

MINI REVIEW



Impact of COVID-19 on women and children and the need for a gendered approach in vaccine development

Kranti Suresh Vora^{a,b}, Aarthi Sundararajan^a, Shahin Saiyed^c, Kuldeep Dhama^d, and Senthilkumar Natesan^{a,c}

^aIndian Institute of Public Health Gandhinagar, Gandhinagar, India; ^bUniversity of Canberra, Bruce, Australia; ^cBiomac Life Sciences Pvt Ltd, Gandhinagar, India; ^dDivision of Pathology, ICAR-Indian Veterinary Research Institute, Izatnagar, India

ABSTRACT

The COVID-19 pandemic has imposed unprecedented health and socioeconomic challenges on public health, disrupting it on a global scale. Given that women and children are widely considered the most vulnerable in the times of emergency, whether in war or during a pandemic, the current pandemic has also severely disrupted access to reproductive and child health services. Despite this, data on the effect of the pandemic on pregnant women and newborns remain scarce, and gender-disaggregated indicators of mortality and morbidity are not available. In this context, we suggest the implementation of a gendered approach to ensure the specific needs of women and their newborns are considered during the development of COVID-19 vaccines. Taking into account gender-based biological differences, the inclusion of pregnant and lactating mothers in clinical trials for the development of COVID-19 vaccines is of vital importance.

ARTICLE HISTORY

Received 19 May 2020
Revised 22 August 2020
Accepted 15 September 2020

KEYWORDS

COVID-19; women and child health; vaccine development; gendered approach; vaccine

Introduction

Women and children are among the most vulnerable in times of disaster. Routine but essential services for women and children, such as antenatal care, contraception, abortion services, and immunization, are some of the most affected during emergencies, as a result of healthcare providers being occupied with other services.

Both the research literature and the guidelines from developmental agencies (e.g. WHO, UNICEF) are calling for practitioners to pay closer attention to women and children to minimize the impact of the pandemic on these vulnerable populations. Despite this, little has been done to evaluate the impact of the current COVID-19 pandemic on women and children. For example, whether the pandemic affects men and women differently is not investigated significantly as not much primary data are published for the same. As a result, a single brush approach, rather than a gendered approach, appears to be currently applied in response to the COVID-19 pandemic including for the development of a vaccine, to the detriment of women and children.

In this article, we examine the current literature on this topic and analyze secondary data to investigate the impact of the pandemic on the health of women and children in low resource settings to understand the context and to evaluate the extent to which a gendered approach is being applied for vaccine development.

We describe the impact of COVID-19 on women and children with a focus on a lack of access to health care and its negative effects on women and children. We also describe efforts to develop a vaccine from a gender perspective to highlight the need for a gendered approach in the development of a successful vaccine against COVID-19.

Methodology

An extensive literature search was performed using several databases, namely PubMed (<https://pubmed.ncbi.nlm.nih.gov/>), Science Direct (<https://www.sciencedirect.com/>), and Google Scholar (<https://scholar.google.co.in/>). With respect to efforts to develop a vaccine using a gendered approach, the following set of criteria were included in the literature search: (1) gender/sex-based differences in response to several virus infections, including SARS-CoV-2; (2) gender/sex-based differences in response to vaccination; (3) pregnant women inclusion/exclusion in vaccine clinical trials; (4) immune response during pregnancy. A further detailed search was conducted for these criteria in specific vaccine studies related to influenza, Diphtheria Tetanus Pertussis (DTP), Measles Mumps Rubella (MMR), and Oral Polio vaccine (OPV).

With respect to ongoing COVID-19 vaccine clinical trials, the draft landscape of vaccine candidates released by developmental agencies such as WHO and the listed relevant clinical trial identifier/registration numbers were used to further explore the studies in more detail, including their eligibility criteria (inclusion, exclusion), the participants, and the study protocols. The following clinical trials search sites were used in this review: (1) Global Clinical Trials registry (<https://clinicaltrials.gov/ct2/home>); (2) ISRCTN registry (<http://www.isrctn.com/>); (3) Chinese Clinical Trial registry (<http://www.chictr.org.cn/enindex.aspx>). A combination of the following keywords was used during searches: “COVID-19,” “SARS-CoV-2,” “pregnancy,” “women & child health,” “contraception,” “family planning,” “birth outcome” and “vaccine development.”

