Review

**Safety of Radiation exposure during pregnancy in COVID-19 affected women**

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Abstract

Radiologic imaging in the evaluation of pregnant patients has significantly grown with the outbreak of the severe acute respiratory syndrome related to SARS-CoV-2 pandemic.

Lung ultrasound is an emerging non-invasive bedside technique used to diagnose interstitial lung syndrome through evaluation and quantitation of the number of B-lines, pleural irregularities and nodules or consolidations.

In pregnant COVID-19 patients, lung ultrasound should be considered on account of its various strengths, such as its being easily carried out bedside by trained sonographers for the monitoring of lung involvement in follow-ups, and its repeatability and affordability.

However, pregnant patients could need chest radiography or computed tomographic (CT) examinations for the diagnosis of pneumonia. Concerns and misconceptions about potential radiation-related risks for the embryo or fetus are still widespread among clinicians, and can lead to excessive anxiety among patients. Several well-recognized guidance documents were published in the last years as to the safety of a single-phase CT or an X-ray chest and related carcinogenic and teratogenic risk.
This paper summarizes the safety of radiological examination for pneumonia in pregnant women affected by COVID 19, based on the estimated embryo-fetal radiation absorption per procedure (mGy).

**Keywords:** SARS-CoV-2 pandemic, radiation exposure, pregnancy, teratogenic effect, radiological imaging

**Introduction**

During SARS-CoV-2 pandemic the use of imaging procedures with ionizing radiations has considerably increased because of the necessity to investigate the severity and the evolution of the interstitial pneumonia caused by novel coronavirus. The increase of cases of pregnant woman affected by SARS-19 disease, that need radiological examination, demand for a more evidence-based disclosure on the effects of ionizing radiations on embryos and fetuses.

Since the first report of the novel coronavirus disease, the number of confirmed cases has been rapidly increasing. The impact of COVID-19 disease on various population segments has been extremely severe, and led to overwhelmed hospitals and the redefinition of ethical standards in the face of deteriorating circumstances in terms of access to care. The impact of the pandemic on pregnant women and their newborns remains largely unknown and under researched.

Data from the WHO suggest that many infections are asymptomatic, but the proportion of asymptomatic cases is not well defined. The most common symptoms related to infection in pregnant people, that are similar to those in non-pregnant individuals,
included cough, headache, muscle aches, fever, sore throat, shortness of breath, ageusia and anosmia (1).

It is known that pregnant women generally constitute a high-risk group for infectious diseases due to gestational changes in their immunological system. According to previous experiences with SARS-CoV, MERS-CoV and influenza H1N1, pregnant women appear to be more vulnerable in developing severe pneumonia in case of respiratory pathogen infection than nonpregnant patients (2).

The Centers for Disease Control and Prevention (CDC) surveillance report from the United States noted that pregnant women were more likely to be admitted to the ICU and receive mechanical ventilation and, in rare cases, ECMO (extracorporeal membrane oxygenation) than non-pregnant women (3).

Data reported by the Italian Obstetric Surveillance System (ItOSS) on 146 women who gave birth during the initial pandemic period are in contrast with CDC. In fact, currently available data suggest that the susceptibility of pregnant women to SARS-CoV2 illness is similar to that described for the general population, with most women developing mild to moderate disease. Among 146 women affected, 47 (32.2 %) developed interstitial pneumonia; ICU admission was necessary for 5 patients (10.6%) with no need for ECMO (extracorporeal membrane oxygenation) and no maternal deaths were reported. Considering neonatal data on 149 infants, NICU admission was necessary in 23 cases (15.6%); 2 stillbirths and no neonatal deaths were described (4).

