Incidence and Clinical Features of Respiratory Syncytial Virus Infections in a Population-Based Surveillance Site in the Nile Delta Region

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Background. Most reports about respiratory syncytial virus (RSV) in developing countries rely on sentinel surveillance, from which population incidence is difficult to infer. We used the proportion of RSV infections from population-based surveillance with data from a healthcare utilization survey to produce estimates of RSV incidence in Damanhour district, Egypt.

Methods. We conducted population-based surveillance in 3 hospitals (2009–2012) and 3 outpatient clinics (2011–2012) in Damanhour district. Nasopharyngeal and oropharyngeal specimens from hospitalized patients with acute respiratory illness and outpatients with influenza-like illness were tested by real-time reverse transcriptase polymerase chain reaction for RSV. We also conducted a healthcare utilization survey in 2011–2012 to determine the proportion of individuals who sought care for respiratory illness.

Results. Among 5342 hospitalized patients and 771 outpatients, 12% and 5% tested positive for RSV, respectively. The incidence of RSV-associated hospitalization and outpatient visits was estimated at 24 and 608 (per 100 000 person-years), respectively. Children aged <1 year experienced the highest incidence of RSV-associated hospitalizations (1745/100 000 person-years).

Conclusions. This study demonstrates the utility of combining a healthcare utilization survey and population-based surveillance data to estimate disease incidence. Estimating incidence and outcomes of RSV disease is critical to establish the burden of RSV in Egypt.

Keywords. respiratory syncytial virus; incidence; population-based surveillance.

Respiratory syncytial virus (RSV) is a common cause of bronchiolitis, pneumonia, and other acute respiratory illnesses among children. The incidence of RSV disease varies widely across geographic regions, with the majority of RSV-associated mortality occurring in developing countries [1, 2]. In Egypt, infectious diseases account for 8% of both deaths and age-adjusted disability-adjusted life-years (DALYs) [3]; among infectious diseases, respiratory infections are the primary contributor to both deaths and DALYs lost.

The majority of published RSV incidence estimates from developing countries have been derived from hospital-based sentinel surveillance. However, studies of healthcare utilization patterns in developing countries have shown that a significant proportion of patients with moderate and severe respiratory illness are treated in outpatient departments and private clinics, and a small but significant proportion do not seek care outside the home [4]. Data from developed countries indicate that RSV contributes to a significant proportion of outpatient visits for respiratory illness [5, 6]. Estimating the total incidence of RSV infections of

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all severities is therefore difficult from hospital-based surveillance alone.

This study estimates the incidence of laboratory-confirmed RSV disease in Damanhour district, Egypt, during 3 years of population-based surveillance for acute respiratory infection in hospital and outpatient settings. Using healthcare utilization survey (HUS) data to adjust for the proportion of the population treated for respiratory disease in various settings, we developed a comprehensive estimate of RSV incidence in Damanhour.

MATERIALS AND METHODS

Hospital Surveillance

The Egyptian Ministry of Health and Population, the US Centers for Disease Control and Prevention (CDC), and the US Naval Medical Research Unit No. 3 (NAMRU-3) established a population-based surveillance for infectious diseases at the International Emerging Infections Program (IEIP) field site in Damanhour in May 2009. Surveillance was initiated in 3 government referral hospitals based on the results of a 2008 HUS, which indicated that >90% of persons hospitalized for an acute respiratory infection (ARI) in Damanhour were admitted to government facilities. The catchment area of the IEIP is defined by the administrative boundaries of Damanhour district, and the study population includes all persons residing within these boundaries. The 3 hospitals began enrolling patients with ARI in May and June 2009.

Hospital admission logbooks were reviewed daily to identify patients admitted with suspected ARI. Patients of any age were eligible if they presented with ≥1 sign of acute infection, (documented fever ≥38°C or history of subjective fever with acute illness, abnormal white blood cell count, or hypothermia <35°C) and ≥1 respiratory symptom. Children aged <5 years meeting the Integrated Management of Childhood Illness definitions for moderate or severe pneumonia [7] were also enrolled. Infants aged <31 days were excluded because study physicians were not comfortable performing nasopharyngeal swabs on ill patients in this age group. Patients who were residents of a district other than Damanhour or had been enrolled previously at a different hospital were also excluded. After consent was obtained from the patient or their legal guardian, study personnel conducted patient interviews and chart reviews to complete questionnaires detailing disease history with the patients' current illness. No follow-up information was collected from patients or their families after discharge or transfer.