Impact of COVID-19 on women and children

With an increasing number of COVID-19 cases around the world, concerns regarding the effects of this disease on pregnant women and their unborn children are increasing. Since the current pandemic is several months old, the majority of women who delivered in the last 6 months were in their last or second trimester at the time the pandemic started, in which case the adverse effects on the then unborn child are likely to be minimal. Congenital malformations are more likely to occur if infection occurs within the first trimester, that is, when the majority of the key organs of the fetus are forming. One study found that women affected by COVID-19 had higher rates of late preterm birth (between 34 and 37 weeks) and higher rates of abortion earlier in the pregnancy. Preeclampsia and cesarean delivery were also found to be more common in these women compared to general population. The study did not find evidence suggestive of vertical transmission in mothers infected in late pregnancy nor specific neonatal symptoms.¹ In addition, another North American study found that pregnant women may not be a representative sample of the entire female population, and that asymptomatic viremia may be increased in pregnant women with COVID-19 compared with non-pregnant women.²

A study of 15 Chinese women found that pregnancy did not aggravate the symptoms of COVID-19 among mothers admitted with pneumonia, and the disease did not impact the pregnancy outcome.³ The majority of women underwent C-section. Another Chinese study also found that the majority of women (93%) underwent a cesarean section, as well as a higher proportion of premature deliveries (21%), 8 of which were induced (7 due to concerns about COVID-19).⁴

To date, there have been no report of an increased risk of congenital malformations or still birth due to COVID-19. Studies and reviews originating in China indicate that SARS CoV-2 does not have any major adverse health consequences on unborn babies, unlike infection with Zika virus or Rubella, the former resulting in major congenital malformation in newborns delivered by infected mothers.¹⁻¹⁶ As such, there is no clarity on whether to continue pregnancy, particularly in the case that mothers are administered antiviral drugs for treatment.³⁻⁹ Unlike Zika, the transmission of SARS-CoV-2 from the mother to child is yet to be confirmed and has not been detected in amniotic fluid nor breast milk.⁴ However, one study evaluated 33 mothers from Wuhan, China, and found that three newborns were positive for COVID-19 after birth.¹⁷ In conclusion, whether COVID-19 can be transmitted from mothers to their unborn children in the womb remains unknown. However, as of now, the virus does not seem to have any major adverse health effects on mothers or their newborns.

In India, the number of pregnant mothers diagnosed with COVID-19 is currently low. However, it is worth noting that around 80% of infections are mild to moderate and mothers may not be tested. Hence, the possibility of exposure to COVID-19 during early pregnancy is not necessarily small. Recently, the ICMR has published guidelines requiring that women who are admitted for delivery be tested for COVID-19.¹⁸

WHO and Royal College of Obstetrics (United Kingdom) agree that pregnant mothers should take precautions to prevent the infection. This has been facilitated by lockdowns, which have, however, limited their access to maternity care, including emergency obstetric care, especially for blood transfusions.^{19,20} According to the Health Management Information Systems of the Government of India, the number of women registered for antenatal care fell by 0.5 million and the number of women receiving 4 or more antenatal visits fell by 0.4 million between January 2020 and March 2020. This may be the result of public sector personnel becoming increasingly busy with COVID-19-related work, as well as fear among the general population.^{9,21}

As the pandemic unfolds, we expect the long-term effects of the virus on newborns to manifest. These effects will have to be studied systematically, such as via virology studies, to evaluate poor birth outcomes as a result of COVID-19 infection, including still births and abortions. To this end, special studies should be instituted as soon as possible.

