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ARTICLE

Epidemiology and population health

Is weight associated with severity of acute respiratory illness?

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Abstract

Background/objectives Obesity was an independent risk factor for severe disease in hospitalized adults during the 2009 pandemic H1N1 influenza season. Few studies have investigated the association between weight and severity of acute respiratory illnesses in children or in adults seeking care in the emergency department (ED) during other winter respiratory seasons.

Subjects/methods We prospectively and systematically enrolled patients ≥2 years of age who presented to the ED or inpatient setting in a single geographic region with fever/acute respiratory illness over four consecutive winter respiratory seasons (2010–2014). We collected demography, height and weight, and high risk co-morbid conditions. Multivariable logistic regression was used for prediction of hospital admission (primary outcome), length of stay and supplemental oxygen requirement among those hospitalized, and antibiotic prescription (secondary outcomes).

Results We enrolled 3560 patients ($N = 749$ children, 2811 adults), 1405 (39%) with normal weight, 860 (24%) with overweight, and 1295 (36%) with obesity. Following multivariable logistic regression, very young or very old age ($p < 0.001$) and high-risk conditions ($p < 0.001$) predicted hospitalization. Risk of hospitalization was decreased for adults with overweight [aOR 0.8 (95% CI 0.6–1.0)], class 1 obesity [aOR 0.7 (95% CI 0.5–1.0)], and class 2 obesity [aOR 0.6 (95% CI 0.4–0.8)] compared to normal-weight. Class 3 obesity was associated with supplemental oxygen requirement in adults [aOR 1.6 (95% CI 1.1–2.5)]. No association was seen in children.

Conclusion Overweight and obesity were not associated with increased risk of hospitalization during winter respiratory seasons in children or adults.

Introduction

Obesity was first identified as a novel independent risk factor for severe influenza disease in studies of hospitalized adult patients during the 2009 pandemic A(H1N1) influenza season [1, 2]. Relatively few investigators have extended this analysis to influenza seasons besides 2009, although some data suggest that obesity may be associated with increased risk of hospitalization during other influenza seasons [3, 4]. One meta-analysis demonstrated that obesity was significantly associated with increased risk of death for both seasonal and pandemic influenza; however, most existing studies investigating risk factors for severe influenza are limited by retrospective design and limited adjustment for covariates [5]. One study found that obesity was not associated with seasonal influenza virus severity but focused only on hospitalized adults [6]. Few studies have investigated the association of obesity and severe influenza disease in pediatric patients, and these results have been inconsistent and have used varying definitions of obesity [7–9]. Very few data exist on the outcomes of acute respiratory infections besides influenza. Studies in adults found an increased number of outpatient visits for acute respiratory infections [10] and increased detection of

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respiratory syncytial virus among adults with overweight and obesity compared to normal weight [11]. Studies on association between obesity and other respiratory illnesses in children are limited by the use of billing codes to define obesity, which dramatically under-document its true prevalence [12–14].

Given the high prevalence of obesity [15], the goals of this prospective study are to identify associations between obesity and severity of acute respiratory infection, measured by hospital admission, length of stay (LOS), supplemental oxygen, and prescription of antibiotics, in both adult and pediatric patients. We sought to test the hypothesis that patients with obesity will have more severe respiratory disease by each of these measures.

Patients and methods

Study setting and population

We prospectively and systematically enrolled patients ≥2 years with fever and/or acute respiratory symptoms at two hospitals over four winter respiratory seasons (2010–2014). Exclusion criteria included identified nonrespiratory source of fever prior to enrollment and lack of respiratory symptoms. Underweight patients were also excluded due to the high likelihood of comorbid conditions that would confound this analysis. Participants were enrolled ≥4 days per week at each hospital from November through April.

Approvals

We obtained written informed consent and child assent, as appropriate. We received approval for this study from the Wake Forest School of Medicine Institutional Review Board with an authorization agreement with the Forsyth Medical Center Institutional Review Board.

Demographic and clinical information

A trained research assistant administered a standardized questionnaire for demographic and medical information to each enrolled patient or guardian. Full influenza vaccination status was verified using the North Carolina Immunization Registry, the primary care provider, or the reported location of administration.

