



Clinical trial paper

Healthcare burden of obstructive sleep apnea and obesity among asthma hospitalizations: Results from the U.S.-based Nationwide Inpatient Sample

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ARTICLE INFO

Article history:

Received 3 December 2015

Received in revised form

24 June 2016

Accepted 25 June 2016

Available online 27 June 2016

Keywords:

Asthma

Obstructive sleep apnea

Obesity

Nationwide Inpatient Sample

Respiratory therapy

ABSTRACT

Background: Studies have highlighted the significant comorbidities of both obesity and obstructive sleep apnea (OSA) among asthma patients in outpatient settings, but such data in the inpatient setting is sparse.

Methods: Using 2009–2011 U.S. Nationwide Inpatient Sample; survey-weighted regression analyses were conducted to address the role of obesity, OSA, and both obesity and OSA on length of stay (LOS), total hospital charges, need for respiratory therapy, and disposition among adults with primary asthma hospitalization ($n = 179,789$).

Results: Males had a higher prevalence of OSA than females (5.23% vs. 3.88%), while females had a higher prevalence of obesity (17.21% vs. 8.95%) and both obesity and OSA (7.11% vs. 6.19%). Increased hospital LOS was associated with presence of obesity (incidence rate ratio [IRR] males = 1.07, IRR females = 1.08), OSA (IRR males = 1.07, IRR females = 1.14), and both obesity and OSA (IRR males = 1.19, IRR females = 1.24). Increased total hospital charges was related to obesity (8.64% for males and 9.61% for females), OSA (15.39% for males and 19.13% for females), and both comorbidities (24.94% for males and 28.50% for females). Presence of OSA alone increased odds of need for respiratory therapy for males (odds ratio [OR] = 2.56) and females (OR = 3.22), as did presence of both comorbidities (OR males = 2.85, OR females = 3.60). Odds of routine disposition was lower among females with both comorbidities (OR = 0.82).

Conclusion: Compared to obesity alone, OSA and both obesity and OSA are associated with increased health resource utilization and poorer inpatient outcomes. This demonstrates the need for further clinical investigations of early detection of OSA among such at-risk populations.

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1. Background

Asthma, a chronic respiratory disease, is characterized by episodes of coughing, wheezing, shortness of breath, and acute exacerbations that can be life threatening without adequate treatment. According to recent epidemiologic reports, 8% of adults in the United States have current asthma, with higher proportions noted among those of low socioeconomic status, females, and ethnic minorities [1]. In addition, estimates note 56 billion dollars of both

direct and indirect annual costs are attributable to asthma [2].

Studies have also highlighted both obesity and obstructive sleep apnea (OSA) as significant comorbidities of asthma [3]. For example, research has uncovered a significant association between increasing weight and higher severity of asthma [4], incidence of asthma [5], asthma hospitalizations [6], and poorer quality of life [7]. In a prospective study among women, weight gain was also shown to increase risk of adult onset of asthma [8], further demonstrating the comorbid conditions. Similarly, studies have demonstrated asthma severity to be associated with higher prevalence of OSA [9], in addition to difficulty sleeping, early morning awakening, snoring, daytime sleepiness [10], and poor sleep quality [11,12]. OSA is associated with poor asthma control [13,14] and

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higher disease burden apart from obesity [14], but also among the obese [15].

Despite such evidence on the comorbidity of asthma to that of obesity and OSA, little research exists on the impact of such conditions on healthcare resource utilization in the inpatient setting. In a study evaluating Maryland Medicaid claims, the authors noted that presence of OSA resulted in higher medical claims and costs among patients with respiratory illness [16], demonstrating the putative increased healthcare burden of OSA. In today's post healthcare reform era, there is a heightened focus on reducing unnecessary healthcare costs, including early preventive measures. As such, studies evaluating the economic healthcare burden of asthma comorbidities are imperative, though yet lacking. In this study, we addressed this literature gap by evaluating the burden of two highly prevalent asthma comorbidities on inpatient health resource utilization.

