Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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COVID-19 in pregnancy: a systematic review of chest CT findings and associated clinical features in 427 patients

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ABSTRACT

Purpose: Our purpose was to conduct a comprehensive systematic review of all existing literature regarding imaging findings on chest CT and associated clinical features in pregnant patients diagnosed with COVID-19.

Materials & methods: A literature search was conducted on April 21, 2020 and updated on July 24, 2020 using PubMed, Embase, World Health Organization, and Google Scholar databases. Only studies which described chest CT findings of COVID-19 in pregnant patients were included for analysis.

Results: A total of 67 articles and 427 pregnant patients diagnosed with COVID-19 were analyzed. The most frequently encountered pulmonary findings on chest CT were ground-glass opacities (77.2%, 250/324), posterior lung involvement (72.5%, 50/69), multilobar involvement (71.8%, 239/333), bilateral lung involvement (69.4%, 231/333), peripheral distribution (68.1%, 98/144), and consolidation (40.9%, 94/230). Pregnant patients were also found to present more frequently with consolidation (40.9% vs. 21.0–31.8%) and pleural effusion (30.0% vs. 5.0%) in comparison to the general population. Associated clinical features included antepartum fever (198 cases), lymphopenia (128 cases), and neutrophilia (97 cases). Of the 251 neonates delivered, 96.8% had negative RT-PCR and/or IgG antibody testing for COVID-19. In the eight cases (3.2%) of reported neonatal infection, tests were either conducted on samples collected up to 72 h after birth or were found negative on all subsequent RT-PCR tests.

Conclusion: Pregnant patients appear to present more commonly with more advanced COVID-19 CT findings compared to the general adult population. Furthermore, characteristic laboratory abnormalities found in pregnant patients tended to mirror those found in the general patient population. Lastly, results from neonatal testing suggest a low risk of vertical transmission.

1. Introduction

On New Year's Eve 2019, Chinese national officials reported an outbreak of a highly-contagious pneumonia of unknown cause in Wuhan, Hubei Province, China to the World Health Organization (WHO).[1] By mid-February, the WHO named the disease caused by this novel infectious agent Coronavirus Disease 2019 (COVID-19).[1] Although data from the WHO suggest that as many as 80% of infections are mild or asymptomatic, common symptoms when present often include shortness of breath, fever, lethargy, sore throat, headache, chest pain, diarrhea, ageusia, and anosmia.[2] Extra-pulmonary features can include renal, gastrointestinal, hepatic, cardiac, neurological, and hematological manifestations.[3] Before reverse transcriptase polymerase chain reaction (RT-PCR) test kits became widely available, chest

Abbreviations: WHO, World Health Organization; COVID-19, Coronavirus Disease 2019; RT-PCR, Reverse Transcriptase Polymerase Chain Reaction; CT, Computed Tomography; SARS-CoV, Severe Acute Respiratory Syndrome Coronavirus; GGOs, Ground-Glass Opacities; NIH, National Institutes of Health; CRP, C-reactive protein; MERS, Middle East Respiratory Syndrome.

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computed tomography (CT) was used in some settings as a tool to confirm diagnosis and track progression of disease.[4–11] The most common features on CT imaging of patients in the general population with COVID-19 are multifocal, patchy, ground-glass opacities (GGOs) with or without superimposed consolidation in a peripheral or posterior distribution.[6,12]

Pregnant patients are a unique population of interest during the COVID-19 pandemic as they are typically young, otherwise-healthy individuals; however, they also experience an altered immunological state due to their expectancy. In 2003, pregnant patients who contracted Severe Acute Respiratory Syndrome Coronavirus 1 (SARS-CoV-1) were found to be at increased risk for spontaneous miscarriage, preterm labor, and maternal death. However, follow-up testing on neonates postnatally was unable to detect serologic evidence of vertical transmission in select cohorts.[13] Currently, there are limited data on COVID-19 in pregnant patients, and potential for vertical transmission remains unclear.[14]

While many guidelines suggest avoidance of ionizing radiation in pregnancy, appropriate shielding and low-dose protocols may allow for relatively safe use of chest CT for situations in which such investigations are clinically indicated.[15] As much of the literature regarding this unique patient population currently remains limited to case reports and case series, the primary purpose of this systematic review was to consolidate the existing knowledge on manifestations of COVID-19 in pregnant patients into a single report. We aimed to identify the most common laboratory abnormalities and imaging features on presenting chest CT, and to compare our findings with reported values in the general adult population.

