



# Impact of congenital heart disease on mortality and other associated outcomes in children hospitalised for acute asthma exacerbation

## Original Article

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### Abstract

**Background:** Acute asthma exacerbation is one of the most common reasons for paediatric emergency room visits and hospital admissions in the United States of America. **Objective:** To assess the impact of CHD on outcomes of children hospitalised for acute asthma exacerbation. **Methods:** Children primarily admitted for acute asthma exacerbation were sampled from 2006, 2009, 2012, and 2016 kid inpatient database of the Healthcare Cost and Utilization Project using ICD codes. The disease outcomes were compared between those with and without CHD using multivariate logistic regressions in Stata version 17. **Results:** There were a total of 639,280 acute asthma exacerbation admissions, of which 5,907 (0.92%) had CHD. The mortality rate was 0.079% for patients without CHD and 0.72% for those with co-existing CHD. Children with CHD had higher odds of mortality (5.51, CI 3.40–8.93,  $p < 0.001$ ), acute respiratory failure (2.84, CI 2.53–3.20;  $p < 0.001$ ), need for invasive mechanical ventilation (4.58, CI 3.80–5.52;  $p < 0.001$ ), acute kidney injury (adjusted odds ratio 3.03, CI 3.03–7.44;  $p < 0.001$ ), and in-hospital cardiac arrest (adjusted odds ratio 4.52, CI 2.49–8.19;  $p < 0.001$ ) when compared with those without CHD. The adjusted mean length of hospital stays (CI 2.91–3.91;  $p < 0.001$ ) and hospital charges (95% CI \$31060–\$47747) among children with acute asthma exacerbation and CHD were significantly higher than in those without CHD. **Conclusion and Significance:** CHD is an independent predictor of mortality, more severe disease course, and higher hospital resource utilisation. Strategies that improve CHD care will likely improve the overall health outcomes of children with CHD hospitalised for acute asthma exacerbation.

Asthma is the most common chronic illness in childhood in the United States of America, with increased prevalence over the past decade.<sup>1–3</sup> It is also one of the most frequent causes of childhood hospitalisations, with a national annual hospital cost of an estimated US\$1.59 billion in 2009 alone.<sup>4</sup> It has a significant impact on the quality of life and is a leading cause of disability among people of all ages.<sup>5</sup> Asthma is a heterogeneous disease characterised by airway inflammation, with variable airflow limitation and symptoms such as wheezing, coughing, and shortness of breath. An acute asthma exacerbation is a worsening of asthma symptoms and may be triggered by viral infections or other environmental substances.

In addition to respiratory viral infections, which account for more than 80% of cases, socio-economic factors and comorbid conditions have been shown to predispose children to severe asthma exacerbations necessitating hospital admissions. In the United States of America, acute asthma exacerbations are more common among African-American, Puerto Rican, or low-income children.<sup>6</sup> Studies have also shown that the frequency of acute exacerbations, hospitalisations, and mortality rates increased in patients with obesity, obstructive sleep apnoea, or diabetes.<sup>7</sup> However, there is relatively little evidence to date about whether cardiovascular comorbidities influence the outcome of children hospitalised for asthma exacerbations.<sup>7</sup> CHD is the most prevalent cause of childhood cardiovascular morbidity and mortality. Also, it is the most common of all congenital defects, affecting nearly 1% of live births.<sup>8</sup> There is a growing population of children and adults living with CHD as advancements in medical and surgical care have increased the survival rates of patients with these conditions.<sup>9</sup> CHD and associated derangements in cardiopulmonary physiology, such as those causing increased pulmonary blood flow, distal airway compression, or elevated pulmonary capillary pressure, may cause recurrent or chronic breathing difficulties similar to asthma, and, in some cases, both may co-exist.