In a more recent preliminary analysis of Italian data on 667 women who gave birth between February 2020 and September 2020, only 18.6% of affected women developed interstitial pneumonia and 2% were admitted to the ICU, with no maternal deaths recorded. Among 681 neonates, only one out of 19 infants found positive to SARS-CoV2 required NICU admission, and no neonatal deaths were reported (5-8).
Diagnosis of interstitial pneumonia is based on:

- Chest Computed Tomography (CT)
- Chest X-ray
- Lung ultrasound

Chest CT is the most important screening tool of the diagnostic workup for COVID-19 pneumonia, thanks to its high sensitivity and convenience. Generally, the findings from chest imaging in COVID-19 are not specific and may overlap with others linked to different infections, including influenza, H1N1, SARS and MERS. However, some chest CT findings may be characteristic of COVID-19 pneumonia (9).

Recent evidence has shown that asymptomatic COVID-19 patients may present identifiable CT changes very early on, and even before testing positive with rRT-PCR. For these reasons, Chinese radiological specialists strongly recommend the use of CT, as the main method for the screen and diagnosis of COVID-19 (10, 11).

Nevertheless, as with chest x-ray, chest CT may be normal soon after the onset of symptoms; lung abnormalities on chest CT showed greatest severity approximately 10 days after initial onset of the disease (12, 13).

A recent meta-analysis described ground-glass opacities, vascular enlargement, interlobular septal thickening and subpleural bands as the most common features in either common and severe patients. Other CT manifestations were more frequent in severe patients, such as traction bronchiectasis, consolidation, crazy-paving pattern, reticulation, pleural effusion, and lymphadenopathy. These differences reflect the progression of the disease, with the increase in alveolar and mucosa involvement, and SARS CoV-2 diffusion in pulmonary interstitium (14).
Chest CT abnormalities in COVID-19 are often bilateral, have a peripheral distribution, and involve the lower lobes (15).

Most radiologic societies do not currently recommend using chest CT for screening or diagnosis of COVID-19 disease because of the incidental findings that could potentially be attributed to COVID-19. In the United States, the American College of Radiology (ACR) recommends reserving the use of chest CT for hospitalized patients when needed for management (16).

Chest radiography may be considered as a tool for identifying COVID-19 pneumonia, although it is less sensitive than CT, with a reported baseline sensitivity of 69%. In a retrospective study of 64 patients in Hong Kong with documented COVID-19, 80 percent demonstrated abnormalities in chest radiographs at some point during their illness. Common abnormal radiograph findings were consolidation and ground-glass opacities; peripheral distribution and lower zone distribution were the more common locations. Lung involvement increased over the course of the illness, which peaked in severity at 10–12 days from symptom onset (17, 18).

A review from the Cochrane Database of Systematic Reviews on chest radiographs concluded that chest x-ray did not improve clinical outcomes for patients with lower respiratory tract infection. However, chest radiographs appeared to be of benefit in the subgroup of patients with an infiltrate on their radiograph; in this subgroup the use of the chest x-ray was associated with a reduction in the length of illness, duration of cough, and duration of sputum production (19).

The American College of Radiology (ACR) noted that CT decontamination required after scanning COVID-19 patients may disrupt radiological service availability and suggests that portable chest radiography may be considered to minimize the risk of cross-
infection. The surfaces of these machines can be easily cleaned, avoiding the need to bring patients into radiography rooms.

As for ultrasound, the sonographic signs are non-specific when considered alone, but observation of some aspects of vertical artifacts can enhance the diagnostic power of the ultrasound examination. In fact, Pneumonia in COVID-19 has peculiar features and can be studied by lung ultrasound in the early approach to suspected patients.

COVID-19 typically induces an interstitial diffuse bilateral pneumonia involving mainly the lung periphery, which makes it particularly suitable for an ultrasound investigation. (20)

Lung ultrasound examination can be a valid alternative to CT scan, with certain advantages, particularly for pregnant women. Ultrasound can be performed directly at the bed-side by a single operator, reducing the risk of spreading the disease among health professionals (21).

Although extensive studies are available on the CT and clinical manifestations of patients with COVID-19 pneumonia, data on pregnant women with COVID-19 pneumonia evaluated by CT remain scarce (22, 23).