2. Materials and methods

2.1. Literature and database search

PubMed, Embase, WHO, and Google Scholar databases were queried using the same keyword search that included the terms “covid*” OR “ncov” OR “sars*” OR “2019-ncov” OR “coronavirus” AND “pregn*” OR “gestation*”. The search query was designed in consultation with an investigator experienced in database searches and subsequently revised by the other investigators. All searches were initially conducted on April 21, 2020 and updated on July 24, 2020. Given the recency of COVID-19 reported cases, searches were limited only to articles published in 2020.

2.2. Qualification and study inclusion

Two reviewers independently assessed each article for study appropriateness. Initially, articles were screened to remove duplicates and those not written in English. Only articles that included details on chest CT findings in pregnant patients diagnosed with SARS-CoV-2 infection were included in the study. All systematic reviews were screened to ensure that there was no subject overlap with any included case reports and case series. Of note, one article was withdrawn from print following the initial search and thus not tabulated in our final summative reporting.

2.3. Risk of bias

The quality of each article was independently rated by two reviewers as per the National Institutes of Health (NIH) Quality Assessment Tool for Case Series Studies (Table 1).[16].

2.4. Synthesis and extraction of data

All articles underwent data extraction and verification by two independent reviewers. For papers that included multiple CT scans per patient, only data from the first CT performed were used. As many articles did not explicitly list all CT findings present, data were supplemented with our own interpretations of images included in the text. Instances in which a given finding or laboratory value could not be definitively excluded with the textual information or imaging provided were not counted in the reported fractional denominators. The number of patients presenting with various clinical findings and laboratory aberrations, such as elevated C-reactive protein (CRP), lymphopenia, and neutrophilia, was also tabulated. These values were compared to reference ranges adjusted for physiological alterations in pregnancy.[17]

3. Results

3.1. Overview of included studies

Once the literature searches were completed and duplicate records were removed, a total of 1737 records were identified for initial screening. After further review, a finalized total of 67 published studies were included in the quantitative data extraction (Fig. 1). Data were extracted from a total of 427 pregnant patients, all of whom were admitted to hospital for acute care related to COVID-19 from December 2019 to July 2020. The average reported age was 30.4 years, with a range of 17 to 49 years. In total, eight maternal deaths were reported.

3.2. Chest CT manifestations

All 427 patients underwent chest CT for either diagnosis or clinical management as per standard-of-care protocols at their respective institutions. For 65 patients, low-dose protocol was explicitly reported. The remainder of cases did not specify radiation dosage. Many CT findings were reported using a wide array of nomenclature; for the purposes of the present study, these were further classified according to standard morphologic descriptors.[6,18,19] We found the following trends in CT manifestations: GGOs (77.2%, 250/324), posterior involvement (72.5%, 50/69), multilobar involvement (71.8%, 239/333), bilateral lung involvement (69.4%, 231/333), peripheral distribution (68.1%, 98/144), and consolidation (40.9%, 94/230). Patients without an explicit presence or absence of a given finding were excluded from the fractional denominators (Tables 2 and 3). Of note, pleural effusion was observed in 30.0% of cases.

