



ASYNCHRONOUS INFLUENZA VACCINATION AND ADVERSE MATERNAL-CHILD HEALTH OUTCOMES IN THE BRAZILIAN SEMIARID, 2013 TO 2018: THE INFLUEN-SA STUDY

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Introduction

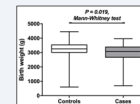
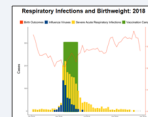
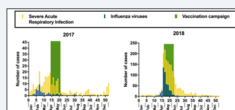
Complicated respiratory infections are well-recognized as an important cause of death in children and the elderly; however, the impact of respiratory infections on pregnant women and fetal development are understudied, particularly in regards to the burden of disease in low- and middle-income countries and adverse effects on birth outcomes, early childhood growth and neurodevelopment. Influenza syndrome and epidemics are associated with high morbidity and mortality, usually in the form of excess rates of pneumonia, hospitalizations associated with influenza, and deaths during epidemics.

Methods

We identified cases of severe acute respiratory infection cases registered in the state of Ceará, Brazil from 2013 to 2018 using the Notifiable Diseases Information System (SINAN-Influenza). A case of severe acute respiratory infection was defined as an individual with fever, even if referred, accompanied by cough, sore throat, dyspnea, O2 saturation <95% or respiratory discomfort, with onset of symptoms in the preceding seven days. In previous studies, multivariate regression analysis has shown that cough and fever are the best predictors of laboratory-confirmed influenza (11). From the SINAM-Influenza case report form we collected data on demographics, education, clinical signs and symptoms, epidemiological risk factors, vaccination status, treatments received, samples collected (nasopharyngeal secretions, bronchial aspirations, tissue or others) and RT-PCR laboratory results for influenza.

Results

During the period between 2013 and 2018, the amount of rainfall and number of cases of severe acute respiratory infections were significantly associated by Spearman correlation analysis. For 312 pairs of data points, the Spearman r was 0.2276 (95% CI: 0.1196 - 0.3303), with a P value (two-tailed) less than 0.0001. We see birth weights fall as peak SARI and influenza season approaches. Birth weights peaked in the first week of the year then fell to their lowest level by week 15, with a ~40 gram decline in average birth weight. Box and whisker plot describes how children born to mothers who had a severe acute respiratory infection had significantly lower birth weights than control children born to mothers who had no documentation of a severe acute respiratory infection.



Object

Earlier single center studies from the state capital Fortaleza, northeast of Brazil (population 2.6 million) showed seasonal influenza peaks 2 to 3 months earlier than in the South and Southeast of Brazil (10), with influenza strains in Fortaleza showing higher parity with Northern hemisphere strains. Despite these well-described epidemiological differences, all of Brazil is subject to the same vaccination schedule, hence pregnant women and their fetuses are inadequately protected against influenza in the semiarid region Brazil. Here we use data science approaches to test the hypothesis that Brazil's current national policy (targeting vaccination only during the months of April and May using the Southern Hemisphere vaccine) inadequately protects against the harmful maternal-fetal effects of influenza.

Conclusion

Mistiming of influenza vaccination in a populous region of Brazil—a middle-income country with high vaccine coverage—has adverse consequences for pregnancy and birth outcomes. Seasonal A/H1N1 and A/H3 viruses are associated with the rainy season. Seasonal influenza is associated with circannual periodicity in birth weight and gestational age at birth. The seasonality of the A/H1N1 and A/H3/seasonal influenza viruses in this region calls for a reassessment of Brazil's national influenza immunization strategy in order to prevent an intergenerational burden of disease.

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Recent models indicate seasonal influenza transmission in Brazil begins each year in the semiarid state of Ceará—before vaccine campaigns begin. To assess the extent and maternal-child health consequences of this misalignment, we examined the burden of severe acute respiratory infections (SARI) and influenza from 2013–2018. Of 3,297 SARI cases, 145 (4%) occurred in pregnancy. Vaccine coverage was >80%; however, campaigns often occurred during or after peak influenza activity. Mean birth weights and gestational age nadired 30–40 weeks following peak influenza and SARI activity. We identified 61 babies of mothers with gestational SARI; they weighed 10% less at birth ($P = 0.019$) and were more often premature (OR: 2.944 ; 95% CI: 1.100 – 7.879) relative to controls ($n=122$). Mistiming of influenza vaccination adversely impacts pregnancy and birth outcomes in Ceará, with critical implications for the first 1000

