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Epidemiology and Clinical Outcomes of Hospitalizations for Acute Respiratory or Febrile Illness and Laboratory-Confirmed Influenza Among Pregnant Women During Six Influenza Seasons, 2010–2016

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Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Abstract

Background.—Pregnant women are at increased risk of seasonal influenza hospitalizations, but data about the epidemiology of severe influenza among pregnant women remain largely limited to pandemics.

Methods.—To describe the epidemiology of hospitalizations for acute respiratory infection or febrile illness (ARFI) and influenza-associated ARFI among pregnant women, administrative and electronic health record data were analyzed from retrospective cohorts of pregnant women hospitalized with ARFI who had testing for influenza viruses by reverse-transcription polymerase chain reaction (RT-PCR) in Australia, Canada, Israel, and the United States during 2010–2016.

Results.—Of 18 048 ARFI-coded hospitalizations, 1064 (6%) included RT-PCR testing for influenza viruses, 614 (58%) of which were influenza positive. Of 614 influenza-positive ARFI hospitalizations, 35% were in women with low socioeconomic status, 20% with underlying conditions, and 67% in their third trimesters. The median length of influenza-positive hospitalizations was 2 days (interquartile range, 1–4), 18% (95% confidence interval [CI], 15%–21%) resulted in delivery, 10% (95% CI, 8%–12%) included a pneumonia diagnosis, 5% (95% CI, 3%–6%) required intensive care, 2% (95% CI, 1%–3%) included a sepsis diagnosis, and <1% (95% CI, 0%–1%) resulted in respiratory failure.

Conclusions.—Our findings characterize seasonal influenza hospitalizations among pregnant women and can inform assessments of the public health and economic impact of seasonal influenza on pregnant women.

Keywords

hospitalization; influenza; pregnant

Acute respiratory illness in hospitalized adults may be due to a variety of respiratory pathogens [1, 2]. Influenza virus infections are one of the few vaccine-preventable etiologies of acute viral respiratory illnesses. Pregnant women are at increased risk of hospitalizations with influenza compared with both nonpregnant women of childbearing age and the general population [3–6]. However, data remain scarce on clinical outcomes of severe influenza among pregnant women and are largely limited to influenza pandemics [6–9]. The few published studies describing pregnant women with severe seasonal influenza include relatively small numbers of women from the United States, and most report data from epidemics before 2009, when the A/H1N1pdm09 virus was not in circulation and molecular diagnostic testing for influenza was infrequently used [10–12]. In addition, few data are available on whether illness severity varies by seasonal influenza virus type or subtype in this population [13]. Information is needed on the epidemiology and clinical outcomes of hospitalized pregnant women with influenza during sequential contemporary seasonal influenza epidemics [14], both to inform assessments of the public health and economic impact of seasonal influenza on pregnant women and to contribute to the global evidence base for recommending seasonal influenza vaccination during pregnancy.

During 2017, a large retrospective cohort study was conducted at sites in Australia, Canada, Israel, and the United States with the primary objective of estimating influenza vaccine effectiveness (VE) against influenza-associated hospitalizations among pregnant women hospitalized with acute respiratory or febrile illness (ARFI). The VE study was nested within the larger cohort and used the test-negative design to compare rates of influenza vaccination among women hospitalized and tested for influenza who were influenza positive versus negative [15, 16]. We used data from this large international cohort to describe characteristics, illness, and pregnancy outcomes at the time of hospital discharge of pregnant women hospitalized with ARFI and tested for influenza by reverse-transcription polymerase chain reaction (RT-PCR) during the influenza season. We also examined the frequency of selected illness severity indicators by influenza virus type and subtype and by pregnancy trimester at hospital admission.