2. Methods

2.1. Data source

We utilized the Nationwide Inpatient Sample (NIS) 2009–2011, the largest public national inpatient database in the United States. Since 1988, NIS has been available annually and is comprised of data from all hospitals participating in the Healthcare Cost and Utilization Project (HCUP), sponsored by Agency for Healthcare Research and Quality (AHRQ). NIS includes 8 million inpatient stays from 1000 hospitals, which reflects a 20% random sample of HCUP participating hospitals. Additional details of NIS could be found elsewhere [17].

2.2. Study population

We utilized International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) 493.x to identify primary hospitalizations for asthma. As a result, a total of 179,789 primary asthma hospitalizations were included in the study, reflective of an extrapolated 896,222 hospitalizations in the nation. NIS further reports up to 24 secondary diagnoses codes. We utilized such codes to identify asthma hospitalizations with comorbid conditions of obesity (ICD-9-CM 278.0x) and OSA (ICD-9-CM 327.23). While OSA diagnosis codes of 780.5x have been used in some studies, these codes are symptom-based, thus we solely used 327.23 code, which offers confidence of an objectively rather than symptom-based OSA diagnosis, and thus reduces the potential bias of inflating the results.

2.3. Dependent variables

The primary outcome of interest was health resource utilization, defined through length of hospital stay and total charges. AHRQ provides edited length of stay and total charges to ensure uniformity within states. In this study, we further adjusted total charges to 2009 USD by utilizing the Gross Domestic Product deflator from the United States Department of Commerce, Bureau of Economic Analysis [18]. Secondary outcomes included respiratory therapy procedures utilizing Clinical Classification Software (CCS) for ICD-9-CM primary procedure code of 216 (respiratory intubation and mechanical ventilation) and disposition of patients, defined as routine discharge to home (set as reference) versus non-routine. Non-routine included: home with health care services, transfers to skilled nursing facility, intermediate care, and other types.

2.4. Independent variables

The exposure variables in our study were asthma comorbidities of obesity and OSA categorized as: obesity only, OSA only, OSA and obesity, and none (absence of both OSA and obesity) as the control group. Confounding variables included both patient and hospital characteristics, in addition to data year. Patient characteristics were defined as age, race/ethnicity, median household income quartiles by zip code, primary expected payer, and Charlson-Deyo Index. The Charlson-Deyo Index is a validated measure of comorbidities for administrative data [19–21] and comprises 17 comorbidities, which include: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease (not including asthma in our study), rheumatic disease, peptic ulcer disease, mild liver disease, diabetes with and without chronic complications, hemiplegia or paraplegia, renal disease, any malignancy (including lymphoma and leukemia, except malignant neoplasm of skin), moderate or severe liver disease, metastatic solid tumor, and human immunodeficiency virus/acquired immunodeficiency syndrome. Since our primary population consisted of asthma hospitalizations, asthma was excluded from the index. Hospital characteristics comprised of hospital type/teaching status, bed size, control/ownership, and geographic region. When evaluating the impact of asthma comorbidities on patient disposition status, the need for respiratory therapy was also included as a covariate.

2.5. Data analysis

We used survey weights for all statistical analyses, unless otherwise stated, in addition to design-based *F* values for variance estimation. All analyses were sex stratified. To evaluate the significant differences in patient and hospital characteristics between each sex, we conducted survey-weighted chi-square analysis. Next, in order to assess the impact of obesity, OSA, and both OSA and obesity on length of stay among asthma hospitalizations, we used survey-weighted multivariable negative binomial regression. We analyzed the impact of such asthma comorbidities on total charges, by conducting survey-weighted multiple linear regression. Due to non-normality of total charges, we further used log-transformation of the variable. In addition, we conducted age-stratified analyses to evaluate if the burden of asthma comorbidities on health resource utilization varied by age group, for each sex. To evaluate the role of obesity and/or OSA on respiratory therapy and patient disposition in our study population, we employed survey-weighted binary logistic regression analyses. A total of 16 multivariable regression analyses were conducted and as such, to reduce bias of multiple testing, we further employed a family-wise correction (Bonferroni) and thus alpha less than 0.0017 was used to establish statistical significance. We used SAS 9.4 (SAS Institute, Inc., Cary, NC) for all statistical analyses except for negative binomial regression where we used STATA 12 package (Stata Corp LP, College Station, TX).

