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Impact of ASD and ADHD on pediatric asthma exacerbations: a retrospective analysis of the Nationwide Inpatient Sample 2005–2020

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Abstract

Background To explore the impact of autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) on in-hospital outcomes in children hospitalized for asthma exacerbations.

Methods This retrospective study utilized data from the Nationwide Inpatient Sample (NIS) database between 2005 and 2020. We included children aged 5 to 19 years admitted for asthma exacerbations. Children were categorized into four groups: those with ASD only, ADHD only, both ASD and ADHD, and neither condition. Propensity score matching was used to balance baseline characteristics.

Results A total of 155,893 children hospitalized for asthma were identified, with 2,443 patients remaining after propensity score matching. Children with both ASD and ADHD had the highest total hospital costs, followed by those with ASD alone. Children with both ASD and ADHD had significantly increased risks of overall complications (aOR = 1.69, 95% CI: 1.27–2.26), including epilepsy (aOR = 3.56, 95% CI: 1.61–7.87), pneumonia (aOR = 2.00, 95% CI: 1.33–3.03), and constipation (aOR = 4.22, 95% CI: 1.58–11.26), compared to those without either condition. Children with ASD alone also had elevated risks for epilepsy (aOR = 3.79, 95% CI: 1.79–8.03) and constipation (aOR = 4.33, 95% CI: 1.78–10.54).

Conclusion In the US children hospitalized for asthma exacerbations, those with both ASD and ADHD, or ASD alone, face significantly greater costs and higher risks of specific complications, particularly epilepsy, pneumonia, and constipation. The findings suggest a compounded impact of these neurodevelopmental conditions on asthma children, emphasizing the need for specialized care to manage these patients effectively and reduce the risks.

Keywords Autism spectrum disorder (ASD), Attention deficit hyperactivity disorder (ADHD), Asthma, Children, In-hospital mortality, Complication

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Background

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by challenges in social interaction, communication, and repetitive behaviors. ASD affects approximately 1 in 36 children in the United States (US), with rising prevalence over the past decade [1, 2]. Children with ASD often face additional health challenges, including difficulties with medication adherence, increased sensitivity to environmental stimuli, and behavioral concerns, all of which contribute to their complex care needs [3]. It is also documented that they have higher rates of emergency department visits compared to individuals without ASD [4]. Additionally, studies have reported that individuals with ASD face an increased risk of premature death [5]. In general, ASD presents a significant healthcare burden, requiring ongoing interventions and support for both patients and their families.

Individuals with ASD often have multiple co-occurring conditions, including psychiatric disorders such as anxiety, bipolar disorder, and depression, as well as neurological conditions like epilepsy [6–8]. Also, medical comorbidities such as infection, immunologic diseases, and neurological diseases are more common in children with ASD than those without ASD [9]. Amongst the comorbidities, attention deficit hyperactivity disorder (ADHD), another neurodevelopmental condition marked by hyperactivity, impulsivity, and inattention, is frequently comorbid with ASD. ADHD also places a significant burden on the healthcare system, contributing to higher rates of healthcare utilization, increased costs, and poorer overall outcomes compared to children without these conditions [10]. Studies indicate that up to 30–50% of children with ASD also have ADHD, further complicating their clinical management [11].

Asthma is one of the most common chronic diseases in children, affecting approximately 6 million children in the US [12]. It is a leading cause of pediatric hospitalizations, with asthma exacerbations frequently resulting in emergency room visits and inpatient stays [13]. Asthma hospitalizations reflect significant morbidity, with contributing factors including inadequate asthma control, exposure to environmental triggers, and adherence to treatment regimens [14]. Children with such as ASD and ADHD may experience additional challenges in managing asthma, given the complex interplay between their behavioral and physical health needs [15]. Comorbid ASD or ADHD in children with asthma may lead to poorer asthma control and an increased risk of hospitalization. This is often due to behavioral factors affecting treatment adherence, communication challenges, and heightened sensitivity to environmental triggers [16, 17].

Given its importance and the limited data available on the impact of ASD and ADHD on pediatric asthma hospitalizations, this study aims to address this gap by exploring how these comorbidities influence outcomes in children hospitalized for asthma, utilizing a nationally representative U.S. dataset.

