Medically-attended respiratory illnesses amongst pregnant women in Brisbane, Australia


Abstract

There are limited community-based data on the burden of influenza and influenza-like illnesses during pregnancy to inform disease surveillance and control. We aimed to determine the incidence of medically-attended respiratory illnesses (MARI) in pregnant women and the proportion of women who are tested for respiratory pathogens at these visits. We conducted a nested retrospective cohort study of a non-random sample of women aged 18 years or over who had a live birth in maternity units in Brisbane, Queensland, from March 2012 to October 2014. The primary outcomes were self-reported doctor visits for MARI and laboratory investigations for respiratory pathogens. Descriptive analyses were performed. Among 1,202 participants, 222 (18.5%, 95% CI 16.3%–20.7%) self-reported MARI during their pregnancy. Of those with a MARI, 20.3% (45/222) self-reported a laboratory test was performed. We were able to confirm with health service providers that 46.7% (21/45) of tests were undertaken, responses from providers were not received for the remainder. Whilst one in five women in this population reported a MARI in pregnancy, only 3.7% (45/1,202) reported a clinical specimen had been arranged at the consultation and the ability to validate that self-report was problematic. As the focus on maternal immunisation increases, ascertainment of the aetiological agent causing MARI in this population will be required and efficient and reliable methods for obtaining these data at the community level need to be established.

Keywords: influenza, incidence, pregnancy, laboratory confirmation

Introduction

Influenza is a global public health issue affecting both human life and economies in our ever-increasingly interconnected world. Some groups in society are at higher risk of getting influenza; infants, the elderly, and people with certain chronic medical conditions. Pregnant women are particularly susceptible to serious consequences from influenza infection, particularly during pandemics. Reasons for this are linked to the number of changes that occur to a woman’s body during pregnancy, which may put pregnant women at higher risk of complications from influenza (e.g. changes to lung function, increased cardiac output, increased oxygen consumption, and impairments to the innate and adaptive immune response). Consequently, the World Health Organization recommends that pregnant women be given the highest priority for influenza vaccine in countries that are initiating or expanding a seasonal influenza program.

While data on hospitalisations for influenza during pregnancy are important, few studies have identified the incidence of medically-attended respiratory illnesses (MARI) during pregnancy at the primary health care level. Fewer still have reported the proportion of these women who have laboratory investigations performed to identify the aetiological agent. This lack of data limits the ability to accurately assess the burden of influenza during pregnancy and the likely effectiveness of interventions, such as influenza vaccination, aimed at preventing disease.

The objective of this study was to investigate the incidence of MARI during pregnancy in women in Brisbane, Queensland. A secondary objective was to identify the proportion of these women who had a laboratory test performed to identify an aetiological agent.

Methods

This study was part of an ongoing broader prospective cohort study (the FluMum Study) investigating the effectiveness of influenza vaccine during pregnancy in preventing laboratory confirmed influenza in infants across 6 Australian capital cities. Women in Brisbane maternity units within 6 participating hospitals (public and/or private) were approached for recruitment by trained research staff, prior to hospital discharge. The selected hospitals included the 2 large tertiary public maternity units in inner Brisbane and 4 units (3 private, 1 public) in suburbs more than 10 km from the city centre.
Women were eligible for inclusion if they were: aged 18 years or over at the time of written informed consent, willing and able to adhere to all protocol requirements, had sufficient verbal English to permit questionnaire completion, and had given birth to a live infant. Women were excluded if they planned to move overseas before the infant reached 6 months of age.

At enrolment, a detailed questionnaire was completed that collected data on self-reported influenza and pertussis vaccination, self-reported maternal medical and obstetric history and socio-demographic indicators. MARIs were determined by asking the participant whether, during her pregnancy, did she ever have a respiratory illness with symptoms like fever, chills, cough, aches and pains, that caused her to see a doctor. If yes, participants were asked whether a test was performed at the visit (nose, throat or blood specimen) but they were not specifically asked if the test was for influenza or other respiratory pathogens. If a test was reported, this was validated by contacting the relevant healthcare provider. Three to five attempts were made by telephone, email and/or facsimile to confirm the test and obtain a diagnosis. Similar attempts were made to confirm self-report of influenza vaccination during and in the 12 months prior to the pregnancy.

We analysed data collected on enrolment from the 1,202 women recruited at the Brisbane site for the years 2012–2014. The primary endpoint was participant-reported attendance at a medical practitioner for a respiratory illness during pregnancy. The secondary endpoints were a) the participant reported clinical specimens collected for laboratory investigations at these visits, and b) the healthcare provider confirmation of those laboratory investigations.

The study was approved by the Royal Brisbane and Women's Hospital Human Research Ethics Committee (HREC/12/QRBW/85), the Mater Mothers Human Research Ethics Committee (2012–16), and The University of Queensland Medical Research Ethics Committee (2012000180).

**Data analysis**

The primary analysis was the proportion of women who reported a MARI during the pregnancy and presented with its 95% confidence interval (CI). Secondary analyses were the proportion of women who reported a test done and of those, the proportion that were confirmed by the health service provider. Descriptive analyses were performed using Stata SE V12 (StataCorp, Texas, USA), including producing proportions and means with 95% CIs, and medians with interquartile ranges.

**Results**

**Participant characteristics**

Between March 2012 and October 2014, 1,713 women were screened and 1,202 (70.2%) were enrolled into the FluMum study in Brisbane. The mean age was 31.5 years (95% CI 31.3–31.8), 2% (23/1,196) identified as Aboriginal and/or Torres Strait Islander and 698 (58.1%) were recruited through public hospitals. More than half of the women for whom data were available (947/1,194, 79%) were in paid employment during their pregnancy; the majority of these being in full-time employment (568, 60%). Approximately half (515/1,035, 49%) had completed a university degree or higher and approximately 8% of women (93/1,195) had smoked during their pregnancy. Of the 1,196 women for whom data were available, 340 (28.4%) self-reported a pre-existing health condition such as heart disease, respiratory conditions, immunosuppressive conditions, cancer or diabetes, or a history of pneumonia requiring hospitalisation in the past 12 months.