METHODS

Study Network and Data Sources

The Pregnancy Influenza Vaccine Effectiveness Network (PREVENT) is an international collaboration between the US Centers for Disease Control and Prevention, Abt Associates, and study sites in Australia, Canada (2 sites), Israel, and the United States [15, 16]. Study sites were chosen based on their ability to meet several inclusion criteria related to the underlying characteristics of the source population, clinical and laboratory practices, and availability of high-quality regional respiratory virus surveillance and electronic medical records (EMR) data. In Australia, the Department of Health Western Australia used 4 primary data sources covering approximately 34 000 annual births to establish a population-based cohort: the Midwives Notification System, a perinatal data collection that includes data on >99% of births in Western Australia; the Hospital Morbidity Data System; the Western Australia Antenatal Influenza Vaccination Database; and pathology testing data from the state reference laboratory. In Alberta, Canada, the Ministry of Health compiled data covering 53 500 annual births from the Canadian Institute for Health Information's Discharge Abstract Database (DAD), the provincial vaccination registry, and the provincial Vital Statistics Registry. In Ontario, Canada, provincial databases included the DAD covering approximately 147 000 annual births, as well as the Ontario Health Insurance Plan and Ontario Drug Benefits databases, all housed at ICES, a nonprofit research organization. These datasets were linked using unique encoded identifiers and analyzed at ICES. In Israel, investigators from Clalit Health Services, the largest integrated healthcare fund in the country that covers approximately 93 000 annual births, extracted data from its EMR system. In the United States, Kaiser Permanente (Northwest, Northern California, and Washington), an integrated healthcare delivery system, also collected data from its EMR. The 3 Kaiser Permanente sites include approximately 56 000 live births annually.

Data were collected during 6 Northern Hemisphere influenza seasons from 2010 to 2016 in Canada, Israel, and the United States and during 4 Southern Hemisphere influenza seasons from 2012 to 2015 in Australia. The influenza season was defined at each site using regional surveillance and/or clinical laboratory records and site-specific standardized criteria for the start and end of influenza virus circulation.

Cohort Identification, Case Ascertainment, and Data Assembly

Each study site used local data to identify a retrospective cohort of all pregnant women aged 18 through 50 years with pregnancies that overlapped at least in part with the local influenza season from 2010 to 2016. Women with pregnancies that ended in a live birth or stillbirth of at least 20 weeks of gestation were eligible for inclusion. An ARFI hospitalization was defined as a hospitalization record with a discharge diagnosis code for ARFI using country-relevant *International Classification of Diseases, Ninth Revision* (ICD-9) or ICD-10 codes based on codes used in previous studies of medically attended influenza [17–19] plus codes for febrile-only, nonrespiratory, or sepsis-like presentations that may be associated with severe influenza [20, 21] (see Supplemental Methods Data Dictionary). The ARFI hospitalizations were included in the main analysis if they included clinical testing of at least 1 respiratory specimen by RT-PCR for influenza viruses with a testing date within 3 days of admission to hospital. Women could contribute multiple ARFI hospitalizations with RT-PCR testing for influenza viruses to the analysis if their hospitalizations were more than 14 days apart.

Data were extracted from administrative databases or EMRs using standardized variable definitions across study sites (see Supplemental Methods Data Dictionary) [16]. Data collected included the following: demographic and maternal characteristics; medical and pregnancy history; influenza immunization status during the current season; indicators of illness severity during the hospitalization including length of hospitalization, diagnoses of pneumonia, sepsis, or respiratory failure, intensive care unit (ICU) admission, extracorporeal membrane oxygenation requirement, and whether the hospitalization resulted in death; pregnancy outcomes during the index hospitalization including whether the hospitalization resulted in continued pregnancy, delivery at term or preterm, or stillbirth; and results of clinical testing for influenza by RT-PCR. Pregnancy outcomes were identified using ICD-9 or ICD-10 codes. When severity indicator or pregnancy outcome data were not available in EMRs or administrative databases, a limited medical record abstraction was performed by study sites that had direct access to medical records. Influenza immunization status data were obtained from immunization registries (Australia and Alberta) or health plan EMRs (Israel, Ontario, and the United States), as previously described [15]. Influenza A/H3N2 subtyping information was not available from sites in the United States and Israel. Data on influenza antiviral treatment were not included in this analysis because data were not available from most sites.

Low socioeconomic status (SES) was defined using the following: site-specific criteria based on a woman’s neighborhood of residence for Western Australia, Canada, and Israel: lowest quintile of relative advantage and disadvantage based on the Socioeconomic Index for Area (SEIFA) for Western Australia; lowest income quintile for Alberta and Ontario, Canada; and lowest income tertile for Israel. Low SES was defined by Medicaid status as of the hospital admission date for Kaiser Permanente sites in the United States.