Methods

Data source

This population-based, retrospective observational study extracted all data from the US National Inpatient Sample (NIS) database, which is the largest all-payer, continuous inpatient care database in the United States, including about 8 million hospital stays each year [18]. The database is administered by the Healthcare Cost and Utilization Project (HCUP) of the US National Institutes of Health (NIH). The patient data consist of primary and secondary diagnoses, primary and secondary procedures, admission and discharge status, patient demographics, projected payment source, hospital stay duration, and hospital characteristics (i.e., bed size/location/teaching status/hospital area). Initial consideration is given to all hospitalized patients for inclusion. The continuously updated, annual NIS database contains patient information from around 1,050 hospitals in 44 states, representing a stratified sample of 20% of US community hospitals as defined by the American Hospital Association.

Ethics statement

This study complies with the NIS data-use agreement established by HCUP. As a secondary data analysis, this study had no direct patient interaction and was exempt from IRB approval.

Study population

This study included hospitalized patients aged 5 to 19 years with a primary discharge diagnosis of asthma from 2005 to 2020 in the NIS database. These children were identified in the NIS database using the International Classification of Diseases (ICD) codes, ninth and tenth editions (ICD-9-CM: 493; ICD-10-CM: J45). The exclusion criteria included incomplete data on age, and sex, missing sample weights, and missing information on study outcomes.

Eligible children were categorized into four groups: those with ASD only (ICD-9-CM: 299.0, 299.8, 299.9; ICD-10-CM: F84.0, F84.5, F84.9), those with ADHD only (ICD-9-CM: 314.0; ICD-10-CM: F90), those with both ASD and ADHD and those with neither condition.

In-hospital outcomes

The outcomes of interest included: (1) in-hospital mortality, (2) length of stay, (3) total hospital costs, and (4) complications during admission, such as epilepsy, pneumonia, sepsis, dehydration, respiratory failure/mechanical ventilation, non-invasive positive pressure ventilation

(NIPPV) usage, and constipation, all identified by the corresponding ICD codes.

Covariates

Covariates included co-existing psychiatric and developmental conditions such as anxiety, suicidal ideation, bipolar disorder, aggressive disorder, depressive disorder, disruptive mood dysregulation disorder, obsessive-compulsive disorder, speech disturbances, developmental speech disorders, and developmental motor function disorders [9]. Medical comorbidities were identified using ICD codes and included malnutrition, obstructive sleep apnea, central sleep apnea, congenital heart anomalies, and neuromuscular disorders, which encompassed conditions such as Duchenne muscular dystrophy (DMD), spinal muscular atrophy (SMA), cerebral palsy, myasthenia gravis, Charcot-Marie-Tooth disease, congenital myopathies, congenital myasthenic syndromes, peripheral neuropathies, Friedreich's ataxia, and congenital muscular dystrophy.

Demographic data, including age, gender, race, and family income-to-poverty ratio, were extracted from the NIS database. Hospital-related characteristics, such as bed size and location/teaching status, were also obtained from the database, consistent with the comprehensive data used in other NIS studies in the literature.

Statistical analysis

The NIS database comprises a 20% sample of annual US inpatient admissions and employs weighted samples, strata, and clusters to generate national estimates. Descriptive statistics of the study population are presented as numbers (n) and weighted percentages (%), or as means ± standard errors (SE). P-values for comparisons between the study groups were calculated by using the PROC SURVEYFREQ and SURVEYREG on categorical and continuous data, respectively. The propensity-score matching (PSM) method using the SAS OneToManyMTCH macro was employed to balance the baseline characteristics of patients across the study groups. The macro prioritizes "best" matches first and then proceeds with "next-best" matches until no more can be made. The patient cohort was matched at a ratio of "With ASD and ADHD", "With ASD alone", "With ADHD alone", and "Neither" = 1: 2: 2: 2 based on age (in years) and sex. Univariate and multivariable logistic regression models determine associations between the study variables and binary outcomes. Multivariable regression analysis adjusted for variables that were significant in univariate analysis. In addition, stratified analyses for the impact of ASD and ADHD on the risk of in-hospital complications were performed by age and (any) medical comorbidities. All p values were two-sided and $p < 0.05$ was considered to represent statistical significance. All statistical analyses were performed using the statistical software package SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Study population selection

The study population selection process is depicted in Fig. 1. A total of 170,915 children aged from 5 to 19 years hospitalized for asthma exacerbations from the NIS database from 2005 to 2020 were included. Patients admitted electively ($n = 11,246$) and those with missing data on sex, in-hospital mortality, hospital costs, or weight values ($n = 3,773$) in the dataset were excluded. Finally, 155,893 patients were included in the study. After matching by propensity scores, 2,443 patients remained for subsequent analyses, consisting of 349 cases for "With ASD and ADHD" and 698 cases for "With ASD alone" "With ADHD alone" and "Neither". This sample could represent a total of 11,972 hospitalized children in the whole US (Fig. 1).