Outpatient Clinic Surveillance

Surveillance for influenza-like illness (ILI) was initiated in March 2011 at the outpatient departments of the 3 government hospitals. All outpatients were screened for ILI, and informed consent was provided to every 10th eligible patient for study enrollment. The case definition for ILI was fever (documented temperature ≥38°C at time of presentation or subjective history of fever with this illness) and cough. The same exclusion criteria used for hospitalized patients was applied.

Laboratory Testing

Nasopharyngeal (NP) and oropharyngeal (OP) specimens were collected from all enrolled patients. Specimens were placed in 2 mL of liquid viral transport media and stored at 4°C for ≤2 days prior to testing. Microbiologists at the IEIP laboratory in Damanhour tested all specimens by real-time reverse transcription polymerase chain reaction (rRT-PCR) assays for RSV, influenza A and B, adenovirus, human parainfluenza viruses 1–3, and human metapneumovirus, using CDC-developed assays [8]. Every third specimen collected from outpatients was tested for RSV due to limited availability of laboratory resources, maintaining the proportion of patients enrolled in surveillance by age group. An aliquot of each specimen was stored in liquid nitrogen and shipped weekly to the NAMRU-3 reference laboratory in Cairo for confirmation.

Healthcare Utilization Survey

To estimate the proportion of patients with respiratory illness who sought care either at a hospital or at other healthcare settings, a healthcare utilization survey (HUS) was conducted in urban and rural areas of Damanhour district during 20 December 2011 to 18 March 2012. Urban households were selected via simple random sampling of geographic coordinates. In rural areas, a 2-stage cluster sampling design was used. The targeted sample size was 3000 households (2000 rural and 1000 urban). In the first stage, 30 clusters were selected from 57 distinct rural villages using probability proportional to size; some villages contained multiple clusters. Sixty-seven geographic points were randomly selected within each cluster, and the closest residential structure was identified at each geographic point. In structures containing multiple residential units, a single residential unit was selected using a random number table. All household members were enrolled.

At each household identified, the head of household or primary caregiver was asked to identify household members who had lower respiratory infection (LRI) during the past year or an episode of ILI during the past 30 days. Similar to HUS surveys conducted at other IEIP sites [4], an episode of LRI was defined as self-reported cough and dyspnea for ≥2 days or diagnosis of pneumonia by a healthcare worker. An episode of ILI was defined as fever and cough. Participants with a history of LRI or ILI were asked if they sought medical care for themselves or their children for the respiratory infection, where they received medical care, and if they were hospitalized. Hospitalization was defined as admission to an inpatient ward for ≥24 hours.

Statistical Analysis

Descriptive Data

Hospitalized patients with ARI enrolled during 23 June 2009–22 June 2012 and outpatients with ILI enrolled during 1 May 2011–30 April 2012 were included for analysis. The number and proportion of patients positive for RSV was stratified by age group (1–11 months, 1–4 years, 5–19 years, 20–49 years, 50–64 years, and ≥65 years) and residence (rural vs urban). We calculated 95% confidence intervals (CIs) for the proportion of RSV infection in hospitalized patients and outpatients using the Wilson score method without continuity correction and Wald and Clopper-Pearson CIs, respectively. It was assumed that patients who were eligible, but who did not participate, and enrolled patients without NP/OP specimens had the same proportion of RSV infection as patients from whom a specimen was obtained, adjusted for sex, age, and residence strata.

We compared characteristics of RSV-positive hospitalized patients <5 years of age to those who were RSV-negative using the Pearson χ^2 test, including the presence of underlying medical conditions known to increase the risk of respiratory infections or risk of severe complications. Characteristics of RSV-positive and RSV-negative outpatients were not compared due to small numbers.

To evaluate the potential impact of climate on the epidemiology of RSV infections, the association between average weekly temperatures and relative humidity with RSV seasonality was evaluated graphically. Meteorological data was obtained from El Nouzha Airport weather station in Alexandria, 64 km north of Damanhour.

RSV Hospitalization Rates

To obtain denominators for incidence calculations, we used the 2006 census for Damanhour district as obtained from Egypt's Central Agency for Public Mobilization and Statistics and applied the estimated national population growth rate of 11.6%.