Among ARFI hospitalizations with influenza testing by RT-PCR, influenza-positive hospitalizations were defined as those with at least 1 respiratory specimen that tested positive for influenza by RT-PCR and influenza-negative hospitalizations as those with no specimens positive for influenza. Pregnancy trimesters were defined according to the

definitions provided by the American College of Obstetrics and Gynecology: first trimester as 0 through 13 weeks of gestation, second trimester as 14 through 27 weeks of gestation, and third trimester as 28 weeks or greater [22]. Stillbirth was defined as a fetus delivered without signs of life at ≥20 weeks of gestation. Respiratory failure, pneumonia, and sepsis were defined by discharge diagnosis codes (see Supplemental Methods, Data Dictionary).

No personal identifiers were shared with other study sites, Abt Associates, or US Centers for Disease Control and Prevention. Sites provided aggregate data tables that included summary statistics rather than individual-level data sets, and low cell counts (ie, <6 participants per variable) were suppressed to meet site-specific data suppression requirements.

Statistical Analysis

The unit of analysis for the main analysis was ARFI hospitalizations with influenza testing by RT-PCR. Frequencies of baseline characteristics, illness severity indicators, and pregnancy outcomes during ARFI hospitalizations were first compared between study sites to assess for differences between sites. We then aggregated all data and described baseline characteristics, illness severity indicators, and pregnancy outcomes using frequencies with 95% confidence intervals (CIs) for categorical values and medians with interquartile ranges (IQRs) for continuous variables. Where cell counts were <6, only 95% CIs are presented to meet site-specific privacy requirements. Selected baseline characteristics of women with influenza-positive and negative ARFI hospitalizations were compared for descriptive purposes by bivariate analysis using χ^2 tests; a P value less than .05 was considered significant. Ninety-five percent CIs were calculated using the mid-P exact method.

Among pregnant women with laboratory-confirmed influenza, proportions of women with pneumonia, ICU admission, and respiratory failure were also described by influenza type and subtype and by pregnancy trimester at hospital admission.

To assess for potential testing bias, we conducted a supplemental analysis to compare characteristics of ARFI hospitalizations in which respiratory specimens were tested for influenza by RT-PCR to ARFI hospitalizations without testing. We used logistic regression to evaluate associations between RT-PCR testing and site, season, season timing (early, peak, late), age (<35 years, ≥35 years), parity, underlying chronic medical conditions, trimester at index hospitalization, influenza vaccination status, whether the hospitalization resulted in delivery, and whether the hospital stay included admission to the ICU. Statistical analyses were performed using OpenEpi Version 3.01 [23].

Ethical Review

The study protocol and procedures were reviewed and approved by Institutional Review Boards (IRBs) (or their equivalents) at each study site and by Abt Associates. The IRB of the US Centers for Disease Control and Prevention relied on the review of the Abt Associates IRB. Each site received a waiver of informed consent for all participants.

RESULTS

Baseline Characteristics of Study Acute Respiratory Infection or Febrile Illness Hospitalizations With Influenza Testing by Reverse-Transcription Polymerase Chain Reaction

Among 18 048 ARFI-coded hospitalizations of pregnant women across 6 influenza seasons (2010–2016), 1064 (6%) included a RT-PCR test and were included in the main analysis (henceforth referred to as study ARFI hospitalizations); 27 women contributed 2 or more study ARFI hospitalizations to the analysis. Overall, 226 of 1064 (21%) study ARFI hospitalizations were in women who were 35–50 years of age and 322 of 989 (33%) in women who had low SES (Table 1). Twenty-five percent of all study ARFI hospitalizations (268 of 1064) occurred in women who had 1 or more underlying chronic medical conditions; the most common condition was asthma (108 of 1064, 10%). The majority of study ARFI hospitalizations occurred in women who were in their third trimester of pregnancy (688 of 1064, 65%). Influenza vaccine uptake was low among women with study ARFI hospitalizations (169 of 1061, 16%), but influenza vaccine uptake varied substantially by site, ranging from a low of 6% in Australia to a high of 50% in the United States.

Baseline Characteristics of Influenza-Positive Study Acute Respiratory Infection or Febrile Illness Hospitalizations

Of the 1064 study ARFI hospitalizations with testing for influenza viruses by RT-PCR, 614 (58%) were influenza positive, including 507 (83%) positive for influenza A viruses (205 [40%] unsubtyped, 177 [35%] influenza A/H1N1, and 125 [25%] influenza A/H3N2) and 110 (18%) for influenza B viruses. The proportion of influenza-positive study ARFI hospitalizations varied by site from 45% at US sites to 64% at Israel sites, and by season, from 52% during 2011–2012 to 61% during 2012–2013.

