Generic protocol:
a prospective cohort study investigating maternal, pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2

Version 3.1
Date: 1 November 2022
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human reproduction programme hrp research for impact
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World Health Organization

Any understanding of the transmission patterns, severity, clinical features and risk factors for infection of an emerging virus will be limited at the start of an outbreak. To address these unknowns, the World Health Organization (WHO) has provided protocols for special investigations in different settings.

In the case of the recent coronavirus disease (COVID-19) pandemic, data collected using these investigation protocols are critical to refine recommendations for case definitions and surveillance; characterize key epidemiological features of COVID-19; help understand the spread, severity and spectrum of the disease, and its impact on the community; and inform guidance for the application of countermeasures such as case isolation and contact tracing. These protocols are designed to enable the rapid and systematic collection of data in a format that facilitates comparison across different settings globally. All WHO protocols for COVID-19 are available on the WHO website, together with the technical guidance documents. This protocol may be subject to revision, pending WHO research governance processes.

For questions related to implementation or other aspects of pregnancy-related COVID-19 research, contact hrp_covid19pregnancycohort@who.int; for questions related to other early investigation protocols, contact earlyinvestigations-2019-nCoV@who.int.

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Preface

This research protocol is one of the World Health Organization (WHO) protocols for coronavirus disease (COVID-19) designed to enable the rapid and systematic collection of data in a format facilitating comparison across different settings. All WHO investigation protocols for COVID-19 are available on the WHO website.

Any partner who wishes to use this protocol can do so freely and without charge or obligations; however, the United Nations Development Programme (UNDP), United Nations Population Fund (UNFPA), United Nations Children's Fund (UNICEF), WHO and the World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP) cannot provide guaranteed support for study implementation. We ask implementing study sites to inform the HRP of their implementation of this protocol and to provide a contact. Please share your information with hrp_covid19pregnancycohort@who.int.

It is important to note that this protocol is designed to answer the key research questions and primary objectives outlined here. The implementation of this study may include additional objectives or study components, as determined by each implementing site. For example, the protocol for this prospective cohort study includes COVID-19 vaccine-related objectives that will require the recruitment of a sufficient number of vaccinated pregnant women. In countries where pregnant women receive COVID-19 vaccines, and as part of the adaptation process of this generic protocol, careful consideration of the feasibility and appropriateness of engaging in selected secondary and optional objectives will be required. Individual study sites can attempt to overcome technical, financial or capacity limitations by pooling/aggregating data in order to achieve an overall sample size with sufficient statistical power to answer the primary research questions.

Implementing partners can opt to manage data onsite or through the central HRP repository, subject to local circumstances. A pooled analysis bringing together all consenting and contributing sites will be discussed with sites implementing the study. Sites that agree to pool data under the coordination of WHO/HRP will have the option to independently publish their own data. The analyses of the pooled data will be made available and widely disseminated in collaboration with all contributing sites. All partners will retain control of their site data, regardless of whether the data are included in the pooled/aggregated analyses or not.

Summary

To better understand how severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection impacts outcomes in women and their neonates during pregnancy and the postpartum period, the World Health Organization (WHO) has developed a generic research protocol for the investigation of coronavirus disease (COVID-19) outcomes in pregnant women. The protocol addresses key research questions, facilitates systematic and harmonized collection of data and biological specimens, and allows for data comparison and aggregation across different locations while minimizing potential biases. The protocol is designed to be adapted to each study site, according to resource availability and local circumstances.

This protocol outlines a prospective cohort study of pregnant or recently pregnant women infected with, as well as pregnant or recently pregnant women not infected with, SARS-CoV-2 during pregnancy. The purpose of this study is to determine whether SARS-CoV-2 infection during pregnancy increases the risk of adverse pregnancy, perinatal, neonatal and postpartum outcomes; assess the number of neonates, fetuses and fetal tissue/products of conception with detectable SARS-CoV-2 RNA as a proportion of all births, stillbirths, miscarriages and induced abortions from infected pregnant women; and describe pregnancy, perinatal, neonatal and postpartum outcomes among women who have received at least one dose of a COVID-19 vaccine during pregnancy.

Additionally, this study will characterize the clinical spectrum of COVID-19 in pregnant women; determine the probability of detecting SARS-CoV-2 RNA in pregnancy-related fluids (i.e. amniotic fluid), breast milk and tissues; follow clinical outcomes of women and their neonates up to 6 weeks after childbirth; and assess COVID-19 vaccine uptake among pregnant women in the study, along with symptoms and events following vaccination.

It is expected that findings from studies implementing this protocol will be published, widely disseminated and used to develop recommendations on the surveillance, management and counselling of women during and after pregnancy, as well as their neonates, in the context of the