In this study, we report the impact of CHD on the outcomes of children who were admitted for acute asthma exacerbation using a national database. We examine the risk of mortality and development of complications, as well as the effects of CHD on the length of stay and hospital

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charges in children with CHD admitted for acute asthma exacerbation. The findings of this study will buttress previous knowledge on the influence of comorbid conditions on both health outcomes and the cost of health care among children with acute asthma exacerbation in the U.S. Also, the result of this study will convey relevant information for future research that is aimed at improving health outcomes for children with asthma and CHD.

## Materials and methods

### Study design and sample

This is a retrospective cohort study of children with acute asthma exacerbation admitted to pediatric hospitals across the U.S in the years 2006, 2009, 2012, and 2016 using the Kids' Inpatient Database. Kids' Inpatient Database is part of the Healthcare Cost and Utilization Project prepared by the Agency for Healthcare Research and Quality.<sup>10</sup> It is the largest publicly available pediatric inpatient care database in the U.S, containing two to three million hospital stays per year. It includes all-payer inpatient pediatric discharges at children's hospitals, both teaching and non-teaching, from 47 participating states in the U.S. The Kids' Inpatient Database is released every 3 years and the four most recently available datasets at the time of analysis of this study were used. The Kids' Inpatient Database has two types of diagnoses: the principal or primary diagnosis is the reason for the hospitalisation while the secondary diagnoses are other discharge diagnoses other than the primary diagnosis. Patients with a primary diagnosis of acute asthma exacerbation are included in this study. Children ages 20 or less are included in the Kids' Inpatient Database and are thus used in this analysis.

### Study outcomes

The primary outcome of this study was in-hospital mortality. The secondary outcomes were the risk of developing disease complications, including acute respiratory failure, acute kidney injury, and sudden cardiac arrest, and healthcare resource utilisation, measured by the length of hospital stay and total charges accrued during hospitalisation.

### Clinical variables

Hospitalised children with a primary diagnosis of acute asthma exacerbation were identified using the International Classification of Disease ninth and tenth revision codes. Data extracted included patient demographic characteristics (age, sex, race, insurance types) as well as the length of stay, death during hospitalisation, and hospital characteristics (bed size, location, and teaching status). From a thorough literature review, we identified common comorbid conditions and complications that have been associated with hospitalised children. These variables are tachyarrhythmias, diabetes, heart failure, conduction disorders, acute respiratory failure, acute kidney injury, use of invasive mechanical ventilation, obstructive sleep apnoea, and sudden cardiac arrest. Patients with these conditions, as well as individual cardiac diagnoses, were identified using the ICD-9 or ICD-10 codes. We adopted the American Heart Association's current adult CHD anatomy classification guideline to subdivide CHDs into simple, moderate, or complex CHD categories to assess for the impact of CHD complexity and, similar to prior publications exploring the impact of CHD on respiratory disease outcomes, we excluded diagnoses

related to patent ductus arteriosus to minimise its effects, which are usually insignificant after infancy.<sup>11-13</sup>

### Statistical analysis

Statistical analyses were performed using Stata version 17. Both descriptive and inferential analyses in this study take into account the complex sampling design of the Kids' Inpatient Database, including stratification, clustering, and weighing.

Bivariate analyses were performed to compare children admitted for acute asthma exacerbation with and without CHD. Similar analyses were generated to compare outcomes among the different groups of CHD based on their complexity. In each of the bivariate analyses, continuous and categorical variables were compared using the student t-test and Fisher exact test, respectively. Univariate regressions were first performed to generate unadjusted odd ratios for the primary and secondary outcomes. We then adjusted for potential confounders using multivariable logistic regression. Binary and continuous outcomes were analysed using logistic and linear regression, respectively. Co-founders were carefully selected by reviewing previous literature on this topic. A univariate screen was first performed on all the selected confounders. Those confounders that were significantly associated with the outcomes with a cut-off p-value of 0.2 were included in the final models of multivariable regressions. The cut-off p-value of 0.2 is based on a previously published and related study using the Healthcare Cost and Utilization Project database.<sup>14</sup> The potential confounders that were adjusted for were age, sex, race, primary payment methods, hospital location, and teaching status. The comorbidities that were adjusted for included diabetes mellitus, heart failure, cardiac conduction disorders, obstructive sleep apnoea, and arrhythmia, as well as the Deyo adaptation of the Charlson Comorbidity Index. We generated odds ratios for the risk of mortality, respiratory failure, the requirement of invasive mechanical ventilation, cardiac arrest, and acute renal failure. Mean differences in the length of hospital stay and total hospital charges were compared between children with and without CHDs. Using the Consumer Price Index Inflation calculator maintained by the US Bureau of Labor Statistics,<sup>15</sup> we accounted for inflation over the studied years. Statistical significance was set at the two-sided p-value of 0.05.