Gender-based Socio-cultural risk factors

The risk of contracting COVID-19 is higher in women, which may be due to the fact that they are more likely to be the primary caregivers of sick relatives. Furthermore, a large proportion of frontline workers, including nursing personnel, are women. In India, there are approximately 2 million grassroot-level workers, such as Auxiliary Nurse Midwives (ANM), Anganwadi Workers (AWW), and Accredited Social Health Activist (ASHA), in rural areas.²² Globally 70% of the health and social care workforce is comprised of women.^{22,23}

In addition to an increased risk of contracting COVID-19 and limited decision-making ability, women are further compromised by disruptions to reproductive health services as a result of the current pandemic. Reproductive health services, such as contraception and abortion services, have been widely documented as either having been shut down or rendered inaccessible as a result of the pandemic.²⁴⁻²⁶ International Planned Parenthood Federation (IPPF) has recently reported on their website that they anticipate widespread shortages of contraceptives. The IPPF reported that lockdown and other measures put in to curtail the pandemic have led to a significant reduction in the manufacturing of contraceptives.²⁵ In addition to limited supplies, IPPF has reported on the closure of over 5,000 clinics that provide community-based care in 64 countries. The lack of personal protective equipment and transportation to the clinics is further limiting access to reproductive health services. In a technical note, the UNFPA reported that measures for the containment of COVID-19 have led to 47 million women in 114 low and middle-income countries to lose their access to contraception.²⁷ In India itself, about 3 million unintended pregnancies are predicted to occur as a result of the pandemic and lockdown.²⁸ On a global scale, an estimated 7 million unplanned pregnancies are expected. To further exacerbate the situation, many of these women will face the early stages of their pregnancy during peak times of the COVID-19 pandemic.²⁹

Fiscal resource distribution should take into account gender-based inequity in power, higher rates of infection in women, and reproductive health issues, including gender-based violence, faced by women during this pandemic. Advocates suggest the use of a sexual, reproductive health, and justice framework for the monitoring of gender issues in terms of the health and social impacts of the COVID-19 pandemic to ensure any injustices are acknowledged and power structures are taken into consideration.^{25–27,30–33}

Gender-specific data, especially with regards to mortality, case fatality rate, and morbidity surveillance data, should be prioritized in the response to the COVID-19 pandemic. Research on the pathophysiology of this virus should highlight the prevalence of vertical transmission and prevalence of infection in women. Moreover, the development of vaccines and treatments for COVID-19 should take into account gender-based differences and their safety in pregnant and lactating women.

Current vaccine development efforts from a gendered perspective

Women tend to be more affected in pandemics for several reasons, including an increased biological vulnerability, their role as primary caregivers to sick relatives, social disadvantages, and the fact that the majority of frontline health workers are women. Therefore, gendered analyses are needed to evaluate the complex relationship between biological and behavioral risk factors in women during the COVID-19 pandemic. None of the countries affected by high COVID-19 mortality rates, including China and Italy, have provided data segregated on the basis of gender, in particular with regards to the case fatality rate, nor taken into account gender-specific susceptibility, behavioral risk factors, or the gender-specific prevalence of comorbidities.^{22,24,31}

Given the rapid transmission of SARS-CoV-2 and high rates of fatality, the majority of prevention measures have focused on controlling the spread of this virus, mainly through social distancing and the promotion of hand hygiene. However, biotechnology-pharmaceutical companies and research institutions are actively pursuing several vaccine development strategies against SARS-CoV-2.³⁴ Recently released landscape document prepared by WHO (29 June 2020) indicates, there are currently 17 candidate vaccines under clinical evaluation.³⁵ These vaccine platforms include: (a) non-replicating adenoviral vectors; (b) inactivated vaccines; (c) DNA plasmid vaccine; (d) lipid nanoparticle encapsulated RNA vaccine; (e) protein subunit vaccine. An online search conducted on ClinicalTrials.gov, the ISRCTN registry, and the Chinese Clinical Trial registry using the relevant identifier/registration number indicated that both men and women participated in these clinical trials. These vaccine trials are focused on assessing the safety, dosage, and immunogenicity of these vaccines. Safety of some of the vaccine candidates has been established in initial phases of trials. However, the gender-based effects of these vaccines can only be evaluated as part of a subgroup analysis.

Differences in women's responses to vaccines and implications for COVID 19

There is currently a need to design vaccine clinical trials with larger number of men and women participants in order to conduct a detailed analysis of differences in response to vaccination due to gender. This is of critical importance in response to the COVID-19 pandemic since men and women respond differently to viral infections and vaccines.^{36–38} These differences could be the result of immunological, hormonal, and genetic factors.³⁹ A study conducted in Wuhan, China found that, compared to men, women had high levels of SARS-CoV-2-specific IgG antibodies in the plasma of severe cases.⁴⁰ In general, women are able to mount a higher inherent and adaptive immune response to viral infections than men.³⁹ However, hyperactive immune responses can lead to a fatal outcome and a higher incidence of autoimmunity in the case of infection and immunization.

