Response Letter

Dear Editors, we received the revisions for the invited manuscript. We appreciate the valuable contributions of the reviewers. You can see the responses in detail below. The changes are stated in the Word Document with using the "Track changes" function.

Sincere Regards.

Reviewer – 1

Question (Q) 1: "*The key problem this study suggested that pregnant women are at high risk of acquiring birth defects to CT-scan. The authors further suggested in order to avoid the exposure of pregnant women toward ionising radiation, ultrasound could be a good option instead of CT-scan to undergo diagnosis and to identify any association of lung complications caused by COVID-19*."

Response (R) 1: Sorry for the misunderstanding, the main advantage of lung ultrasound is not only reducing the exposure to ionizing radiation, but also reducing the risk of contamination and decrease the burden on the health system. Moreover, it enables monitoring (repetitive measurements).

Line 86-89: "The main advantage of lung ultrasound is not only reducing the exposure to ionizing radiation but also reducing the risk of contamination and decrease the burden on the health system. Moreover, it enables monitoring (repetitive measurements)."

Q 2: *In the subheading "The advantages of LUS" the sentence "Owing to these facts, CT is not an optimal screening tool and not feasible in monitoring the patient clinical situation" it should be "the patent's clinical situation" please change.*

R 2: It is corrected.

Q 3: "Please add page numbers."

R3: It is added.

Q 4: "*Last paragraph of "Monitoring with LUS and other areas of use" 3rd sentence, the word "Decisiozn" please correct this word."*

R 4: It is corrected.

Q 5: *"Second last point of LUS score=1 "Weekly phone calls to check for new onset symptoms to reduce unnecessary admission to the hospital" this sentence has syntactical errors please take necessary step. In the last point please mention the types of new symptoms, please specify.*

R 5: The sentence Syntactical errors are corrected. The types of new symptoms are specified in the mentioned figure.

Q6: *It is reasonable to offer LUS for the triage and monitoring the clinical progress of patients with leaving the indication of chest CT scan as reserved only for the more complex cases" Please mention the complex cases in brief.*

R6: Thanks for the contribution, the "complex cases" are detailed as: "*such as unexpected deterioration in clinical progress and patients with previous lung diseases.*" in Line 185-186.

Q7: "*Please mention the disadvantages or limitations of using LUS in a separate paragraph kindly include the procedural limitation if found."*

R7: An additional section is added that discusses the limitations of LUS in a separate paragraph starting with 201.

"Limitations of LUS

Despite the several advantages of LUS in the COVID-19 pandemic setting, the diagnostic accuracy of LUS may be affected by the patient's characteristics and co-morbidities including elevated body-mass index and pre-existing interstitial lung diseases[38-39]. The findings of preexisting interstitial inflammation, scarring, and pleural thickening can mimic the initial COVID-19 imaging. In addition, heart failure causing pulmonary edema or end-stage renal disease may lead to diagnostic confusion with the interstitial inflammation caused by COVID-19. Approximately 70% of the lung surface can be visualized with a systematic LUS examination, however, lesions located in the blind area of ultrasound can be missed[31].

The studies investigating the use of LUS in the COVID-19 pandemic have included small sample sizes and much effort is needed to increase the quality of those studies to promote the LUS scanning in the triage of COVID-19[15]. The specific protocols for triage should be formed and the effects of the clinicians' experience and the inter-operator agreement should be further studied[40-42].

User-related limitations can be challenging in the management of the patient that depends on the LUS scores. It is postulated that less-experienced users are tended to label the mild abnormalities in a single lung field as compatible with COVID-19. The ultrasound settings of the LUS can affect the interpretation of LUS images such as undergained or overgained images may lead to false-negative or positive assessments[18]."

Q8: "*Please discuss in brief how LUS can be useful to distinguish between pneumonia, COVID-19, and other viral pneumonia."*

R8: As the reviewer also questioned, LUS is not very useful in differentiating the SARS-CoV-2 infection from other viral pneumonia causes, however, it is a well-accepted approach to consider every pregnant women either with or without symptoms as a possible COVID-19 positive case during the outbreak. Besides, the diagnostic accuracy of the PCR testing is not 100% which may explain the very few cases with the negative PCR test results and positive LUS imaging.

Brief information about specific LUS patterns that can be helpful in recognizing the COVID-19 imaging findings is added to the Line72.

Line 72-75: *"B lines, small consolidated area and broken pleural lines are suggestive of COVID-19. Bacterial pneumonia is mainly represented with isolated large lobar consolidation with or without pleural effusion and dynamic air bronchograms."*

Q 9: "*In the advantages of LUS subheading section, the sentence "Our study investigating the universal testing strategy for SARS-CoV-2 infection with RT-PCR in pregnant women who were admitted to the hospital showed an overall and asymptomatic infection diagnosis rate of 7.77% and 4%, respectively" Please be specific it is not 4%, please mention it accurately."*

R 9: It is corrected.

