## PEER REVIEW HISTORY



## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | Prevalence and impact of SARS-CoV-2 infection on maternal and infant health in African populations: protocol of a multi-centre prospective cohort study (MA-CoV project) |
| **AUTHORS** | Figueroa-Romero, Antía; Mendes, Anete; Mombo-Ngoma, Ghyslain; Mischlinger, Johannes; Esen, Meral; Vogler, Michael; Mazuze, Maura; Mombo-Nzamba, Lionel; Mbadinga, Benjamin; Sanz, Sergi; Ramharter, Michael; Saute, Francisco; Nhampossa, Tacilta; Menendez, Clara; González, Raquel |

## VERSION 1 – REVIEW

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| **REVIEWER** | Ofman, Gaston<br>The University of Oklahoma Health Sciences Center |
| **REVIEW RETURNED** | 31-Aug-2022 |

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| **GENERAL COMMENTS** | Romero et al. present a protocol for a prospective two center study to determine the prevalence and health effects of maternal SARS-CoV-2 infection in selected sites from Gabon and Mozambique. In addition of adding valuable data on the effects of COVID-19 on vulnerable population, this well-designed study will inform into the interactions between SARS-CoV-2 infections and other prevalent infection diseases such as Malaria and HIV. In addition the data and samples collection is very interesting specially the collection of human milk and placental tissue.<br><br>The primary objective of the MA-CoV (Maternal CoVid) study is to determine the prevalence and incidence of SARS-CoV-2 infection during pregnancy. Secondary objectives include to describe the effects of maternal SARS-CoV-2 infection on pregnancy and perinatal outcomes, to<br>characterize the clinical features of COVID-19 disease in pregnancy, and to assess the potential<br>vertical transmission and through breastfeeding of SARS-CoV-2 from infected mothers to their<br>offspring. The main study hypotheses are: (1) SARS-CoV-2 infection during pregnancy may<br>influence maternal and perinatal outcomes, (2) SARS-CoV-2 clinical manifestations may be<br>different in pregnant women compared to non-pregnant adults, and (3) SARS-CoV-2 can be<br>transmitted from mother to child prenatally and postnatally.<br>.<br>Comments<br><br>1.For the hypothesis number 2, where the authors state that infection in pregnant women may have different clinical |

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| | manifestations tan non-pregnant women, do they recruit non pregnant women and assess their clinical manifestation?<br><br>2.The authors describe that this new study will leverage the structure of another ongoing clinical trial. In this sense it would be important for the readers to include a brief paragraph about the goal and design of the mother study as well as the clinicaltrial.gov number.<br><br>3.It would be useful for the authors to include as supplement the case report forms in order to inform other to make them available for other researchers across the globe or other investigators that might want to collaborate with them based on the information the study will be collecting.<br><br>4.Could the authors clarify if there are there any exclusion criteria?<br><br>5.An important aspect that the authors should clarify is how will they account for asymptomatic COVID-19 infection (about half based on other studies).<br><br>6.The antenatal follow-up description states that the pregnant women will attend clinic once a month, but it is unclear what would happen if they have symptoms of COVID-19 in between their visits.<br><br>7.A strength of the study would, if possible, to investigate IgA in breastmilk or viral neutralization in order to assess the ability of breastfeeding mothers to continue to protect their infants.<br><br>8.In order to assess neonatal vertical transmission a single PCR swab may be insufficient. Most pediatric societies recommend a follow up swab at 48-72 hs to correct for early false negative/contamination samples. |

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| **REVIEWER** | Chionuma, Joy Onyinyechi<br>Lagos State University, Obstetrics and Gynaecology |
| **REVIEW RETURNED** | 27-Jan-2023 |

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| **GENERAL COMMENTS** | The proposal was well written, easy to understand and addressed most areas of importance. The research findings will contribute to the knowledge about COVID-19 infection in pregnancy especially in sub-Saharan Africa. I believe it is a good proposal. |