Among influenza-positive study ARFI hospitalizations, 19% (119 of 614) were among women aged 35–50 years and 35% (197 of 571) were in women with low SES. Eighty percent (493 of 614) of influenza-positive study ARFI hospitalizations were in women who were previously healthy (ie, did not have an underlying medical condition). There was no significant difference in the frequencies of older maternal age, low SES, or tobacco smoking between influenza-positive and -negative hospitalizations. However, underlying medical conditions were less frequent among women with influenza-positive study ARFI hospitalizations than influenza-negative hospitalizations (20% vs 33%, $P < .01$).

Illness Severity Indicators and Pregnancy Outcomes of Influenza-Positive Study Acute Respiratory Infection or Febrile Illness Hospitalizations

Overall, the median length of influenza-positive study ARFI hospitalizations was 2 days (IQR, 1–4), with a median of 2 days (IQR, 1–3) among hospitalizations that did not result in deliveries and 3 days (IQR, 2–6) among delivery hospitalizations (Table 2).

Ten percent (95% CI, 8%–12%) of influenza-positive study ARFI hospitalizations included a diagnosis of pneumonia, 5% (95% CI, 3%–6%) resulted in an ICU admission, 2% (95% CI, 1%–3%) included a diagnosis of sepsis, and <1% (counts and percentages suppressed

to meet site-specific data suppression rules) resulted in respiratory failure. None of the 614 influenza-positive study ARFI hospitalizations included treatment with extracorporeal membrane oxygenation or resulted in maternal death.

The majority of influenza-positive study ARFI hospitalizations (82%; 95% CI, 79–85) resulted in a continued pregnancy at the end of the hospital stay (Table 2). Of the 110 influenza-positive hospitalizations that resulted in deliveries during the hospital stay, 101 (92%) were singleton gestation deliveries of live births with available outcome data. Of these 101 deliveries, based on 95% CIs, 0%–6% were stillbirths and 94%–100% were live births, 66%–83% of which were term deliveries and 25%–34% were preterm deliveries [1].

Among the 412 influenza-positive study ARFI hospitalizations with complete influenza type and subtype information, a larger percentage of influenza A/H1N1-positive study ARFI hospitalizations was associated with pneumonia than influenza A/H3N2 (19% vs 8%, $P < .01$) and influenza B hospitalizations (19% vs 5%, $P < .01$), although proportions that resulted in respiratory failure or ICU admission were similar by influenza type and subtype (Figure 1). The proportions of influenza-positive study ARFI hospitalizations that included pneumonia, respiratory failure, or ICU admission were also similar by trimester (Figure 2).

Hospitalization Characteristics Associated With Reverse-Transcription Polymerase Chain Reaction Testing for Influenza

Among all ARFI hospitalizations, testing prevalence varied by site and season (Supplemental Table 1). Hospitalizations were more likely to include RT-PCR testing for influenza if they occurred during the peak of influenza season and if they occurred in women who were in their second trimester, multiparous, or required intensive care (Supplemental Table 1). Hospitalizations were less likely to include RT-PCR testing if they occurred in women who were vaccinated against influenza or delivered during the hospitalization. Among all ARFI hospitalizations regardless of testing, 80% occurred in women who were unvaccinated against influenza.

DISCUSSION

We describe the clinical epidemiology of more than 1000 hospitalizations among pregnant women admitted with ARFI who had RT-PCR testing for influenza viruses during 6 influenza seasons in 4 high-income countries. Laboratory-confirmed influenza was associated with more than half of these hospitalizations. Among influenza-positive hospitalizations, 80% occurred in previously healthy women without underlying medical conditions and 1 in 3 occurred among women of low SES. Of influenza-positive hospitalizations that resulted in deliveries, 25%–34% were preterm deliveries, substantially higher than the estimated baseline preterm birth prevalence of 9% among the general population of pregnant women in high-income countries [24]. A higher proportion of influenza A/H1N1 hospitalizations were associated with a diagnosis of pneumonia compared with influenza A/H3N2 and influenza B hospitalizations, consistent with findings from studies in the general adult population [20]. The large majority of study ARFI hospitalizations and influenza-positive study ARFI hospitalizations occurred in women who had not received the influenza vaccine.