During the development of a vaccine for COVID-19, lessons learned from the gender-based differences observed in vaccines against previous respiratory viral infections, such as influenza should be remembered, where women exhibited higher local and systemic responses to vaccines.^{41,42} The antibody response of women to seasonal influenza vaccine is higher than in men, with half a dose of vaccine generating an antibody response in women equivalent to the response following a full dose of vaccine in men.^{43,44} Therefore, clinical studies in response to the current COVID-19 pandemic should focus on gender-based differences since these have implications on vaccine dosage, as well as on the side effects of any vaccine and their impacts on immunogenicity.

Previously, the side effects of DTP vaccination were found to show gender-based differences, with female infants showing increased rates of hospitalization post-vaccination.⁴⁵ Similar adverse events were also increasingly common among young girls who received DTP, measles, and OPV vaccine together or the MMR vaccine alone.^{46,47} The subcutaneous administration of yellow fever vaccine and several other vaccines has also demonstrated higher adverse events among women compared to men.⁴⁸ With respect to COVID-19, co-morbidity-associated risk factors, such as cardiovascular diseases, have demonstrated gender-specific clinical manifestations.⁴⁹ These studies should be evaluated against current vaccine trials for SARS-CoV-2 from a gendered perspective.

Additionally, in the ongoing vaccine clinical trials against SARS-CoV-2, pregnancy has been added as an exclusion criteria for participation since it can be checked from the relevant clinical trial identifier/registration number given in the recently issued draft landscape of COVID-19 candidate vaccines by WHO.³⁵ Some of these trials specifically excluded breastfeeding women and women who intended to become pregnant during the study, similar to during Ebola and Zika vaccine development.^{50–52} However, the exclusion of participants without justification from vaccine clinical trials continues despite the recent elimination of pregnant women as “vulnerable” owing to pregnancy in the guidelines published by CIOMS in collaboration with WHO.⁵³ The inclusion of pregnant women in a vaccine

clinical trial should be based on informed consent, and the potential benefits/risks of participation should be assessed during fatal pandemics. In addition, the results from vaccine clinical trials involving non-pregnant women cannot be generalized to pregnant women since the immunological and physiological make-up changes drastically during pregnancy.⁵⁴ Therefore, a lack of information on the effects of candidate vaccines against SARS-CoV-2 specific to pregnant women and the subsequent birth outcome poses a risk to the health of these women during the ongoing pandemic.

Vaccination strategies being developed against other viruses and tested in clinical trials involving pregnant women could be adapted for use in the current pandemic. In addition, vaccines routinely recommended for pregnant women, such as influenza and tetanus, should be evaluated to determine the type of vaccination strategy that is best for pregnant women in terms of safety and protection.⁵⁵ Vaccine candidates against SARS-CoV-2 involving minimal risk as well as potential benefits to pregnant women and fetuses should be developed and introduced into clinical trials to encourage participation of pregnant women.

Among the ongoing clinical and pre-clinical vaccine trials against SARS-CoV-2, strategies involving inactivated vaccine, subunit vaccine, non-replicating adenoviral vector-based vaccines, and DNA vaccines are generally considered safe and offer low-risk approaches for designing vaccine trials with pregnant women.⁵⁶ Although the inclusion of pregnant women in clinical trials is an important issue, the process of inclusion is not straightforward. It is complicated by legal issues that might arise if pregnancy complications occur in participating pregnant women which may or may not be due to the vaccine in trial. There are no easy solutions to address this issue. One solution might be to strengthen preclinical studies of vaccines, such as evaluation of vaccine safety in pregnant non-human primate animal models, comprehensively assessing the occurrence of vaccine-induced pregnancy complications.

In order to assess the risk-benefit parameters of including pregnant women in vaccine development against SARS-CoV-2, it is critical that health information systems consistently collect data relevant to maternal and birth outcomes, along with data on comorbidities established as risk factors for mortality among infected mothers.