To calculate numerators, we first extrapolated the HUS results to the entire district using sample weights and accounting for the complex survey design. The proportion of respondents by sex and age were adjusted using population census data. HUS respondents reporting an episode of respiratory illness (either LRI or ILI) were categorized into hospitalized patients and outpatients. To produce estimates of RSV hospitalizations for Damanhour district adjusted for patterns of healthcare utilization, we divided the number of RSV-positive hospitalized patients with ARI by the proportion of HUS respondents who reported hospitalization at surveillance facilities. We then used this adjusted estimate to calculate the incidence rate per 100 000 population in each sex/age stratum.

RSV Outpatient Clinic Visit Rates

The RSV incidence for outpatients with ILI was calculated differently due to the low proportion of HUS respondents who reported receiving outpatient care at surveillance facilities. RSV incidence was calculated by applying the proportion of RSV-positive outpatients to the proportion of HUS respondents who reported either LRI or ILI that did not result in hospitalization. HUS respondents were asked to recall episodes of ILI during the past 30 days, and the proportion of respondents reporting these episodes was adjusted to an annual total based on the proportion of eligible outpatients with ILI presenting to surveillance sites per month. The proportion of patients with RSV infection in the outpatient clinics was applied to all nonhospitalized HUS respondents reporting an episode of respiratory illness.

We used SPSS software (version 19.0) to calculate 95% CIs for the incidence of hospitalized and outpatient RSV infections. For hospitalized patients, we used the variance of the proportion of RSV positivity in each age group. For outpatients, 95% CIs were calculated by applying the upper and lower bounds applying the upper and lower bounds of the proportion of HUS respondents receiving outpatient care to the upper and lower bounds of the proportion of outpatients testing positive for RSV in each age group.

Human Subjects Review

The surveillance and HUS protocols were approved by institutional review boards at NAMRU-3 in Cairo, Egypt, and the CDC, and by the Egyptian Ministry of Health and Population. Verbal informed consent was provided by patients or their legal guardians before study enrollment; a separate verbal informed consent was provided for future use of specimens. Verbal informed consent was provided by the head of household prior to administering the HUS questionnaire. The study protocols (numbers 802 and 906) were approved by the NAMRU-3 Institutional Review Board in compliance with all applicable federal regulations governing the protection of human subjects.

RESULTS

Hospital Surveillance

From 23 June 2009–22 June 2012, 9903 hospitalized patients with possible ARI were screened. Of these, 5342 (54%) patients met the case definition and 4993 (93%) consented to enrollment. An NP/OP swab was collected from 4683 (94%) enrolled patients. A total of 518 (11%) specimens were positive for RSV by rRT-PCR. The proportion of RSV infection detected was

$$\text{RSV Incidence} = \left[\left(\frac{\text{No. RSV positive hospitalized patients/Proportion of patients hospitalized at surveillance facilities}}{\text{Population Estimate}} \right) \times 100000 \right]$$

Table 1. Hospitalized Patients With Respiratory Syncytial Virus Infection—Damanhour District, Egypt (1 April 2009–31 March 2012)

Age Group	Rural No. Samples Tested	Rural Patients Positive for RSV, % (95% CI)		Urban No. Samples Tested	Urban Patients Positive for RSV, % (95% CI)		Total No. Samples Tested	Total Patients Positive for RSV, % (95% CI)	
1 mo–4 y	1333	28	(26–31)	345	27	(24–32)	1678	28	(26–30)
1–11 mo	617	45	(41–49)	166	45	(38–52)	783	51	(42–48)
1–4 y	716	13	(11–16)	179	12	(8–17)	895	15	(11–16)
5–19 y	420	2	(4–8)	144	5	(2–9)	564	3	(2–4)
20–49 y	917	1	(0–3)	347	1	(0–4)	1264	1	(0–2)
≥50 y	755	1	(0–2)	422	2	(1–4)	1177	2	(0–2)
Total	3425	11	(10–12)	1258	9	(8–11)	4683	11	(10–12)

Abbreviations: CI, confidence interval; RSV, respiratory syncytial virus.

highest in children aged 1–11 months in both rural and urban patients (45% each), followed by children aged 1–4 years (13% in rural patients and 12% in urban patients) (Table 1).

