol



Correlation analyzed with 1. Clinical disease category (WHO), 2. Lab inflammatory markers, 3. Maternal fetal outcome

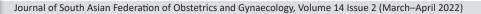
Table 1: Demographic	profile of enrolled	pregnancy cases
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Demographic factors	Total pregnant women enrolled N = 185 (%)	Women with normal chest X-ray (CXR) RALE score = 0 group I N = 147 (%)	Women with abnormal CXR RALE score ≥ 1 group II N = 38 (%)	p value
Age (mean + SD)	26.97 ± 4.94		11 - 56 (70)	pvalue
20–30	144 (77.8)	118 (80.2)	26 (68.4)	0.11
30–40	41 (22.2)	29 (19.7)	12 (31.5)	
Gravida				
G1	76 (41)	61 (41.5)	15 (39.4)	0.82
G2	109 (59)	86 (58.5)	23 (60.5)	
Gestational age (mean + SD)	33.06 ± 7.52			
14–28 weeks (second trimester)	41 (22.2)	32 (21.7)	9 (23.6)	0.799
29–40 weeks (third trimester)	144 (77.8)	115 (78.2)	29 (76.3)	
Religion				
Hindu	164 (88.6)	130 (88.4)	34 (89.4)	0.86
Muslim	21 (11.3)	17 (11.5)	4 (10.5)	
Rural	54 (29.2)	25 (17)	29 (76.3)	0.00
Urban	131 (70.8)	122 (82.9)	9 (23.6)	
Obstetrical complications	39	24 (previous ISCS-18, twins-2, PE-2, Rh negative-1, IHCP-11)	15 (previous ISCS-4, twin-3, Rh negative-2, primi breech-1, BOH-2, gest. HTN-1, GDM-2, IHCP-3)	0.001

LSCS, lower segment cesarean section; PE, pre-eclampsia; HTN, hypertension; GDM, gestational diabetes mellitus; IHCP, intrahepatic cholestasis of pregnancy

 Table 2: Clinico-biochemical parameters of enrolled pregnancy cases in two groups

Parameters	<i>Total pregnant women enrolled N = 185 (100%)</i>	Women with normal CXR RALE score = 0 group I N = 147 (79.4%)	Women with abnormal CXR RALE score ≥1 group II N = 38 (20.5%)	p value
WHO clinical category				
Asymptomatic	97 (52.4)	93 (63.2)	4 (10.5)	0.00
Symptomatic	88 (47.6)	54 (36.7)	34 (89.4)	
Mild	63 (34)	54 (36.7)	9 (23.6)	NA
Moderate	7 (3.7)	0 (0)	7 (18.4)	
Severe	10 (5.4)	0 (0)	10 (26.3)	
Critical	8 (4.3)	0 (0)	8 (21)	
Biochemical laboratory values				
NLR	129 (69.7)	102 (69.3)	27 (71)	0.149
NLR (mean \pm SD)		5.6 <u>+</u> 4.1	6.7 <u>+</u> 4.6	
SGPT (>40 IU/L)	73 (39.4)	57 (38.7)	16 (42)	0.836
SGPT (mean <u>+</u> SD)		60.9 <u>+</u> 77	58.1 <u>+</u> 64.4	
SGOT (>40 IU/L)	94 (50.8)	70 (47.6)	24 (63.2)	0.95
SGOT (mean \pm SD)		65.9 <u>+</u> 83	65.1 <u>+</u> 52.2	
CRP (>6 mg/L)	107 (57.8)	79 (53.7)	28 (73.6)	< 0.0001
CRP (mean \pm SD)		12 ± 14.4	51.3 <u>+</u> 46.6	
LDH (>480 U/L)	47 (25.4)	26 (17.6)	21 (55.2)	0.00
LDH (mean \pm SD)		377.3 <u>+</u> 200.4	772.6 <u>+</u> 854.4	
Ferritin (>30 ng/mL)	111 (60%)	79 (53.7%)	32 (84.2%)	0.00
Ferritin (mean <u>+</u> SD)		56.5 <u>+</u> 76.9	127.9 <u>+</u> 185.0	
D-dimer (>2 mg/dL)	61 (32.9)	41 (27.8)	20 (52.6)	0.033
D-dimer (mean \pm SD)		2.1 ± 2.2	3.0 <u>+</u> 2.8	
IL-6 (>6 pg/mL) [#] IL-6 (mean ± SD)	23 (12.4)	Done in 13 cases 42.9 <u>+</u> 33.6	Done in 10 cases 174.3 <u>+</u> 194.9	0.020