3. Results

Table 1 summarizes the study population of adult asthma hospitalizations. Both OSA and obesity were present in 6.19% of males, in comparison to 7.11% of females. Obesity was more prevalent in females than males (17.21% vs. 8.95%), while males had a higher prevalence of OSA than females (5.23% vs. 3.88%). Significant differences were also noted for several other patient (age, race/ethnicity, Charlson-Deyo, and payer type) and hospital (setting, control, and geographic location) characteristics between males and females. For example, a higher percent of males reported two or more score of Charlson-Deyo Index of comorbidities (21.34%) as

Table 1

Characteristics of study population of asthma hospitalizations, Nationwide Inpatient Sample 2009–2011 (n = 179,789; N = 896,222). Weighted Percentage and 95% Confidence Interval.

	Male	Female	P value
OSA/Obesity			<0.0001
None	79.63 (78.98, 80.28)	71.79 (71.16, 72.42)	
Obesity only	8.95 (8.56, 9.34)	17.21 (16.74, 17.68)	
OSA only	5.23 (4.90, 5.56)	3.88 (3.68, 4.09)	
OSA and obesity	6.19 (5.87, 6.52)	7.11 (6.79, 7.44)	
Age			<0.0001
18–34 years	14.99 (14.35, 15.63)	11.54 (11.17, 11.92)	
35–49 years	23.89 (23.23, 24.55)	24.59 (24.10, 25.08)	
50–64 years	30.01 (29.42, 30.60)	31.93 (31.52, 32.33)	
65 years or more	31.10 (30.11, 32.10)	31.94 (31.17, 32.71)	
Race/ethnicity			<0.0001
White	51.93 (49.36, 54.49)	54.96 (52.58, 57.34)	
Black	28.60 (26.62, 30.58)	26.75 (24.94, 28.56)	
Hispanic	12.15 (10.59, 13.71)	12.49 (10.94, 14.04)	
Other	7.32 (6.03, 8.61)	5.80 (4.65, 6.96)	
Charlson-Deyo index			<0.0001
0	54.76 (53.92, 55.59)	52.21 (51.59, 52.82)	
1	23.91 (23.42, 24.39)	28.80 (28.45, 29.15)	
2 or more	21.34 (20.70, 21.98)	18.99 (18.53, 19.46)	
Neighborhood income			0.2848
\$1–\$38,999	37.62 (35.22, 40.02)	37.48 (35.28, 39.67)	
\$39,000–\$47,999	24.90 (23.44, 26.36)	25.33 (23.97, 26.68)	
\$48,000–\$62,999	21.66 (20.40, 22.93)	21.82 (20.56, 23.07)	
\$63,000 or more	15.82 (14.16, 17.47)	15.38 (13.88, 16.88)	
Payer type			<0.0001
Private including HMO	22.64 (21.64, 23.63)	24.70 (23.83, 25.58)	
Medicare	40.68 (39.59, 41.76)	42.00 (41.19, 42.81)	
Medicaid	18.35 (16.91, 19.79)	21.67 (20.45, 22.89)	
Other	18.33 (17.30, 19.37)	11.63 (10.94, 12.32)	
Hospital setting			<0.0001
Rural	12.61 (11.45, 13.77)	14.17 (12.99, 15.35)	
Urban non-teaching	43.45 (40.92, 45.99)	44.61 (42.31, 46.92)	
Urban teaching	43.94 (41.20, 46.69)	41.22 (38.70, 43.73)	
Bed size			0.4365
Small	13.70 (12.21, 15.20)	14.10 (12.82, 15.39)	
Medium	26.79 (24.66, 28.92)	26.74 (24.80, 28.68)	
Large	59.51 (57.05, 61.97)	59.16 (56.93, 61.38)	
Hospital Control			0.0008
Government, nonfederal	14.02 (11.32, 16.73)	12.79 (10.62, 14.95)	
Private, non-profit	71.13 (68.03, 74.22)	71.63 (68.93, 74.32)	
Private, investor-own	14.85 (13.01, 16.69)	15.59 (13.80, 17.37)	
	Male	Female	P value
Geographic location			<0.0001
Northeast	27.66 (24.84, 30.48)	26.18 (23.69, 28.66)	
Midwest	22.01 (20.13, 23.88)	21.69 (20.04, 23.35)	
South	34.49 (32.13, 36.85)	37.78 (35.56, 40.00)	
West	15.85 (14.35, 17.35)	14.35 (13.04, 15.65)	
Year			0.5727
2009	35.36 (32.33, 38.39)	35.25 (32.34, 38.16)	
2010	33.08 (30.23, 35.93)	32.79 (30.14, 35.43)	
2011	31.56 (28.86, 34.26)	31.96 (29.38, 34.54)	