Conclusion

In the current pandemic, women and children are being disproportionately impacted. However, data on the effects of the pandemic on pregnancy and newborns are scarce, gender-disaggregated indicators are not available, and the provision of reproductive health services remains limited. Research on vaccines and treatment will need to adopt a gender-based approach to ensure the specific needs of women are considered. At the same time, the inclusion of pregnant women and lactating mothers in vaccine trials is vital to evaluate their safety.

As we move forward in the pandemic, the impact of COVID-19 on pregnant women and newborns will become more clear. However, a gendered approach should be implemented soon in order to tackle the pandemic while protecting

vulnerable populations, such as women and children. Because women are at higher risk of contracting infection, the safety of pregnant women should be taken into account during vaccine development. A gender balance should also be implemented in clinical trials to evaluate the safety and efficacy of a vaccine in women, in particular pregnant women.

Disclosure of potential conflicts of interest

Authors declare no conflict of interest with respect to the publication of this article.

Funding

Preparation of this article required no substantial funding to be stated.

ORCID

Kranti Suresh Vora  <http://orcid.org/0000-0001-5999-1118>
Kuldeep Dhama  <http://orcid.org/0000-0001-7469-4752>

References

1. Di Daniele M, Asma K, Gabriele S, Giuseppe R, Danilo B, Marco L, Jacopo V, Luigi N, Giovanni S, Vincenzo B, et al. Outcome of coronavirus spectrum infections (SARS, MERS, COVID 1-19) during pregnancy: a systematic review and meta-analysis. *Am J Obs Gynecol MFM*. 2020;PII:S2589-9333(20)30037-9. doi:10.1016/j.ajogmf.2020.100107.
2. Miller ES, Grobman WA, Sakowicz A, Rosati J, Peaceman AM. Clinical implications of universal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing in pregnancy. *Obstet Gynecol*. 2020 May 19;136(2):232–34. Epub ahead of print. PMID: 32433449. doi:10.1097/AOG.0000000000003983.
3. Dehan L, Lin L, Xin W, Dandan Z, Jiazheng W, Lian Y, Chuansheng Z. Pregnancy and perinatal outcomes of women with coronavirus disease (COVID-19) pneumonia: a preliminary analysis. *Am J Roentgenol*. 2020;215:1–6. doi:10.2214/AJR.20.23072.
4. Chen L, Li Q, Zheng D, Jiang H, Wei Y, Zou L, Feng L, Xiong G, Sun G, Wang H, et al. Clinical characteristics of pregnant women with Covid-19 in Wuhan, China. *N Engl J Med*. 2020 Apr 17;382(25):e100. Published Online First. doi:10.1056/NEJMc2009226.
5. David S. An analysis of 38 pregnant women with 2 COVID-19, their newborn infants, and maternal-fetal transmission of SARS-CoV-2: maternal coronavirus infections and pregnancy outcomes. *Arch Pathol Lab Med*. 2020. Forthcoming [published online ahead of print, 2020 March 17]. doi:10.5858/arpa.2020-0901-SA.
6. Chen S, Huang B, Luo DJ, Li X, Yang F, Zhao Y, Nie X, Huang BX. Pregnant women with new coronavirus infection: a clinical characteristics and placental pathological analysis of three cases. 2020. *Zhonghua Bing Li Xue Za Zhi*. 2020;49:E005. doi:10.3760/cma.j.cn112151-20200225-00138.
7. Favre G, Pomar L, Musso D, et al. 2019-nCoV epidemic: what about pregnancies? *Lancet*. 2020;395. (published online February 6). [https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(20\)30311-1.pdf](https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)30311-1.pdf).
8. Rasmussen SA, Smulian JC, Lednicki JA, Wen TS, Denise J. Jamieson. Coronavirus disease 2019 (COVID-19) and pregnancy: what obstetricians need to know. *Am J Obstet Gynecol*. 2020;222(5):415–26. doi:10.1016/j.ajog.2020.02.017.
9. Nan Y, Li W, Kang Q, Xiong Z, Wang S, Lin X, et al. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. *Lancet Infect Dis*. 2020. doi:10.1016/S1473-3099(20)30176-6.