Chest CT could be used as a tool to confirm diagnosis and track progression of disease, even in pregnant patients. In a systematic review of 427 pregnant patients diagnosed with COVID-19, the most frequently encountered pulmonary findings on chest computed tomography were ground-glass opacities, posterior lung involvement, multilobar involvement, bilateral lung involvement, peripheral distribution, pleural effusion and consolidation (26).

Teratological data on radiation exposure in pregnancy could be referred from previous and consolidated studies on the use of these radiological techniques.
Radiation exposure from CT procedures varies depending on the number and spacing of adjacent image sections. A fetal radiation dose less than 50 mGy is considered “acceptable” in a balance of risk and benefit. By using typical imaging parameters, it is unlikely that a single-phase CT scan reach this dose level. The fetal dose becomes important when the fetus is included in the field of view. A chest CT or CT pulmonary angiography are considered “low-to moderate-dose examinations (0.1-10 mGy). The radiation exposure to the fetus from spiral CT is comparable with conventional CT.

Chest radiography with typical two views is considered a “very low dose examinations” (< 0.1 mGy) (25,26) (Table I).

Fetal growth restriction microcephaly and intellectual disability are the most common adverse effects from high-dose (>610mGy) radiation exposure (27,28).

The ISUOG interim guidance encourages performing a chest CT scan in pregnant women with COVID-19 infection as an essential instrument for evaluation of the clinical condition in epidemic areas. Informed consent should be acquired and a radiation shield be applied over the gravid uterus.

The ISUOG guidelines stress that the radiation dose during single chest CT or even CT pulmonary angiogram is much lower than the one potentially causing fetal complications (29).

Before obtaining a protocol, clinicians have to ask themselves if the information could be obtained by the use of no-ionizing radiation and without contrast agents and ask themselves if the information gained would affect patient survival or care.

No ultrasound appearance that would be pathognomonic of COVID-19 has been identified so far. Lung ultrasound can reveal a typical pattern of diffuse interstitial lung
syndrome, characterized by multiple or confluent bilateral B-lines with spared areas, thickening of the pleural line with pleural line irregularity and peripheral consolidations.

While the ability of a chest x-ray to distinguish between a bacterial pneumonia and a non-bacterial infection is no more than 60%, lung Ultrasound has a higher degree of sensitivity (80%).

Lung Ultrasound could be used in pregnant woman as a bedside evaluation of lung involvement, reducing the use of chest x-rays and CT (30,32).

**Evaluation on radiation safety based on radiation absorbed dose**

Thousands of pregnant women are inadvertently exposed to diagnostic radiation especially in the periconceptional period when pregnancy is still unknown. A misinformation on the teratological risks related to diagnostic examinations in pregnancy causes anxiety in medical-doctors and patients and could lead to an unjustified voluntary interruption of pregnancy. Several well-recognized guidance documents provide information regarding safety on risks related to imaging of pregnant women. The International Commission on Radiological Protection (ICRP) states that “Prenatal doses from most properly done diagnostic procedures present no measurably increased risk of prenatal death, malformation, or impairment of mental development over the background incidence of these entities.” Article 62 of the European Directive 2013/59/Euratom states that if pregnancy cannot be excluded, depending on the medical radiological procedure, special attention shall be given to the justification and optimization, considering both the pregnant mother and the unborn child (32).
With few exceptions, radiation exposure through radiography, computed tomography (CT) scan, or nuclear medicine imaging techniques is at a dose much lower than the exposure associated with fetal harm (33).

The International System of Units (SI) has 4 units of measurement for ionizing radiations: Sievert (Sv), Coulomb (C), Gray (Gy) and Becquerel (Bq). The potential radiation exposure from medical diagnostic procedure is described by Gray (Gy) or milligray (mGy); however, radiation absorbed dose (rad) is the predominant measure used, considering that 1 Gy=100 rad.

