




## Coronavirus disease 2019 and pregnancy is déjà vu all over again

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Over the past two decades, the world has faced a series of public health emergencies, all requiring a robust international response. These include the severe acute respiratory syndrome (SARS) outbreak of 2003, the 2009 H1N1 influenza pandemic, the Ebola virus outbreak in West Africa in 2014–16, the Zika virus outbreak in 2015/16 and, most recently, the coronavirus disease 2019 (COVID-19) pandemic. Each of these emerging infections has required that obstetricians and other obstetric healthcare providers react quickly to protect their pregnant patients as well as the fetus. These outbreaks have presented different challenges to obstetric healthcare providers – ranging from increased severity of illness during pregnancy with 2009 H1N1 influenza<sup>1</sup> to substantial effects on the fetus, despite minimal effects on the pregnant woman's health, with Zika virus.<sup>2</sup> In each case, months passed before data on the effects of the infection on pregnancy and the fetus were available. In the meantime, obstetrics providers had no choice but to base clinical decision-making not on evidence, but on expert opinion, often with rapidly changing guidelines as more information became available. In addition, while treatment (e.g. oseltamivir for 2009 H1N1 influenza) and prophylaxis (e.g. vaccines for Ebola and COVID-19) became available for the general population, these measures were not studied during pregnancy, once again leaving obstetrics providers without evidence on which to make recommendations to patients. Finally, obstetrics providers sometimes faced potential risks to their own health because knowledge of how to prevent infectious transmission to healthcare providers during labour and delivery was limited.<sup>3</sup>

Although many have framed COVID-19 as a once-in-a-lifetime pandemic, this is unlikely to be the case. One important lesson from the recent succession of emerging

infections (those for which the incidence has risen in the past two decades or threatens to arise in the future) is that emerging infections will continue to occur. One reason for the increasing emergence of infectious diseases is the interconnectedness of the world's population; the ability to rapidly travel anywhere in the world means that an emerging infection anywhere is an emerging infection everywhere. This concept was well demonstrated by COVID-19, which spread rapidly from a small number of cases in China in December of 2019 to cases transmitted around the world, with declaration of a pandemic by the World Health Organization on 11 March 2020. Another reason is climate change: diseases in which the pathogen spends a significant amount of time outside its human host are particularly vulnerable to climate change. These include pathogens spread by vectors such as mosquitoes and ticks, and pathogens that spread in water and in food.<sup>4</sup> In addition, as human populations are more frequently encroaching on wildlife habitats, they are placed in close contact with animals that could spread pathogens to humans.<sup>5</sup> Most emerging infections and almost all pandemics have originated in animals (most in wildlife), with emergence driven by ecological, behavioural or socio-economic changes.<sup>6</sup>

Much has been written about the need to prepare for the next pandemic. A recent National Academy of Medicine initiative identified six steps to strengthen pandemic resilience in the USA, including launching a commission to evaluate the US COVID-19 response, strengthening and modernising health and public health systems, renewing the status of the USA as a global public health leader and partner, reinforcing a science-based approach to public health policy, increasing federal funding and political independence for pandemic agencies, and supporting One Health (which emphasises the connections among people,

animals, plants and the environment) and efforts to mitigate underlying drivers of pandemics.<sup>7</sup> Improved public health infrastructure is needed not only in the USA, but globally, so that countries have the ability to prevent, detect and respond to outbreaks quickly.

General pandemic preparedness efforts are critical, but special considerations are needed to improve our response to emerging infections among pregnant women. Obstetric healthcare providers and public health researchers that focus on maternal and child health also need to prepare for the next pandemic, and public health leaders at the national, sub-national and local levels need to recognise the importance of maternal and child health as part of pandemic preparedness so that addressing these issues can be prioritised. These preparedness efforts for pregnant women will require a collaborative approach to include not only obstetrics providers and maternal and child health researchers, but also experts in infectious disease, public health, epidemiology, data science and information technology, among others.

As part of the influenza pandemic preparedness efforts initiated in the USA in 2005, emphasis was placed on 'vulnerable populations'; as part of these efforts, specific plans to address issues related to pregnant women were developed by the US Centers for Disease Control and Prevention (CDC).<sup>8</sup> Once the H1N1 pandemic influenza virus emerged in 2009, these plans were used to guide the response. A collaborative response effort was developed quickly to address the pandemic's effects during pregnancy;<sup>9</sup> however, after the pandemic ended, that infrastructure was dismantled and had to be rebuilt during the CDC's emergency response to Zika virus. The infrastructure developed to respond to COVID-19 and pregnancy needs to be maintained and further developed so that expertise is not lost and response activities can be ramped up quickly at the time of the next public health emergency.