10. Swartz DA, Graham AL. Potential maternal and infant outcomes from (Wuhan) coronavirus 2019-nCoV infecting pregnant women: lessons from SARS, MERS, and other human coronavirus infections. *Viruses*. 2020;12(2):194. doi:10.3390/v12020194.
11. Mojgan KZ, Hossein N, Seyed AD, Hajar A, Seyed RM, Athena B, Farzad F, Reza B. Vertical transmission of coronavirus disease 19 (COVID-19) from infected pregnant mothers to neonates: a review. *Fetal Pediatr Pathol*. 2020. doi:10.1080/15513815.2020.1747120.
12. Thornton JG. COVID-19 in pregnancy. *BJOG*. 2020 May 7;127(9):1122–1122. Epub ahead of print. PMID: 32378774. doi:10.1111/1471-0528.16308.
13. Shanes ED, Mithal LB, Otero S, Azad HA, Miller ES, Goldstein JA. Placental Pathology in COVID-19. Version 2. *Am J Clin Pathol*. 2020 Jun 8;154(1):23–32. PMID: 32441303; PMCID: PMC7279066. doi:10.1093/ajcp/aqaa089.
14. Simões E Silva AC, Leal CRV. Is SARS-CoV-2 vertically transmitted? *Front Pediatr*. 2020 May 15;8:276. PMID: 32574285; PMCID: PMC7243472. doi:10.3389/fped.2020.00276.
15. Penfield CA, Brubaker SG, Limaye MA, Lighter J, Ratner AJ, Thomas KM, Meyer JA, Roman AS. Detection of severe acute respiratory syndrome coronavirus 2 in placental and fetal membrane samples. *Am J Obs Gynecol MFM*. doi:10.1016/j.ajogmf.2020.100133.
16. Juan J, Gil MM, Rong Z, Zhang Y, Yang H, Poon LC. Effect of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcome: systematic review. *Ultrasound Obstet Gynecol*. 2020 Jul;56(1):15–27. PMID: 32430957; PMCID: PMC7276742. doi:10.1002/uog.22088.
17. Zeng L, Xia S, Yuan W, Yan K, Xiao F, Shao J, Zhou W. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. *JAMA Pediatrics*. 2020;174(7):722. doi:10.1001/jamapediatrics.2020.0878.
18. Guidance for Management of Pregnant Women in COVID-19 Pandemic. ICMR - national institute for research in reproductive health. [accessed 1 Jul 2020] https://www.icmr.gov.in/pdf/covid/techdoc/Guidance_for_Management_of_Pregnant_Women_in_COVID19_Pandemic_12042020.pdf
19. Coronavirus disease (COVID-19) technical guidance: Maintaining Essential Health Services and Systems. World health organization. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/maintaining-essential-health-services-and-systems>
20. RCOG, Royal College of Midwives, RCPCH, et al. Coronavirus (COVID-19) infection in pregnancy: information for healthcare professionals. Royal College of Obstetricians and Gynaecologists 2020; (published online 28 March) <https://www.rcog.org.uk/globalassets/documents/guidelines/2020-03-28-covid19-pregnancy-guidance.pdf>
21. Data Reporting Status All India level data, 2019–2020. Standard reports. Health management information system (HMIS). Ministry of health & family welfare, government of India. The data is retrieved from https://nrhm-mis.nic.in/hmisreports/frmstandard_reports.aspx on 29th April, 2020
22. India's auxiliary nurse-midwife, anganwadi worker, accredited social health activist, multipurpose worker, and lady health visitor programs by: Kerry Scott, Dena Javadi, and Jessica Gergen (comments from Dr. Rajani Ved and contributions from Rachel Strodel). <https://www.chwcentral.org/blog/indias-auxiliary-nurse-midwife-anganwadi-worker-accredited-social-health-activist-multipurpose>.
23. Kelli SH, Goleen S, Samantha G, Sara EC, Dazon DD, Miriam O, Rachel TM, Micaela EM, Terry M. Centring sexual and reproductive health and justice in the global COVID-19 response. *Comment. Lancet*. 395:1175–77.
24. Coronavirus Disease (COVID-19) Preparedness and Response - UNFPA Technical Briefs V March 23_2020. Gender equality and addressing gender-based violence (GBV) and coronavirus disease (COVID-19) prevention, protection and response.