3.3. Extra-pulmonary manifestations/constitutional symptoms

Several extra-pulmonary manifestations were also recorded. However, as many articles tended only to report pertinent positives and often did not explicitly indicate absence of a given abnormality, we were unable to tabulate exact proportions for these findings. Nevertheless, 150 patients were reported to present with elevated CRP, 128 patients with lymphopenia, 97 patients with neutrophilia, 73 patients with leukocytosis, 51 patients with elevated D-dimers, 24 patients with anemia, and 24 patients with elevated procalcitonin. Likewise, a total of 198 patients had documented fevers prior to delivery (antepartum), and 67 had fevers in the postpartum period. Additionally, 15 patients had gastrointestinal involvement/diarrhea, and 12 patients had cardiac involvement. Of those who experienced cardiac complications, a total of eight patients succumbed to cardiac arrest and were unable to be resuscitated. Three of these fatal cases were attributed to refractory hypotension, including one patient who experienced severe heart failure with an ejection fracture of 10–15% and another patient who experienced left-sided heart failure with an ejection fraction of 25%.[20–22] In addition, one patient was found to have a nonfatal pericardial effusion[23] (Table 4).

3.4. Neonatal outcomes

A total of 298 patients gave birth during admission to 304 neonates, 85 of which were born prematurely. Gestational ages at the time of delivery ranged between 28 and 41.3 weeks (28–41^{+2} weeks), with an average gestational age of 35.2 weeks (~35^{+1} weeks). Of the 304

Table 1
Quality rating of articles using the National Institutes of Health (NIH) Quality Assessment Tool for Case Series Studies.[16]

First author [Reference #]	Question[a]									Overall rating	
	1	2	3	4	5	6	7	8	9	Rater 1	Rater 2
Wang[52]	Yes	Yes	NA	NA	Yes	NA	Yes	NA	Yes	Fair	Fair
Wang[53]	Yes	Yes	NA	NA	Yes	NA	Yes	NA	Yes	Fair	Fair
Uzel[54]	Yes	Yes	NA	NA	Yes	Yes	CD	NA	Yes	Fair	Fair
Wen[55]	Yes	Yes	NA	NA	Yes	NA	Yes	NA	Yes	Fair	Fair
Taghizadieh[56]	Yes	Yes	NA	NA	Yes	Yes	CD	NA	Yes	Fair	Fair
Du[57]	Yes	Yes	NA	NA	Yes	Yes	CD	NA	Yes	Fair	Fair
Song[58]	Yes	Yes	NA	NA	Yes	NA	Yes	NA	Yes	Fair	Fair
Lu[59]	Yes	Yes	NA	NA	Yes	Yes	CD	NA	Yes	Fair	Fair
Ashokka[60]	Yes	NA	NA	NA	NA	NA	CD	NA	Yes	Fair	Fair
Chen[61]	Yes	Yes	NA	NA	CD	CD	CD	NA	Yes	Fair	Fair
Liao[62]	Yes	Yes	NA	NA	CD	NA	Yes	NA	Yes	Fair	Fair
Liu[27]	Yes	Yes	CD	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Zhu[63]	Yes	Yes	CD	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Chen[64]	Yes	Yes	CD	Yes	CD	Yes	CD	Yes	Yes	Fair	Fair
Cao[65]	Yes	Yes	CD	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Xiong[66]	Yes	Yes	NA	NA	Yes	Yes	CD	NA	Yes	Fair	Fair
Chen[67]	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair
Yang[68]	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair
Liu[69]	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair
Cheng[70]	Yes	Yes	CD	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Yu[71]	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair
Yang[72]	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair
Xie[73]	Yes	Yes	Yes	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Xu[74]	Yes	Yes	CD	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Xu[75]	Yes	Yes	CD	Yes	Yes	Yes	CD	NR	Yes	Fair	Fair
Liu[76]	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair
Zheng[77]	Yes	Yes	CD	Yes	Yes	Yes	Yes	NA	Yes	Fair	Fair
Justino[78]	Yes	Yes	NA	NA	Yes	Yes	CD	NA	Yes	Fair	Fair
Fontanella[79]	Yes	Yes	CD	Yes	Yes	Yes	CD	NA	Yes	Fair	Fair
Ai[23]	Yes	Yes	NA	NA	Yes	Yes	Yes	NA	Yes	Fair	Fair
Gong[80]	Yes	Yes	CD	Yes	Yes	Yes	CD	NR	Yes	Fair	Fair
Yang[81]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair
Xia[82]	Yes	Yes	NA	NA	Yes	NA	Yes	NA	Yes	Fair	Fair
Lee[83]	Yes	Yes	NA	NA	Yes	NA	Yes	NA	Yes	Fair	Fair
Kelly[84]	Yes	Yes	NA	NA	Yes	Yes	CD	NR	Yes	Fair	Fair
Khan[85]	Yes	Yes	NR	Yes	Yes	Yes	CD	NR	Yes	Fair	Fair
Chen[86]	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair
Kalafat[87]	Yes	Yes	NA	NA	Yes	NA	NA	NA	Yes	Fair	Fair
Yassa[88]	Yes	Yes	CD	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Chen[89]	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair
Li[90]	Yes	Yes	CD	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Hantoushzadeh[22]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair
Lucarelli[91]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NR	Yes	Fair	Fair
Yu[92]	Yes	Yes	CD	Yes	Yes	Yes	CD	NA	Yes	Fair	Fair
Mehta[93]	Yes	Yes	NA	NA	Yes	NA	CD	NA	Yes	Fair	Fair
Kolkova[94]	Yes	Yes	NA	NA	Yes	NA	CD	NA	Yes	Fair	Fair
Mohammadi[95]	Yes	Yes	NA	NA	Yes	NA	CD	NA	Yes	Fair	Fair
Romagano[96]	Yes	Yes	CD	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Fan[97]	Yes	Yes	NR	Yes	Yes	NR	Yes	NR	Yes	Fair	Fair
Tutiya[98]	Yes	Yes	CD	Yes	Yes	Yes	CD	NA	Yes	Fair	Fair
Dong[99]	Yes	Yes	NA	NA	Yes	NA	CD	NA	Yes	Fair	Fair
An[100]	Yes	Yes	CD	Yes	Yes	Yes	CD	CD	Yes	Fair	Fair
Liu[101]	Yes	Yes	Yes	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Zamaniyan[102]	Yes	Yes	NA	NA	Yes	NA	Yes	NA	Yes	Fair	Fair
Martinelli[43]	NR	Yes	NA	NA	Yes	NA	CD	NA	Yes	Fair	Fair
Wu[103]	Yes	Yes	NR	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Perrone[104]	Yes	Yes	CD	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Yang[105]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair
Reis[106]	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair
Alzamora[107]	Yes	Yes	NA	NA	Yes	NA	Yes	NA	Yes	Fair	Fair
Zhang[108]	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair
Shojaei[20]	Yes	Yes	NA	NA	Yes	NA	Yes	NA	Yes	Fair	Fair
Huang[109]	Yes	Yes	CD	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Peng[110]	Yes	Yes	NA	NA	Yes	NA	Yes	NA	Yes	Fair	Fair
Zeng[111]	Yes	Yes	CD	Yes	Yes	Yes	CD	Yes	Yes	Fair	Fair
Wu[112]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Fair	Fair