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Clinical outcome				
Oxygen requirement	25 (13.5)	0 (0)	25 (65.7)	NA
Ventilator	10 (5.4)	1 (0.68)	9 (23.6)	0.0001
Deliveries	95 (51.35)	78 (53.1)	17 (44.7)	
Vaginal	44 (46.3)	38 (48.7)	6 (35.3)	0.31
Cesarean	51 (53.7)	40 (51.2)	11 (64.7)	
Apgar (mean \pm SD)		7.98 <u>+</u> 0.85	7.43 ± 0.72	
IUD/SB	6 (6.32)	0 (0)	6 (35.3)	NA
Maternal death	10 (5.4)	1 (0.68)	9 (23.6)	0.000

*IL-6 done in few cases due to monitory constraints

Table 3: X-ray-	finding	spectrum	in COVID-19	pregnancies

Modified RALE score				
	Group IIA Score <4	Group IIB		
N = 38		Score ≥ 4 N = 25 (65 7%)		
	N = 13 (34.2%)	N = 25 (65.7%)		
Mean RALE score \pm SD	1.76 ± 0.43	5.52 ± 1.47		
Lung involvement				
Unilateral	3 (23)	1 (4)		
Bilateral	10 (76.9)	24 (96)		
Type of lesion				
GGOs	12 (92.3)	6 (24)		
Consolidation	1 (7.7)	7 (28)		
GGOs + consolidation	0 (0)	12 (48)		
Distribution				
Peripheral	13 (100)	9 (36)		
Central + peripheral	0 (0)	16 (64)		
Zonal involvement				
Upper	0 (0)	10 (40)		
Middle	0 (0)	15 (60)		
Lower	13 (100)	23 (92)		

critical disease. Statistically significant more number of symptoms were found in women with score ≥ 4 of which dyspnea was the cardinal symptom and virtually present in all. Majority of women reported within 5–10 days of symptoms onset and showed significant positive correlation of temporal association with radiological findings. Further Kendall's tau_b correlation coefficient showed a positive correlation of biomarkers with radiological severity as depicted in Table 4.

Requirement of oxygen, steroid, heparin, and mechanical ventilation was significantly more in Group IIB with SS \geq 4. Gross difference was notified in maternal and neonatal morbidity and mortality too.

Overall 4.3% maternal mortality was notified in women of Group IIB with X-ray (score \geq 4) compared to 0.5 in Group IIA (score <4) and none in Group I (normal X-ray). Receiver-operating characteristic analysis revealed that an X-ray score of "5.5" has the best prognostic significance of maternal death with sensitivity of 87.5 and 96.6%, specificity. This clarifies that for all practical purposes, X-ray score cutoff of "5" can be well considered to define the high probability of a poor outcome (morbidity and mortality) at the time of admission itself and care be given accordingly. As per the ROC findings of maternal death, and X-ray scores were statistically significant parameters for prognosis of maternal death in our study (Fig. 1).

DISCUSSION

Coronavirus disease-2019 virus spread via droplet infection and causes pneumonia, later the host immunological response leads to multisystem affection. Therefore, lung imaging has an important role in the management of SARS-CoV-2 and the disease severity categorization is based on lung affection along with clinical findings as described by WHO. Initial data from China indicated that pregnant women have nonsevere disease as compared to same-age nonpregnancy cases suggesting the effect of pregnancy hormones.⁸ But later, it was observed over the world that symptomatic COVID-19 pregnant women experienced more adverse outcomes. Severity in pregnancy could be attributed to the anatomical and physiological adaptive changes like reduction in total lung capacity, inability to clear secretion due to hyperemia and edema of the mucosal surfaces mediated by elevated progesterone, and the immunosuppressive status and hypercoagulability of pregnant women.9