25. Contraception and COVID-19: disrupted supply and access. 15 Apr 2020. <https://www.ippf.org/blogs/contraception-and-covid-19-disrupted-supply-and-access>.
26. Andy H, Enrique B, Anita B, David LH, Matthew JH. Centring sexual and reproductive health and justice in the global COVID-19 response. *Lancet*. 2020 Apr 11;395(10231):1175–77. COMMENT]. doi:10.1016/S0140-6736(20)30801-1.
27. Interim Technical Note: Impact of the COVID-19 Pandemic on Family Planning and Ending Gender-based Violence, Female Genital Mutilation and Child Marriage. Pandemic threatens achievement of the transformative results committed to by UNFPA. By UNFPA, with contributions from avenir health, Johns Hopkins University (USA) and Victoria University (Australia) dated 27th April 2020.
28. Impact of COVID 19 on Family Planning Program. Policy Brief May 2020. FRHS India. [accessed 29 May 2020]. https://pratigya_campaign.org/wp-content/uploads/2020/05/impact-of-covid-19-on-indias-family-planning-program-policy-brief.pdf
29. Vora KS, Saiyed S, Natesan S. Impact of COVID-19 on family planning services in India. *Sex Reprod Health Matt*. 2020 Jun 19;1–3. Epub ahead of print. PMID: 32552622. doi:10.1080/26410397.2020.1785378.
30. Enabling Delivery of Essential Health Services during the COVID 19 Outbreak: Guidance note. MOHFW guidelines for COVID 19. [accessed 25 Apr 2020] <https://www.mohfw.gov.in/pdf/EssentialservicesduringCOVID19updated0411201.pdf>
31. Wenham C, Smith J, Morgan R. COVID-19: the gendered impacts of the outbreak. *Lancet*. 2020;395:846–48. doi:10.1016/S0140-6736(20)30526-2.
32. Peterman P, O'Donnell T, Shah O-P, van Gelder, 2020. Pandemics and Violence Against Women and Children. CGD Working Paper 528. Washington (DC): Center for Global Development. <https://www.cgdev.org/publication/pandemics-and-violence-against-women-and-children>.
33. COVID-19 and violence against women What the health sector/system can do. World health organization. 26 Mar 2020. <https://www.who.int/reproductivehealth/publications/emergencies/COVID-19-VAW-full-text.pdf?ua=1>
34. Amanat F, Krammer F. SARS-CoV-2 vaccines: status report. *Immunity*. 2020 Apr 14;52(4):583–89. doi:10.1016/j.immuni.2020.03.007.
35. Draft landscape of COVID 19 candidate vaccines. World health organization. 29 Jun 2020. <https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines>
36. Channappanavar R, Fett C, Mack M, Ten Eyck PP, Meyerholz DK, Perlman S. Sex-based differences in susceptibility to severe acute respiratory syndrome coronavirus infection. *J Immunol*. 2017 May 15;198(10):4046–53. doi:10.4049/jimmunol.1601896.
37. Klein SL, Hodgson A, Robinson DP. Mechanisms of sex disparities in influenza pathogenesis. *J Leukoc Biol*. 2012 Jul;92(1):67–73. doi:10.1189/jlb.0811427.
38. Fischinger S, Boudreau CM, Butler AL, Streeck H, Alter G. Sex differences in vaccine-induced humoral immunity. *Semin Immunopathol*. 2019 Mar;41(2):239–49. doi:10.1007/s00281-018-0726-5.
39. Klein SL, Flanagan KL. Sex differences in immune responses. *Nature Rev Immunol*. 2016;16:626–38. doi:10.1038/nri.2016.90.
40. Zeng F, Dai C, Cai P, Wang J, Xu L, Li J, Hu G, Wang Z, Zheng F, Wang L. A comparison study of SARS-CoV-2 IgG antibody between male and female COVID-19 patients: a possible reason underlying different outcome between sex. *J Med Virol*. 2020 May 8. doi:10.1002/jmv.25989.
41. Beyer WE, Palache AM, Kerstens R, Masurel N. Gender differences in local and systemic reactions to inactivated influenza vaccine, established by a meta-analysis of fourteen independent studies. *Eur J Clin Microbiol Infect Dis*. 1996 Jan;15(1):65–70. PMID: 8641306. doi:10.1007/BF01586187.