NIH = National Institute of Health, NR = not recorded, CD = cannot determine, NA = not applicable.

[a] NIH Quality Assessment Tool for Case Series Studies[16] poses the following nine questions: 1 = Was the objective clearly stated?, 2 = Was the study population clearly and fully described, including a case definition?, 3 = Were the cases consecutive?, 4 = Were the subjects comparable?, 5 = Was the intervention clearly described?, 6 = Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?, 7 = Was the length of follow-up adequate?, 8 = Were the statistical methods well-described?, 9 = Were the results well-described? Adapted from Salehi et al. (doi.org/10.2214/AJR.20.23034). NIH = National Institutes of Health.

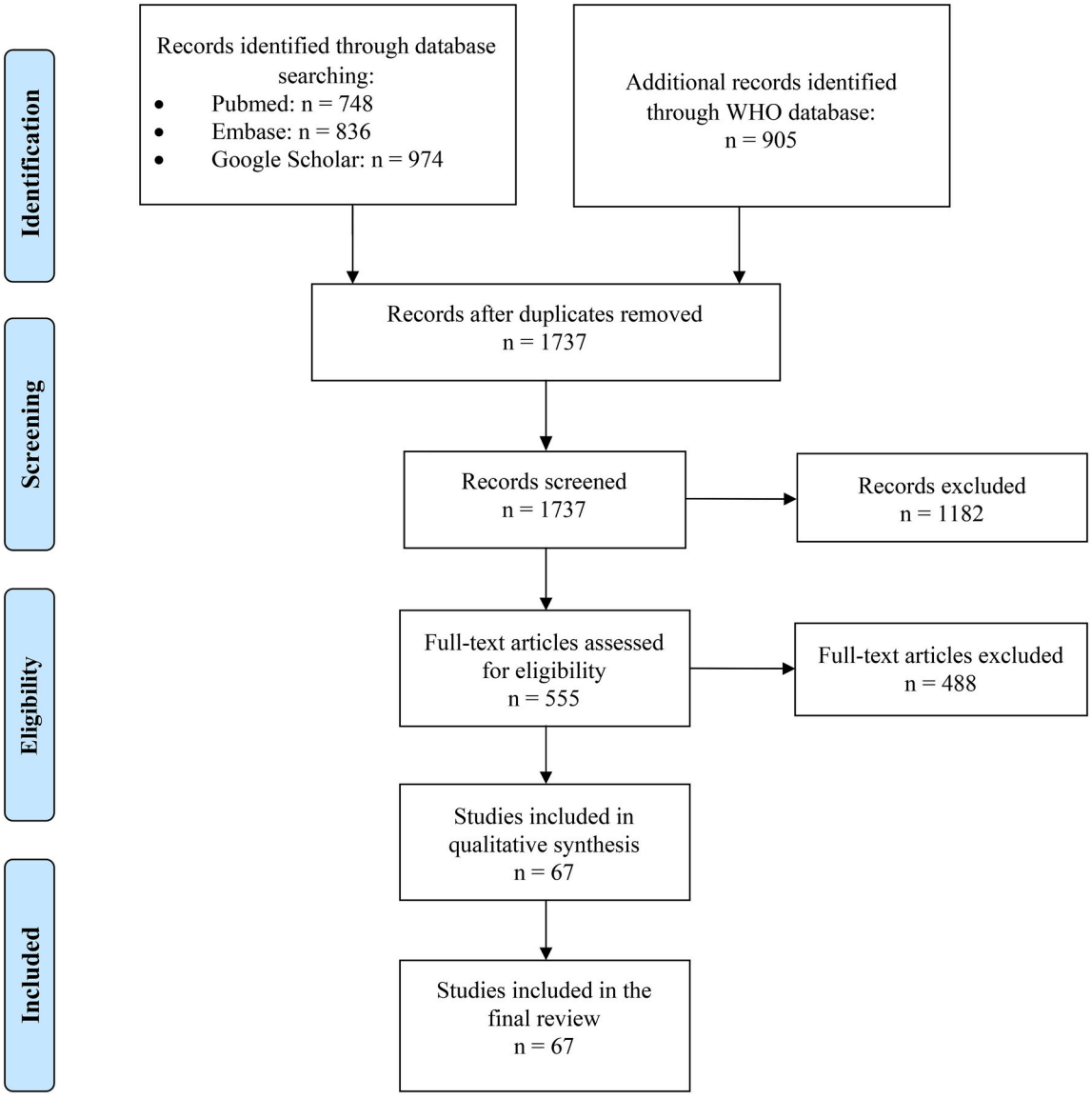

Fig. 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram, showing study selection process. Embase is a product of Elsevier. WHO = World Health Organization.
Adapted from Salehi et al. (doi.org/10.2214/AJR.20.23034).

Table 2
Common patterns and distributions on initial CT images of 427 pregnant patients with COVID-19.

Imaging finding	No. of reported cases/total no. of patients	% of report cases
Bilateral involvement	231/333	69.4
Unilateral involvement	102/333	30.6
Multilobar involvement	239/333	71.8
Peripheral distribution	98/144	68.1
Central distribution	11/144	7.64
Peripheral & central distribution	35/144	24.3
Subpleural distribution	24/68	35.3
Anterior involvement	1/69	1.45
Posterior involvement	50/69	72.5
Anterior & posterior involvement	18/69	26.1
Ground-glass opacities (GGOs)	250/324	77.2
Consolidation	94/230	40.9
Pleural effusion	45/150	30.0

Table 3
Additional findings on initial CT images of 427 pregnant patients with COVID-19.