In our multinational study of 614 hospitalizations of pregnant women with laboratory-confirmed seasonal influenza, 5% of hospitalizations required intensive care, <1% resulted in respiratory failure, the median length of stay was 2 days, and there were no maternal deaths. We avoided direct statistical comparisons of illness severity indicators between influenza-positive and negative study ARFI hospitalizations because of differences in baseline characteristics such as underlying medical conditions and possible differences in reasons for hospitalization between the groups that might influence illness severity. Our findings for influenza-positive hospitalizations are similar to those of a smaller case series describing pregnant women hospitalized with laboratory-confirmed influenza in the United States (4% intensive care, 2% respiratory failure, median length of stay of 2 days) [21]. However, a smaller proportion of hospitalizations in our study required intensive care or resulted in respiratory failure than those in another case series of 5270 adults hospitalized with laboratory-confirmed influenza in the United States (15% intensive care, 9% respiratory failure), a large proportion of whom were elderly or had underlying medical conditions [20]. These data suggest that although clinical outcomes of pregnant women hospitalized with seasonal influenza may be less severe than for some other high-risk groups, the burden of critical illness in pregnant women is not trivial. Differences in the proportions of hospitalizations that included ICU admission and respiratory failure between pregnant women in our study and other high-risk groups in earlier studies may also reflect a lower threshold for hospitalization of pregnant women, as opposed to a true difference in severity [6].

Although influenza vaccination is recommended for pregnant women in all the countries in this study [25–27], 84% of all study ARFI hospitalizations occurred among unvaccinated women, and 80% of all ARFI hospitalizations regardless of influenza testing occurred in unvaccinated women. Even in the United States, where vaccine uptake was highest among study sites, half of study ARFI hospitalizations occurred in unvaccinated women, consistent with influenza vaccination coverage estimates for pregnant women in the United States during the study years. The World Health Organization includes pregnant women as a target group for influenza vaccination [28], and multiple studies, including randomized-controlled trials and a previously published analysis from the PREVENT dataset, have demonstrated that inactivated influenza vaccine is moderately effective at preventing influenza in pregnant women [15, 17, 22, 29] and provides protection to infants of vaccinated mothers during the first few months of life [22, 29–34].

In our study, influenza virus testing occurred at the discretion of the clinician or according to hospital protocols, and a supplemental analysis of all ARFI hospitalizations documented that testing frequency varied among the 5 sites. Only 6% of all study ARFI hospitalizations included testing for influenza viruses, which means that there were likely many influenza-associated hospitalizations among the >18 000 identified study ARFI hospitalizations that went undetected. Over half (58%) of study ARFI hospitalizations that included testing were influenza virus positive. This positivity rate is higher than in 2 previous studies of patients of all ages hospitalized with respiratory illness during influenza season in temperate climates, where influenza positivity rates ranged from 20% to 32% [35, 36]. However, these studies involved systematic active surveillance throughout the influenza season. In contrast, in our

study, the bulk of influenza testing occurred during the peak of the influenza season [15], which likely explains some of the higher positivity rate for influenza.

Strengths of our study include the large size of the cohort that allowed examination of relatively rare indicators of illness severity, use of laboratory confirmation with highly sensitive and specific influenza RT-PCR testing to identify hospitalizations associated with influenza, and a multisite, multicountry approach that supports the generalizability of results to similar settings. However, several limitations should be considered when interpreting our study findings. First, only 6% of ARFI hospitalizations during the influenza season included RT-PCR testing for influenza, and a supplemental analysis of all ARFI hospitalizations showed that hospitalizations with selected characteristics were more likely to include influenza testing. Future studies examining the clinical epidemiology of influenza among hospitalized pregnant women should include systematic testing for influenza. Second, the infrequent influenza testing reduced our ability to evaluate rare clinical outcomes (eg, extracorporeal membrane oxygenation requirement). Third, the analysis relied on discharge diagnosis codes to identify ARFI hospitalizations, and it is possible that some ARFI hospitalizations with influenza testing may have been missed if they did not include one of the codes used in this study. Fourth, the analysis was not designed to directly compare characteristics of pregnant women hospitalized with ARFI or influenza-associated ARFI with the general population of pregnant women and did not include a comparison group drawn from the general population. Finally, we pooled data from 4 high-income countries in a population with relatively high insurance coverage or publicly funded healthcare. Therefore, our results may not be generalizable to women in low- and middle-income countries where clinical course and outcomes of influenza during pregnancy may be different.