compared to females (18.99%), while more females were hospitalized in the South than males (37.78% vs. 34.49%).

Table 2(a and b) displays the survey-weighted length of stay (days) and total charges (percent change) among asthma hospitalizations with secondary diagnoses of, obesity only, OSA only, presence of both OSA and obesity, compared to absence of both obesity and OSA. As noted in Table 2a, in males, mean length of stay for all age groups combined, was highest (4.21 days) among those with both OSA and obesity, followed by OSA alone (4.02 days), obesity alone (3.74 days), as compared to 3.47 days among the control group (no comorbidity present). A similar trend was noted for females among each age group, with highest length of stay among asthma hospitalizations with both comorbid OSA and obesity (4.90 days), followed by OSA only (4.63 days), obesity only (4.12 days), and neither (3.86 days). Similarly, in regards to total hospital charges, among males overall, total charges were the highest for those with both OSA and obesity (\$70,250), followed by OSA (\$64,077), obesity (\$53,473), as compared to those lacking both (\$50,880). Charges increased with older age, such that the highest charges were incurred in males aged 65 years or more, where presence of OSA increased charges to \$75,852, while obesity increased total charges to \$68,266, in comparison to lack of both OSA and obesity (\$62,109). Similar overall and age-group trends were seen among females, such that among those aged 65 years or more, presence of and both OSA and obesity, OSA or obesity, increased such charges to \$90,713; \$77,417 and \$74,741, respectively, relative to \$62,596 in those lacking of OSA and obesity comorbidities. For both males and females, OSA demonstrated a higher burden on both length of stay and charges, than compared to obesity.

Table 3a and b display the impact of asthma comorbidities on health resource utilization, by age groups, upon five independent regression analyses for each sex. Results demonstrate that relative to the control groups, presence of both comorbidities (OSA and obesity) among asthma hospitalizations significantly increased length of stay by 19% for males and 24% for females. Additionally, presence of OSA increased length of stay by 7% and 14% for males and females, respectively, while obesity by 7% for males and 8% for females. Such asthma comorbidities, particularly OSA, also increased total charges for males and females. For example, in males with obesity we observed 8.64% increases in total charges, while presence of OSA only and both OSA and obesity, further doubled (15.39%) and tripled (24.94%) these charges, respectively. Likewise, females with obesity, OSA, and both OSA and obesity demonstrated 9.61%, 19.13%, and 28.50% increases in total charges. Age-stratified data analysis showed that among males, presence of obesity increased length of stay for those 35–49 years, while presence of both comorbidities increased such an outcome among all age groups, with the exception of those over 65 years.

Total charges were significantly higher upon presence of obesity

Table 2a

Health resource utilization for asthma hospitalizations with or without OSA and obesity, among males, by age group, Nationwide Inpatient Sample 2009–2011.