Characteristics of the study population

Statistics of demographics, comorbidities, hospital-related information, and outcomes of the study population are summarized in Tables 1 and 2, and Supplementary Table 1. The mean age of all patients was 9.6 years. 58.6% were male, 31.3% were White, and 57.2% had insurance covered by Medicare/Medicaid. The most common complication was pneumonia (10.0%). Significant differences were observed in total hospital cost, several complications, age, sex, race, psychiatric comorbidities, medical comorbidities, insurance status, and hospital-related information across the four composite groups (Supplementary Table 1). After PSM, age and sex distributions were balanced between the groups. However, significant differences remained in certain study variables (i.e., race/ethnicity, psychiatric and medical comorbidities, insurance type, admitted at the weekend, year of admission, and hospital location/teaching status and region) (Table 1). Only 1 child (0.04%) died during hospitalization across the entire study sample. Children with both ASD and ADHD had the highest total hospital costs, averaging $21,800, followed by those with ASD alone at $19,500. The overall LOS was 2.3 days, with no significant differences observed between the groups The frequencies of epilepsy, constipation, and pneumonia showed significant variation between the study groups (Table 2).

Associations between ASD, ADHD, and complications

Associations between the presence of ASD, ADHD, or both, and complications among children admitted for asthma are summarized in Table 3 and Supplementary Table 2.

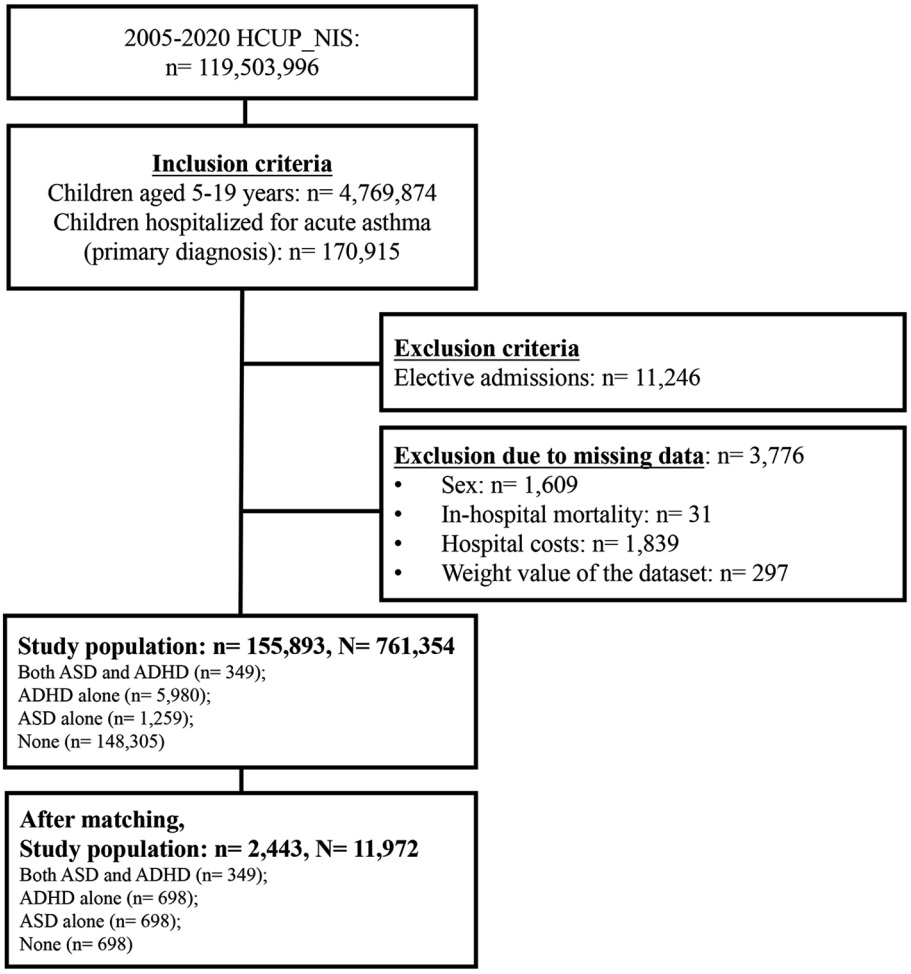

Fig. 1 Flow diagram of the study population selection

After adjusting for relevant confounders, compared with children with neither ASD nor ADHD, the multivariable analysis revealed that children with ASD alone had significantly increased risks of overall complications (adjusted odd ratio [aOR] = 1.44, 95% confidence interval [CI]: 1.14–1.82, $p = 0.003$), including increased risks of epilepsy (aOR = 3.79, 95% CI: 1.79–8.03, $p = 0.001$), constipation (aOR = 4.33, 95% CI: 1.78–10.54, $p = 0.001$) and pneumonia (aOR = 1.69, 95% CI: 1.20–2.39, $p = 0.003$).