CONCLUSIONS

In our study, the majority of pregnant women hospitalized and tested for influenza were previously healthy, without underlying medical conditions, and were in the third trimester of pregnancy. Although severe outcomes such as ICU admission, respiratory failure, and death were less frequent compared with what has been reported in some other high-risk groups, the impact of hospitalization itself during pregnancy should not be underestimated. Multiple studies confirm that influenza vaccines effectively prevent influenza in pregnant women and provide protection to their infants in the first months of life. Thus, a large proportion of influenza-positive hospitalizations among pregnant women are likely vaccine preventable, yet more than 80% of ARFI hospitalizations in our study occurred among women who had not received the current season’s influenza vaccine. Our findings characterize seasonal influenza hospitalizations among pregnant women and can be used to inform assessments of the public health and economic impact of seasonal influenza on pregnant women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Potential conflicts of interest.

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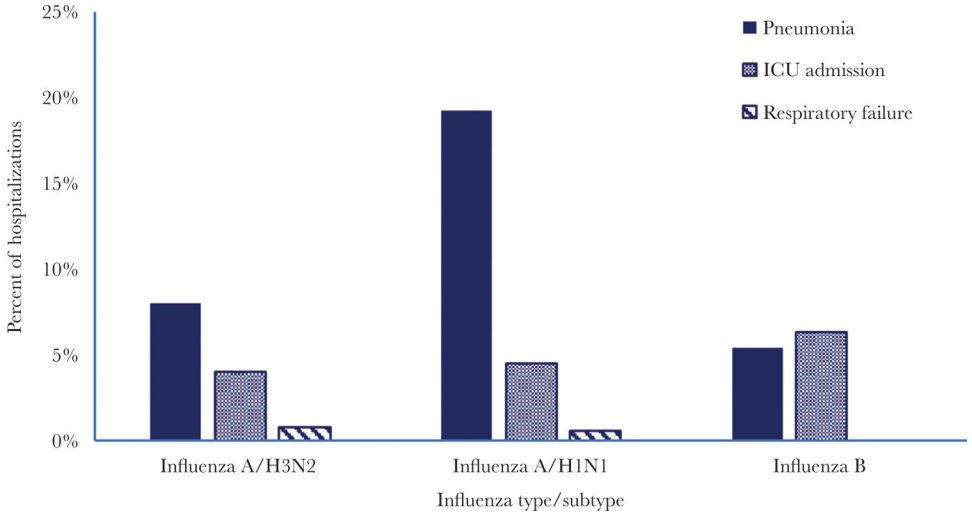

Figure 1.

Percentage of influenza-positive hospitalizations for acute respiratory illness or fever with pneumonia, intensive care unit (ICU) admission, or respiratory failure by influenza type/subtype (only includes influenza-positive hospitalizations for which complete influenza type and subtype information were available), Pregnancy Influenza Vaccine Effectiveness Network (PREVENT) sites 2010–2016 (N = 412). Respiratory failure was defined as presence of at least 1 of the following discharge diagnosis codes: *International Classification of Diseases, Ninth Revision* (ICD-9) codes 518.81, 799.1 or ICD-10-AM/ICD-10-CA codes J96.0, J96.00-J96.02, J96.2, J96.90-J96.92, R09.2. The proportion of influenza A/H1N1-positive acute respiratory infection or febrile illness hospitalizations that was associated with pneumonia was statistically significantly higher than the proportions of influenza A/H3N2 and influenza B hospitalizations. The proportions of hospitalizations associated with ICU admission and respiratory failure did not differ by influenza type/subtype.