Data extracted during systematic chart review included age, sex, past medical history, specifically high-risk comorbid conditions, smoking status, insurance status, diagnostic testing, and medical treatments. Medical conditions were considered high risk if they are associated with severe influenza disease and/or have a condition-specific influenza vaccine recommendation. This includes cancer, diabetes, hemoglobinopathy, immunodeficiency, pregnancy, and any chronic cardiac, pulmonary, renal, hepatic, or neuromuscular disease. Asthma was considered separately from other high-risk conditions given the established association of severe disease with obesity in both adults and children [16–19].

Weight status

Participant weight and height were determined by both standardized interview and chart review. Weights were recorded from the patient chart at the time of ED or hospital check-in. Heights were not uniformly recorded in the chart so were either determined from patient/parent report or measured at the time of study enrollment. Age, sex, height, and weight were used to calculate body mass index (BMI), BMI percentile, and BMI z-score according to Center for Disease Control guidelines [20, 21]. Outliers with BMI z-score > 2.5 (children) or BMI > 50 (adults) had measurements verified or corrected by manual review of the medical record. BMI was analyzed categorically as normal-weight (children: 5−<85%ile, adults 18.5–25), overweight (children: 85−<95%ile, adults: 25−<30), and obesity (children ≥95%ile, adults ≥30). For adults, obesity was further subcategorized as class 1 (BMI 30−<35), class 2 (BMI 35−<40), and class 3 (BMI ≥ 40).

Outcomes

Our primary outcome was need for hospital admission, as an indication of severity of illness. In addition, we collected data for all patients on treatment with antibiotics (either by prescription or administration). For hospitalized patients, we extracted data on LOS and need for supplemental oxygen.

Power calculation

We performed post-hoc power calculations for both children and adults. Based on our experience, we anticipated that 25% of normal-weight children and 40% of normal-weight adults would require hospital admission. A difference of 15% would be meaningful from a clinical and resource utilization standpoint. We would be able to detect this difference with 80% power by Pearson chi-square test with 152 children in each group and 173 adults in each group.

Statistical analysis

Results were analyzed using descriptive statistics to determine the prevalence of normal-weight, overweight, and obesity by demographic conditions, clinical outcomes, and

Table 1 Counts and percentages of the study population by weight category

a. Pediatrics

	All $n = 749$ N (%)	Normal weight $n = 420$ N (%)	Over-weight $n = 157$ N (%)	Obese $n = 172$ N (%)	Overall p value[a]
Age in years					<0.0001
2–4	230 (31)	158 (38)	36 (23)	36 (21)	
5–9	204 (27)	123 (29)	33 (21)	48 (28)	
10–17	159 (21)	70 (17)	40 (25)	49 (28)	
18–21	156 (21)	69 (16)	48 (31)	39 (23)	
Year					0.91
2010–2011	185 (25)	102 (24)	38 (24)	45 (26)	
2011–2012	218 (29)	118 (28)	46 (29)	54 (31)	
2012–2013	214 (29)	127 (30)	45 (29)	42 (24)	
2013–2014	132 (18)	73 (17)	28 (18)	31 (18)	
Female	404 (54)	213 (51)	91 (58)	100 (58)	0.14
Race-ethnicity					0.64
Non-Hispanic White	250 (33)	142 (34)	57 (36)	51 (30)	
Black or African American	399 (53)	223 (53)	77 (49)	99 (58)	
Hispanic, other or unknown	100 (13)	55 (13)	23 (15)	22 (13)	
Any private insurance[b]	157 (21)	93 (22)	29 (18)	35 (20)	0.61
High-risk condition					0.91
Asthma	246 (33)	137 (33)	50 (32)	59 (34)	
Other[c]	63 (8.6)	36 (8.6)	11 (7.0)	16 (9.3)	
None	440 (59)	247 (59)	96 (61)	97 (56)	
Full vaccination	134 (18)	80 (19)	26 (17)	28 (16)	0.65
Fever (reported or measured)	527 (70)	308 (73)	108 (69)	111 (65)	0.09