Imaging finding	No. of reported cases
Opacities NOS	64
Fibrotic bands	11
Cardiomegaly/change in heart size	4
Vascular changes	5

Opacities NOS = opacities not otherwise specified.

neonates, 251 were tested for SARS-CoV-2 infection by RT-PCR and/or IgG antibody testing, with a resulting 96.8% negative test rate. Eight cases (3.2%) of suspected neonatal infection were reported, six of which tested positive by RT-PCR and two of which tested positive by IgG antibody assay. The six positive RT-PCR tests were conducted on samples collected between 16 and 72 h postpartum. The two cases of positive IgG antibody assays subsequently tested negative on follow-up RT-PCR. Furthermore, testing of cord blood, placenta, breastmilk, and/or vaginal secretions was conducted in four of the eight cases, all of which

Table 4
Extra-pulmonary and constitutional symptoms of 427 pregnant patients with COVID-19.

Manifestation	No. of reported cases
Elevated C-reactive protein (CRP)	150
Lymphopenia	128
Neutrophilia	97
Leukocytosis	73
Elevated D-dimers	51
Anemia	24
Elevated procalcitonin	24
Antepartum fever	198
Postpartum fever	67
Gastrointestinal involvement/diarrhea	15
Cardiac involvement	12
Maternal death	8

were negative for the presence of SARS-CoV-2. The overall neonatal survival rate was 93.14%.

4. Discussion

In the era of COVID-19, pregnant patients pose as a uniquely susceptible and understudied population. While routine exposure to ionizing radiation is discouraged during pregnancy, current guidelines recommend that chest CT should not be withheld when clinically indicated as the radiation dose from a single scan remains sub-threshold to cause teratogenic effects when appropriate precautions are taken.[24–26] At the beginning of the COVID-19 pandemic, chest CT scans were frequently used in many patients,[9–11] including those who were pregnant. As knowledge of the disease became more disseminated and RT-PCR testing kits were made more readily available, chest CT use has since been curtailed at many institutions. Nevertheless, despite a plethora of literature discussing imaging findings and clinical features of COVID-19 in the general adult population, specifics regarding disease presentations in the pregnant population are lacking. Thus, this systematic review represents one of the most comprehensive analyses of the existing literature regarding initial chest CT findings and associated clinical features of pregnant COVID-19 patients to date.

In a systematic review of 919 adults, Salehi et al. found that 87.5% of patients demonstrated bilateral lung involvement, 76.0% demonstrated peripheral lesion distribution, and 80.4% demonstrated posterior lung involvement. Furthermore, 88.0% of their patients presented with GGOs and 31.8% presented with consolidation.[6] Similarly, Liu et al. identified bilateral involvement in 79% of their non-pregnant patients, but only 21% of non-pregnant patients presented with evidence of consolidation.[27] Compared with our results, these findings suggest that pregnant patients may have a slightly lower prevalence of bilateral lung involvement than the general population (69.4% vs. 79–87.5%), which is consistent with published data suggesting lower rates of bilateral disease in younger populations.[28] Additionally, our results suggest that pregnant patients may present with lower rates of GGOs (77.2% vs. 88.0%) and higher rates of consolidation (40.9% vs. 21.0–31.8%) compared to the general population. These observations are further detailed in Table 5. Also of note, pregnant patients were found to have higher rates of pleural effusion when compared to that of the general population (30.0% vs 5.0%).[29] Currently, limited data exist on the baseline prevalence of pleural effusion in pregnancy. However, though pregnancy is a known risk factor for pleural effusion, our results still suggest a 3-fold higher prevalence of pleural effusion in COVID-19 pregnant patients when compared to preliminary observational data taken from an asymptomatic pregnant cohort.[30,31] Considering that consolidation and pleural effusion are indicative of more severe disease progression, our results suggest that pregnant patients may be more prone to presentation at advanced disease stages.[32]