Outpatient Clinic Surveillance

From 1 May 2011 to 30 April 2012, 19 856 patients presented to surveillance outpatient clinics, of whom 7107 (36%) met the ILI case definition. Every tenth eligible outpatient was enrolled (859 [12%]). NP and OP swabs were collected from 771 (90%) patients; 269 (36%) NP/OP specimens were then selected for RSV testing. The highest proportion of RSV-positive specimens occurred among children aged 1–11 months (16%) in the rural areas and among adults aged 20–49 years (11%) in the urban areas (Table 2), although the differences among age groups were not statistically significant.

RSV-Positive vs RSV-Negative Hospitalized Patients

Among children aged <5 years hospitalized for suspected ARI, those testing positive for RSV differed significantly from RSV-negative hospitalized patients with respect to clinical presentation, intensive care admission, and infection with another respiratory virus (Table 3). Other respiratory viruses were more frequently identified among the children testing negative for RSV (P < .0001; Table 3).

Few hospitalized patients aged <5 years had underlying medical conditions such as congenital heart disease and asthma. Such conditions were also less common among children with RSV infection than RSV-negative children (1% vs 5%, P < .0001; Table 3). Among hospitalized patients aged >5 years, the proportion of RSV-positive and RSV-negative patients reporting a chronic disease was similar (22% vs 19%, P = .61). RSV-positive patients >5 years were significantly more likely to report an underlying condition than RSV-positive patients aged <5 years (P < .0001). One RSV-associated death was captured among hospitalized patients with ARI, occurring in an adult female aged ≥65 years with no underlying conditions.

RSV Seasonality

There were 3 distinct peaks of RSV activity in hospitalized patients: April 2010, January 2011, and December 2011–January

Table 2. Outpatients With Respiratory Syncytial Virus Infection–-Damanhour District, Egypt (1 May 2011–30 April 2012)

Age Group	Rural No. Samples Tested	Rural Patients Positive for RSV, % (95% CI)		Urban No. Samples Tested	Urban Patients Positive for RSV, % (95% CI)		Total No. Samples Tested	Total Patients Positive for RSV, % (95% CI)	
1 mo–4 y	94	5	(2–12)	32	3	(0–16)	126	5	(1–9)
1–11 mo	31	16	(3–29)	8	0	(0–32)	39	4	(2–10)
1–4 y	63	0	(0–6)	24	4	(1–20)	87	1	(.01–6)
5–19 y	46	2	(0.05–12)	22	5	(0.01–23)	68	3	(.03–7)
20–49 y	39	8	(2–21)	9	11	(0–48)	48	8	(1–16)
≥50 y	17	0	(0–19)	4	0	(0–60)	21	0	(0–16)
Total	196	5	(2–9)	67	5	(0–13)	263	5	(2–7)

Abbreviations: CI, confidence interval; RSV, respiratory syncytial virus.

Table 3. Characteristics of Respiratory Syncytial Virus (RSV)–Positive vs RSV-Negative Hospitalized Patients Aged <5 years—Damanhour District, Egypt

Characteristic	RSV-Positive (n = 467)		RSV-Negative (n = 1211)		OR (95% CI)
	No.	%	No.	%	
Female	199	(43)	494	(41)	1.1 (.9–1.3)
Age					
1–11 mo	350	(75)	433	(36)	5.4 (4.3–6.9)
1–4 y	117	(25)	778	(64)	0.2 (.2–.3)
Rural residence	417	(90)	1040	(86)	1.4 (1.0–1.9)
Underlying condition reported[a]	7	(1)	65	(5)	0.3 (.1–0.6)
Intensive care unit required	11	(2)	76	(6)	0.4 (.2–.7)
Ventilation required	0	(0)	0	(0)	NA
Influenza positive	11	(2)	570	(14)	0.1 (.06–.3)
Adenovirus positive	33	(7)	185	(15)	0.9 (.7–1.2)
Human metapneumovirus positive	11	(2)	172	(14)	0.5 (.4–.7)
Human parainfluenza virus positive	8	(2)	104	(9)	0.1 (.1–.2)
Symptomology					
Cough	465	(100)	1168	(96)	9.6 (2.3–39.8)
Abnormal breath sounds	425	(91)	864	(72)	4.0 (3.0–5.5)
Tachypnea[b]	354	(76)	528	(44)	3.7 (3.0–5.0)
Dyspnea	313	(67)	421	(35)	3.2 (2.6–3.9)
Sputum	258	(55)	616	(51)	1.3 (1.1–1.6)
Documented fever ≥38°C	247	(53)	795	(66)	0.7 (.6–.8)
Grunting	243	(52)	332	(28)	2.7 (2.2–3.3)
Nasal flaring	227	(47)	310	(26)	2.8 (2.3–3.4)
Indrawing	148	(32)	812	(67)	3.9 (3.2–5.0)
Low O_2 saturation[c]	60	(47)	67	(53)	2.3 (1.7–3.3)
Lethargy	10	(2)	26	(2)	0.8 (.4–1.6)
Convulsions	9	(2)	81	(7)	0.2 (.1–.5)
Stridor	8	(2)	10	(1)	2.1 (1.0–4.5)