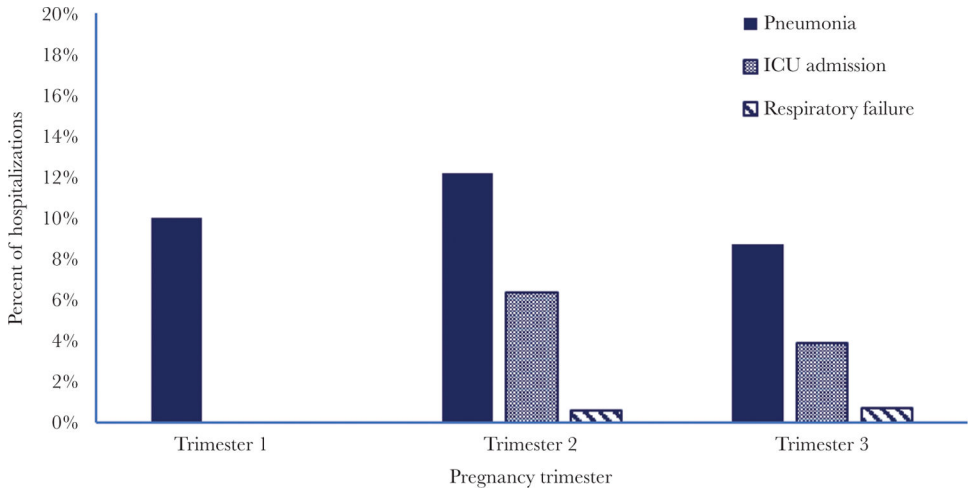

Figure 2.

Percentage of influenza-positive hospitalizations for acute respiratory illness or fever with pneumonia, intensive care unit (ICU) admission, or respiratory failure by pregnancy trimester (there was no statistically significant difference in the proportions of influenza-positive acute respiratory infection or febrile illness hospitalizations that were associated with pneumonia, respiratory failure, or ICU admission by trimester), Pregnancy Influenza Vaccine Effectiveness Network (PREVENT) sites, 2010–2016 (N = 614). Respiratory failure was defined as presence of at least 1 of the following discharge diagnosis codes: *International Classification of Diseases, Ninth Revision* (ICD-9) codes 518.81, 799.1 or ICD-10-AM/ICD-10-CA codes J96.0, J96.00-J96.02, J96.2, J96.90-J96.92, R09.2.

Table 1.

Characteristics of Pregnant Women Hospitalized With Acute Respiratory or Febrile Illness and Tested for Influenza by RT-PCR, PREVENT Network Sites, N = 1064

Characteristics	Influenza Positive		Influenza Negative		Total	
	n = 614		n = 450		N = 1064	
	n	%	n	%	n	%
Age						
18–34 years	495/614	81%	343/450	76%	838/1064	79%
35–50 years	119/614	19%	107/450	24%	226/1064	21%
Low SES[a]	197/571	35%	125/418	30%	322/989	33%
Current smoker[b]	51/322	16%	55/271	20%	106/593	18%
Obesity based on prepregnancy BMI[c]	43/202	21%	40/152	26%	83/354	23%
Previously healthy	493/614	80%	303/450	67%	796/1064	75%
>1 pre-existing medical conditions[d]	121/614	20%	147/450	33%	268/1064	25%
Asthma	51/614	8%	57/450	13%	108/1064	10%
Blood disorder	35/614	6%	42/450	9%	395/1064	37%
Metabolic disease	32/614	5%	30/450	7%	62/1064	6%
Chronic lung disease (other than asthma)	15/614	2%	47/450	10%	62/1064	6%
Heart disease	11/614	2%	20/450	4%	31/1064	3%
Diabetes	8/614	1%	8/450	2%	16/1064	2%
Immune disorder	6/614	1%	7/450	2%	13/1064	1%
Parity						
0	183/602	30%	128/444	29%	311/1046	30%
1	207/602	35%	155/444	35%	362/1046	35%
>2	212/602	35%	161/444	36%	373/1046	36%
Multiple gestation	24/612	4%	25/448	6%	49/1060	5%
Trimester[e]						
First	30/614	5%	35/450	8%	65/1064	6%
Second	172/614	28%	139/450	31%	311/1064	29%
Third	412/615	67%	276/450	61%	688/1064	65%