Children with ADHD alone were significantly associated with a higher risk of constipation compared to those without ASD or ADHD (aOR = 4.05, 95% CI: 1.65–9.95, $p = 0.002$); however, no increased risks were observed for other complications.

Further, compared to children with neither ASD nor ADHD, children with both ASD and ADHD had significantly increased risks of overall complications (aOR = 1.69, 95% CI: 1.27–2.26, $p < 0.001$), epilepsy (aOR = 3.56, 95% CI: 1.61–7.87, $p = 0.002$), constipation (aOR = 4.22, 95% CI: 1.58–11.26, $p = 0.004$) and pneumonia (aOR = 2.00, 95% CI: 1.33–3.03, $p = 0.001$) (Table 3.)

The crude associations of ASD with ADHD and the complications in the univariate analysis are presented in Supplementary Table 2.

Stratified associations between ASD, ADHD, and complications

The results of stratified analysis based on age groups are depicted in Table 4. After adjusting for confounding factors, we found that patients aged under 10 years and with ASD alone had significantly higher risks of epilepsy compared to those with neither ASD nor ADHD; patients aged under 10 years and with both ASD and ADHD had significantly higher risks of (any) complications, epilepsy, and pneumonia compared to those with neither ASD nor ADHD. For the stratification of children aged over 10 years, similar results were observed, where children with ASD alone and those with both ASD and ADHD had significantly higher risks of (any) complications, epilepsy, and pneumonia compared to those with neither ASD nor ADHD (Table 4).

