

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Cohort profile: COVID-19 in a cohort of pregnant women and their descendants, the MOACC-19 study
AUTHORS	Llorca, Javier; Lechosa-Muñiz, Carolina; Gortazar, Pilar; Fernández-Ortiz, María; Jubete, Yolanda; Cabero, Maria

VERSION 1 – REVIEW

REVIEWER	Joao Guilherme Alves Instituto de Medicina Integral Prof. Fernando Figueira (IMIP) Brazil
REVIEW RETURNED	29-Oct-2020

GENERAL COMMENTS	<p>Thank you for the opportunity to review this manuscript. The study deals with a very important issue and may contribute to answer some questions of SARS-CoV-2 infection in the mother-child binomial. Basically, a project of a gestational cohort study with some preliminary results is presented. I have a few comments:</p> <p>Abstract The Conclusion is missing.</p> <p>Introduction It seemed to me long (8 paragraphs) and in need of deepening the justification for the study. Second paragraph: “non-pharmacological preventive measures for general population include ...”. It sounds like there are pharmacological preventive measures.</p> <p>Last paragraph: Objective – “To compare pregnancy outcomes occurred in a pre-COVID-19 cohort in the same hospital”. This cohort study should be presented previously and not in the Methods section. Reference 34 is a cross-sectional study. Reference 35 just states: “Medical records of both mothers and neonates were reviewed in order to gather information on maternal age, educational level, occupational situation and smoking habits. Regarding neonate information, we recorded gestational age, birth order and nursery attendance.” Besides type of feeding. I could not identify pregnancy outcomes as Table 1 shows for this study – Medical History. I think this needs clarification.</p> <p>Methods Objective (5), to evaluate the relationship between socio-economic status and risk of infection by SARS-CoV-2 in pregnant women.</p>
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	<p>Socio-economic aspects of COVID-19 should be addressed in the introduction.</p> <p>Context: update the data. According to the WHO: October 27 - 1,046,132 cases and 34,752 deaths.</p> <p>Sub-cohort 2: "The later their date of delivery, the lower their exposure to COVID-19 in the third trimester." This should be reconsidered in the face of the second wave of COVID in Spain.</p> <p>Follow-up: How development, general and psychomotor, will be evaluate?</p> <p>Sample size: deserves some comment.</p> <p>Results and Discussion</p> <p>Results were not compared to previous cohort study (Pre-COVID-19).</p> <p>Discussion have only two paragraphs: limitations (5) and strengths (5). Important results as the finding of negative tests in seven newborns from women testing positive to RT-PCR should be comment.</p> <p>Funding information is missing.</p>
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REVIEWER	Tirso Pérez HOSPITAL UNIVERSITARIO PUERTA DE HIERRO, MADRID
REVIEW RETURNED	25-Nov-2020

GENERAL COMMENTS	<p>This is just a project for a future research.</p> <p>The research plan is well designed and, with enough time, it will be an excellent research.</p> <p>Nowadays, the number of patients is too short.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. João Alves, Instituto de Medicina Integral Prof. Fernando Figueira (IMIP) Comments to the Author: Thank you for the opportunity to review this manuscript. The study deals with a very important issue and may contribute to answer some questions of SARS-CoV-2 infection in the mother-child binomial. Basically, a project of a gestational cohort study with some preliminary results is presented. I have a few comments:

Answer: Thank you very much for your constructive comments.

Abstract

The Conclusion is missing.

Answer: Our manuscript is a cohort profile; therefore, the results must be considered provisional. In this regard, BMJ Open submission guidelines indicate that the Abstract in cohort profiles should have these headings: Purpose, Participants, Findings to date, Future plans, and Registration (if linked to a clinical trial, which is not the case of our cohort). Therefore, we still stay with the structure we used for the abstract in the first version. However, we have updated the paragraph "Findings to date" and all tables according to the evolution of the cohort.

Introduction

It seemed to me long (8 paragraphs) and in need of deepening the justification for the study.

Second paragraph: “non-pharmacological preventive measures for general population include ...”. It sounds like there are pharmacological preventive measures.

Answer: We have omitted the second paragraph, which was too general about COVID-19 but was unrelated with our specific cohort. Although the expression “non-pharmacological preventive measures” does no longer appear in the manuscript, we want to clarify that our usage of that expression came from the terminology used by the ECDC. For instance: “Guidelines for the implementation of non-pharmaceutical interventions against COVID-19”. 24 September 2020. Available at: <https://www.ecdc.europa.eu/sites/default/files/documents/covid-19-guidelines-non-pharmaceutical-interventions-september-2020.pdf> (accessed 16 January 2021).