Ideally, the CT scan is suggested to be the best modality along with the inflammatory markers for monitoring the COVID-19 disease. But in lower middle income countries (LMICs) and in resource limited areas, aforementioned investigations are neither feasible nor affordable. We planned our study to investigate whether in pregnant patients with COVID-19 infection, X-ray imaging at time of admission along with clinical findings can be used as an alternative to CT scan in disease categorization and deciding the management plan. Our study although retrospective and small, with only 185 participants, found that simple X-ray modified RALE scoring system showed good correlation with the clinico-biochemical parameters and can be used in prognosticating morbidity and mortality. Further, single chest X-ray carries no more risk of radiation exposure than CT scan (0.0005-0.01 mGy and 0.01-0.66 mGy, respectively), and hence not associated with abnormal pregnancy outcome or fetal loss.¹⁰ In order to control the infection, the American College of Radiology has also recommended the use of portable chest X-ray as first-line triage tool and reserving CT scan for progressive disease.¹¹

In our study, in normal X-ray Group I, majority of COVID RT-PCR-positive pregnant women were clinically asymptomatic (63.2%) or had mild disease (36.7%) with benign course of illness and short hospital stay. None of them had severe or critical disease and all presented primarily with one or other obstetrical complaint in third trimester. Maternal as well as fetal outcome was significantly better with only 0.68% mortality rate, and all live births. While in pregnant women with abnormal X-ray findings, 89.4% women were symptomatic having severe and critical illness in 26.3 and 21% cases, respectively.

In our study, GGOs, bilaterally with peripheral distribution affecting lower zones, were commonest radiological findings. Xu et al.¹² and Chong et al. also reported that GGO on CT

Table 4: Clinico-biochemica	I profile and outcome	based on X-ray severity score
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	Abnormal CXR cases $N = 38$				
	Group IIA	Group IIB		Kendall's tau_b	
	Score <4	Score ≥ 4		correlation	
Parameters	N = 13 (34.2%)	N = 25 (65.7%)	p value	coefficient	Sig. (two-tailed)
Clinical category (WHO)					
Asymptomatic	4 (30.7)	0 (0)	NA		
Symptomatic	9 (69.2)	25 (100)			
Asympt/mild	13 (100)	0 (0)			
Moderate	0 (0)	7 (28)			
Severe	0 (0)	10 (40)			
Critical	0 (0)	8 (32)			
Symptoms ≥3	2 (15.3)	12 (48)	<0.001		
Symptoms <3	11 (84.7)	13 (52)			
Mean duration from symptom onset	2.3 ± 1.0	4.8 ± 3.07		0.459	0.000
Hospital stay (mean \pm SD)	9 ± 3.72	7 <u>+</u> 3.49	0.144		
Biochemical laboratory values	<u> </u>	/ <u>+</u> 5.17	0.111		
NLR >3.5	6 (46.2)	21 (84)	0.00	0.084	0.148
NLR (mean \pm SD)	3.82 ± 1.5	8.26 ± 5.01	0.00	0.001	0.110
PLR (mean \pm SD)	0.08 ± 0.04	0.22 ± 0.18	0.009	0.102	0.081
SGOT >40 IU/L	6 (46.2)	18 (72)	0.007	0.102	0.001
SGOT (mean \pm SD)	40.33 ± 21.73	77.98 ± 58.81	0.007		
SGPT $>$ 40 IU/L	3 (23)	13 (52)	0.059		
SGOT (mean \pm SD)	36.15 ± 29.91	69.46 ± 74.47	0.037		
CRP (>6) mg/L	6 (46.2)	22 (88)	0.001	0.287**	0.000
CRP (mean \pm SD)	20.70 ± 34.01	67.18 ± 44.75	0.001	0.207	0.000
LDH (>480 U/L)	20.70 ± 34.01 5 (38.5)	16 (64)	0.232		
LDH (mean \pm SD)	5(30.3) 540.40 ± 402.38	893.34 ± 1000.07	0.232		
Ferritin (>30 ng/mL)	7 (53.8)	25 (100)	0.02	0.281**	0.000
Ferritin (mean \pm SD)	54.39 ± 44.68	166.08 ± 217.59	0.02	0.201	0.000
D-dimer (>2 mg/dL)	4 (30.7)	16 (64)	0.211	0.133*	0.022
D-dimer (mean \pm SD)	2.17 ± 2.48	3.39 ± 2.93	0.211	0.155	0.022
IL-6 (done in 10 pt.) [#]	176.1 ± 208.03	173.87 ± 205.15	0.991	0.238**	0.000
Maternal and neonatal outcome	170.1 ± 200.05	175.07 <u>+</u> 205.15	0.991	0.230	0.000
Oxygen requirement	2 (15.3)	25 (100)	0.00		
Ventilator	1 (7.6)	8 (32)	0.00		
Delivery	8	o (32) 9	0.00		
Vaginal	° 4 (30.7)	2 (8)	0.43		
Cesarean	4 (30.7)		0.43		
IUD/stillbirth	4 (30.7) 0 (0)	7 (28) 6 (24)	0.00 NA		
Maternal death	0 (0) 1 (7.6)	8 (32)	0.00		