Table 1 Characteristics of the study population after propensity score matching

Characteristics	Total (*n* = 2,443)	With ASD alone (*n* = 698)	With ADHD alone (*n* = 698)	With ASD-ADHD (*n* = 349)	Neither [a] (*n* = 698)	*p*-value
Demography						
Age, years	10.0 ± 0.1	10.1 ± 0.1	10.0 ± 0.1	10.0 ± 0.2	9.9 ± 0.1	0.880
5–9	1218 (49.9)	348 (50.0)	348 (49.8)	174 (49.9)	348 (49.9)	0.140
10–14	961 (39.4)	256 (36.6)	282 (40.6)	141 (40.3)	282 (40.5)	
15–19	264 (10.7)	94 (13.4)	68 (9.6)	34 (9.8)	68 (9.6)	
Sex						1.000
Male	2184 (89.5)	624 (89.5)	624 (89.4)	312 (89.3)	624 (89.5)	
Female	259 (10.6)	74 (10.5)	74 (10.6)	37 (10.7)	74 (10.5)	
Race/ethnicity						**< 0.001**
White	808 (37.1)	240 (39.0)	232 (36.9)	151 (47.7)	185 (29.8)	
Black	799 (36.6)	192 (31.4)	271 (42.5)	96 (30.7)	240 (39.0)	
Hispanic	403 (18.3)	118 (19.2)	95 (14.9)	43 (13.4)	147 (23.6)	
Other	174 (8.0)	65 (10.5)	36 (5.7)	26 (8.2)	47 (7.7)	
Missing	259	83	64	33	79	
Psychiatric comorbidities	268 (11.0)	65 (9.3)	120 (17.2)	74 (21.3)	9 (1.3)	**< 0.001**
Anxiety state	134 (5.5)	27 (3.9)	59 (8.4)	43 (12.5)	5 (0.7)	**< 0.001**
Bipolar disorder	52 (2.2)	6 (0.9)	27 (3.9)	19 (5.4)	0 (0.0)	-
Aggressive disorder	1 (0.04)	1 (0.15)	0 (0.00)	0 (0.00)	0 (0.00)	-
Depressive disorder	41 (1.7)	6 (0.9)	29 (4.2)	5 (1.5)	1 (0.1)	**< 0.001**
Disruptive mood dysregulation disorder	2 (0.1)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	-
Obsessive-compulsive disorder	28 (1.2)	4 (0.6)	7 (1.0)	16 (4.7)	1 (0.1)	**< 0.001**
Speech disturbance	9 (0.4)	3 (0.4)	4 (0.6)	1 (0.3)	1 (0.2)	0.618
Developmental disorders of speech	53 (2.2)	25 (3.6)	14 (2.1)	12 (3.4)	2 (0.3)	**< 0.001**
Developmental disorders of motor function	3 (0.1)	1 (0.2)	0 (0.0)	2 (0.6)	0 (0.0)	-
Medical comorbidities	135 (5.6)	57 (8.2)	29 (4.2)	29 (8.4)	20 (2.9)	**< 0.001**
Malnutrition	5 (0.2)	3 (0.4)	1 (0.1)	1 (0.3)	0 (0.0)	-
Obstructive sleep apnea	81 (3.4)	32 (4.7)	24 (3.5)	15 (4.4)	10 (1.5)	**0.004**
Central Sleep Apnea	1 (0.04)	0 (0.00)	0 (0.00)	0 (0.00)	1 (0.20)	-
Congenital anomalies of the heart	23 (1.0)	11 (1.6)	2 (0.3)	9 (2.6)	1 (0.2)	**< 0.001**
Neuromuscular disorder	31 (1.3)	14 (2.0)	2 (0.3)	6 (1.7)	9 (1.3)	**0.011**
Insurance status/Primary Payer						**< 0.001**
Medicare/Medicaid	1532 (63.0)	434 (62.2)	463 (66.6)	230 (67.2)	405 (58.1)	
Private including HMO	759 (31.1)	224 (32.0)	209 (30.0)	95 (27.3)	231 (33.2)	
Self-pay/no-charge/other	144 (5.9)	40 (5.8)	24 (3.4)	19 (5.6)	61 (8.8)	
Missing	8	0	2	5	1	
Weekend admission	712 (29.1)	186 (26.6)	192 (27.5)	118 (33.8)	216 (30.8)	**0.029**
Year of admission						**< 0.001**
2005–2008	532 (21.0)	107 (14.8)	147 (20.4)	40 (10.7)	238 (33.1)	
2009–2012	601 (24.3)	155 (22.0)	187 (26.3)	77 (21.8)	182 (25.9)	
2013–2016	697 (29.1)	197 (28.6)	224 (32.8)	108 (31.4)	168 (24.8)	
2017–2020	613 (25.6)	239 (34.7)	140 (20.5)	124 (36.1)	110 (16.2)	
Hospital characteristics						
Hospital bed size						0.596
Small	405 (16.3)	107 (15.2)	121 (17.1)	68 (19.2)	109 (15.3)	
Medium	580 (24.0)	167 (24.3)	162 (23.5)	82 (23.6)	169 (24.6)	
Large	1451 (59.6)	423 (60.6)	412 (59.5)	199 (57.2)	417 (60.1)	
Missing	7	1	3	0	3	
Location/teaching status						**< 0.001**
Rural	141 (5.8)	35 (5.1)	43 (6.3)	11 (3.2)	52 (7.4)	
Urban nonteaching	367 (14.8)	92 (13.0)	91 (12.8)	35 (9.7)	149 (21.1)	
Urban teaching	1928 (79.4)	570 (82.0)	561 (80.9)	303 (87.1)	494 (71.5)	
Missing	7	1	3	0	3	

Table 1 (continued)

Characteristics	Total (*n* = 2,443)	With ASD alone (*n* = 698)	With ADHD alone (*n* = 698)	With ASD-ADHD (*n* = 349)	Neither [a] (*n* = 698)	*p*-value
Hospital region						**< 0.001**
Northeast	628 (26.0)	180 (26.1)	175 (25.3)	93 (26.9)	180 (26.3)	
Midwest	484 (19.7)	135 (19.2)	161 (23.0)	76 (21.7)	112 (16.0)	
South	955 (38.9)	250 (35.9)	287 (40.9)	136 (38.8)	282 (39.9)	
West	376 (15.4)	133 (18.8)	75 (10.8)	44 (12.7)	124 (17.8)	

Continuous variables are presented as mean ± SE

Categorical variables are presented as unweighted counts (weighted percentages)

