Influenza immunisation in pregnancy is efficacious and safe, but questions remain

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Influenza immunisation in pregnancy is efficacious and safe, but questions remain

Pregnant women and infants are at high risk of severe influenza.[1,2] Since 2012, WHO has recommended influenza immunisation during pregnancy in any trimester and targets pregnant women as a high priority in annual influenza vaccination programmes. Although trivalent seasonal inactivated influenza vaccine (IIV) has shown efficacy against influenza infections in both pregnant women and infants,[3,4] the optimal timing of vaccination and effect on infant outcomes and safety remain controversial. The Bill & Melinda Gates Foundation funded three large randomised controlled trials in South Africa, Mali, and Nepal, which were done between 2011 and 2014, to increase the evidence base for the effects of maternal influenza immunisation.[5–7] The three trials showed that IIV was effective in preventing laboratory-confirmed influenza in pregnant women and in infants younger than 6 months. In the trial done in Nepal, maternal immunisation reduced the frequency of low birthweight infants by 15%.

In *The Lancet Respiratory Medicine*, Saad B Omer and colleagues[8] report the pooled analysis of these three trials, which included 10 002 pregnant women (5017 assigned to IIV and 4985 assigned to control) and 9800 liveborn infants (4910 livebirths from women who received IIV, and 4890 livebirths from women who received control) representing the largest dataset on women and newborns concerning influenza immunisation during pregnancy.

Several lessons can be learned from the results of Omer and colleagues' study. First, trivalent IIV administered at any time during pregnancy is effective in protecting pregnant women against PCR-confirmed influenza with a vaccine efficacy of 42% (95% CI 12–61) during pregnancy and 60% (36–75) in the postpartum period. Efficacy lasted until 6 months after vaccination (49%, 95% CI 29–63), which has implications for countries with year-round influenza virus circulation.

Second, although maternal immunisation appears to be effective in protecting infants up to 6 months of age (vaccine efficacy 35% [95% CI 19 to 47] on cumulative episodes of PCR-confirmed influenza), this protection is significant only up to 4 months of age (56% [28 to 73] before 2 months and 39% [11 to 58] between 2 and 4 months) but not between 4 and 6 months of age (19%, 95% CI –9 to 40) underscoring the progressive decline in maternal antibody titre. This finding has two implications. First, it supports the immunisation strategy based on the passive transplacental transfer of anti-influenza antibodies, which allows for effective protection of children who cannot be vaccinated against influenza, because influenza vaccines are not approved in children 0–6 months old. Second, it shows that there is a period between the ages of 4 months (disappearance of maternal antibodies) and 6 months (possible start of vaccination) when children are no longer protected, which should be considered in immunisation strategies based on recombinant or high dose or adjuvanted influenza vaccines during pregnancy. Moreover, in this pooled analysis, the vaccine was not effective against influenza B in infants (vaccine efficacy 13%, 95% CI –21 to 37). This finding could be explained by the frequent mismatch between vaccine and circulating influenza B strains in trivalent IIV. Research on the use of the quadrivalent IIV in pregnant women, which would probably improve the overall vaccine efficacy and the

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See **Articles** page 597

efficacy against influenza B, especially in children, is therefore warranted.

Third, the optimal timing of immunisation during pregnancy remains unclear. Whether the gestational stage of pregnancy affects responses to vaccines has not yet been extensively studied and conflicting results on seroconversion after seasonal influenza immunisation exist. In this study, there was no difference in efficacy against PCR-confirmed influenza in infants when the mothers were vaccinated before or after 29 weeks of gestation. Concerning the mothers, there was no efficacy against PCR-confirmed influenza when they were vaccinated before 29 weeks gestational age (vaccine efficacy 30%, 95% CI −2 to 52). As explained by the authors, this absence of efficacy in mothers vaccinated before 29 weeks gestational age is probably due to statistical considerations (lack of power), rather than a real difference in efficacy, as this would be inconsistent with studies that have shown a waning serological response to influenza immunisation as pregnancy progresses.[9]

Fourth, these results confirm that seasonal influenza vaccination during pregnancy is safe. In addition to studies that did not show an increased incidence of adverse events in mothers,[3] safety in fetuses and newborns was also shown when considering low birthweight, stillbirth, preterm birth, and small for gestational age. However, contrary to what was suggested in the trials in Bangladesh[4] and Nepal,[7] the pooled data show no positive association between maternal immunisation and low birthweight. These findings would be a strong argument for recommending generalised maternal influenza immunisation in resource-limited countries and suggest that further research considering the heterogeneity of the findings across countries is needed.

In conclusion, these pooled data confirm that influenza immunisation during pregnancy is safe and effective for protecting both women and infants. Further research is warranted to consider more immunogenic vaccines to fill the protection gap in infants between 4 and 6 months of age and improve understanding of the association between maternal immunisation and child weight and length at birth at 6 months of age.

PL has received personal fees and non-financial support from Pfizer and Sanofi Pasteur. VT has received personal fees from Alexion and grants and personal fees from Roche Diagnostics and is a member of the scientific board of Obseva. OL has received personal fees from Sanofi Pasteur, grants, personal fees, and non-financial support from Pfizer, Janssen, and Sanofi Pasteur-Merck Sharp & Dohme, and grants, and non-financial support from GlaxoSmithKline.

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Challenges in the interpretation and application of typical imaging features of COVID-19

Published Online
May 18, 2020
https://doi.org/10.1016/
S2213-2600(20)30233-2

The detailed report by Timothy Harkin and colleagues[1] of an unusual case of respiratory illness eventually diagnosed as COVID-19 raises issues about the role of imaging in the management of the disease. The causative virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can result in lethal pneumonia, so might chest imaging