Q 10: "*Refer the citation 25 and please explain in another sentence with reasoning and your understanding about LUS positive and LUS negative patients, mainly the intensity of the lungs complications beside the cause of such complication. Please add while explaining why in Negative COVID-19 group, 3 patients were LUS positive. Please add it in suitable section. Please mention which patients had only pneumonia and which patients were suffering from COVID-19 or other viral pneumonia as per LUS and RT-PCR result.*

R 10: - Dear Reviewer, in our article that we shared our results of the universal screening program, those 3 patients with positive LUS scanning and negative PCR testing were due to the previous lung diseases that interfere with the LUS images. Those belonged to benign previous lung diseases including atelectasis and bronchiectasis. This is corrected in Line 159-164: "*The false positivity of LUS was due to previous benign lung diseases where the main maternal symptom status comes forward in the interpretation of LUS findings. In our routine approach, LUS comes prior to the maternal symptomatology because mild COVID-19 symptoms can interfere with the natural pregnancy-related symptoms, moreover, we observed that LUS signs can alert the clinician before bothersome symptoms occur".*

For example, LUS score 3 is considered severe lung complication in a patient, he/she also has covid-19 along with LUS 3. So, How would you name the complication as per (Severe, mild and moderate pneumonia with/without Covid-19 positive or Covid-19 negative)?"

- The radiological severity of pneumonia (mild/moderate and severe) was already discussed in the "The scoring system for LUS" section.

How LUS score could be helpful to determine and distinguish that? The reference [25] cited in this article lacks reasoning in the discussion section of the original article. No doubt the cohort study factually provided a wise technique to identify and distinguish different levels of lung complication. Hence, please provide with more rationales and reasons in this existing opinion review. Please classify the patients as per asymptomatic or symptomatic covid-19 positive or negative respectively.

- The underlying understanding mechanism is detailed in Line 164-168:

"*In our algorithm for the interpretation of LUS findings that combines the lung imaging and the maternal symptomatology; a LUS score of 1 was accepted as a normal finding in asymptomatic pregnant women with*

aiming to reduce the false positivity of LUS imaging. Lung ultrasound scores of 2 and 3 were adopted as abnormal regardless of the symptom status.".

Q 11: "*I believe that ultrasound could be useful to distinguishing pneumonia and viral pneumonia as well as it can determine and distinguish the complicated or severe viral pneumonia in patients, only when the probe of ultrasound is in correct hand. But the ultrasound will give confusing output for a patient with historic severe lung disease, this is a disadvantage. Please refer for more limitations and please add."*

R 11: This limitation is mentioned in "Limitation of LUS" section.

Q 12: "*Please conclude on the basis of changes to be made as per the above suggested points."*

R 12: Conclusion section is revised.

Q 13: "*Since, the scoring procedures are discussed. If possible please provide the snapshots (at least 4 symptomatic and asymptomatic patients) of different ultrasound reports as per LUS score 0-3."*

R 13: Thanks for this valuable contribution. However, we currently lack snapshots available because we need further ethical permission. Very detailed ultrasound images are already available in our published case series (*Yassa, M., Birol, P., Mutlu, A. M., Tekin, A. B., Sandal, K., & Tug, N. (2021). Lung Ultrasound Can Influence the Clinical Treatment of Pregnant Women With COVID-19. Journal of Ultrasound in Medicine, 40(1), 191-203.)* and didactic article (*Yassa, M., Mutlu, M. A., Kalafat, E., Birol, P., Yirmibeş, C., Tekin, A. B., ... & Tug, N. (2020). How to perform and interpret the lung ultrasound by the obstetricians in pregnant women during the SARS-CoV-2 pandemic. Turkish Journal of Obstetrics and Gynecology, 17(3), 225.).*

<u>Reviewer – 2</u>

Q: "*Dear authors I have read this article with interest. COVID-19 pandemic raises significant challenges in the management of patients. This article has described the role of lung ultrasound in the triage of pregnant women during this pandemic. It needs a wider literature review and mention about similar studies and its success rate. A brief paragraph about the use of lung ultrasound in other lung infections will also be helpful. Overall, the concept is innovative and lung US will be very helpful in pregnant patients who should avoid CT scans. Tables are helpful in these kinds of reviews. CT scan-based severity scoring systems are well established and followed as standard of care – and we will need larger multicenter studies before we can make strong recommendations. English language needs revision- I quote a line that needs revision- Pregnant women are a vulnerable, special population in medically and socially thinking."*

R: Thank you for your precious suggestions. A new table (Table 1) including a more detailed literature review is formed and references related to the mentioned studies are added.

- Line 143 is revised as: "*Pregnant women are vulnerable population that possess medical and social burdens.*"

Science Editor: *"Self-cited references: There are 8 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated".*

- We have only 4 self-cited references which account for 9.5% self-referencing rate. Indeed, those articles are essential for proper reasoning for this review and they form the perceptual base for this invited review.

"*The title is too long, and it should be no more than 18 words.*"

- Indeed, the title was proposed by the journal itself for this invited review. The title has 15 words.

"*Before final acceptance, the author(s) must add a figure to the manuscript*".

- This review has one figure and one table.