	All age groups	18–34 years	35–49 years	50–64 years	65 or more years
Mean length of stay (days)					
No OSA or obesity	3.47	2.40	2.87	3.53	4.35
Obesity only	3.74	2.64	3.38	3.98	4.46
OSA only	4.02	2.94	3.40	4.03	4.67
OSA and obesity	4.21	3.32	4.00	4.43	4.68
Mean total charges (\$)					
No OSA or obesity	50,880	37,150	41,499	53,285	62,109
Obesity only	53,473	37,412	46,165	56,279	68,266
OSA only	64,077	50,935	55,387	61,352	75,852
OSA and obesity	70,250	58,141	64,129	77,053	75,610

Table 2b

Health resource utilization for asthma hospitalizations with or without OSA and obesity, among females, by age group, Nationwide Inpatient Sample 2009–2011.

	All age groups	18–34 years	35–49 years	50–64 years	65 or more years
Mean length of stay (days)					
No OSA or obesity	3.86	2.56	3.22	3.90	4.70
Obesity only	4.12	3.15	3.62	4.25	5.11
OSA only	4.63	3.57	3.95	4.59	5.35
OSA and obesity	4.90	3.83	4.34	5.06	5.78
Mean total charges (\$)					
No OSA or obesity	51,661	36,821	42,163	52,076	62,596
Obesity only	57,831	42,582	48,955	60,110	74,741
OSA only	66,957	43,350	60,024	65,525	77,417
OSA and obesity	75,731	57,965	65,334	79,101	90,713

Table 3a

Impact of OSA and obesity on health resource utilization for asthma hospitalizations among males, by age group, Nationwide Inpatient Sample 2009–2011.

	All age group	18–34 years	35–49 years	50–64 years	65 or more years
Length of stay, IRR and 95% CI^a					
None	Ref.	Ref.	Ref.	Ref.	Ref.
Obesity only	1.07 (1.04, 1.10)*	1.07 (0.98, 1.16)	1.13 (1.07, 1.19)*	1.08 (1.02, 1.13)	1.02 (0.96, 1.08)
OSA only	1.07* (1.03, 1.11)	1.16 (1.01, 1.32)	1.10 (1.01, 1.20)	1.07 (0.99, 1.14)	1.05 (0.99, 1.11)
OSA and obesity both	1.19 (1.15, 1.23)*	1.31 (1.17, 1.47)*	1.27 (1.20, 1.35)*	1.18 (1.10, 1.27)*	1.05 (0.98, 1.12)
Total charges, percent change and 95% CI^a					
None	Ref.	Ref.	Ref.	Ref.	Ref.
Obesity only	8.64 (5.41, 11.86)*	8.43 (1.98, 14.88)	12.08 (6.69, 17.47)*	7.81 (2.97, 12.65)*	6.15 (0.34, 11.96)
OSA only	15.39 (11.31, 19.48)*	29.92 (17.08, 42.77)*	18.45 (10.89, 26.02)*	14.20 (7.67, 20.72)*	12.06 (5.89, 18.24)*
OSA and obesity both	24.94 (20.81, 29.07)*	35.28 (25.80, 44.76)*	32.57 (26.02, 39.12)*	22.39 (15.79, 28.99)*	11.16 (3.82, 18.50)

Table 3b

Impact of OSA and obesity on health resource utilization for asthma hospitalizations among females, by age group, Nationwide Inpatient Sample 2009–2011.