One theory as to why pregnant patients may be more susceptible to severe progression of COVID-19 is that they may experience thoracic cage splaying and reduced functional residual capacity due to the expansive volume of the gravid uterus.[32,33] In a study comparing pregnant and non-pregnant patients with SARS-CoV-1, two-thirds of deaths in the pregnant cohort occurred during the second or third trimester, coincident with the time when these physiological changes are most evident.[33] These same changes could theoretically increase risk of developing severe complications of COVID-19 by reducing ability to clear secretions, which could in turn lead to a higher likelihood of developing consolidative pneumonia. Another theory is that altered immune functionality during pregnancy predisposes patients to acute pulmonary injury.[33,34] This could explain the fewer instances of GGOs and greater instances of consolidation seen in our cohort. The lungs of these particularly susceptible patients could be compensating with a stronger inflammatory response, which could in turn predispose to lesion progression to consolidation on CT imaging. Furthermore, most fatal cases in our cohort resulted from cardiac complications with low ejection fraction. Pregnancy is in and of itself a known risk factor for cardiomyopathy; however, as myocardial injury is also a known manifestation of COVID-19, it is possible that additive effects of disease may not just be limited to pulmonary complications and may in fact extend to other organ systems.[3,35]

Table 5
Comparison between rates of imaging findings in pregnant patients and the general population.

Imaging finding	Pregnant rate (%)	General population rate (%)
Bilateral involvement	69.4	79.0–87.5
Peripheral distribution	68.1	76.0–100
Posterior involvement	72.5	80.4
Multilobar involvement	71.8	78.8
Ground-glass opacities (GGOs)	77.2	88.0
Consolidation	40.9	21.0–31.8
Pleural effusion	30.0	5.0

The data referenced for the rate of occurrence of each imaging finding in the general COVID-19 patient population was obtained from Salehi et al., Liu et al., and Ojha et al.[6,27,29]

Of note, 150 patients in our cohort presented with elevated CRP levels (>10 mg/L), and 24 patients presented with elevated procalcitonin levels (>0.1 ng/mL). A small meta-analysis previously found that an increase in procalcitonin was correlated with advanced progression of COVID-19 by nearly fivefold[36]; however, only 2 of the 24 patients with elevated procalcitonin levels in our study eventually required mechanical ventilation, and 23 patients recovered fully. In addition, 51 patients exhibited elevated D-dimers ≥2.0 μg/mL. While elevated D-dimers have been associated with a greater morbidity and mortality in COVID-19,[37–41] all 51 patients with elevated D-dimer levels in our study population made a complete recovery. As physiological pregnancy is known to be associated with elevated D-dimers and pro–coagulability, the implications of elevated D-dimers in this clinical context remain unclear.[42] Notably, only one out of the 427 patients in this study was found to have a pulmonary embolism. On admission, this patient's D-dimer value was 16.4 μg/mL, and a small segmental pulmonary embolism was detected on hospital day 7 via CT imaging. The 17-year-old patient had a successful emergent C-section, and both mother and neonate were later discharged.[43]

Among patients with reported laboratory values, 128 patients presented with lymphopenia and 97 patients presented with neutrophilia, which is consistent with existing data for SARS-CoV-2 infection as reported in the literature.[44] However, Wei et al. found that the extent of lymphopenia and neutrophilia in the pregnant COVID-19 population tends to be much higher than that of the general population.[45] Some authors have suggested that these findings may be indicative of an altered immune response in the setting of a hyperinflammatory state, which may in turn coincide with greater risk for severe disease progression. When considering other historical coronavirus epidemics, similar trends of lymphopenia and/or neutrophilia were also observed

with both SARS-CoV-1 and Middle East Respiratory Syndrome (MERS).[44,46,47]

Of the 298 patients who gave birth during admission, we found an estimated preterm birth rate of 28.0%. A study comparing pregnancy outcomes among SARS-CoV-1, MERS, and SARS-CoV-2 patients previously showed that these three diseases had associated preterm birth rates of 15.03%, 0%, and 41.11%, respectively.[48] In contrast to these related viral pneumonias, the values reported by Di Mascio et al.[48] and our study suggest that COVID-19 may lead to higher preterm birth rates when compared to global preterm birth rates of 12% and 9% in underdeveloped and developed countries, respectively.[49] Further investigation is needed to better characterize these risks and associated causalities.

