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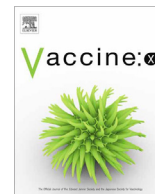
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SARS-CoV-2 variants and pregnant Women: A cause for Concern?

Joy Onyinyechi Chionuma^{a,*}, Helen Onyeaka^b, Osmond C. Ekwebelem^c,
Nnabueze Darlington Nnaji^c

^a College of Medicine, Lagos State University, Lagos, Nigeria

^b School of Chemical Engineering, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK

^c Faculty of Biological Sciences, University of Nigeria, Nsukka, Nigeria



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ABSTRACT

During pregnancy, women are at an increased risk of getting sick from respiratory viruses and when compared to non-pregnant women, pregnant women are more susceptible to severe illness from COVID-19. Owing to this fact and the emergence of a more infectious COVID-19 variants, pregnant women are currently classified as a vulnerable population, along with pediatric patients and older adults. While scientists are still learning more about the new variants, it is becoming clear that COVID-19 infected pregnant women are also at a real increased risk of poor pregnancy outcomes, as premature birth and babies born with lifelong health issues are possible if people become infected during pregnancy. Added to these facts, recommendation for COVID-19 has largely varied globally. The conspiracy-laden information on social media has led to pregnant women being hesitant about getting COVID-19 vaccine. Furthermore, as the transmissibility of COVID-19 is higher with this variant and the health system for maternal care in many countries regarded as “very bad” there is need to clearly highlight the impacts of the variants and for countries to speed up vaccination programme to reach all members of society.

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Commentary

Pregnant women make up a high risk group in the population who have to deal with the challenges and uncertainties associated with the pandemic caused by the novel SARS-CoV-2 coronaviruses in addition to that associated with the pregnant state.

Pregnancy is characterized by physiological changes in various systems of the woman's body which include the immune, respiratory and cardiovascular systems among others. [1] The alteration in function results from hormonal changes associated with pregnancy. The response to infections including COVID-19 depends on an active immune system for clearance of the infectious agent. [2] During pregnancy, there is an adaptation of the immune system aimed to protect the developing fetus. [3] This modulation of maternal immunity may affect the required clearance response to infections especially viruses. [4] There is alteration in normal inflammatory response to viral infections in pregnancy. The resultant effect of these changes may impact on the course, treatment and prevention of COVID-19 infection in affected women. [1] Also known is that the total lung capacity is reduced in pregnancy. There is associated impaired clearance of broncho-alveolar secretions. The

reduction in total lung capacity and impaired clearance of secretions may increase the woman's susceptibility to severe respiratory infections. [5] Pregnancy fulfils the Virchow's triad (hypercoagulation, increased thrombin formation and intravascular inflammation) which increases the risk for thromboembolic events and death. [6] COVID-19 infection is observed to be associated with increase risk of thromboembolic complications and thus, may further worsen the risk of thrombosis and severe disease in pregnancy [1].

The impact of COVID-19 on the pregnant women and their unborn babies is an area of interest globally. Surprisingly, this interest has tripled with the emergence of COVID-19 variants (Alpha B.1.1.7, Beta B.1.351, Gamma P.1, Delta B.1.617.2 and more recently Omicron). An in-depth understanding of the effect of the virus on the different stages of pregnancy and puerperium is essential for accurate diagnosis, treatment and prevention of the disease. Available data suggest pregnant women are not more prone to COVID-19 infection than their non-pregnant counterparts or the general population. [7] Most infected pregnant women are also not symptomatic. [8] There is however, evidence that those with symptoms are at an increased risk of severe disease compared to pregnant women without symptoms especially in the third trimester. [9] In a study conducted in the UK [10] suggest pregnant women who were older, obsessed non-whites, blacks or Hispanics, and those with preexisting hypertension, diabetes, asthma or

* Corresponding author.

E-mail address: joy.agbara@lasucom.edu.ng (J. Onyinyechi Chionuma).

cardiac disease were observed to be more at risk of severe disease.. There is increased risk of preterm births in symptomatic women which is largely indicated caesarean deliveries due to either maternal or fetal complication [11,12], and intensive care unit admissions and ventilation [13]. The report from a systematic and meta-analysis review of global data revealed that there were poorer outcomes of pregnancies during the pandemic with increased maternal mortality, still births, maternal depression and ruptured ectopic pregnancy [14]. The risk of vertical transmission of the virus from mother to fetus is said to be rare. Neonatal outcomes in babies delivered to COVID-19 positive mothers have been reassuring. [15].

COVID-19 vaccination has commenced in most countries in the world. While priority populations such as frontline workers, older age groups and people with pre-existing comorbidities are readily encouraged to be vaccinated, there was initially conflicting recommendations on vaccination of pregnant women and nursing mothers for achieving immunity against the virus. Most of the preliminary studies conducted on the available vaccines worldwide excluded these special cohort of the population leading to limited data. Although preliminary result from the analysis of the available data suggests that these vaccines (which are largely mRNAs) are safe in pregnancy and breastfeeding mothers, the data was considered insufficient to offer a generalized overview and recommendation or vaccination in pregnancy had thus varied. While the World Health Organization(WHO) initially advised that the available vaccines be offered only to pregnant women at high risk and those with comorbidities following due consultation with her physician, American College of Obstetricians and Gynaecologists (ACOG), Society of Maternal and Fetal Medicine (SMFM) and the Centers for Disease Control and Prevention (CDC) believe that the vaccine should not be withheld from women who choose to be vaccinated [16,17].