P-values < 0.05 are shown in bold

[a] Patients with neither ASD nor ADHD

Table 2 Outcome of the study population after propensity score matching

Outcomes	Total (*n* = 2,443)	With ASD alone (*n* = 698)	With ADHD alone (*n* = 698)	With ASD-ADHD (*n* = 349)	Neither [b] (*n* = 698)	*p*-value
In-hospital mortality	1 (0.04)	0 (0.00)	0 (0.00)	0 (0.00)	1 (0.15)	-
LOS, days[a]	2.3 ± 0.04	2.3 ± 0.07	2.2 ± 0.06	2.4 ± 0.17	2.3 ± 0.08	0.651
Total hospital cost, per 1,000 USD[a]	18.3 ± 0.7	19.5 ± 0.8	16.5 ± 0.7	21.8 ± 2.5	17.2 ± 1.8	**0.021**
Complications	558 (23.0)	187 (26.8)	139 (20.1)	107 (30.8)	125 (18.0)	**< 0.001**
Epilepsy	79 (3.2)	40 (5.7)	10 (1.4)	20 (5.8)	9 (1.3)	**< 0.001**
Constipation	69 (2.8)	28 (4.0)	22 (3.1)	14 (4.0)	5 (0.7)	**< 0.001**
Pneumonia	231 (9.5)	82 (11.7)	52 (7.6)	46 (13.2)	51 (7.3)	**< 0.001**
Sepsis	17 (0.7)	5 (0.7)	3 (0.4)	2 (0.6)	7 (1.0)	0.450
Dehydration	86 (3.6)	24 (3.5)	21 (3.1)	15 (4.4)	26 (3.8)	0.684
Respiratory Failure/ Mechanical ventilation	129 (5.3)	36 (5.2)	38 (5.5)	23 (6.6)	32 (4.6)	0.543
(NIPPV)	50 (2.1)	14 (2.0)	19 (2.8)	8 (2.4)	9 (1.3)	0.206

Abbreviation: ASD, Autism spectrum disorder; ADHD, attention deficit hyperactivity disorder; LOS, length of stay; NIPPV, non-invasive positive pressure ventilation

[a] Excluded in-hospital mortality patients

[b] Patients with neither ASD nor ADHD

Table 3 Adjusted associations between ASD, ADHD, and complications in children admitted for asthma

Outcomes	Compared with children without ASD or ADHD					
	ASD alone		ADHD alone		ASD-ADHD	
	aOR (95% CI)	*p*-value	aOR (95% CI)	*p*-value	aOR (95% CI)	*p*-value
Complications, any	1.44 (1.14–1.82)	**0.003**	1.05 (0.82–1.35)	0.689	1.69 (1.27–2.26)	**< 0.001**
Epilepsy	3.79 (1.79–8.03)	**0.001**	0.97 (0.37–2.55)	0.956	3.56 (1.61–7.87)	**0.002**
Constipation	4.33 (1.78–10.54)	**0.001**	4.05 (1.65–9.95)	**0.002**	4.22 (1.58–11.26)	**0.004**
Pneumonia	1.69 (1.20–2.39)	**0.003**	1.11 (0.76–1.61)	0.596	2.00 (1.33–3.03)	**0.001**
Sepsis	0.81 (0.32–2.05)	0.652	0.44 (0.15–1.28)	0.130	0.72 (0.18–2.92)	0.641
Dehydration	0.70 (0.41–1.18)	0.177	0.70 (0.40–1.23)	0.217	0.86 (0.46–1.61)	0.639
Respiratory Failure/ Mechanical ventilation	0.97 (0.63–1.50)	0.895	0.99 (0.63–1.56)	0.967	1.15 (0.68–1.96)	0.599
Non-invasive positive pressure ventilation (NIPPV)	0.99 (0.45–2.18)	0.972	1.40 (0.67–2.91)	0.367	0.96 (0.36–2.59)	0.942

Abbreviations: ASD, autism spectrum disorder; ADHD, attention deficit hyperactivity disorder; aOR, adjusted odds ratio; CI, confidence interval

All models were adjusted for related variables of p-value < 0.05 in univariate analysis, including psychiatric comorbidities, medical comorbidities, and year of admission

P-values < 0.05 are shown in bold

Discussion

This study revealed several important findings regarding the impact of ASD and ADHD on pediatric acute asthma exacerbations. Children with both ASD and ADHD had the highest total hospital costs, followed by those with ASD alone. Despite the in-hospital mortality being low, children with both ASD and ADHD had the highest risk of complications, with overall complication rates being 1.7-fold, epilepsy being more than 3.5-fold higher, and constipation over 4.2-fold higher compared to those with neither condition. The risk of pneumonia was also doubled in this group. Compared to children with neither condition, those with ASD alone had significantly elevated risks as well, with epilepsy nearly 3.8 times higher

Table 4 Stratified associations of ASD, ADHD, and complications in children admitted for asthma