Several strategies are needed to address pandemic preparedness for pregnant women. These include ensuring that comprehensive plans for surveillance and research to better understand the effects of the infection during pregnancy are in place before the next pandemic, addressing issues that limit the inclusion of pregnant women in the testing of interventions for treatment and prophylaxis (including vaccines) during an emergency, and improving the expertise in the obstetrics community related to infectious disease, prevention of infectious transmission and rapid development of guidelines.

Setting up surveillance and research activities during an emergency response is challenging. Hence, developing systems in advance of a public health emergency that can be quickly adapted to collect and share real-time data is critical.<sup>10</sup> As an example, because of delays in the implementation of research studies on 2009 H1N1, the National

Institute for Health Research in the UK developed a portfolio of projects that were 'hibernated', with plans for them to be activated in the event of a new influenza pandemic. Most of these projects, including one that focused on pregnancy and the postpartum period, were activated during COVID-19, which allowed early collection of data on pregnancy. Within 3 days of activation, data began to be collected across all obstetric units in the UK, and information on the effects of COVID-19 in pregnant women was published online on 8 June 2020.<sup>11,12</sup> Another example is the CDC's Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET): built on the infrastructure of the US Zika Pregnancy and Infant Registry, the CDC initiated support to state, local and territorial health departments in 2019 to collect data on mothers and infants in the event of an emerging health threat. This system was activated during the COVID-19 response, with data on nearly 4500 live-born infants born to mothers with SARS coronavirus 2 infection during pregnancy made available online on 2 November 2020.<sup>13</sup> Although these data were critical, this analysis of SET-NET included data on COVID-19 from only 16 jurisdictions (13 states, one territory, one county and one city). Expansion of SET-NET to more jurisdictions is needed so that data can be collected more quickly and can be nationally representative.

Another important area of research related to maternal health is related to transmission of infectious pathogens in the obstetric setting. Even basic questions such as whether vaginal or cesarean deliveries are aerosol-generating procedures remained unanswered early in the COVID-19 pandemic,<sup>3</sup> and the paucity of knowledge in this area was detrimental early in the COVID-19 pandemic when N95 respirators were reserved for healthcare providers performing aerosol-generating procedures. Better understanding of transmission of infections in obstetric settings is necessary to protect healthcare workers and their patients.

Another critical issue in preparing for the next pandemic is ensuring ethical inclusion of pregnant women in the testing of therapeutics and vaccines. As is often the case, pregnant women were specifically excluded from clinical trials of COVID-19 vaccines, once again leaving them and their healthcare providers without data to guide decisions about vaccination. In fact, at the time of emergency use authorisation by the US Food and Drug Administration, developmental and reproductive toxicology studies (animal studies to study the effects of vaccines on pregnant animals) were not yet available for the Pfizer vaccine.<sup>14</sup> This was despite the fact that much work has been done since the 2009 H1N1 pandemic to address issues related to the inclusion of pregnant women in clinical trials, including their inclusion in vaccine clinical trials, and that immunisation

during pregnancy for influenza and pertussis has been included as standard of care for many years.<sup>15,16</sup> Recently a multidisciplinary working group developed a set of 22 recommendations to ensure that the interests of pregnant women were included when vaccines against future emerging infections are developed and deployed.<sup>17</sup> Addressing these recommendations will be necessary to ensure that pregnant women have earlier access to vaccines in future public health emergencies.

In preparation for the next pandemic, another need is to develop more expertise in emerging infectious diseases, epidemiology and public health among obstetric health-care providers. In recent years, obstetric practice has increasingly focused on using evidence-based medicine, requiring obstetric training to include how to critically interpret the literature underlying evidence-based medicine. However, training in obstetrics needs to include additional emphasis on epidemiology so that obstetric healthcare providers are able to rapidly interpret surveillance data regarding evolving trends in the spread of disease in their location and to review epidemiological data to understand issues such as severity of disease during pregnancy and safety and efficacy of vaccines. Professional organisations such as the American College of Obstetricians and Gynecologists and the Royal College of Obstetricians and Gynaecologists have played a key role in recent public health emergencies, but given the pace of evolving information, obstetric healthcare providers also need to be able to interpret the surveillance and research data on their own. In addition, future thought leaders in obstetrics will be needed to guide these professional organisations in the future. Finally, public health agencies need to recruit more obstetric healthcare providers who have in-depth knowledge of epidemiology, infectious disease and public health, but who also understand the issues involved in caring for pregnant women.

As we emerge from more than a year of this devastating pandemic, we have already seen many positive trends including increasing COVID-19 vaccination rates and rapidly declining COVID-19 case counts and deaths. We are looking forward to many positive developments in the coming months such as full reopening of schools and businesses. However, as we return to some degree of post-pandemic 'normal', we must not become complacent. Now is the time to plan for the next pandemic, and it is critical that pregnancy issues be included in these planning efforts.

### Disclosure of interests

The authors have no relevant conflicts of interests. Completed disclosure of interests form is available to view online as supporting information.

### Contribution to authorship

SAR and DJJ contributed equally to authoring this manuscript.

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