**Medically attended respiratory illnesses during pregnancy**

Overall, 222 of 1,202 women (18.5%, 95% CI, 16.3–20.7) reported a respiratory illness that caused them to visit a health practitioner during their pregnancy. Of these, 39 women reported 2 episodes, eight reported 3 episodes, and two reported 4 episodes. Forty-five (20.3%, 95% CI 15.0–25.6) of the 222 women with a MARI reported that a clinical specimen was collected at the time (nose swab n=15, and/or throat swab n=10, and/or a blood test n=35). No tests were reported in episodes subsequent to the initial presentation. Seventy-two (21.2%) of the 340 women with a self-reported pre-existing health condition reported a MARI during their pregnancy and 22 (30.6%) of these women reported they had a test done.

Despite multiple attempts to secure information from providers, confirmation of the test request was obtained in 21 (46.7%) episodes. Of the confirmed episodes in which a blood test was taken (n=13), 7 providers reported the bloods were not tested for respiratory viruses. This information was not provided for the remaining 6 episodes.

**Discussion**

Influenza is an important cause of morbidity during pregnancy but the lack of systematic surveillance for disease during pregnancy at the community level limits the ability to reliably estimate the burden of disease and the effectiveness
of interventions, particularly vaccination. This study had identified that almost one in 5 women will present to a health care provider during their pregnancy for a respiratory illness. Collection of clinical specimens during the visit is reported but is difficult to confirm. This leads to doubts about the reliability of those reports with respect to testing for respiratory pathogens.

There are limited comparable data with which to compare the MARI incidence in our study given differences in study designs, study populations, and the case definitions used for respiratory illness and/or influenza-like illness. In a randomised controlled trial of inactivated influenza vaccine in HIV-negative pregnant women in South Africa that employed active surveillance for respiratory illnesses,10 17.2% (95% CI 14.9–19.6) of women in the control group reported an influenza-like illness in the period from the time of vaccination to up to 24 weeks post-birth of the infant; 65.2% (95% CI 62.2–68.1) reported having any respiratory illness.14 The incidence of illness during pregnancy only was not reported. In a cohort study that used administrative datasets, Lindsay et al11 reported 8% of 8,323 healthy (no underlying chronic conditions) pregnant and post-partum women in Washington, United States of America, experienced an influenza-like episode that resulted in health-care use (total person weeks of observation = 301,778).11

Blood was the predominant specimen women reported as being collected. This is unusual given there are few clinical indications for serology in acute, uncomplicated respiratory illness at the community level.12 For those who reported a MARI episode, we asked "thinking now about the 1st episode of respiratory illness during your pregnancy that caused you to see a doctor, can you tell me the tests done?" We then sought further information on who had done the test, the diagnosis, gestational age at the time of the test and the treating doctors contact details. We also sought similar information for each subsequent MARI. Whilst we made reference to episodes of respiratory illness, it is possible that there may have been some misunderstanding or uncertainty for participants such that the information provided may not have directly related to specimens collected at a MARI presentation that were specifically for a respiratory diagnosis. This is partially supported by the number of reports from providers stating bloods were not tested for respiratory viruses.

The difficulties encountered in confirming the test with the health care provider is problematic for influenza surveillance and control in this population and for estimating the effectiveness of maternal influenza and/or pertussis vaccination during pregnancy at the population level, particu-

larly in non-pandemic periods. With the exception of hospitalised cases, there are limited population-based data on both the burden of influenza and the effectiveness of influenza vaccination during pregnancy. This lack of data is recognised as a contributing factor towards determining the real risk of influenza associated with pregnancy.13, 14 Such data would enhance public health policy recommendations and facilitate discussions between health care providers and pregnant women on the risks of influenza and why the vaccine is recommended in pregnancy.

This study has some limitations that necessitate caution in interpreting the findings. The FluMum study9 population is derived from English speaking women giving birth to a live infant in metropolitan maternity units and may not be representative of non-English speaking women and those with high risk pregnancies and adverse pregnancy outcomes, nor of women in rural and remote areas where access to health care and the viability of specimen collection, transport, and processing for respiratory illnesses may differ. While the proportion of Aboriginal and Torres Strait Islander women enrolled in the study was low (1.7%), it does approximate the 2011 estimated resident Indigenous population of the greater Brisbane region (2.0%).15 Further possible selection and measurement biases that may be affecting our findings are potential differences between vaccinated and unvaccinated women that would influence their decision to participate in the study and their recall of MARI. Finally, as data were collected retrospectively, misclassification due to poor recall may have occurred resulting in an over- or under-estimation of MARI frequency and of testing for MARI.

MARI during pregnancy is not uncommon yet the investigation of these illnesses to determine an aetiological agent is infrequent. While laboratory investigation of all community-based MARI during pregnancy may be unwarranted clinically, sentinel surveillance of these events in sites representative of Australian pregnant women would be a useful contribution to further understanding the risk and outcomes of influenza during pregnancy. Such surveillance would provide more comprehensive estimates of influenza vaccine effectiveness to inform public health policy.

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Author contributions

PFA analysed the data and wrote the first draft of the manuscript. RMA, SBL and KFO are chief investigators on the overall FluMum study. RMA and KFO devised this current paper & KFO prepared the final draft. LMCh, SLW, JZ, DA & CS all contributed substantially to study implementation and the preparation of data for analysis. All authors had full access to the study data and contributed to and approved the final manuscript.

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