Outcomes	Compared with children without ASD or ADHD [a]					
	ASD alone		ADHD alone		ASD-ADHD	
	aOR (95% CI)	*p*-value	aOR (95% CI)	*p*-value	aOR (95% CI)	*p*-value
Age < 10 years						
Complications, any	1.27 (0.93–1.75)	0.135	0.95 (0.68–1.31)	0.737	1.54 (1.05–2.26)	**0.027**
Epilepsy	3.94 (1.58–9.83)	**0.003**	1.27 (0.39–4.15)	0.688	3.39 (1.20–9.54)	**0.021**
Pneumonia	1.28 (0.81-2.00)	0.293	1.03 (0.64–1.65)	0.915	1.95 (1.19–3.20)	**0.008**
Age ≥ 10 years						
Complications, any	1.67 (1.20–2.32)	**0.002**	1.17 (0.84–1.63)	0.355	1.91 (1.28–2.85)	**0.002**
Epilepsy	3.77 (1.35–10.52)	**0.011**	0.77 (0.21–2.83)	0.691	3.70 (1.31–10.43)	**0.013**
Pneumonia	2.38 (1.51–3.75)	**< 0.001**	1.19 (0.74–1.90)	0.472	2.06 (1.12–3.77)	**0.020**

Abbreviations: ASD, autism spectrum disorder; ADHD, attention deficit hyperactivity disorder; aOR, adjusted odds ratio; CI, confidence interval; NA, no event occurred in one group

P-values < 0.05 are shown in bold

[a] Adjusted for related variables of p-value < 0.05 in univariate analysis (except for the stratified variable), including psychiatric comorbidities, medical comorbidities, and year of admission

and constipation 4.3 times higher. Children with ADHD alone had a 4-fold increased risk of constipation but no significant increase in other complications than those with neither condition. Importantly, ASD had a greater impact on complication risks than ADHD, while having both ASD and ADHD led to even higher risks than ASD alone. These findings indicate the compounded effect of dual diagnoses on asthma hospitalization outcomes among US children.

Firstly, it should be noted that whether there is a causal relationship between ASD and asthma has been investigated. Although earlier meta-analyses [19] of epidemiological studies did not support a direct relationship between asthma and ASD, a recent study [20] using various genetically informed designs, evidence of familial co-aggregation between asthma and ASD was found, suggesting that the weak association between these disorders may be influenced by shared genetic factors. Future studies are still needed to strengthen the evidence.

The focus of the present study is to determine whether ASD or co-occurring ASD/ADHD negatively impacts hospital outcomes in children with asthma exacerbations. The elevated risk of pneumonia among children with ASD observed in our study may be explained by the well-documented immune dysregulation and heightened inflammatory response often seen in individuals with this neurodevelopmental disorder [21]. This underlying vulnerability, compounded by the complexities of asthma management, likely contributes to the higher incidence of pneumonia in pediatric asthma exacerbations. Individuals with ASD may be more susceptible to respiratory infections, possibly due to immune system abnormalities and difficulties in managing respiratory symptoms. For example, a study by Zandam et al. [22] reported that autistic adults had higher odds of presenting to the emergency department with respiratory infections (aOR = 1.83), including lower respiratory infections (aOR = 1.37) and pneumonia (aOR = 2.42), compared to non-autistic adults. They were also more likely to be hospitalized for respiratory infections (aOR = 3.87), including upper and lower respiratory infections, pneumonia, and bronchitis, which aligns in part with our findings.

ASD and ADHD are both increasing in prevalence and frequently co-occur. They strongly impact individuals' functions and are often unrecognized [23]. Children with comorbid ASD and ADHD tend to experience more severe symptoms, including more challenging behaviors, heightened anxiety, and worse overall outcomes compared to those diagnosed with either condition alone [24]. Few studies have assessed the impact of co-occurring ASD and ADHD on common healthcare outcomes, such as asthma management. In our analysis, the combined presence of both disorders significantly increased the costs and risk of complications during asthma exacerbations, underscoring the joint impact of these neurodevelopmental conditions. These findings contribute insights to the existing knowledge on how co-occurring ASD and ADHD affect healthcare outcomes.

We found that the risk of epilepsy is elevated in children hospitalized with asthma who also have underlying ASD or ASD/ADHD. This aligns with the well-established association between ASD and seizure disorders, as seizures are more common in individuals with ASD compared to the general population, with epilepsy affecting approximately 10–30% of those with ASD [25]. Hospitalizations and acute medical conditions, such as asthma exacerbations, may trigger seizures due to stress, medication interactions, or underlying neurological vulnerabilities in individuals with ASD.

While the association between asthma and seizures remains under debate [26], the physiological stress of an exacerbation or certain treatments (e.g., corticosteroids) may increase seizure risk in predisposed individuals [27]. Based on our analysis, close monitoring for seizures may

be warranted in individuals with ASD during hospitalization for asthma exacerbations.

In addition, the high rate of constipation observed in children with ASD and ADHD in our study likely reflects the common gastrointestinal issues associated with these neurodevelopmental disorders. Previous research has shown that children with ASD frequently experience gastrointestinal dysregulation, including motility issues that contribute to constipation [28, 29]. Behavioral factors, such as selective eating and difficulty communicating discomfort, may further exacerbate these problems.