b. Adults

	All $n = 2811$ N (%)	Normal weight $n = 985$ N (%)	Over-weight $n = 703$ N (%)	Class 1 $n = 413$ N (%)	Class 2 $n = 358$ N (%)	Class 3 $n = 352$ N (%)	Overall p value[a]
Age in years							<0.0001
22–34	599 (21)	222 (23)	161 (23)	74 (18)	72 (20)	70 (20)	
35–49	707 (25)	184 (19)	163 (23)	134 (32)	106 (30)	120 (34)	
≥50	1505 (54)	579 (59)	379 (54)	205 (50)	180 (50)	162 (46)	
Year							0.19
2010–2011	399 (14)	151 (15)	99 (14)	52 (13)	48 (13)	49 (14)	
2011–2012	769 (27)	272 (28)	196 (28)	104 (25)	88 (25)	109 (31)	
2012–2013	951 (34)	351 (36)	232 (33)	143 (35)	121 (34)	104 (30)	
2013–2014	692 (25)	211 (21)	176 (25)	114 (28)	101 (28)	90 (26)	
Female	1704 (61)	523 (53)	446 (63)	214 (52)	245 (68)	276 (78)	<0.0001
Race-ethnicity							<0.0001
Non-Hispanic White	1422 (51)	544 (55)	369 (52)	208 (50)	154 (43)	147 (42)	
Black or African American	1281 (46)	407 (41)	300 (43)	193 (47)	183 (51)	198 (56)	
Hispanic, other or unknown	108 (3.8)	34 (3.5)	34 (4.8)	12 (2.9)	21 (5.9)	7 (2.0)	
Any private insurance[b]	1398 (50)	505 (51)	356 (51)	216 (52)	170 (47)	151 (43)	0.049
Smoker	1012 (36)	406 (42)	253 (36)	133 (33)	113 (32)	107 (31)	0.0002
High-risk condition							<0.0001

Table 1 (continued)

b. Adults

	All $n = 2811$ N (%)	Normal weight $n = 985$ N (%)	Over-weight $n = 703$ N (%)	Class 1 $n = 413$ N (%)	Class 2 $n = 358$ N (%)	Class 3 $n = 352$ N (%)	Overall p value[a]
Asthma	823 (29)	243 (25)	166 (24)	127 (31)	127 (35)	160 (45)	
Other[c]	1235 (44)	453 (46)	325 (46)	180 (44)	148 (41)	129 (37)	
None	753 (27)	289 (29)	212 (30)	106 (26)	83 (23)	63 (18)	
Full vaccination	1017 (36)	326 (33)	269 (38)	161 (39)	125 (35)	136 (39)	0.093
Fever (reported or measured)	1430 (51)	510 (52)	381 (54)	211 (51)	159 (44)	169 (48)	0.030

[a] p values are for comparison of characteristics across body weight groups (normal weight, overweight, and 3 obesity classes) based on a chi-squared test

[b] Individuals with unknown insurance status are included with those who have no private insurance

[c] Other high-risk conditions: chronic cardiac or pulmonary diseases (excluding asthma), diabetes, cancer, immunodeficiency, HIV, transplant, chronic renal or hepatic diseases, cognitive or neurological disorders, hemoglobinopathies, and pregnancy

markers of resource utilization. Age was analyzed categorically, with four groups of children (2–4 years, 5–9 years, 10–17 years, and 18–21 years) and three groups of adults (22–34 years, 35–49 years, and 50+ years). Children and adults were analyzed separately. Comparison between groups was done using chi-square analysis or Fisher exact test. Multivariable logistic regression modeling was performed for the outcomes of hospitalization (primary outcome), LOS > 2 days, oxygen requirement, and antibiotic prescription. The models included age, weight status, gender, race, insurance, year, vaccination status, and high-risk medical conditions as covariates. Smoking status was added in a second set of models in adults for all outcomes. Results are reported as adjusted odds ratios with 95% confidence intervals. A p value of 0.05 was used as the cutoff for statistical significance. All analyses were performed using SAS v 9.4 (Cary, NC).