	All age group	18–34 years	35–49 years	50–64 years	65 or more years
Length of stay, IRR and 95% CI^a (Ref. = none)					
None	Ref.	Ref.	Ref.	Ref.	Ref.
Obesity only	1.08 (1.07, 1.10)*	1.19 (1.15, 1.24)*	1.10 (1.07, 1.13)*	1.06 (1.03, 1.08)*	1.06 (1.03, 1.09)*
OSA only	1.14 (1.11, 1.17)*	1.30 (1.15, 1.46)*	1.18 (1.12, 1.24)*	1.12 (1.07, 1.16)*	1.12 (1.06, 1.17)*
OSA and obesity both	1.24 (1.21, 1.27)*	1.35 (1.27, 1.44)*	1.30 (1.25, 1.35)*	1.22 (1.18, 1.26)*	1.18 (1.13, 1.23)*
Total charges, percent change and 95% CI^a (Ref. = none)					
None	Ref.	Ref.	Ref.	Ref.	Ref.
Obesity only	9.61 (7.42, 11.80)*	12.42 (8.37, 16.47)*	8.87 (5.69, 12.04)*	7.68 (4.80, 10.56)*	11.63 (8.63, 14.62)*
OSA only	19.13 (16.11, 22.15)*	17.50 (5.89, 29.10)	23.45 (17.29, 29.60)*	19.42 (15.17, 23.67)*	15.45 (10.93, 19.96)*
OSA and obesity both	28.50 (25.50, 31.49)*	30.17 (22.33, 38.01)*	31.32 (26.76, 35.89)*	27.64 (23.80, 31.48)*	24.95 (20.44, 29.45)*

*Bonferroni $P < .0017$.

Ref. = reference category, IRR = incidence rate ratio, CI = confidence interval.

^a Model adjusted for patient and hospital characteristics, in addition to data year.

in those aged 35–64 years, and among all age groups upon presence of OSA only. Both comorbidities significantly increased total charges among those aged less than 65 years. Among females, all age groups demonstrated significantly longer length of stay upon presence of each comorbidity, alone or together. Similarly higher total charges upon presence of obesity, OSA (with the exception of 18–34 year age group), and both comorbidities were further noted.

Table 4 displays the impact of asthma comorbidities on our secondary outcomes of interest: respiratory therapy and patient disposition, by sex. In this study population of asthma

hospitalizations, presence of both OSA and obesity significantly increased the likelihood of respiratory therapy for males (adjusted odds ratio [aOR] = 2.85) and females (aOR = 3.60), as compared to those without such comorbidities. Additionally, presence of OSA increased odds of respiratory therapy by 156% and 222% for males and females, respectively. On the other hand, obesity alone did not yield significant results. Similarly, likelihood of routine disposition was 22% lower among females hospitalized for asthma with presence of both OSA and obesity, versus those without such comorbidities. Such non-routine disposition included home health care

Table 4
Impact of OSA and obesity on respiratory therapy and patient disposition for asthma hospitalizations, by sex, Nationwide Inpatient Sample 2009–2011.

	Respiratory therapy ^a OR (95% CI) ^c		Disposition ^b OR (95% CI) ^d	
	Male	Female	Male	Female
None	Ref.	Ref.	Ref.	Ref.
Obesity only	0.97 (0.81, 1.17)	1.01 (0.92, 1.11)	1.17 (1.05, 1.30)	1.05 (0.99, 1.10)
OSA only	2.56 (2.16, 3.05)*	3.22 (2.84, 3.65)*	1.24 (1.08, 1.42)	1.01 (0.92, 1.12)
OSA and obesity	2.85 (2.45, 3.32)*	3.60 (3.18, 4.09)*	1.19 (1.05, 1.35)	0.82 (0.076, 0.88)*

Ref. = reference category, OR = odds ratio, CI = confidence interval.

*Bonferroni $P < .0017$.

^a CCS code of 216 including respiratory intubation and mechanical ventilation.

^b Routine disposition includes discharge to home.

^c Models adjusted for patient and hospital characteristics, and data year.

^d Models adjusted for patient and hospital characteristics, respiratory therapy, and data year.

(140 per 1000 discharges) and other transfers (60 per 1000 discharges), such as, skilled nursing facility, intermediate care, and other type, in addition to in-hospital death (1.7 per 1000 discharges). Asthma comorbidities were not significantly associated with disposition for males in our study.