## Results

### Patient characteristics

There were 12,851,665 weighted hospitalisations in 2006, 2009, 2012, and 2016 in the United States of America, of which 639,280 had the primary diagnosis of acute asthma exacerbation. Table 1 shows the characteristics of the study sample. The mean age of children with acute asthma exacerbation was 6 years (SE 0.027) and 185,797 (39.8%) were females. A higher proportion were Whites (226,961; 35.5%), had Medicaid (364,617; 57.0%), and were admitted in large-bed capacity hospitals. Children with CHD constituted 0.92% of acute asthma exacerbation admissions. Their mean age was 4 years (SE 0.083) compared to 6.1 years (SE 0.026) in those without CHD. They are more likely to have tachyarrhythmias (3.2% versus 1.8%), heart failure (3.2% versus 0.06%), and conduction disorders (1.2% versus 0.04%) than patients admitted for acute asthma exacerbation without CHD (Table 2). Fig. 1 shows the distribution of acute asthma exacerbation admissions by age among children with and without CHD while Fig. 2 shows the number of in-hospital deaths by age in children with and without CHD. Acute asthma exacerbation occurred more

**Table 1.** Patients and hospital characteristics of acute asthma diagnosis.

Variables	n	%
<b>Total asthma cases</b>	639280	100
<b>Mean age in years (SE)</b>	6.0 (0.027)	
<b>Female</b>	185797	39.8
<b>Race</b>		
White	226961	35.5
Black	210805	32.9
Hispanic	144507	22.6
Asian/Pacific Islander	15,906	2.4
Native American	5791	0.9
Others	35,307	5.5
<b>Primary payer</b>		
Medicare	1389	0.21
Medicaid	364617	57.0
Private insurance	226079	35.3
Self-pay	26,735	4.1
No charge	1072	0.1
Others	19,384	3.0
<b>Hospital bed size</b>		
Small	82,332	12.8
Medium	161293	25.2
Large	395653	61.8
<b>Hospital location</b>		
Rural	61,369	9.5
Urban non-teaching	151088	23.6
Urban teaching	426822	66.7
<b>Year</b>		
2006	171408	26.8
2009	184329	28.8
2012	161284	25.2
2016	122257	19.1
SE = standard error		

frequently early in life before trailing off to lower numbers after approximately age 10 in both children with and without CHD.

### *In-hospital mortality*

The overall in-hospital mortality rate was 0.085%. The rate was 0.079% for patients without CHD and 0.72% for those with any type of co-existing CHD. In the unadjusted model, children with CHD were 9 times more likely to die during hospital admission for acute asthma exacerbation than those without CHD (95% CI 6.3–13.5;  $p < 0.001$ ), as seen in Table 3. This relationship was maintained in an adjusted logistic model though with a lower odds ratio (aOR 5.51, CI 3.40–8.93,  $p < 0.001$ ). Table 4 shows the results of the multivariate logistic regression of the impact of CHD on acute asthma exacerbation in-hospital mortality.