Results

We enrolled 3560 patients, including 749 children and 2811 adults. Clinical and demographic information is summarized in Table 1. Overall, 24.2% were overweight (21.0% children, 25.0% adults) and 36.4% had obesity (23.0% children, 40.0% adults). In adults, 14.7% had class 1 obesity, 12.7% had class 2 obesity, and 12.5% had class 3 obesity. Significant differences in the prevalence of overweight and obesity were noted by age, year, gender, and race/ethnicity, with obesity more common in enrolled older, female, and Black patients. Asthma was more common in patients with obesity, especially severe obesity. Patients with overweight or obesity were more likely to have at least one high-risk medical condition and to be fully vaccinated against influenza.

The bivariate analysis is summarized in Table S1 and was used to identify variables for inclusion in multivariable logistic regression modeling, displayed for pediatric and adult patients in Tables 2 and 3, respectively. Age and high-risk conditions had the strongest association with all markers of severe respiratory illness, with more severe illness noted for the youngest patients (ages 2–4 years) and oldest patients (>50 years). Asthma alone was associated with increased risk of hospitalization and need for supplemental oxygen. Children with other high-risk conditions had more severe disease across all our outcomes. In contrast, adults in that category only had increased hospitalization and supplemental oxygen. In adults, fully vaccinated patients were more likely to be admitted and to require supplemental oxygen. Weight status was not significantly associated with increased risk of any of the clinical outcomes investigated, except for need for supplemental oxygen in adults with class 3 obesity (OR 1.6, 95% CI 1.1–2.5). Both overweight and class 1 and 2 obesity were associated with a slight decrease in hospitalization risk in adults.

Discussion

We did not identify significant associations between obesity and increased severity of acute respiratory illness in either pediatric or adult patients, except for an association between supplemental oxygen requirement and class 3 obesity in hospitalized adult patients. Initial studies documenting associations between obesity and mortality from acute respiratory illness were done during the 2009 pandemic H1N1 influenza season, which was not included here. Several of the prior studies [3, 10] investigating seasonal influenza or other respiratory infections relied on self-reported BMI, which may result in inaccurate classification [22]. Another study that reported an association between obesity and seasonal influenza in 2011 identified the majority of their subjects using an Influenza A/H1N1

Table 2 Predictors of clinical outcomes in children (multivariable logistic regression)

	All patients		Admitted patients	
	Hospital admission ($N = 749$) aOR (95% CI)	Antibiotic prescription ($N = 749$) aOR (95% CI)	Length of stay > 2 days ($N = 134$) aOR (95% CI)	Oxygen requirement ($N = 134$) aOR (95% CI)
Weight status				
Normal weight	Ref	Ref	Ref	Ref
Overweight	0.7 (0.4–1.3)	0.7 (0.5–1.2)	1.5 (0.4–5.1)	0.5 (0.2–1.7)
Obese	1.2 (0.7–2.0)	0.8 (0.6–1.3)	0.7 (0.3–1.9)	1.3 (0.5–3.3)
Age				
2–4 years	Ref	Ref	Ref	Ref
5–9 years	0.7 (0.4–1.1)	**0.5 (0.3–0.9)**	0.8 (0.3–2.4)	0.7 (0.2–1.8)
10–17 years	**0.3 (0.2–0.6)**	0.9 (0.5–1.4)	0.8 (0.2–2.7)	**0.2 (0.1–0.7)**
18–21 years	**0.3 (0.1–0.6)**	**2.0 (1.2–3.2)**	**13.2 (2.3–74.9)**	**0.1 (0.02–0.4)**
Gender				
Female	Ref	Ref	Ref	Ref
Male	1.0 (0.6–1.5)	**0.6 (0.4–0.9)**	0.5 (0.2–1.2)	0.5 (0.2–1.2)
Race				
Non-Hispanic White	Ref	Ref	Ref	Ref
Black or African American	**0.5 (0.3–0.8)**	1.0 (0.7–1.5)	1.1 (0.4–3.1)	1.0 (0.4–2.7)
Hispanic/other/unknown	0.5 (0.3–1.1)	1.0 (0.6–1.8)	2.3 (0.5–9.8)	0.8 (0.2–3.5)
Insurance				
Public/none/unknown	Ref	Ref	Ref	Ref
Any private	**2.4 (1.4–4.0)**	1.3 (0.8–2.0)	1.0 (0.4–2.6)	0.5 (0.2–1.2)
Year				
2010–2011	Ref	Ref	Ref	Ref
2011–2012	**2.1 (1.2–3.9)**	**0.6 (0.4–1.0)**	0.8 (0.2–2.8)	0.8 (0.2–2.5)
2012–2013	**2.1 (1.1–3.8)**	**0.6 (0.4–1.0)**	1.4 (0.4–4.7)	0.8 (0.2–2.8)
2013–2014	0.2 (0.2–1.3)	**0.4 (0.2–0.7)**	0.1 (0.01–2.2)	0.4 (0.1–3.2)
Vaccination				
No or incomplete vaccination	Ref	Ref	Ref	Ref
Full vaccination	1.2 (0.7–2.1)	1.1 (0.7–1.7)	0.5 (0.2–1.3)	1.1 (0.4–2.9)
High-risk condition				
None	Ref	Ref	Ref	Ref
Asthma	**2.8 (1.8–4.5)**	0.9 (0.6–1.3)	1.0 (0.4–2.9)	**4.2 (1.5–11.4)**
Other	**8.0 (4.0–15.7)**	**2.4 (1.4–4.3)**	**5.2 (1.5–17.2)**	**6.3 (1.9–21.2)**