The past months have been characterized by emergence of more pathogenic variants of the SARS-CoV-2 virus. This development is of great concern globally as it may impact on vaccines efficacy and safety concerns about vaccination of pregnant women. Among those identified are the United Kingdom (UK) B117, California, Brazil, Indian, South African delta and omicron variants. The new variants were projected to be 30–50% more virulent than the wild or original type. The variants are said to result from mutations of spike proteins required for binding to receptors in infected cells, common among which is the K417N and E484K documented in the South Africa and Brazil variants [18]. Wei BW et.al, in their work on some of the variants of the SARS-CoV-2 virus, reported that they observed that with mutation of these spike proteins, there was enhancement in the receptor binding affinity of these proteins in host cells and a reduction in affinity for binding to neutralizing antibodies. This translates to a possibility of an increased risk of viral transmission and concomitant reduction in the ability of infected host to mount an appropriate immune response [18]. The newest variant, omicron, is said to be associated with less severe symptoms than the delta variant, but is highly infectious and can cause adverse maternal and neonatal outcomes especially in the unvaccinated. [19] The implication of these findings on the impact of the disease on the population and specifically pregnancy thus raises concern.

Recently, there has been reports which suggest that pregnant women were being infected by these new variants at a higher rates and that the severity, complications of disease and outcomes were worse than those documented for the primary or wild virus. The UK variant, Alpha B.1.1.7 has been documented to be more transmissible than the other variants and observed to survive for a longer period in those infected. This variant has been suggested to be responsible for increase in COVID-19 infections seen in UK and other countries, and the susceptibility to severe disease in

pregnant women. This claim however, is yet to be validated as preliminary analysis [18] did not show any evidence that the B.1.1.7 UK variant was particularly more infective or causes more severe disease in pregnant women specifically than other variants do during the 2nd wave. Perhaps another frightening phenomenon is the reported reduced response to currently available vaccines and antibody therapies observed with the Brazil and South African variants. [20].

During the first wave of the pandemic, one study reported that maternal death from COVID-19 infection was low at 0.19%, a figure which was comparable to 0.25% in the non-pregnant women. This was lower than maternal deaths from severe acute respiratory syndrome (SARS) 13% and Middle East respiratory syndrome (MERS) 40% [21]. In their work, Chiu-Lin et.al [22], observed that women who developed pneumonia had similar ICU admission compared with non-pregnant women. However, a higher rate of caesarean section occurred with COVID-19 infection [22]. They documented a case fatality rate of 1% in affected pregnant women This was much lower than 25% and 27% recorded with SARS and MERS respectively [21]. This pattern however, is observed to have changed during the 2nd and 3rd waves, with increasing risk of complications and requirement for hospitalization, intensive care management and even invasive oxygenations on account of acute severe respiratory failure observed in affected women. Outcomes of pregnancies complicated by COVID-19 were documented to be worse in low- and middle-income countries that already had poor health indices compared with high income countries in a review [23].

The Royal Brompton Hospital, London UK had reported that more pregnant or newly delivered women were infected during the 2nd wave of the pandemic possibly caused by the new variant. The course of the disease was said to be more severe with most of the women requiring intensive care along with extra corporeal membrane oxygenation (ECMO) on account of severe acute respiratory failure [23]. They [23] received more referrals (62 vs 34 in 2nd and 1st wave respectively) of mostly women about to deliver or newly delivered. Similar pattern of referrals and admissions was documented in another audit [24] comparing admissions, need for intensive care and invasive ventilation among pregnant and newly delivered women between 1st and 2nd waves of COVID-19 infection: The results showed that more women required admissions and ventilation in the 2nd wave compared to the first (13% vs 8.9%) and (14% vs 8%) respectively [24]. In the light of the frightening reports that the variants of the COVID-19 have been more aggressive in pregnant women, Brazil warned women to postpone pregnancy until the worst of the COVID-19 pandemic is contained. [25].

More experts are calling for vaccination of pregnant women to prevent these complications and provide a relief for the already stretched resources. Canada was one of the few countries that earlier had authorized the vaccination of pregnant women irrespective of the gestational age and also included are breastfeeding mothers. In the new recommendation by the Royal College of Obstetricians and Gynaecologists (RCOG) [9], UK, vaccination of pregnant women in all trimesters against COVID-19 has been strongly recommended. Among the available vaccines (Pfizer-BioNTech, Moderna, Oxford-AstraZeneca and Janssen), Pfizer and Moderna which are both mRNA vaccines are most preferred. [26] The vaccine is to be given in two doses just like the general population based on age and clinical risk. [9] Booster dose given after the 1st two doses are also being advocated. A study [27] show that pregnant women who received two doses and a booster (or three doses) of vaccine (combined data on Pfizer, Oxford-AstraZeneca and Moderna) are 88% less likely to be admitted to hospital with the omicron variant than those who have not been vaccinated. World Health Organization [28] in her interim recom-

mentation advocates for pregnant women to be vaccinated when the benefits outweigh the potential risks. Information on vaccines including its benefits and side-effects should be given to these women to assist them in making well informed choices. Breast-feeding mothers are not excluded from vaccination as evidence of the presence of antibodies against the COVID-19 virus in neonatal cord blood and breastmilk in women both women who were infected with the virus [29] and those who were vaccinate respectively. [30] There is some evidence that newborn can acquire some maternal antibodies through transplacental transfers which developed in response to vaccines given to mothers in pregnancy. [31].

Conclusion

The continued emergence and transmission of more virulent variants of the SARS-CoV-2 virus is said to be increasing the demands on healthcare resources with more deaths and ICU admissions. There is need for robust data on the safety of vaccines in pregnancy to assist in liberalization and uptake of vaccination against COVID-19 and subsequently increase herd immunity so as to prevent further mutations and their impact on vaccine effectiveness and outcomes of pregnancy.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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