Lastly, a primary concern when studying viral infections in pregnant patients is that of the potential for vertical transmission. Significant rates of maternal-fetal transmission were not observed with other coronavirus epidemics, including SARS-CoV-1 and MERS.[48] As more literature regarding COVID-19 becomes available, there is a growing body of evidence to suggest that the risk of vertical transmission with COVID-19 remains similarly negligible.[50] We found that 96.8% of patients in our data set showed no signs of vertical transmission at delivery. For the eight cases (3.2%) in which suspected neonatal infection was reported, six were diagnosed by positive RT-PCR. However, as testing was performed on samples collected up to 72 h postpartum, the possibility of extrauterine exposure must be considered. One such example was shown in Mehta et al., a case series that reported delivery of a pair of fraternal twins in which only one of the two neonates tested positive for SARS-CoV-2 by RT-PCR.[51] As vertical transmission to only one of the two neonates in the shared intrauterine environment would seem unlikely, a more plausible explanation is that Twin A may have been infected during the 72-hour postpartum period prior to sample collection. In addition, the remaining two cases of neonatal infection were diagnosed by IgG antibody positivity on samples collected 2 h postpartum. However, as IgG antibodies are known to cross transplacentally, it is also possible that the IgG antibodies detected in the neonates' blood were of maternal origin. This hypothesis was supported by negative results on all subsequent RT-PCR tests in both cases.

4.1. Study limitations

There were several factors that limited our study. Firstly, as the findings from this systematic review were aggregated primarily from case reports and case series, we acknowledge a risk of sampling bias in that such reports often tend to skew toward only reporting positive findings. Secondly, a number of the articles included in this systematic review did not adhere to a standardized lexicon to describe the chest CT findings of COVID-19. As a result, many of the reported imaging findings required investigator interpretation for appropriate classification using standard morphologic descriptors. For this reason, we argue in favor of adopting a common lexicon for describing COVID-19-associated features, as described by Salehi et al.[18] Use of a standardized reporting system will improve both patient care and future research by facilitating clear and concise communication when discussing features of COVID-19 pneumonia. Additionally, another limiting factor was the scarcity of published case reports of COVID-19 in pregnant patients, which made it difficult to assemble a larger sample size. Lastly, many articles did not clearly state the radiation dose administered, which may have affected the resolution of images and ability to detect subtle findings.

5. Conclusion

Our data from 427 pregnant patients diagnosed with COVID-19 suggest a higher prevalence of consolidation and pleural effusion on chest CT compared to the general adult population. In addition, a lymphopenia/neutrophilia pattern was observed in our study cohort, which is in concordance with data from existing COVID-19 literature. These laboratory abnormalities were similarly reported in patients evaluated during prior SARS-CoV-1 and MERS epidemics. Lastly, despite an increased rate of prematurity as compared to the world preterm birth rate, we do not observe frequent vertical transmission of COVID-19 infection. While our results suggest more advanced presentations than would be otherwise expected for age, further study is needed to more definitively quantify our findings against historical controls.

CRediT authorship contribution statement

RSL and DM conducted the initial literature search and screening of articles. RRO and MYCC conducted the subsequent literature search and screening of articles with assistance from NLD and BKKF. RRO and MYCC extracted the quantitative data from each of the selected papers and assessed the quality of each publication. RRO and MYCC drafted the manuscript with support from NLD, BKKF, and AG, who conceived the idea. All authors provided edits on the manuscript prior to submission. RRO and MYCC contributed equally to the work and should be considered as co-first authors.

The authors declare that they had full access to all of the data in this study and the authors take complete responsibility for the integrity of the data and the accuracy of the data analysis.

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Disclosures

None.

Declaration of competing interest

None.

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