### *Disease complications*

Acute respiratory failure was more common in patients with CHD than in those without CHD (11.2% versus 3.9%). In the unadjusted model, the odds of development of acute respiratory failure were 3 times higher in children with CHD than those without CHD (OR 3.12, CI 2.79–3.49;  $p < 0.001$ ), and the significant relationship was also true when adjusted for confounders (aOR 2.84, CI 2.53–3.20;  $p < 0.001$ ). Acute kidney injury occurred in 49 children with CHD (0.8%) versus 886 children without CHD (0.1%). The odds of development of acute kidney injury were greater in those with CHD than those without CHD (aOR 3.03, CI 3.03–7.44;  $p < 0.001$ ). For the entire cohort, the overall rate of in-hospital cardiac arrest was 0.078%. There was a higher proportion of cardiac arrest among children with CHD (31, 0.5%) than in those without CHD (468, 0.07%). Furthermore, cardiac arrest odds were 7 times greater in children with CHD in the unadjusted model (OR 7.42, CI 4.80–11.46;  $p < 0.001$ ), and this risk decreased to 4 times when other co-founders were factored in the analysis (aOR 4.52, CI 2.49–8.19;  $p < 0.001$ ), with both relationships being statistically significant. Invasive mechanical ventilation was required for 7,455 children, with an overall utilisation rate of 1.16%. Of those children with CHD, 5.5% required invasive mechanical ventilation compared to 1.1% of those without CHD. Multivariate logistic analysis showed that the odds of requiring invasive mechanical ventilation were at least 4 times higher in children with CHD than in those without CHD (aOR 4.58, CI 3.80–5.52;  $p < 0.001$ ).

### *Resource utilisation*

Resource utilisation was based on hospital length of stay and total hospital charges. The overall mean length of stay was 2.5 days (95% CI 2.50–2.580), 6.4 days for those with CHD, and 2.5 days for those without CHD. After adjusting for possible confounders, CHD was associated with a significant increase in the mean hospital length of stay (adjusted mean length of stay: 3.41 days, CI 2.91–3.91;  $p < 0.001$ ). In the adjusted model, the presence of other comorbid conditions like arrhythmia, diabetes, and underlying heart failure was correlated with an increase in the overall length of stay of those with CHD. The mean total hospital charges for all acute asthma exacerbations within the studied period were \$16427.22 (CI \$15822–\$17031). While the mean total hospital charges for children without CHD were \$16003, children with CHD accrued a mean total charge of \$61890, a relationship that is significant in both the bivariate (95% CI \$36562–\$55,211) and multivariate (95% CI \$31060–\$47747) analyses as shown in Table 4. Furthermore, Figure 3 shows the relationship between total hospital charges when accounting for inflation. The inflation-adjusted mean total hospital charges for children with CHD were about \$118,920.06 (95% CI \$74919.59–\$128644.3) and were at least three times greater than in children without CHD (\$33,432.94, 95% CI \$26482.56–\$30745).

### *Outcomes among different CHD classes*

Supplementary Table 1 compared the outcomes of acute asthma exacerbation among the different classes of CHD in this study. There were no statistically significant differences in both primary and secondary outcomes among different degrees of CHD complexity.

**Table 2.** Comparison of patients' characteristics in children with and without CHD.

Variable	CHD				p-value
	Yes		No		
	n	%	n	%	
<b>Acute asthma</b>	5907	0.92	633373	99.0	
<b>Mean age in years (SE)</b>	4(0.083)		6.1(0.026)		<0.01
<b>Gender</b>					0.13
Male	3480	58.9	381227	60.1	
Female	2426	41.0	252145	39.8	
<b>Race</b>					<0.01
White	2442	41.35	224530	35.4	
Black	1248	21.12	209583	33.0	
Hispanic	1332	22.5	142825	22.5	
Asian/Pacific Islander	146	2.4	15,707	2.4	
Native American	53	0.9	5700	0.9	
Others	326	5.5	35,025	5.5	
Mean of length of stay (days)	6.4		2.5		<0.01
Mean total hospital charges	61,890		16,003		<0.01
In-hospital death	43	0.72	506	0.079	<0.01
<b>Comorbidity</b>					
Tachyarrhythmias	193	3.2	11,844	1.8	<0.01
Diabetes	26	0.4	3166	0.5	0.67
Heart failure	191	3.2	373	0.06	<0.01
Conduction disorders/heart block	76	1.2	253	0.04	<0.01
<b>Complications</b>					
Acute respiratory failure	666	11.2	24,764	3.9	<0.01
Acute kidney injury	49	0.8	886	0.1	<0.01
Invasive mechanical ventilation	325	5.5	7220	1.1	<0.01
Sudden cardiac arrest	31	0.5	468	0.07	<0.01