[#]IL-6 can be done in few cases due to monitory constraints; ^{*}Correlation is significant at the 0.05 level (2-tailed); ^{**}Correlation is significant at the 0.01 level (2-tailed)

corresponds to pathological diffuse alveolar damage which may actually be filled with water, pus, or blood in most viral infections.¹³

Radiographic assessment of lung edema score with SS <4 demonstrated mild-to-moderate clinical illness with few symptoms corroborating radiologically with GGOs, predominantly in lower lung zone, while severe and critical diseases and multiple symptoms (>3) were noted with a score \geq 4 in our study. This was correlated well with bilateral lung involvement on chest X-ray, especially by consolidation in middle and upper lung zones in our study, consistent with findings in literature where

the presence of pure consolidation at initial lung imaging was associated with severe COVID-19 pneumonia in pregnancy.¹⁴ Ong et al. also highlighted that the chest X-ray features such as the presence of bilateral and multifocal opacities, or any upper or middle zone affection were associated with severe illness requiring supplemental oxygen.¹⁵

Xu et al. reported that chest CT detects minor lesions in an early disease but they cannot demonstrate the prognostic role of it because they could not find any correlation between imaging and course of disease.¹² Similarly, another study by Homayounieh



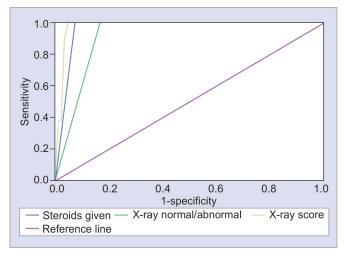


Fig. 1: ROC curve

et al. notified that CT pneumonia could not define a significant difference in area under the curve (AUC) of quantitative features for predicting disease severity (AUC 0.94–0.97) and outcome (AUC 0.7–0.77) (p >0.5).¹⁶ Jiang et al. reported that 70–80% accuracy for artificial intelligence (AI) framework based on patient symptoms and laboratory values for assessing disease severity and outcome that is actually not possible in developing countries.¹⁷

To our surprise, four (10.5%) women in abnormal X-ray group with score <4 remained asymptomatic throughout course of admission and this created the dilemmas during their clinical management and they received steroids and even plasma therapy based on X-ray findings. Rest nine cases with score of <4 had mild disease. However, with experience, this discordance could be explained as a result of either acquiring immunity from a previous infection or being in the healing phase as reported by a few in literature.^{5,18}

Atypical clinical findings in pregnant COVID-19 cases increase the difficulty in initial categorization of disease. Liu et al. also reported predominantly that peripheral and bilateral distributions in 98 and 67% cases, respectively, on CT and mixed consolidation were quite common in pregnancy cases. In our study, sole GGOs and combined GGOs + consolidation each were found in 47 and 31% pregnancy cases on X-ray.¹⁹ Our findings are in consensus with previous studies on chest X-rays and chest CT scans.^{20,21}

Studies also highlighted the transformation of initial GGOs to consolidation during the second week of illness (6–12 days), thus representing peak chest X-ray severity score at 6–10 days from symptom onset. Majority of the patients with abnormal X-ray, especially with score \geq 4 in our study, had reported within 5–10 days of symptoms onset, and hence, we could find a positive temporal correlation between the two. On history analysis, we also found that most of the pregnancy cases reported between 4th and 8th day of their symptom onset to hospital as few opted telemedicine facility, home remedies, and various surveillance mobile app for initial consultation during pandemic initially.

Correlation with Inflammatory Markers

As pneumonia in COVID-19 is an inflammatory process and the modulations in maternal immune system during pregnancy may affect the inflammatory response to infection, making the interpretations of biomarkers a bit challenging. Previous studies have highlighted lymphocytopenia,²² a high NLR,²³ CRP²⁴ linked with disease severity, or mortality along with hypercytokinemia

(IL-6 and IL-8) involved in immune-related lung injury in severe COVID-19 and ARDS.²⁵ Hence, we also looked for the correlation of hematological, biochemical, and inflammatory parameters with severity and chest X-ray score. In our study, NLR, liver enzymes, CRP, LDH, D-dimer, ferritin, IL-6, all were found raised in both Group I and Group II (normal vs abnormal), but their values were much higher in women with abnormal X-ray and showed a significant positive correlation with those having score \geq 4.