In relation to possible harmful effects on embryos and fetus caused by radiations, we have to consider that it is partially protected by surrounding soft tissues and uterus of the mother. Besides, detrimental effects are dependent on the radiation dose and the trimester of the pregnancy. Adverse pregnancy outcomes include pregnancy loss, malformations, neurobehavioral anomalies, fetal growth retardation and cancer. The underlying mechanism is known as “all-or-one” response, because pregnancy loss, malformations, neurobehavioral anomalies and fetal growth retardation have a deterministic effect, so they manifest themselves only if a threshold of radiation dose is exceeded. Consequently, the severity of the adverse effect is directly proportional to the absorbed radiation dose. On the other hand, cancer has a stochastic effect, whereby the more radiation given, the greater the risk of the disease (34).

The epidemiological data suggest that the lowest dose of X- or Y-radiation for which good evidence exists of increased cancer risks in humans is 10 –50 mSv for an acute exposure and 50 –100 mSv for a protracted exposure (34).

According to the review by Sreetharan et al. (35), human data on the effects of prenatal exposure to ionizing radiation are predominantly based on high-dose exposures (such as the bombing of Hiroshima and Nagasaki), while there are limited human data for low-
doses exposures (such as the majority of medical radiologic procedures). In rodent models, radiation exposure during pre-implantation of embryo seemed to follow the “all-or-none” response, with a complete lethality at higher dose or no effects. However, there is evidence that it could be not true at lower doses. Radiation exposures during organogenesis and fetal development have led to neurobehavioral changes, effects on the central nervous system, delay in the appearance of physiological markers of development, low birth weight and growth reduction.

The American College of Radiology established that fetal doses below 100 mGy should not be considered a reason for terminating a pregnancy (36). The American College of Obstetricians and Gynecologists (37) published the following policy statement: “Women should be counseled that X-ray exposure from a single diagnostic procedure does not result in harmful fetal effects. Specifically, exposure to < 5 rad (50 mGy) has not been associated with an increase in fetal anomalies or pregnancy loss.” According to these documents, the risk to the unborn baby from radiation doses of < 50 mGy is negligible. Doubling that dose (i.e., 100 mGy), the increase over background incidence for organ malformation and the development of childhood cancer combined results in about 1%.

Deterministic effects exhibit a threshold of around 100 mGy even during the most sensitive phase of organogenesis. Termination of pregnancy should only really be considered for conceptus doses above 100 mGy, depending on the phase of pregnancy.

In pregnancy, the major biological effects of fetal demise, growth restriction, organ malformations and cognitive deficits are seen only with doses in excess of routine diagnostic imaging (38).

A consensus has emerged that when the fetal radiation dose is less than 50 mGy, the noncarcinogenic risk, which includes abortion or malformation, is negligible when compared to other risks of pregnancy. By using typical imaging parameters, it is unlikely
that a single-phase CT scan would reach this dose level. A fetal dose of less than 100 mGy also should not be considered a reason to terminate pregnancy. If the fetal dose reaches levels greater than 150 mGy, there is stronger likelihood of malformation (Table II).

Regarding the body part exposed to the imaging procedure, this is the most important factor for determining the uterus radiation:

- Imaging without ionizing radiation and imaging of the extremities or the head and neck are justified as in non-pregnant women. As radiation exposure is absent or irrelevant, the examinations can be performed anytime.

- Imaging of the torso without direct radiation to the conceptus will cause some scatter radiation and a dose of well below 1 mGy to the conceptus.

Examinations of this category will usually be performed when deemed warranted.

Normally, during a full-term pregnancy, the estimated radiation dose to the mother from background radiation that naturally occurs averages approximately 2.3 mSv worldwide and varies according to geographic location and altitude. Average fetal dose is approximately 0.5–1 mSv because of attenuation through the mother's tissue. The conceptus radiation dose for common radiologic examination is as follows: abdominal radiograph 0.001 - 0.003 Gy (0.1– 0.3 rads), intravenous pyelogram 0.006 Gy (0.6 rads), lumbar spine radiograph 0.006 Gy (0.6 rads), CT pelvis 0.02-0.05 Gy (1.5 rads).