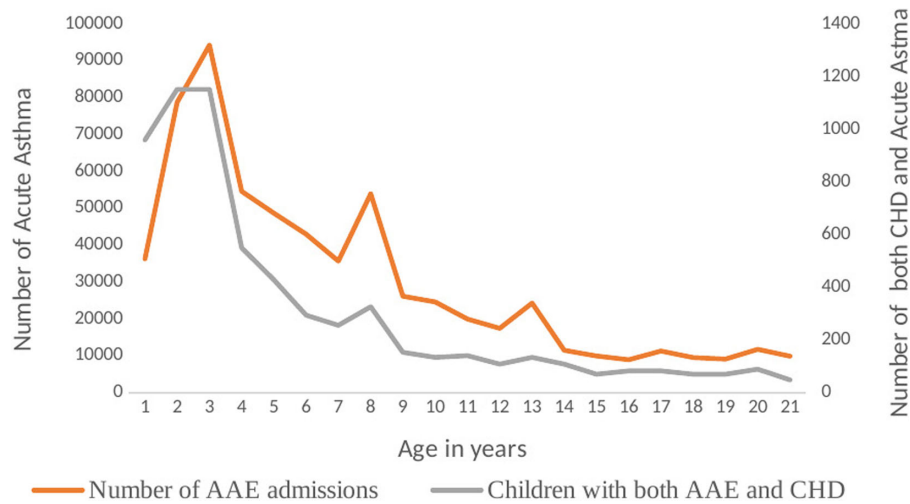
## Discussion

We have shown in this study that CHD is a major independent comorbid predictor of mortality in children who are admitted for acute asthma exacerbation. Also, concomitant CHD and acute asthma exacerbation are associated with an increased risk of developing major hospital complications, including the requirement of mechanical ventilation, acute respiratory failure, acute renal failure, and cardiac arrest. Children with CHD admitted for acute asthma exacerbation have increased hospital resource utilisation in the length of hospital stay and total hospital charges.

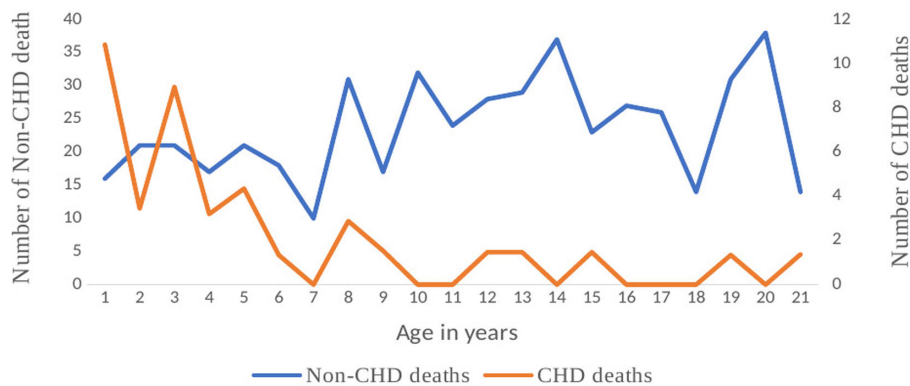
CHD has been frequently reported as a major comorbid condition in childhood, contributing to worse treatment outcomes in both respiratory and non-respiratory conditions. In a study by Diller et al. on children admitted for viral pneumonia, CHD was associated with an increase in in-hospital death for children with CHD when compared to the non-CHD cohort.<sup>12</sup> The authors reported an overall in-hospital case fatality rate of 8.5% in children with CHD compared to 3% in non-CHD pairs. Similarly, using the Kids' Inpatient Database, Ghimire et al. found children with CHD to have 2.8-fold increased odds of mortality when admitted for