## VERSION 1 – AUTHOR RESPONSE

Comments from the reviewers:
Romero et al. present a protocol for a prospective two center study to determine the prevalence and health effects of maternal SARS-CoV-2 infection in selected sites from Gabon and Mozambique. In addition of adding valuable data on the effects of COVID-19 on vulnerable population, this well-designed study will inform into the interactions between SARS-CoV-2 infections and other prevalent infection diseases such as Malaria and HIV. In addition, the data and samples collection is very interesting specially the collection of human milk and placental tissue.
The primary objective of the MA-CoV (Maternal CoVid) study is to determine the prevalence and incidence of SARS-CoV-2 infection during pregnancy. Secondary objectives include to describe the effects of maternal SARS-CoV-2 infection on pregnancy and perinatal outcomes, to characterize the

clinical features of COVID-19 disease in pregnancy, and to assess the potential vertical transmission and through breastfeeding of SARS-CoV-2 from infected mothers to their offspring. The main study hypotheses are: (1) SARS-CoV-2 infection during pregnancy may influence maternal and perinatal outcomes, (2) SARS-CoV-2 clinical manifestations may be different in pregnant women compared to non-pregnant adults, and (3) SARS-CoV-2 can be transmitted from mother to child prenatally and postnatally.

R: We thank the reviewer for his comments. They will help us improve the final version of the article. We have provided a response for each of the comments/questions and we have modified the manuscript accordingly.

Comments

1. For the hypothesis number 2, where the authors state that infection in pregnant women may have different clinical manifestations than non-pregnant women, do they recruit non-pregnant women and assess their clinical manifestation?

R: The study will not enroll non-pregnant women. However, the clinical presentation of COVID-19 have been well described among non-pregnant individuals. Thus, we will be able to compare the present study findings regarding signs and symptoms of maternal SARS-CoV-2 infection with reports from non-pregnant women.

2. The authors describe that this new study will leverage the structure of another ongoing clinical trial. In this sense it would be important for the readers to include a brief paragraph about the goal and design of the mother study as well as the clinicaltrial.gov number.

R: The goal and design of the mother study as well as the clinicaltrial.gov number have been included in the revised manuscript.

3. It would be useful for the authors to include as supplement the case report forms in order to inform other to make them available for other researchers across the globe or other investigators that might want to collaborate with them based on the information the study will be collecting.

R: We appreciate this suggestion. The study case report forms have been included as supplementary material.

4. Could the authors clarify if there are there any exclusion criteria?

R: There is one exclusion criterion: woman planning to move out the study area in the following 7 months from enrolment. We have included it in the revised manuscript.

5. An important aspect that the authors should clarify is how will they account for asymptomatic COVID-19 infection (about half based on other studies).

R: We will be able to account for asymptomatic infections since we will determine SARS-CoV-2 nucleocapsid (N) antibodies. Asymptomatic COVID-19 infection will be defined as presence of SARS-CoV-2 nucleocapsid (N) antibodies with and/or a positive COVID-19 PCR without COVID-19 associated symptoms. Women with baseline SARS-CoV-2 N antibodies will be considered infected before study enrolment. We have updated this information in the revised manuscript.

We have updated the Laboratory tests section in order to update the information on the essay that will be used for detection of SARS-CoV-2 N and S antibodies since it differs from the first version of the protocol that was presented on July 2022 when this manuscript was submitted.

6. The antenatal follow-up description states that the pregnant women will attend clinic once a month, but it is unclear what would happen if they have symptoms of COVID-19 in between their visits.

R: Study participants reporting being sick at the health facilities (including suspicion of COVID-19) will be seen by study personnel. Every unscheduled visit of the woman from enrolment until the post-partum visit will be recorded into a study CRF specifically designed for these visits. We have updated the revised manuscript with this information.

7. A strength of the study would, if possible, to investigate IgA in breastmilk or viral neutralization in order to assess the ability of breastfeeding mothers to continue to protect their infants.

R: We agree with the reviewer suggestion, and we also believe that investigating IgA and/or other immunoglobulins in breastmilk would be an added value of our study. We will take this suggestion into account for potential ancillary analysis.

In order to assess neonatal vertical transmission a single PCR swab may be insufficient. Most pediatric societies recommend a follow up swab at 48-72 hs to correct for early false negative/contamination samples.
R: We agree with the reviewer and doing only one PCR it may be a limitation to assess vertical transmission. Nevertheless, study teams test newborns following their national guidelines.