No single inflammatory marker or cytokine is specifically defined for COVID-19 yet and pregnancy further complicates the situation having raised CRP and D-dimer. Pathophysiology of COVID-19 involves the coagulation cascade and responsible for mortality also. In our study, mean D-dimer was found to be significantly low in those with normal X-ray as compared to those with abnormal findings (p = 0.03), but the difference was not found significant between scores less than and more than "4" (p = 0.21). Ferritin, another marker, is associated with anemia (reduced ferritin) which is the most common problem during pregnancy in developing countries like India. Significantly raised mean ferritin values were notified in normal vs abnormal X-ray cases (p < 0.0001) and showed a positive correlation with higher severity score ≥ 4 . Consistent with other studies revealing its association of raised levels with disease severity, it serves a key mediator in immune dysregulation and cytokine storm.²⁶

C-reactive protein, D-dimer, IL-6, and ferritin found well correlated significantly with X-ray score in our study (Table 4). Similarly, Francone et al.²⁷ and Saeed et al.²⁸ also showed positive correlation of CT severity score with lymphopenia, increased serum CRP, D-dimer, and ferritin levels (p < 0.0001). A study by Gupta et al. also reported individually that raised levels of serum ferritin, LDH, and CRP were significantly associated with severe lung involvement on high-resolution CT among COVID-19 patients.²⁹ Further among liver enzymes, aspartate transaminase (AST) serum glutamic oxaloacetic transaminase (SGOT) was significantly higher in women with score \geq 4 similar to data published by Lei et al., demonstrating strong association of AST with mortality risk in COVID-19.³⁰

Correlation with Outcome

Studies in literature have demonstrated association and correlation of X-ray RALE score with outcomes in terms of severity of disease, hospitalization, ICU admission, oxygen requirement, mechanical ventilation, and mortality.

Our study demonstrated that women with X-ray score ≥ 4 experienced more severe disease and required O_2 support along with steroids and heparin as compared to women with score <4. Eight women among 25 with score ≥ 4 required mechanical ventilation and then could not be recovered, i.e., 32% mortality rate in Group IIB. Receiver-operating characteristic analysis and AUC identified that abnormal X-ray findings can predict outcomes. Ong et al. in his study highlighted the similar association with severity and oxygen requirement.¹⁵

In our study, cutoff for modified RALE score is 5.5 for severe and critical disease with 87.5% sensitivity and 96.6% specificity, which is almost near similar to study by Slehria et al.³¹ where score threshold of 4.5 was reported for recognizing severe disease with 79.2% sensitivity and 96.3% specificity. Another study by Yasin and Gouda³² estimated severity score ranged between 6 and 8 association with more disseminated lung involvement.

Statistical significant difference noted in the mode of delivery as pregnant women with abnormal X-ray (Group II) had high Cesarean section rate (64.7%) as compared to 50% in those with normal X-ray (Group I). However, C-section was done only for the one or other obstetrical reason. Initial reports from Western countries reported very high cesarean section in virtually all symptomatic pregnant COVID-19 women, probably due to initial uncertainties regarding the feto-maternal outcome, risk of hypoxia in utero, and potential SARS-CoV-2 fetal transmission.^{33,34}

CONCLUSION

Our retrospective study concludes that X-ray chest analysis with modified RALE score done at admission (4–8 days of symptom onset) in pregnancy cases of second and third trimesters is well correlated to predict maternal and fetal prognosis and outcome. As per ROC, X-ray RALE score of 5.5 can prognosticate maternal mortality with 87.5% sensitivity and 96.6% specificity. X-ray scores are also well correlated with clinico-biochemical and inflammatory markers and treatment should be started timely based on X-ray findings available with mobile digital units immediately in low resource setting well before the laboratory reports are available to have a better feto-maternal outcome.

ORCID

Ritu Sharma https://orcid.org/0000-0002-2178-3417 *Ruchi Pandey* https://orcid.org/0000-0002-4653-6738

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