Last paragraph: Objective – “To compare pregnancy outcomes occurred in a pre-COVID-19 cohort in the same hospital”. This cohort study should be presented previously and not in the Methods section. Reference 34 is a cross-sectional study. Reference 35 just states: “Medical records of both mothers and neonates were reviewed in order to gather information on maternal age, educational level, occupational situation and smoking habits. Regarding neonate information, we recorded gestational age, birth order and nursery attendance.” Besides type of feeding. I could not identify pregnancy outcomes as Table 1 shows for this study – Medical History. I think this needs clarification.

Answer: Reference 34 reported results from the initial cross-section at cohort inception. This was a mistake of ours. We have substituted that reference for Lechosa-Muñiz et al. Factors associated with duration of breastfeeding in Spain: a cohort study. *Int Breastfeed J* 2020;15:79. [PubMed Doi: 10.1186/s13006-020-00324-6](https://pubmed.ncbi.nlm.nih.gov/3511186/), which had not been accepted by the time we sent the first version of this cohort profile. References to the pre-COVID-19 cohort now appear in the introduction section, although we believe it could be inappropriate to describe it in full as this is not the purpose of the current cohort profile.

Methods

Objective (5), to evaluate the relationship between socio-economic status and risk of infection by SARS-CoV-2 in pregnant women. Socio-economic aspects of COVID-19 should be addressed in the introduction.

Answer: In this version, we have introduced socio-economic status in the introduction as follows: Finally, some studies have reported higher risk of COVID-19 in the most deprived (30) or with lower educational attainment (31). In pregnant women, however, the impact of socio-economic status on SARS-CoV-2 infection is still little known and only ecological studies with small sample size have been published (32).

Context: update the data. According to the WHO: October 27 - 1,046,132 cases and 34,752 deaths.

Answer: We have updated data to 14th Dec, last day available in ECDC web page.

Sub-cohort 2: “The later their date of delivery, the lower their exposure to COVID-19 in the third trimester.” This should be reconsidered in the face of the second wave of COVID in Spain.

Answer: We have updated Figure 1 using the recent pandemic evolution, so that we can now better explain the exposure to COVID-19 in each sub-cohort.

Follow-up: How development, general and psychomotor, will be evaluate?

Answer: Psychomotor development will be evaluated using the Denver Developmental Screening Test (DDST-II). This is now specifically stated in the text.

Sample size: deserves some comment.

Answer: The possibility that sample size be insufficient is commented in the limitations paragraph. As the pandemic is still ongoing and the current incidence trend in Spain is towards increasing number of cases, there is still room for our sample size to be sufficient. Otherwise, we explicitly state in the text that we would enlarge the recruitment period.

Results and Discussion

Results were not compared to previous cohort study (Pre-COVID-19).

Answer: We believe that this is not possible yet. Such a comparison is a relevant objective of this cohort, but it could be appropriate only when the recruitment of both mother and children be finished. In this version, we explicitly indicated so under the Ongoing statistical analysis heading.

Discussion have only two paragraphs: limitations (5) and strengths (5). Important results as the finding of negative tests in seven newborns from women testing positive to RT-PCR should be comment.

Answer: Under the Strengths and limitations subheading we include those of this cohort design, rather than those of our results, which are currently provisional. We do believe this is in the spirit of a cohort profile manuscript. However, we have expanded the information about children born from mothers testing positive to PCR, as their number has reached 14.

Funding information is missing.

Answer: Funding information is included at the end of the text.

Reviewer: 2

Dr. Tirso Pérez Medina, Hospital Universitario Puerta de Hierro Majadahonda Comments to the Author:

This is just a project for a future research.

The research plan is well designed and, with enough time, it will be an excellent research.

Nowadays, the number of patients is too short.

Answer: We thank you very much the reviewer for his constructive comments. By this time, the number of women has reached 1167 and that of children is 603. We have updated this information in both text and tables, so that most figures in tables have changed.

VERSION 2 – REVIEW

REVIEWER	Joao Guilherme Bezerra Alves Instituto de Medicina Integral Prof. Fernando Figueira (IMIP) Brazil
REVIEW RETURNED	09-Feb-2021
GENERAL COMMENTS	This version is suitable for publication