For the objective of this paper, it is clear that chest radiography and CT are responsible of a fetal radiation absorption that is much lower than 100 mGy (0.01 mGy and 0.06-0.96 mGy, respectively) (33, 39).
Conclusion

The guiding principle of radiation safety is ALARA “as low as reasonably achievable”. This principle means that however small the dose, if receiving such a dose has no direct benefit, it should be avoided. As far as medical imaging is concerned, medical error and misdiagnosis or discrepancy are not easily distinguished concepts. The diagnostic process is not in fact a binary relation, hence detecting a given pathological condition is often challenging. Errors in radiology are closely tied to the diagnostic process, and they can therefore be defined as diagnostic errors, which commonly lead to litigation and medical malpractice lawsuits against radiologists (40). As for the risks arising from ionizing radiation, they can be minimized by adhering to both the ALARA principle and established guidelines regarding contrast agent administration.

If the clinical and therapeutic benefits are greater than the fetal risks, it is acceptable to use these radiological techniques during pregnancy and consider them safe for the fetus.

Clinicians must provide adequate counseling with the thorough provision of information regarding risks possibly arising from imaging examinations.
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Conflicts of Interest: The authors declare no competing interests.

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<table>
<thead>
<tr>
<th>Procedure</th>
<th>Fetal Dose (mGy)</th>
<th>Maternal Dose (mSv)</th>
<th>Breast Dose (mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest radiography, AP/PA views</td>
<td>0.00525</td>
<td>0.175</td>
<td>&lt; 0.04</td>
</tr>
<tr>
<td>Abdominal radiography:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP view</td>
<td>2.9</td>
<td>0.7</td>
<td>na</td>
</tr>
<tr>
<td>PA view</td>
<td>1.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumbar spine radiography:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP view</td>
<td>7.5</td>
<td>1.4</td>
<td>na</td>
</tr>
<tr>
<td>PA view</td>
<td>0.57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lat view</td>
<td>0.91</td>
<td></td>
<td></td>
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<tr>
<td>CT chest/ pulmonary angiography</td>
<td>0.335</td>
<td>21.35</td>
<td>39</td>
</tr>
<tr>
<td>CT abdomen/pelvis</td>
<td>3.6/35</td>
<td>15</td>
<td>na</td>
</tr>
<tr>
<td>CT lumbar spine</td>
<td>2.8</td>
<td>8.5</td>
<td>0</td>
</tr>
</tbody>
</table>

Table I. Mean fetal, maternal and breast absorbed dose in different procedures using ionizing radiations. mGy: Milligray, mSv: Millisievert. CT: computerized tomography. AP: anterior-posterior, PA: posterior-anterior, Lat: lateral.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Potential Deterministic Effects</th>
</tr>
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<tbody>
<tr>
<td>&lt;50 mGy radiation dose</td>
<td></td>
</tr>
<tr>
<td>&lt;2 weeks</td>
<td>all or-none effect</td>
</tr>
<tr>
<td>&gt;2 weeks</td>
<td>no clinically detectable</td>
</tr>
<tr>
<td>&gt;50-100 mGy radiation dose</td>
<td></td>
</tr>
<tr>
<td>&lt; 25 weeks</td>
<td>teratogenic; organogenesis (malformation, IUGR)</td>
</tr>
<tr>
<td>between 8-15 weeks</td>
<td>mental retardation and microcephaly</td>
</tr>
<tr>
<td>&gt; 25 weeks</td>
<td>No teratogenic effect observed</td>
</tr>
<tr>
<td>------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td><strong>100-500 mGy radiation dose</strong></td>
<td></td>
</tr>
<tr>
<td>&gt;500 mGy radiation dose</td>
<td>Clinically concrete risk of fetal damage</td>
</tr>
</tbody>
</table>

Accurate counseling on the circumstance (maternal neoplasia that need radiological cross-sectional imaging, radiation therapy, interventional procedures) about decision to abort fetus or not.

Table II. Potential deterministic effects for different weeks of pregnancy and different mGy (milligray) radiation dose.