influenza infection.<sup>13</sup> CHD also adds a significant increase in the odds of death in children who undergo non-cardiac surgery. For example, by examining a large multi-institutional database, Baum et al. found that children with CHD undergoing inpatient non-cardiac surgical procedures have significantly greater mortality, regardless of whether mortality is measured at 1, 3, or 30 days postoperatively.<sup>16</sup> Several factors may explain higher rates of mortality in children with CHD after acute asthma exacerbation. Anatomical compression is often an unrecognised complication of CHD.<sup>17</sup> Children with CHD may have underlying obstructive lung diseases, such as peribronchial cuffing, airway compression, vocal cord paralysis, or massive cardiomegaly, which can compress the left main bronchus or the lower left lung lobe. Respiratory infections are the major cause of acute asthma exacerbation, and children with CHD may have greater cardiovascular compromise from the inflammatory response from respiratory infections. Also, common pathologic pulmonary conditions associated with CHD such as restrictive lung diseases with impaired lung growth or impaired lung compliance, diffusional impairments with altered gas exchange associated with pulmonary oedema (intrapulmonary





**Figure 1.** Distribution of acute asthma exacerbation admissions by age, with and without CHD.



**Figure 2.** Distribution of in-hospital deaths by age among children with and without CHD.

shunt in the case of left to right shunting lesions), and reduced pulmonary blood flow (increased physiologic dead space) are important factors that may contribute to increased mortality in children with CHD.

Our study found an increased risk of severe in-hospital complications, such as respiratory failure, use of invasive mechanical ventilation, acute kidney injury, and cardiac arrest among children with CHD. These findings are in keeping with previous findings. For example, among similar age groups of children with bronchiolitis, mechanical ventilation use was higher in children with CHD compared to non-CHD children.<sup>18</sup> Much of the increased risk of these complications is due to the underlying CHD, which can worsen during any acute disease condition such as acute asthma exacerbation. Children with CHD had three times higher odds of acute kidney injury in this study. Although cardiopulmonary bypass surgery is the most common cause of acute kidney injury in children undergoing cardiac surgery, many other complex cardiorenal interactions can also cause acute kidney injury.<sup>19</sup> Different degrees of nephropathy are often seen in children with CHD, and those with cyanotic CHD have a higher risk of developing renal impairment over time spontaneously or during acute illness.<sup>20</sup> Since children with CHD and acute asthma exacerbation have a higher risk of acute kidney injury, it is important to pay good attention to fluid balance when correcting acute dehydration in these children. There is increasing evidence that fluid overload is associated with a higher risk of acute kidney injury and imposes great morbidity and mortality in children.<sup>21</sup>

In acute asthma exacerbation, there is air trapping with ventilation-perfusion mismatch; both can lead to increased intrathoracic pressure, increased pulmonary vascular resistance, and right ventricular systolic pressure overload. Children with CHD may have less myocardial reserve and haemodynamic instability that may make them prone to early cardiovascular arrest not directly due to acute respiratory failure. Also, arrhythmias and conduction disorders are more frequently seen in children with CHD, and these are major comorbidities that may increase the risk of cardiac arrest. The complexity of CHD in this study did not have any significant impact on the outcomes of acute asthma exacerbation admissions while the presence of CHD itself had significant negative effects. It may be intuitive that children with complex or cyanotic CHD will have poorer outcomes if admitted for acute illnesses like asthma exacerbation. However, this depends on the patient's baseline cardiac functions. Children with corrected transposition of great arteries and total anomalous pulmonary venous return with good baseline cardiac function may not necessarily be at higher risk of poor outcomes. But as pertaining to this study, more than two-thirds of the children included had simple or moderate CHD while only 12% had complex disease. Our sample may not be large enough to detect a difference in impact between complex and other types of CHD.

