The burden of vaccine-preventable diseases in pregnancy in low-resource settings

Substantial gains have been made globally for many of the Millennium Development Goals health targets, but progress in the improvement of health has been unequal with respect to the most vulnerable populations, and major discrepancies persist across regions and socioeconomic status.

Maternal immunisation is a unique opportunity to improve maternal and infant health. Vaccines are one of the most successful interventions to protect pregnant women and their fetuses and infants from diseases that cause substantial morbidity and mortality.[1,2] However, pregnant women have been systematically left out of vaccine research, which limits the availability of safety and efficacy data in pregnancy and, consequently, reduces the access of this special population to effective treatment.[2]

Data describing the burden and impact of infections in pregnancy, a period that is unique in presentation and outcome because of the altered physiology, is incomplete and poor.[3] A complete understanding of the epidemiology of common pathogens such as group B streptococcus, respiratory syncytial virus, *Bordetella pertussis,* and influenza virus, which can be prevented through maternal immunisation, is a priority.[3] Little is known about the prevalence of these infections in pregnancy, and accurate information about the illness incidence, its severity, and outcomes is often unavailable. Rigorous data collection and adequate clinical and epidemiological surveillance systems are needed for neonates, young infants, and pregnant women.[4] To what extent these pathogens contribute to maternal morbidity and mortality, and how much the infections determine fetal development and perinatal and infant survival, are unresolved questions. This information is especially needed from low-income countries, where the shortage of data is particularly manifest.[5,6]

Adequate information about the burden of vaccine-preventable diseases in pregnancy is needed for several reasons: to understand the need for and to advocate for such vaccines,[7] to monitor the success of their implementation, for vaccine optimisation, and to improve policy recommendations. Certainly, lessons can be learnt from the universal tetanus vaccine strategy, which did not necessitate broad burden information because the effect was clinically evident, or the case of the influenza vaccine, for which substantial evidence arose from several pandemics; in the 2009 influenza A (H1N1) epidemic, pregnant women were 7·2 times more likely than non-pregnant women to get admitted to hospital.[8] Rigorous and robust burden data will be indispensable for making the case for new vaccines against pathogens such as group B streptococcus, respiratory syncytial virus, and *B pertussis*, about which little is known. Additionally, the role of diseases that are highly prevalent in some areas, such as malaria and HIV, in modifying the burden and in generating adequate immune responses to vaccines during pregnancy is important to understand. Placental damage caused by these comorbidities, especially malaria, might have a role in reducing antibody transfer across the placenta.[9,10]

Collaborative work between research institutions in low and middle-income countries with long track records in conducting biomedical research at the highest quality standards will be instrumental to achieve this goal. These institutions offer the necessary research facilities and infrastructure to generate robust evidence from limited resource settings and to transform the data into interventions with direct benefits for the population.[11] Examples of collaborative work, leading to excellent data gathering and documentation of the burden in low-resource settings, illustrate their added value in disease burden determination and potential for translation into policies.[12] Likewise, partnerships that bring maternal and infant health experts together with the vaccine and immunisation communities are crucial.[3] Major gains can be obtained from the expertise of maternal health programmes in understanding the health problems affecting mothers and their infants, and the determinants of success and failure of interventions delivered through the antenatal care platform.

In the next decade, low-income and middle-income countries will be introducing new life-saving vaccines into their routine immunisation programmes. Maternal immunisation has a tremendous potential to improve the health of infants during their most vulnerable stages

of life. A comprehensive picture of the real burden of vaccine-preventable diseases in pregnancy is a necessary step for a successful maternal immunisation strategy and for the development of maternal immunisation policies in high-burden settings.

Azucena Bardají, Mark Steinhoff, Eusebio Macete, Teresa Aguado, Clara Menéndez

ISGlobal, Barcelona Centre for International Health Research, Hospital Clínic – Universitat de Barcelona, Barcelona 08036, Spain (AB, TA, CM); Centro de Investigação em Saúde da Manhiça, Maputo, Mozambique (EM); and Global Health Center, Cincinnati Children´s Hospital, Cincinnati, OH, USA (MS)
abardaji@clinic.ub.es

1   Bratton KN, Wardle MT, Orenstein WA, Omer SB. Maternal influenza immunization and birth outcomes of stillbirth and spontaneous abortion: a systematic review and meta-analysis. *Clin Infect Dis* 2015; **60:** e11–19.

2   Chu HY, Englund JA. Maternal immunization. *Clin Infect Dis* 2014; **59:** 560–68.

3   Sobanjo-Ter Meulen A, Abramson J, Mason E, et al. Path to impact: a report from the Bill and Melinda Gates Foundation convening on maternal immunization in resource-limited settings; Berlin—January 29–30, 2015. *Vaccine* 2015; **33:** 6388–95.

4   Shi T, McLean K, Campbell H, Nair H. Aetiological role of common respiratory viruses in acute lower respiratory infections in children under five years: a systematic review and meta-analysis. *J Glob Health* 2015; **5:** 010408.

5   Feikin DR, Ope MO, Aura B, et al. The population-based burden of influenza-associated hospitalization in rural western Kenya, 2007–2009. *Bull World Health Organ* 2012; **90:** 256–263A.

6   Madhi SA, et al., Influenza vaccination of pregnant women and protection of their infants. *N Engl J Med* 2014; **371:** 2340.

7   Steinhoff M, MacDonald N, Pfeifer D, Muglia LJ. Influenza vaccine in pregnancy: policy and research strategies. *Lancet* 2014; **383:** 1611–13.

8   Creanga AA, Johnson TF, Graitcer SB, et al. Severity of 2009 pandemic influenza A (H1N1) virus infection in pregnant women. *Obstet Gynecol* 2010; **115:** 717–726.

9   Moro L, Bardají A, Nhampossa T, et al. Malaria and HIV infection in Mozambican pregnant women are associated with reduced transfer of antimalarial antibodies to their newborns. *Infect Dis* 2015; **211:** 1004–14.

10   Naniche D, Serra-Casas E, Bardají A. Reduction of antimalarial antibodies by HIV infection is associated with increased risk of *Plasmodium falciparum* cord blood infection. *J Infect Dis* 2012; **205:** 568–77.

11   Whitworth J, Kokwaro G, Kynyanjui S, et al. Strengthening capacity for health research in Africa. *Lancet* 2008; **372:** 1590–93.

12   Kotloff KL, Nataro JP, Blackwelder WC, et al. Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. *Lancet* 2013; **382:** 209–22.