[a] Bold confidence intervals indicate significance at the 5% level

strain-specific qualitative RT-PCR, suggesting that the association with obesity may be specific to that virus [23]. Finally, Cocoros et al. performed a case-cohort study during two typical influenza seasons (2003–2004 and 2004–2005) and during the 2009 H1N1 pandemic. Although their crude OR for obesity and hospitalization for influenza-like illness was 1.65 (95% CI 1.31–2.08), it was no longer significant once they adjusted for age, gender, and medical comorbidities [4]. Therefore, the association between obesity and severe respiratory illness seems strongest for 2009 H1N1 influenza, with few data supporting an association for other seasons or viruses. One recent study demonstrated that obesity was not associated with ICU admission, mechanical ventilation, or diagnosis of bacterial pneumonia in adult patients hospitalized with influenza [6]. Of note, comparison between these studies is difficult due

Table 3 Predictors of clinical outcomes in adults (multivariable logistic regression)

	All patients	Admitted patients		
	Hospital admission ($N = 2811$) aOR (95% CI)	Antibiotic prescription ($N = 2770$) aOR (95% CI)	Length of stay > 2 days ($N = 1438$) aOR (95% CI)	Oxygen requirement ($N = 1438$) aOR (95% CI)
Weight status				
Normal weight	Ref	Ref	Ref	Ref
Overweight	**0.8 (0.6–1.0)**	1.0 (0.8–1.2)	1.0 (0.7–1.3)	0.9 (0.7–1.2)
Class 1 Obesity	**0.7 (0.5–1.0)**	1.0 (0.8–1.3)	0.8 (0.6–1.2)	1.0 (0.7–1.4)
Class 2 Obesity	**0.6 (0.4–0.8)**	0.9 (0.7–1.2)	**0.7 (0.5–1.0)**	1.3 (0.9–2.0)
Class 3 Obesity	0.9 (0.6–1.2)	1.0 (0.8–1.3)	0.9 (0.6–1.2)	**1.6 (1.1–2.5)**
Age			/	
22–34 years	Ref	Ref	Ref	Ref
35–59 years	**2.6 (1.9–3.6)**	1.1 (0.9–1.4)	1.3 (0.8–2.3)	**1.6 (1.0–2.8)**
>50 years	**7.5 (5.6–10.2)**	**1.2 (1.0–1.5)**	**1.6 (1.0–2.5)**	**3.0 (1.8–4.9)**
Gender				
Female	Ref	Ref	Ref	Ref
Male	**1.3 (1.0–1.5)**	1.0 (0.9–1.2)	1.1 (0.9–1.4)	0.8 (0.7–1.1)
Race				
Non-Hispanic White	Ref	Ref	Ref	Ref
Black or African American	**0.6 (0.5–0.7)**	**0.8 (0.7–0.9)**	0.9 (0.7–1.1)	0.8 (0.7–1.1)
Hispanic/other/ unknown	0.7 (0.4–1.2)	0.9 (0.6–1.3)	0.7 (0.4–1.5)	1.2 (0.6–2.5)
Insurance				
Public/none/ unknown	Ref	Ref	Ref	Ref
Any private	**2.1 (1.7–2.6)**	**0.7 (0.6–0.8)**	1.0 (0.7–1.2)	0.9 (0.7–1.2)
Year				
2010–2011	Ref	Ref	Ref	Ref
2011–2012	**1.6 (1.2–2.3)**	1.0 (0.7–1.2)	1.0 (0.7–1.5)	1.3 (0.9–2.0)
2012–2013	**1.7 (1.2–2.3)**	0.9 (0.7–1.1)	1.0 (0.7–1.5)	1.0 (0.7–1.4)
2013–2014	**0.4 (0.3–0.6)**	**0.5 (0.4–0.7)**	**0.6 (0.4–0.9)**	0.7 (0.4–1.1)
Vaccination				
No or incomplete vaccination	Ref	Ref	Ref	Ref
Full vaccination	**1.6 (1.3–2.0)**	1.0 (0.9–1.2)	1.0 (0.8–1.2)	**1.4 (1.1–1.8)**
High-risk condition				
None	Ref	Ref	Ref	Ref
Asthma	**4.9 (3.7–6.6)**	1.0 (0.8–1.2)	1.4 (0.9–2.2)	**4.4 (2.7–7.1)**
Other	**7.4 (5.6–9.8)**	1.0 (0.8–1.2)	1.4 (0.9–2.2)	**2.3 (1.5–3.5)**