4. Discussion

The literature has elucidated significant comorbidity of obesity [4,22,23] and obstructive OSA [11,12,24,25] among those with asthma, though studies evaluating the impact of such comorbidities on inpatient and hospital outcomes remain limited. In this study, we addressed such a gap in the literature by utilizing the largest publically available inpatient data in the United States, to assess the role of such asthma comorbidities on health resource utilization (length of stay and total charges), need for respiratory therapy, and patient disposition status among those hospitalized for asthma. We found: 1) both males and females hospitalized for asthma had longer length of stay and higher charges in the presence of either obesity or OSA, as compared to none; 2) the burden on such health resource utilization was higher in the presence of OSA; 3) the two comorbidities together had a multiplicative effect on health resource utilizations; 4) need for respiratory therapy was significant for those with asthma–OSA comorbidity or presence of both obesity and OSA with asthma, and 5) finally, likelihood of routine disposition was lower among females hospitalized for asthma with both OSA and obesity.

A major finding from our study is that among asthma hospitalizations, the comorbidity of obesity and OSA demonstrated a multiplicative effect on increased length of stay and total charges, with a higher burden noted for females for each comorbidity independently and as well as combined. According to national estimates, 5.2% and 8.6% prevalence of asthma are noted among adult males and females, respectively [26], demonstrating a higher burden among the latter sex. Additionally, some studies have also found that the association between asthma and obesity differs between males and females. For example, in a longitudinal study in Canada, Chen and colleagues noted that baseline obesity was significantly associated with asthma among females, but not males [27]. Similarly, Beckett et al. found asthma incidence to be significantly associated with body mass index, in a J-shaped curve only among females [28]. As such, the sex-differences noted in our study could be attributable to such differences in asthma prevalence, though we further advance the literature by evaluating the impact

of asthma comorbid conditions on health resource utilization.

On the other hand, the literature primarily notes higher prevalence of OSA among males in the general population, with factors such as neck circumference, upper airway dimensions and reporting by bed-partner, often cited as potential attributable reasons for such differences [29–31]. For example, in a study with over 5000 participants, Larsson and colleagues noted that nearly 18% of males, as compared to 7.4% of females, reported snoring or relatives reported witnessing OSA [32]. Similarly, sleep-disordered breathing was noted to be in 10% of males aged 30–49 years, compared to 3% females of similar age group in the Wisconsin Sleep Cohort Study [33]. Larsson and colleagues further noted that compared to males, females who reported snoring were more likely to report daytime sleepiness, all while being less likely to be referred to sleep laboratories [32]. Our study results, however, demonstrated that despite males having a higher prevalence of OSA, the burden of OSA was more severe among females than males.

Such literature, in addition to our results, demonstrate that the potential under-diagnosis of OSA among females could lead to more long-term worse outcomes and thus increased healthcare burden, as noted in our study, and the need for sex-specific screening mechanism for such asthma comorbidity. Banno and group [34] reported that women with obstructive OSA syndrome had higher healthcare utilization in the year preceding sleep-clinic evaluation, thus highlighting the need for early screening. As noted in our study, the potential burden of OSA among women hospitalized for asthma remains a significant clinical and public health issue.

Our results on age-differences in the outcomes warrant further discussion. Age-stratified analyses also showed that the impact of asthma comorbidities on health resource utilization was significant for all age groups for females, but only for younger males, further demonstrating the sex and age disparities in the burden of asthma and need for targeted interventions for high-risk groups. Nationally, 6.3% of individuals aged 65 years or older reported current asthma, as compared to those aged 20–24 years (7.2%), 25–34 years (6.6%), and 35–64 years (7.3%) [26]. Despite a lower prevalence of asthma among older populations, our results demonstrated increasing mean length of stay and mean total charges with increasing age. Such differences across age could be putatively due to the presence of more comorbidities and their greater impact, in the older populations [35], and thus the greater health resource utilization.