Characteristics	Influenza Positive		Influenza Negative		Total	
	n = 614		n = 450		N = 1064	
	n	%	n	%	n	%
Site						
Australia	56/614	9%	57/450	13%	113/1064	11%
Canada (Alberta)	102/614	17%	84/450	19%	186/1064	17%
Canada (Ontario)	212/614	35%	127/450	28%	339/1064	32%
Israel	176/614	29%	99/450	22%	275/1064	26%
USA	68/614	11%	83/450	18%	151/1064	14%
Influenza Season[f]						
2010–2011	94/614	15%	67/450	15%	161/1064	15%
2011–2012	69/614	11%	63/450	14%	132/1064	12%
2012–2013	117/614	19%	74/450	16%	191/1064	18%
2013–2014	117/614	19%	80/450	18%	197/1064	19%
2014–2015	90/614	15%	78/450	17%	168/1064	16%
2015–2016	127/614	21%	88/450	20%	215/1064	20%
Received current season's influenza vaccine	75/611	12%	94/450	21%	169/1061	16%
Virus Type/Subtype						
A	507/614	83%	–	–	507/1064	48%
Unsubtyped	205/507	40%	–	–	205/1064	19%
A/H1N1	177/507	35%	–	–	177/1064	17%
A/H3N2	125/507	25%	–	–	125/1064	12%
B	110/614	18%	–	–	110/1064	10%

Abbreviations: BMI, body mass index; PREVENT, Pregnancy Influenza Vaccine Effectiveness Network; RT-PCR, reverse-transcription polymerase chain reaction; SES, socioeconomic status.

[a] Site-specific definitions.

[b] Data on smoking status were not available from the Canadian (Ontario) site.

[c] Data on obesity status were not available from the Canadian sites.

[d] Data suppressed for renal disease, neurologic disease, and cancer to meet site requirements because 1 or more cell counts were <6.

[e] First trimester defined as 0 through 13 6/7 weeks of gestation; second trimester 14 0/7 through 27 6/7 weeks of gestation; and third trimester 28 0/7 weeks or greater.

[f] In Australia, seasons correspond to the second year in the stated range. For example, the 2012 season in Australia corresponds to the 2011–2012 season at other sites.

Table 2.

Illness Severity and Pregnancy Outcomes of Pregnant Women Hospitalized With Acute Respiratory or Febrile Illness and Tested for Influenza by RT-PCR, PREVENT Network Sites, N = 1064

	Influenza Positive		Influenza Negative		Total	
	n = 614		n = 450		N = 1064	
Severity Indicator	**N**	**% (95% CI) or IQR**	**n**	**% (95% CI) or IQR**	**n**	**% (95% CI) or IQR**
Illness Severity Indicators[a]						
Hospital length of stay (days, median [IQR])	2	1–4	3	2–5	3	2–4
Nondelivery hospitalizations[b] (days, median [IQR])	2	1–3	3	1–4	2	1–3
Delivery hospitalizations[b] (days, median [IQR])	3	2–6	5	3–8	3	2–4
Pneumonia	60/614	10 (8–12)	139/450	31 (27–35)	199/1064	19 (16–21)
Intensive care unit admission	27/592	5 (3–6)	43/433	10 (7–13)	70/1025	7 (5–8)
Intensive care unit length of stay (days, median [IQR])	2	1–4	3	1–4	2	1–4
Sepsis	10/614	2 (1–3)	24/450	5 (4–8)	34/1064	3 (2–4)
Respiratory failure	†	(0–1)	17/450	4 (2–6)	†	(1–3)
Pregnancy Outcomes During Hospitalization						
Continued pregnancy	504/614	82 (79–85)	339/450	75 (71–79)	843/1064	79 (77–82)
Delivered	110/614	18 (15–21)	111/450	25 (21–29)	221/1064	21 (18–23)
Live birth[c]	101/103	98 (94–100)	98/101	97 (92–99)	199/204	98 (95–99)
Term live birth	†	(66–83)	†	(52–71)	†	(62–75)
Preterm live birth	†	(25–34)	†	(29–48)	†	(25–38)
Stillbirth[c,d]	†	(0–6)	†	(1–8)	†	(1–5)

Abbreviations: CI, confidence interval; IQR, interquartile range; PREVENT, Pregnancy Influenza Vaccine Effectiveness Network; RT-PCR, reverse-transcription polymerase chain reaction.

[a] There were no hospitalizations that resulted in death. One hospitalization in a woman who was influenza negative included an extracorporeal membranous oxygenation requirement.

[b] A nondelivery hospitalization was defined as a case hospitalization during which no delivery of a live or stillborn infant took place, whereas a delivery hospitalization was defined as one in which a deliery did take place.

[c] Data on delivery outcomes only available for singleton gestations.

[d] Stillbirth defined as fetus delivered without signs of life at ≥20 weeks gestation.

† Counts suppressed to meet site requirements because 1 or more cell counts for the variable were <6.