Abbreviations: CI, confidence interval; NA, not applicable; OR, odds ratio; RSV, respiratory syncytial virus.

[a] Underlying conditions included asthma, cardiomyopathy, congenital heart disease, diabetes, heart disease, cerebral palsy, chronic obstructive pulmonary disorder, epilepsy, hepatitis, liver failure, mitral stenosis, myopathy, renal failure, lupus, and tuberculosis.

[b] Tachypnea was defined as >50 breaths per minute for infants aged 31 days to <1 year, and >40 breaths/minute for children aged 1 year to <5 years.

[c] Low oxygen saturation defined as <90.

2012, with sustained transmission between the first and second peaks (Figure 1). In the 2011–2012 respiratory season, a higher proportion of hospitalized patients tested positive for RSV than in previous seasons. Peak activity tended to follow periods of low temperatures and high relative humidity.

HUS Results and RSV Incidence

The HUS was completed in 2938 households (1931 rural and 1017 urban households), comprising 27 255 individuals (12 155 rural and 15 100 individuals). Overall, 17.9% of persons reported ILI in the past 30 days, of whom 97% sought medical care and 6.9% were hospitalized, and 0.7% reported LRI in the previous year, of whom 97.6% sought medical care and 13.0% were hospitalized. Among respondents reporting hospitalization for an acute respiratory illness, 98% were admitted to a surveillance hospital (78% rural, 100% urban). The overall incidence of hospitalized RSV infection in Damanhour district was 24 per 100 000 person-years, with the highest incidence occurring in the <1 year age group (Table 4). Among respondents receiving outpatient care, 8% were treated at a surveillance facility (12% rural, 7% urban). The overall incidence of RSV in outpatient ARI episodes was 608 per 100 000 person-years, with the highest incidence occurring in children aged <5 years (2300/100 000 person-years; Table 4).

DISCUSSION

This study is the first to use HUS data to estimate respiratory pathogen-specific incidence in urban and rural areas of Egypt. The results of the HUS demonstrate that our surveillance system captures the overwhelming majority of hospitalized patients in Damanhour district. Therefore, our incidence estimates of hospitalized RSV have a high degree of accuracy. Rates of RSV hospitalizations were higher among rural children compared to urban children, although outpatient rates of RSV were higher among urban children.

Our estimates of hospitalized RSV incidence are similar to hospitalized RSV incidence estimates reported from both developing and industrialized countries. Hospitalized RSV incidence has been estimated to be 300 per 100 000 person-years among US children aged <5 years [9], and 2830 and 130 per 100 000 person-years among British children aged <1 year and 1–4 years, respectively [10]. Published estimates of hospitalized RSV incidence from hospital-based surveillance in Thailand (46/100 000 person-years overall; 1087 and 406/100 000 person-years in the age groups 1–11 months and 1–4 years, respectively) [8] and Kenya (293/100 000 person-years among children aged <5 years) [11] were also comparable to our estimates. This similarity between developing and industrialized country incidence has been demonstrated in previous comparisons [12].