Our analysis revealed that CHD is a major contributor to a longer length of hospital stay and higher hospital charges following admission for acute asthma exacerbations. CHD has been associated with increased length of stay in various medical and surgical

**Table 3.** Primary and secondary outcomes of the impact of CHD on admissions for acute asthma exacerbation.

Variables	Unadjusted			Adjusted		
	Odds ratio	95% CI	p-value	Odds ratio	95% CI	p-value
In-hospital mortality	9.27	6.3–13.5	<0.01	5.51	3.40–8.93	<0.01
Hospital length of stay (mean)	3.89	3.3–4.4	<0.01	3.41	2.91–3.91	<0.01
Acute respiratory failure	3.12	2.79–3.49	<0.01	2.84	2.53–3.20	<0.01
Invasive mechanical ventilation	5.05	4.30–5.93	<0.01	4.58	3.80–5.52	<0.01
Acute kidney injury	6.20	4.45–8.64	<0.01	4.75	3.03–7.44	<0.01
Sudden cardiac arrest	7.42	4.80–11.46	<0.01	4.52	2.49–8.19	<0.01

**Table 4.** Multivariate logistic regression of the impact of CHDs on in-hospital mortality in acute asthma exacerbation\*.

Variables	aOR	CI	P-value
Congenital heart disease	4.4	2.57–7.60	<0.01
Ages 6–10	1.8	1.31–2.50	<0.01
Ages >10	5.3	4.10–7.07	<0.01
Female	1.0	0.85–1.33	0.555
<b>Race</b>			
Black	0.79	0.587–1.076	0.138
Hispanic	0.69	0.491–0.990	0.043
Asian/pacific Islander	0.68	0.294–1.574	0.369
Other races	0.864	0.552–1.352	0.524
<b>Payment</b>			
Medicaid	0.534	0.310–0.918	0.023
Private insurance	0.469	0.269–0.817	0.008
Self-pay	0.283	0.124–0.646	0.003
<b>Hospital</b>			
Urban non-teaching	2.4	0.937–5.505	0.067
Urban teaching	6.7	2.740–16.54	<0.01
<b>Comorbidity</b>			
Tachyarrhythmias	2.45	1.570–3.822	<0.01
Diabetes	0.69	0.352–1.379	0.301
Heart failure	3.08	1.465–6.490	0.003
Heart conduction disorders	1.79	0.508–6.323	0.364
Obstructive sleep apnoea	1.39	0.656–2.731	0.422
Charlson Comorbidity Index $\geq 2$	4.73	3.929–5.704	<0.01

\*Age group 0–5, White, Medicare, and Charlson Comorbidity Index of 1 were set as the reference value.

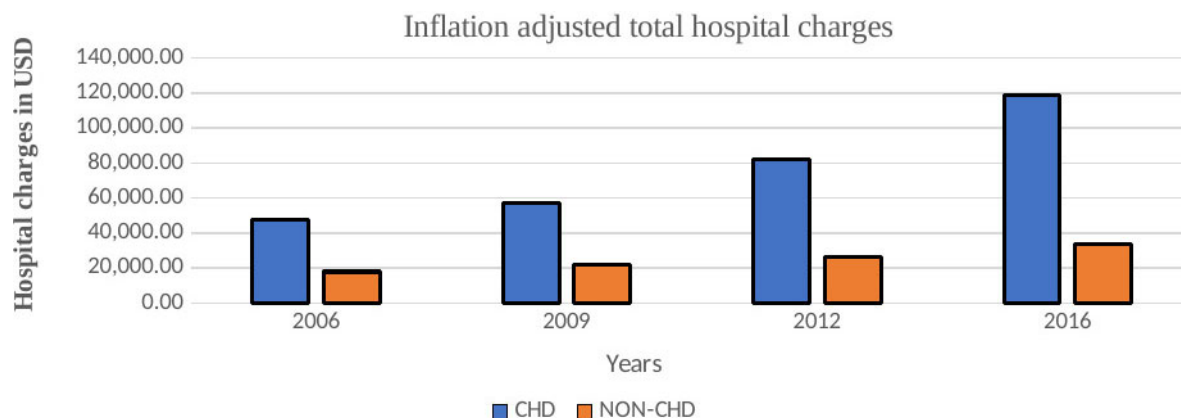
admissions. In a population study using the Kids' Inpatient Database, Edelson et al. found that the length of stay was 4.97 days in CHD versus 1.67 days in the non-CHD cohort and inflation-adjusted hospital charges to be 10-fold higher in children with CHD.<sup>22</sup> Also, Ghimire et al. found that the median length of stay in children with CHD who were admitted for influenza infection was 4 days compared to 2 days in those without CHD<sup>13</sup>. Our study found the mean total inflation-adjusted hospital charges of children with CHD and acute asthma exacerbation to be \$76,355.44 compared to \$25,006 in children without CHD,