[a] Bold confidence intervals indicate significance at the 5% level

to variations in cohort identification. Several studies identified eligible patients by positive laboratory testing [2, 6–9, 23] or by diagnosis code [3, 4, 10]; one additionally required fever as a symptom of disease [4]. Our study examines patients with fever and/or acute respiratory symptoms seeking care in the ED, who may have a wider range of initial disease severity, and demonstrates that obesity is not associated with increased risk of hospitalization. In contrast, we found a decreased risk of hospitalization among adults with overweight, class 1, or class 2 obesity. It is possible that these patients were more likely to seek care in the ED for relatively mild illness, thus decreasing the proportion requiring hospital admission. Or it is possible that they had less severe disease overall.

These cannot be differentiated from the data obtained in this study.

We did find that age, race, insurance status, and high-risk medical conditions were significant independent risk factors for severe disease, as measured by hospitalization, in both adults and children. The elderly have previously been found to have higher risk of hospital admission and mortality from both seasonal and pandemic influenza [5]. As expected, high-risk medical conditions were associated with increased likelihood of hospitalization. In adults, but not in children, smoking, gender, and vaccination status were also found to be independent predictors of hospitalization. We suspect that the association with vaccination status represents an increased likelihood of physician contact and recommendation for immunization among higher-risk patients, and this topic should be explored further in future studies.

There are several limitations to this study. Our patients were primarily enrolled in the ED; therefore, the results may not be generalizable to other populations who are less likely to seek care in the ED for respiratory illnesses. It is possible that severity at presentation to the ED varied systematically by weight status. It is also possible that patients of different BMI categories varied in their likelihood to seek care in the ED; for example, if patients of normal weight were more likely to be seen by a primary provider, only the most severely ill among them might be seen in the ED and subsequently admitted to the hospital. Although two facilities are included, both represent a single geographic location. Our data collection focused on host factors associated with severity of illness with limited information on the infecting organism. The analysis was limited by small sample sizes, especially for hospitalized and pediatric patients. Height and weight inaccuracies are possible, although we attempted to correct for this by manually reviewing outliers. Some heights were obtained by patient or parent report, which may increase risk of inaccuracy. Furthermore, BMI as a measure does not take body composition into account, so it may not reflect increased adiposity in all patients.

In conclusion, we did not identify any significant associations between obesity and increased severity of respiratory illness in this prospective study.

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Compliance with ethical standards

Conflict of interest Dr. Poehling reports grants for observational studies from National Institutes of Health and MedImmune during the conduct of the study. Dr. Peters reports grants from MedImmune during the conduct of the study. Dr. Snively and Ms. Suerken report grants from National Institutes of Health during the conduct of the study. The remaining authors declare that they have no conflict of interest.

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