We found higher rates of RSV infections requiring hospitalization among children aged <5 years in the rural population relative to the urban population, although this difference was not statistically significant (P = .06). In studies comparing rural and urban populations in Kenya and The Gambia, rural children had a lower rate of hospitalization for respiratory episodes, which is thought to be related to the distance from hospital facilities [13, 14]. In a previous HUS in Damanhour, all rural respondents who sought care at a hospital reported the travel time from home to hospital as <2 hours, and 96% of those reported a travel time of <1 hour; this suggests that distance to a
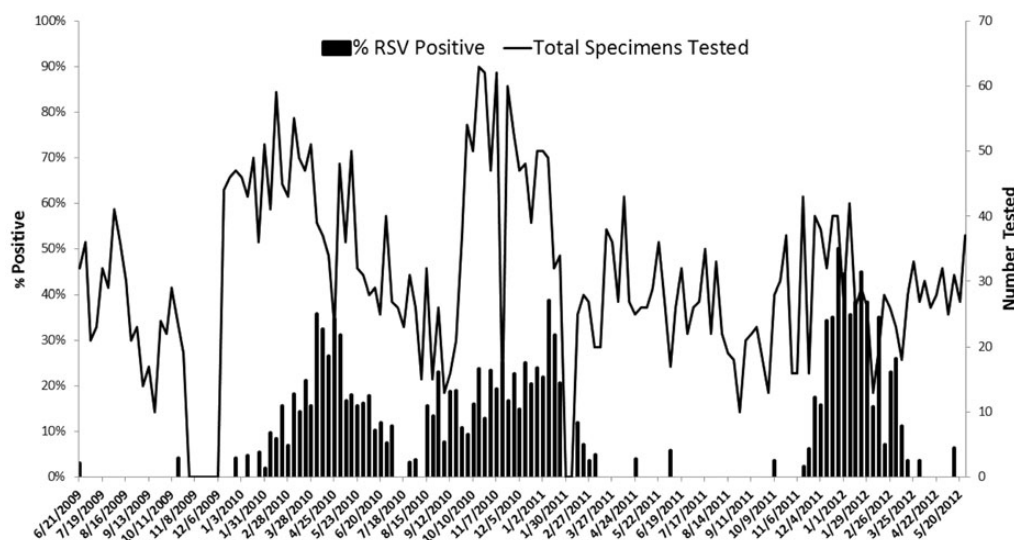
Figure 1. Samples tested from hospitalized patients and proportion postive for respiratory syncytial virus (RSV), Damanhour district, Egypt, June 2009–May 2012.

healthcare facility may not be a barrier to hospital usage in this population.

Rates of RSV infections treated as outpatients among urban children were not significantly higher than those among rural children (*P* = .22). A study from Kenya showed that although healthcare usage for respiratory infections was higher in urban populations, rates of disease, reported through community surveillance in households, were higher in rural areas [15]. It is possible that rural families in Damanhour reported fewer episodes of outpatient respiratory disease because these episodes did not result in seeking care outside the home and therefore may have been subject to a greater degree of recall bias.

Although the total numbers were small, a significantly higher percentage of hospitalized RSV-positive patients aged >5 years reported underlying conditions compared to patients aged <5 years. This is consistent with data from previous studies demonstrating that these conditions are risk factors for hospitalization for RSV infections in older populations.

Table 4. Incidence of Hospitalized Respiratory Syncytial Virus (RSV) Cases vs Outpatient RSV Cases by Rural vs Urban Residence—Damanhour District, Egypt, 2012

Age Group	Rural		Urban		Total	
	Rate	(95% CI)	Rate	(95% CI)	Rate	(95% CI)
Incidence of hospitalized RSV, per 100 000 person-years						
1 mo–4 y	271.2	(250–294)	173.6	(61–84)	242.5	(228–260)
1–11 mo	2053.4	(1884–2223)	a	a	1745.0	(1622–1874)
1–4 y	77.9	(66–93)	16.8	(11–24)	67.4	(58–79)
5–19 y	2.3	(1–4)	1.7	(.8–3)	2.6	(2–4)
20–49 y	4.1	(2–4)	1.3	(0–2)	1.9	(.2–3)
≥50 y	5.2	(.3–10)	6.7	(3–11)	6.2	(.4–10)
50–64 y	5.9	(.3–12)	6.6	(3–11)	6.5	(4–11)
≥65 y	a	a	7.3	(.4–21)	5.0	(2–13)
Incidence of outpatient RSV, per 100 000 person-years						
1–4 y	1310	(336–3594)	1902	(33–11 764)	2300	(1814–2795)
5–19 y	143	(2–1143)	1031	(3–7937)	459	(318–732)
20–49 y	257	(32–1163)	939	(9–7114)	517	(325–3075)
≥50 y	0	(0–1303)	0	(0–13 842)	0	(0–1374)

Abbreviations: CI, confidence interval; RSV, respiratory syncytial virus.