In addition, among asthma hospitalizations, presence of OSA raised a higher demand for health resources than that of obesity alone, highlighting the substantial burden of OSA and need for improved screening and early intervention. Although the effects of treatment for coexistent OSA commencing during an exacerbation remain to be tested, indeed, continuous positive airway pressure (CPAP) treatment for OSA in the outpatient setting relates to improved asthma control [24,36]. Additionally, several interventional studies of CPAP for OSA in asthma, in that same setting have shown improved asthma control indices including asthma symptoms, bronchodilator use, peak flow rates, and disease-specific quality of life [37–40]. Corroborating with these reports, the new data implicate OSA as a frequent contributor to the clinical and economic burden posed of asthma in all, inpatient and outpatient settings.

Our secondary outcomes of interest were the need for respiratory procedures, including intubation and mechanical ventilation and disposition status of those hospitalized for asthma. For both males and females, we found that OSA alone did increase the likelihood of respiratory procedures, while obesity did not; furthermore, the presence of both comorbidities had a multiplicative negative impact on the study population. Interestingly, only

among females, presence of both comorbidities lowered the likelihood of routine disposition, perhaps as a result of more intense and prolonged in-hospital treatments, as suggested by the apparent longer length of stay and increased charges in this group. Cumulatively, such results illustrate the significant burden of asthma-related comorbidities, especially of OSA, and the particular higher burden among females in whom asthma is generally more prevalent.

In recent years, significant public health efforts have been targeted towards reducing the obesity epidemic, both in the United States and globally. Our results illustrate, that while obesity negatively impacts those hospitalized for asthma, the burden is greater for those with OSA and with both, OSA and obesity. The literature has further shown OSA to be significantly associated with poorer outcomes, including heart failure and mortality [41–43]. For example, in a recent study among patients with type 2 diabetes, Seicean and colleagues demonstrated an association between obstructive OSA and asthma comorbidity comparable to that of heart failure and atrial fibrillation [44]. Researchers have also shown that patients with asthma and obstructive OSA reported significantly higher decline in forced expiratory volume 1 (FEV1), as compared to those who did not have OSA [45]; all cumulatively highlighting the negative burden of OSA on asthma. Thus, the need for respiratory therapy, as found in our study, could be attributable to such lower lung function. The results from our study, in addition to the current herein reviewed evidence, further demonstrate the imperative need for efforts at routine screening for obstructive OSA among the asthmatic population. As further stated by Punjabi, the need for reducing the threshold for sleep center referral is critical, as is the improved clinical education in identifying at-risk patients, especially those with other comorbidities [46], such as asthma, as illustrated by our study. In today's post-healthcare reform era, the focus from volume to value [47,48] demands a paradigm shift in healthcare where early prevention is central to improved population health. As such, vigilance in addressing OSA as a public health problem, similar to the health promotion measures against obesity, remains imperative.

The results of our study are not without limitations. The lack of patient identifiable information limits our ability to evaluate out-of-hospital utilization of other healthcare services, including pharmacy, community clinics, and/or outpatient centers; thus potentially underreporting the burden of asthma comorbidities on health resource utilization. Additionally, the NIS database does not provide out-of-hospital mortality rates and thus post-discharge death attributable to asthma comorbidities could not be evaluated. The impact of menopause on sleep apnea severity is documented in the literature, which may be affecting the magnitude of the burden noted in this study [49]. Although we did not specifically address menopause in our analyses, we do present results that are sex and age specific. Future work may uncover specific associations with hospital and patient outcomes among this subpopulation. The major strength of this study stems from utilizing a large national sample of inpatients; thus, our results were not limited to sampling issues often faced in recruiting participants, which reduces the external threat to validity often encountered in smaller scale studies, and thus are generalizable to inpatient stays in the nation. In summary, our results strengthen the literature demonstrating a substantial negative impact on asthma by its comorbidities, particularly OSA, extending to inpatient setting; especially among females.

Conflict of interest

The authors report no conflict of interest or funding sources for this research.

Acknowledgements

The authors report no conflict of interest. MBB was funded by Faculty Professional Grant.

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