indicating more than a threefold increase. This is in keeping with a higher cost of hospitalisation for non-cardiac diagnosis previously reported in adult patients with CHD.<sup>23</sup> The increased total hospital charges may stem from the additional cost of managing complications, including required procedures, and the longer hospital stay. Children with severe CHD sometimes require admission to the ICUs which is often more expensive, with an average daily cost of admissions more than threefold higher than in the general ward.<sup>24</sup>

This study is not without limitations. First, the Kids' Inpatient Database is an administrative database collected primarily for medical coding and billing, and ICD-9 and 10 were used to identify patients and their diagnoses. Though several Healthcare Cost and Utilization Project quality control measures ensure the internal validity of the data, there is a possibility of human errors in the classification of diagnosis. Also, Healthcare Cost and Utilization Project data are limited to certain hospitals and do not contain data on hospital admissions of less than 24 hours. Depending on the severity, children with asthma may have exacerbations necessitating multiple hospital admissions in a year. The de-identification in Healthcare Cost and Utilization Project limits our ability to recognise repeat hospital admissions. Hence, a small number of the studied patients may account for a disproportionate number of encounters. Finally, information on medical treatments received by the patients is not provided in Healthcare Cost and Utilization Project data and thus is not accounted for in our analyses. Many of the medications used to manage asthma, such as beta-adrenoreceptors, muscarinic, corticosteroids, and theophylline, have indirect effects on cardiac rhythm disorders, and accounting for them would have yielded a higher internal validity of this study.

To our knowledge, this study is the first to examine the impact of CHD on children admitted specifically for acute asthma exacerbation at a national level. We analysed the largest public database of paediatric hospitalisations in the United States of America. It is a nationally representative sample of 4,000 US community hospitals including patients from small, medium, and larger, teaching, and non-teaching hospitals, rural and urban, privately or publicly owned, or for-profit and not-for-profit hospitals. Hence, our results should have very low beta error and be reflective of children with acute asthma exacerbation admitted to the hospital across the United States of America.

In conclusion, CHD is an independent predictor of mortality among children admitted to the hospital for acute asthma exacerbation. It is also associated with more serious disease outcomes in patients with acute asthma exacerbation, such as higher incidences of acute respiratory failure leading to more frequent use of invasive mechanical ventilation, acute kidney failure, and sudden cardiac arrest. Also, CHD is significantly



**Figure 3.** Inflation-adjusted total hospital charges of paediatric acute asthma hospitalisations with and without CHD.

associated with increased utilisation of hospital resources, including increased length of stay and total hospital charges. Strategies that improve CHD care, optimise management of acute asthma exacerbation, and identify and treat modifiable risk factors for asthma will significantly improve the overall health outcomes of children with both asthma and CHD.

**Supplementary material.** The supplementary material for this article can be found at <https://doi.org/10.1017/S1047951123003803>.

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