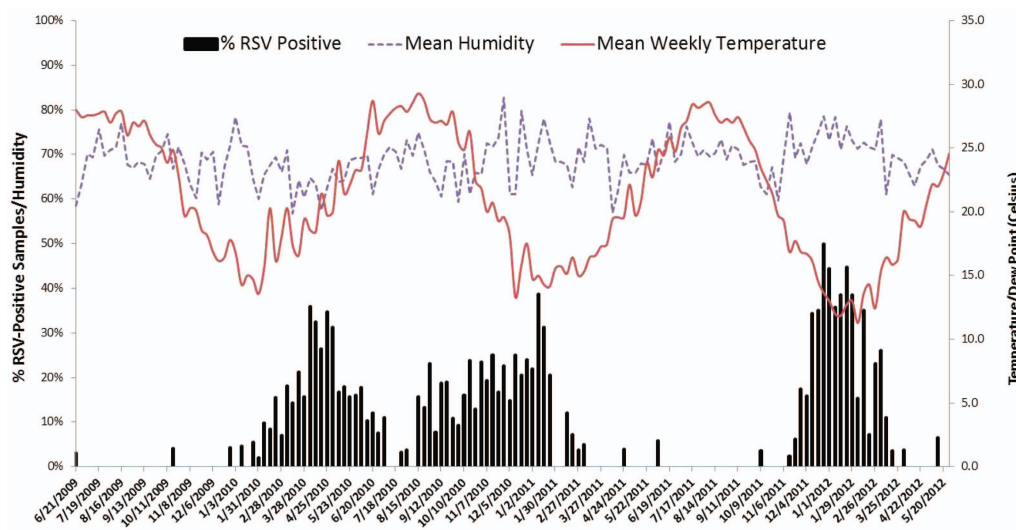[a] No survey respondents in this stratum reported a hospitalization for acute respiratory illness.

Figure 2. Proportion of respiratory syncytial virus (RSV)–positive hospitalized cases, mean weekly temperature, and relative humidity, Damanhour district, Egypt, June 2009–May 2012.

Over 3 years of hospital surveillance, no consistent seasonality of RSV cases was observed in Damanhour. Several studies have posited that transmission of RSV in nontropical climates has an inverse relationship with temperature; our results support that theory (Figure 2). While peak activity tended to follow periods of low temperatures and high relative humidity, RSV circulation was sustained from the peak during March–April 2010 through January 2011. Data from other studies also demonstrate inconsistent seasonality, with a wide range of interepidemic periods that may be due to nonclimatic factors not examined in our study, such as indoor crowding during school season, which may sustain transmission once an outbreak is under way [11, 12, 16].

Our study has several limitations. Our population-based surveillance excluded infants aged <31 days. Recent data have demonstrated a significant burden of RSV in this age group [17], and excluding these patients may have resulted in an underestimate of RSV incidence in the <1 year age group. Similarly, use of fever in the ILI case definition may have excluded older children and adults as well as younger children with RSV infections, resulting in an underestimate of the total burden of disease [18–20]. Our estimates of RSV incidence in Damanhour district were based on healthcare utilization patterns for a broad definition of self-reported ARI, regardless of self-reported disease severity; however, similar studies of healthcare utilization for respiratory infections have determined that self-reported disease severity is not necessarily associated with hospitalization [11, 21].

A uniform proportion of RSV infection was applied to outpatient HUS respondents reporting recent ARI. In reality, the proportion of respiratory illnesses due to RSV infection has been shown to vary by severity of ARI [5]. Last, our enrollment sites included only government facilities. It is possible that the proportion of RSV infections detected in nonsurveillance outpatient facilities differs from those detected in the surveillance outpatient clinics, given the range in the proportion of RSV in different types of outpatient settings previously reported in the United States [5].

These data provide a preliminary picture of RSV incidence in Damanhour by combining population-based surveillance data with healthcare utilization patterns. In addition to a substantial burden of pediatric hospitalization, our data suggest a high incidence of outpatient RSV disease across all age groups. Expanding surveillance to a broader range of outpatient facilities and sampling older patients without fever to capture RSV reinfections would produce more refined estimates. Given the near-universal infection with RSV by age 5 years, national RSV incidence for Egypt could be inferred from this study, but these estimates would not account for differences in healthcare utilization patterns across different settings. Estimating the incidence of RSV disease and RSV-associated outcomes is a critical first step to establish the burden of RSV in Egypt, as well as the cost-effectiveness of future RSV vaccines and treatment modalities.