42. Nichol KL, Margolis KL, Lind A, Murdoch M, McFadden R, Hauge M, Magnan S, Drake M. Side effects associated with influenza vaccination in healthy working adults. A randomized, placebo-controlled trial. *Arch Intern Med.* 1996 Jul 22;156(14):1546–50. PMID: 8687262. doi:10.1001/archinte.1996.0044130090009.
43. Engler RJ, Nelson MR, Klote MM, VanRaden MJ, Huang CY, Cox NJ, Klimov A, Keitel WA, Nichol KL, Carr WW, et al. Walter reed health care system influenza vaccine consortium. Half- vs full-dose trivalent inactivated influenza vaccine (2004–2005): age, dose, and sex effects on immune responses. *Arch Intern Med.* 2008 Dec 8;168(22):2405–14. PMID: 19064822. doi:10.1001/archinternmed.2008.513.
44. Cook IF. Sexual dimorphism of humoral immunity with human vaccines. *Vaccine.* 2008 Jul 4;26(29–30):3551–55. Epub 2008 May 9. PMID: 18524433. doi:10.1016/j.vaccine.2008.04.054.
45. Andersen A, Bjerregaard-Andersen M, Rodrigues A, Umbasse P, Fisker AB. Sex-differential effects of diphtheria-tetanus-pertussis vaccine for the outcome of paediatric admissions? A hospital based observational study from Guinea-Bissau. *Vaccine.* 2017;35:7018–25. doi:10.1016/j.vaccine.2017.10.047.
46. Agergaard J, Nante E, Poulstrup G, Nielsen J, Flanagan KL, Østergaard L, Benn CS, Aaby P. Diphtheria-tetanus-pertussis vaccine administered simultaneously with measles vaccine is associated with increased morbidity and poor growth in girls. A randomised trial from Guinea-Bissau. *Vaccine.* 2011;29:487–500. doi:10.1016/j.vaccine.2010.10.071.
47. Khalil MK I, Al-Mazrou YY, Al-Ghamdi YS, Tumsah S, Al-Jeffri M, Meshkhas A. Effect of gender on reporting of MMR adverse events in Saudi Arabia. *East Mediterr Health J.* 2003;9(1–2):152–58. Jan-Mar.
48. Klein SL, Marriott I, Fish EN. Sex-based differences in immune function and responses to vaccination. *Trans R Soc Trop Med Hyg.* 2015 Jan;109(1):9–15. doi:10.1093/trstmh/tru167.
49. Gao Z, Chen Z, Sun A, Deng X. Gender differences in cardiovascular disease. *Med Novel Technol Dev.* 2019;4:100025. doi:10.1016/j.medntd.2019.100025.
50. Gomes MF, De La Fuente-Nunez V, Saxwna A, Kuesel AC. Protected to death: systematic exclusion of pregnant women from Ebola virus disease trials. *Reprod Health.* 2017;14:47–55.
51. Bebell LM, Oduyebo T, Riley LE. Ebola virus disease and pregnancy - A review of the current knowledge of Ebola virus pathogenesis, maternal and neonatal outcomes. *Birth Defects Res.* 2017 Mar 15;109(5):353–62. doi:10.1002/bdra.23558.
52. Schwartz DA. Clinical trials and administration of Zika virus vaccine in pregnant women: lessons (that should have been) learned from excluding immunization with the Ebola vaccine during pregnancy and lactation. *Vaccines (Basel).* 2018;6:81. doi:10.3390/vaccines6040081.
53. International ethical guidelines for health-related research involving humans. [accessed 12 May 2020]. <https://cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research-involving-humans/>
54. Mor G, Cardenas I. The immune system in pregnancy: a unique complexity. *Am J Reprod Immunol.* 2010 June;63(6):425–33. doi:10.1111/j.1600-0897.2010.00836.x.
55. Vojtek I, Dieussaert I, Doherty TM, Franck V, Hanssens L, Miller J, Bekkat-Berkani R, Kandeil W, Prado-Cohrs D, Vyse A. Maternal immunization: where are we now and how to move forward? *Ann Med.* 2018 May;50(3):193–208. doi:10.1080/07853890.2017.1421320.
56. Ward P et al. COVID-19 vaccine and antiviral drug development, faculty of pharmaceutical medicine blog, 8 Apr 2020. <https://www.fpm.org.uk/blog/covid-19-vaccine-and-antiviral-drug-development/>