Interestingly, a recent study found that in children with asthma, ASD was associated with fewer exacerbations and lower odds of airflow obstruction, yet higher odds of being prescribed asthma controllers [16]. This seems to contrast with our results that ASD is associated with pneumonia in asthma exacerbation. A possible explanation for the contrast between our findings and the recent study could be differences in the severity of ASD or comorbidities in the study populations. Children with more severe ASD may face greater challenges in managing respiratory symptoms, increasing the risk of pneumonia. Further, we have no data on asthma medications or specific treatment details, which limits our ability to fully compare the outcomes.

These findings have key clinical implications for managing pediatric asthma hospitalizations in children with ASD and ADHD. Children with ASD, especially those with co-occurring ADHD, are at significantly higher risk of complications, including epilepsy, pneumonia, and constipation, during asthma exacerbations. This suggests a need for more tailored management strategies, such as close monitoring for respiratory infections and seizure activity, particularly in children with severe forms of ASD. The increased hospital costs and higher complication rates in this population indicate that specialized care approaches may help reduce these risks and improve outcomes.

Strengths and limitations

This study has several strengths. It used data from the NIS, which provides a large, nationally representative sample, making the findings applicable to the broader US pediatric population. The use of rigorous statistical methods, including propensity score matching, helped balance baseline characteristics and minimize confounding between study groups. Additionally, the study examined a comprehensive range of outcomes, such as in-hospital mortality, complications, hospital costs, and length of stay, providing a thorough understanding of the impact of comorbid ASD and ADHD on pediatric asthma hospitalizations. The 16-year span of data also allowed for the analysis of trends over time. However, the study has some limitations. The NIS database lacks detailed clinical information, such as the severity of asthma, ASD, and ADHD, and medication adherence, or environmental factors, which could affect the results. Diagnoses were based on ICD codes at the time of hospitalization, so the long-term progression of conditions was not captured, and there is potential for coding errors or misclassification. Since the study focused only on hospitalized patients, the findings may not apply to children with asthma who do not require hospitalization. Finally, despite adjusting for many variables, unmeasured factors like socioeconomic status, diet, or specific treatments for ASD or ADHD may have influenced the results.

Conclusions

This study highlights the significant impact of ASD and ADHD on pediatric asthma exacerbations. Children with ASD, ADHD, or both are at a substantially higher risk of in-hospital complications, particularly epilepsy, constipation, and pneumonia. Notably, ASD has a greater influence on these risks than ADHD, and the presence of both conditions further amplifies the risk. These findings emphasize the need for tailored clinical management strategies for children with asthma and co-occurring neurodevelopmental disorders to improve outcomes and reduce healthcare burdens. Enhanced awareness and specialized care approaches are essential for this vulnerable population. Future studies should further investigate the biological and behavioral mechanisms behind these associations to inform more effective clinical interventions.

Abbreviations

ASD	Autism spectrum disorder
ADHD	Attention deficit hyperactivity disorder
NIPPV	Non-invasive positive pressure ventilation
DMD	Duchenne muscular dystrophy
SMA	Spinal muscular atrophy

Supplementary Information

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Supplementary Material 1

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Author contributions

DXL: Conception and design; Acquisition of data; Analysis and interpretation of data; Critical revision of the manuscript; Drafting of the manuscript; definition of intellectual content; literature research; Supervision. YTC: Conception and design; Acquisition of data; Analysis and interpretation of data; Critical revision of the manuscript; Drafting of the manuscript; definition of intellectual content; literature research; Supervision. YCL: Conception and design; Acquisition of data; Analysis and interpretation of data; Critical revision of the manuscript; Final approval of the manuscript. SMW: Conception and design; Acquisition of data; Analysis and interpretation of data; Critical revision of the manuscript. All authors read and approved the final manuscript.

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Data availability
The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
All data were obtained through a request to the Online Healthcare Cost and Utilization Project (HCUP) Central Distributor (available at: https://www.distributor.hcup-us.ahrq.gov/), which administers the database (certificate # HCUP-863FXU18I). This study conforms to the NIS data-use agreement with HCUP. Because this study analyzed secondary data from the NIS database, patients and the public were not involved directly. The study protocol was submitted to the Institutional Review Board (IRB) of Chang-Gung Memorial Hospital, which exempted the study from IRB approval. Since all data in the NIS database are de-identified, the requirement for informed consent was also waived.

Consent for publication
Not applicable.

Competing interests
The authors have no conflicts of interest to declare.

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