Notes

Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the US Government.

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Weber MW, Mulholland EK, Greenwood BM. Respiratory syncytial virus infection in tropical and developing countries. Trop Med Int Health 1998; 3:268–80.

2. Nair H, Nokes DJ, Gessner BD, et al. Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. Lancet 2010; 375: 1545–55.

3. World Health Organization. The global burden of disease: 2004 update. Geneva, Switzerland: WHO, 2008.

4. Deutscher M, Van Beneden C, Burton D, et al. Putting surveillance data into context: the role of health care utilization surveys in understanding population burden of pneumonia in developing countries. J Epidemiol Glob Health 2012; 2:73–81.

5. Hall CB, Weinberg GA, Iwane MK, et al. The burden of respiratory syncytial virus infection in young children. N Engl J Med 2009; 360:588–98.

6. Hall CB. The burgeoning burden of respiratory syncytial virus among children. Infect Disord Drug Targets 2012; 12:92–7.

7. World Health Organization. Model IMCI handbook: integrated management of childhood illness. WHO/FCH/CAH/00.12. Geneva, Switzerland: WHO, 2005.

8. Fry AM, Chittaganpitch M, Baggett HC, et al. The burden of hospitalized lower respiratory tract infection due to respiratory syncytial virus in rural Thailand. PLoS One 2010; 5:e15098.

9. Iwane MK, Edwards KM, Szilagyi PG, et al. Population-based surveillance for hospitalizations associated with respiratory syncytial virus, influenza virus, and parainfluenza viruses among young children. Pediatrics 2004; 113:1758–64.

10. Müller-Pebody B, Edmunds WJ, Zambon MC, Gay NJ, Crowcroft NS. Contribution of RSV to bronchiolitis and pneumonia-associated hospitalizations in English children, April 1995–March 1998. Epidemiol Infect 2002; 129:99–106.

11. Nokes DJ, Ngama M, Bett A, et al. Incidence and severity of respiratory syncytial virus pneumonia in rural Kenyan children identified through hospital surveillance. Clin Infect Dis 2009; 49:1341–9.

12. Robertson SE, Roca A, Alonso P, et al. Respiratory syncytial virus infection: denominator-based studies in Indonesia, Mozambique, Nigeria and South Africa. Bull World Health Organ 2004; 82:914–22.

13. Bigogo G, Audi A, Aura B, Aol G, Breiman RF, Feikin DR. Health-seeking patterns among participants of population-based morbidity surveillance in rural western Kenya: implications for calculating disease rates. Int J Infect Dis 2010; 14:e967–73.

14. Weber MW, Milligan P, Sanneh M, et al. An epidemiological study of RSV infection in the Gambia. Bull World Health Organ 2002; 80:562–8.

15. 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 2011; 90:256A–263A.

16. Welliver R. The relationship of meteorological conditions to the epidemic activity of respiratory syncytial virus. Paediatr Respir Rev 2009; 10(suppl 1):6–8.

17. Cho HJ, Shim S-Y, Son DW, Sun YH, Tchah H, Jeon I-S. Respiratory viruses in neonates hospitalized with acute lower respiratory tract infections. Pediatr Int 2013; 55:49–53.

18. El-Radhi AS, Barry W, Patel S. Association of fever and severe clinical course in bronchiolitis. Arch Dis Child 1999; 81:231–4.

19. Walsh EE, Peterson DR, Falsey AR. Is clinical recognition of respiratory syncytial virus infection in hospitalized elderly and high-risk adults possible? J Infect Dis 2007; 195:1046–51.

20. Grom AA. Fever and the inflammatory response. In: Long SS, Pickering LKGrober CG, eds. Principles and practice of pediatric infectious diseases. 4th ed. Saunders, Philadelphia, 2012:91–5.

21. Jordan HT, Prapasiri P, Areerat P, et al. A comparison of population-based pneumonia surveillance and health-seeking behavior in two provinces in rural Thailand. Int J Infect Dis 2009; 13:355–61.