OBSTETRICS

Severity of influenza and noninfluenza acute respiratory illness among pregnant women, 2010–2012

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OBJECTIVE: The objective of the study was to identify characteristics of influenza illness contrasted with noninfluenza acute respiratory illness (ARI) in pregnant women.

STUDY DESIGN: ARI among pregnant women was identified through daily surveillance during 2 influenza seasons (2010-2012). Within 8 days of illness onset, nasopharyngeal swabs were collected, and an interview was conducted for symptoms and other characteristics. A follow-up telephone interview was conducted 1-2 weeks later, and medical records were extracted. Severity of illness was evaluated by self-assessment of 12 illness symptoms, subjective ratings of overall impairment, highest reported temperature, illness duration, and medical utilization.

RESULTS: Of 292 pregnant women with ARI, 100 tested positive for influenza viruses. Women with influenza illnesses reported higher symptom severity than those with noninfluenza ARI (median score, 18 vs 16 of 36; $P < .05$) and were more likely to report severe subjective feverishness (18% vs 5%; $P < .001$), myalgia (28% vs 14%; $P < .005$), cough (46% vs 30%; $P < .01$), and chills (25% vs 13%; $P < .01$). More influenza illnesses were associated with fever greater than 38.9°C (20% vs 5%; $P < .001$) and higher subjective impairment (mean score, 5.9 vs 4.8; $P < .001$). Differences in overall symptom severity, fever, cough, chills, early health care–seeking behavior, and impairment remained significant in multivariate models after adjusting for study site, season, age, vaccination status, and number of days since illness onset.

CONCLUSION: Influenza had a greater negative impact on pregnant women than noninfluenza ARIs, as indicated by symptom severity and greater likelihood of elevated temperature. These results highlight the importance of preventing and treating influenza illnesses in pregnant women.

Key words: acute respiratory illness, illness severity, influenza, influenza vaccine, pregnancy

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Pregnant women are at greater risk of hospitalization and serious complications from influenza virus illness than nonpregnant women.[1] Women in their third trimester[2,3] and those with comorbid conditions[4,5] are especially vulnerable to hospitalization. Little is known about the clinical characteristics and severity of laboratory-confirmed influenza illness among nonhospitalized pregnant women or how influenza illness differs from noninfluenza acute respiratory illness (ARI) in pregnant women.

In a previous study, we examined the relationship between vaccination status and influenza positivity.[6] This study examined symptom severity and

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duration of laboratory-confirmed influenza illness among pregnant women compared with noninfluenza ARI during 2 influenza seasons. Although the number of confirmed influenza cases was limited, we conducted exploratory analyses to assess whether influenza illness severity was higher among the women with comorbid conditions or in their third trimester and whether vaccination with a seasonal influenza vaccine was associated with less severe illness among those women with vaccine failure.

Materials and Methods

Recruitment and eligibility

The study methodology[7] and recruitment of the study participants have been described in detail previously.[6] Eligible participants were Kaiser Permanente members who made at least 1 prenatal visit in the Portland, OR (Kaiser Permanente Northwest), or San Francisco, CA, metropolitan areas (Kaiser Permanente Northern California) during the study period, had an expected delivery date after Nov. 15, 2010, and were at least 16 years of age for Kaiser Permanente Northwest or at least 18 years of age for Kaiser Permanente Northern California. The study instruments, procedures, and written consent documents were approved by the institutional review boards at both sites.

Surveillance

The influenza season was defined by the regional/state health department and the Centers for Disease Control and Prevention influenza surveillance data. Thresholds for the beginning and end of the season were defined a priori at each site. During both study seasons, we identified potential ARIs using daily surveillance of electronic medical records (EMRs) for medically attended acute respiratory illness using *International Classification of Diseases*, ninth revision (ICD-9) codes 460-466, 480-488, and 490-491.

The women were contacted by telephone, screened for eligibility, and asked to provide written consent for study participation. Inclusion criteria included enrollment in the health plan for the study season and completion of the enrollment interview.

During the first season, weekly Internet- or telephone-based surveillance monitored the occurrence of nonmedically attended ARI among a prospective cohort of participants at both sites.[7] First-season participants were encouraged to contact staff directly if they became ill; those who did not complete a weekly surveillance report received a reminder e-mail or telephone call to assess current ARI status. For both seasons, nasopharyngeal swab specimens were collected at the homes of women with self-reported cough and fever, feverishness, or chills within 8 days of illness onset.

Participant characteristics

Sociodemographic characteristics were assessed during an enrollment interview. Health status prior to illness was assessed with 3 measures. First, overall self-rated health was assessed using a standard question on current health (poor, fair, good, very good, or excellent) on the enrollment interview.[8] Second, we identified high-risk comorbidities associated with an increased risk of influenza complications by the presence, during 2 or more visits over 1 year prior to conception, of the following conditions: cancer, diabetes mellitus, neurological disorders, chronic pulmonary disease, chronic cardiac disease, immunosuppressive disorders, and chronic renal disease.[9] Third, pregnancy complications, from conception to start of surveillance, were identified from EMRs, using ICD-9 codes related to adverse pregnancy outcomes. All ICD-9 codes are available upon request. Obesity was defined by body mass index, calculated using self-reported prepregnancy weight and height.

Illness characteristics

Illness characteristics were assessed during an illness episode interview at specimen collection and again at a follow-up telephone contact approximately 8 days later. In the first season, participants who were still ill were called again approximately 14 days after the original illness interview.

We assessed 5 indicators of illness severity. First, participants rated the presence and severity of 12 symptoms, using a 4 point scale (0, absent; 1, mild; 2, moderate; and 3, severe). Ten participants who initially reported a cough at the screening interview described a cough as absent during their illness interview; in these instances, responses were recoded as 1 (mild). All symptom ratings were summed to form a 12 symptom severity score, ranging from 1 (a single mild symptom) to 36 (all symptoms severe), as described previously.[10]

Second, participants assessed the overall subjective severity of illness from 0 (normal health) to 9 (worst possible health) and the extent of illness impairment from 0 (able to perform usual activities) to 9 (unable to do so), as described previously.[11]

Third, we examined febrile severity using the subjective severity of feverishness (mild, moderate, or severe) and the highest temperature recorded using any of the following: EMR vital signs (if the illness was medically attended), self-reported highest temperature at either the illness interview or 8−14 day follow-up interview(s), or measured temperature by visiting study staff. Severe fever was defined as 38.9°C, which represents the threshold for assessing teratogenic exposure in the fetus.

Fourth, we calculated illness duration by subtracting the illness onset date (determined from screening or illness episode interview) from the date of symptom resolution as indicated in follow-up interviews. Seventy-eight women (53 noninfluenza and 25 influenza) who either were unable to recall a recovery date or had not yet recovered when the follow-up interview occurred were excluded from our analysis of illness duration.

Fifth, we examined medical utilization and self-care as indicated by the following: (1) any or more than 1 medical visit, (2) any illness-associated hospitalization, (3) seeking health care within 2 days of onset, and (4) use of antibiotic, over-the-counter (OTC), or antiviral medications associated with the ARI as reflected in an EMR-confirmed prescription or self-reported use of a medication during the illness.