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RESEARCH

Congenital Heart Defects and Concurrent Diagnoses in Influenza Hospitalization in the Pediatric Health Information System Study, 2004–2019

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Abstract

Influenza is associated with adverse outcomes in children, although modification by additional medical conditions is not well-documented. We aimed to compare outcomes in children with versus without congenital heart defects (CHDs) who were hospitalized for influenza. We retrospectively evaluated patients 1-18y hospitalized for influenza in the Pediatric Health Information (PHIS) database from 2004 to 2019. Outcomes were compared by CHD presence and then by CHD severity (minor biventricular, major biventricular, and single ventricle disease) using log-binomial regression adjusted for propensity scores accounting for age at admission, sex, and history of asthma. Outcomes included inpatient mortality, intensive care unit (ICU) admission, mechanical ventilation, and length of stay (LOS) > 12 days. To evaluate for effect modification by genetic diagnoses, analyses were repeated stratified by CHD and genetic diagnosis. Among 55,161 children hospitalized for influenza, 2369 (4.3%) had CHDs, including 963 with minor biventricular, 938 with major biventricular, and 468 with single ventricle CHDs. Adjusting for propensity scores, children with CHDs had higher mortality (4.1% versus 0.9%) compared to those without CHDs (risk ratio [RR] 2.5, 95% confidence interval [CI] 1.9–3.4). Children with CHDs were at higher risk of mechanical ventilation (RR 1.6, 95% CI 1.6–1.7), ICU admission (RR 1.9, 95% CI 1.8–2.1), and LOS > 12 days (RR 2.2, 95% CI 2.0–2.3). Compared to those with neither CHD nor genetic condition, children with both had significantly higher risk of all outcomes, with the largest difference for LOS > 12 days (RR 2.3, 95% CI 2.0–2.7). Children with CHDs hospitalized for influenza are particularly susceptible to adverse outcomes compared to those without CHDs. Future studies are needed to corroborate findings in light of influenza vaccination.

Keywords Influenza infection · Congenital heart disease · Intensive care admission · Mortality · Extracorporeal membrane oxygenation · Mechanical ventilation

Introduction

Approximately 9% of children in the United States (US) are diagnosed with influenza viral infection every year, with annual estimates of hospitalization ranging from 7000 to 26,000 [1, 2]. Infected children, particularly those under age 5 years, are at increased risk of developing serious complications and death [3–6]. Higher morbidity and mortality among children with chronic disease who have influenza infection is previously documented, including in asthma, bronchopulmonary dysplasia, and sickle cell disease with the majority of influenza-associated deaths in the general population occurring in children with chronic disease [5, 7–9]. Further, survivors are more likely to be admitted to intensive care units, have longer admissions, and need

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mechanical ventilation compared to those without chronic disease [10–13].

However, differences in outcome risk between children with congenital heart defects (CHDs) admitted for influenza with and without co-occurring conditions is not well-understood. CHDs are of particular interest because, by definition, many CHDs are characterized by impaired cardiac, pulmonic, and systemic blood flow, often limiting adequate oxygen delivery [14]. Given influenza's additional association with respiratory disease, it follows that children with the combination of CHDs and influenza infection may be particularly vulnerable to poor outcomes compared to infected children without CHDs. Prior literature posits that the limited respiratory and cardiac reserves observed in children with CHDs may contribute to their increased mortality, particularly as the increased cardiorespiratory demand of active infection may not be accommodated in these patients due to their cardiac disease [12, 15]. Therefore, there may be further compromised cardiac function if infection promotes an acute systemic inflammatory response [12, 15]. The aim of this study was therefore to characterize associations between CHDs and inpatient outcomes in a large cohort of children hospitalized for influenza infection.

Methods

Data Source and Study Population

This retrospective cohort study evaluated data collected in the Pediatric Health Information Systems (PHIS) database. Maintained by the Children's Hospital Association (CHA), PHIS is a database containing clinical and administrative data from emergency and inpatient encounters from more than 49 pediatric tertiary centers in the US. PHIS currently accounts for 20% of all pediatric tertiary center care in the US [16]. Inpatient data in PHIS includes clinical diagnostic and procedural codes, medication data, and hospital charges by patient and hospitalization ID. Data from each hospitalization is accompanied with a hospital code corresponding to its respective center. Data quality assurance efforts are performed by participating centers and the CHA [16]. One primary and a maximum of 40 secondary clinical diagnoses at each encounter are documented using International Classification of Disease (ICD) codes, 9th (ICD-9) and 10th (ICD-10) editions. This study was approved by the Institutional Review Board approval at Baylor College of Medicine and the Committee for the Protection of Human Subjects at the University of Texas Health Science Center.

Children ages 1 to < 18 years of age at the time of hospitalization with a primary diagnosis of influenza viral infection (ICD-9 codes 487.0, 487.1, 487.8, ICD-10 codes J09-J18) between January 1, 2004 and December 31, 2019 were included. When a patient had more than one hospitalization, only the first hospitalization was considered. Based on PHIS' inclusion of exclusively pediatric tertiary centers, we anticipate that the likelihood of children being transferred to another hospital for higher level of care, and subsequently having another hospitalization not otherwise captured, is minimal. Of note, because several severe CHDs are associated with a high risk of mortality within the first year of life, we excluded children with influenza who were less than 1 year of age at the time of admission [17–22].

Primary Exposure and Covariates

The primary exposure of interest was a dichotomized diagnosis of CHD. For secondary analyses (described below), CHD type was then stratified based on severity (single ventricle disease [e.g., hypoplastic left heart syndrome], major biventricular disease [e.g., interrupted aortic arch], or minor biventricular disease [e.g., isolated ventricular or atrial septal defects]; Supplemental Table 1). Children with > 1 CHD were hierarchically categorized into the CHD category of highest severity. For example, a patient with tricuspid atresia (single ventricle disease), aortic coarctation (major biventricular), and ventricular septal defect (minor biventricular) were classified as having single ventricle disease. Other variables collected included demographics (age at admission, sex, race/ethnicity, admission year), with age at admission evaluated as a categorized variable based on decile. To ensure adequate cell sizes, admission year was categorized as 2004–2010, 2011–2015, and 2016–2019. Asthma, hospital of care (coded), and genetic conditions were defined using ICD-9 and 10 codes (Supplemental Table 2).

Outcomes

The primary outcome was death during hospitalization. Secondary outcomes were intensive care unit (ICU) admission, mechanical ventilation, and length of hospital stay (LOS) > 12 days. Death during hospitalization, ICU admission, and LOS were ascertained from the patient's medical record chart and are recorded as individual variables in PHIS. LOS was dichotomized as either > 12 or ≤ 12 days (i.e., based on the 90th percentile in LOS among all patients). Secondary outcomes were coded according to their respective ICD-9 and 10 codes (defined in Supplemental Table 2).

Statistical Analysis

The cohort was first described using counts and percentages for categorical variables and medians with corresponding interquartile ranges (IQR) for continuous variables. Chi-square and Wilcoxon rank-sum test were used to evaluate differences in categorical and continuous variables

(respectively) by CHD presence (yes/no). Using hospital as a random effect, mixed-effects log-binomial regression was used to generate unadjusted risk ratios (RRs) and corresponding 95% confidence intervals (CIs) for the association between dichotomized CHD and each outcome.

To adjust for covariates, propensity scores were generated using logistic regression to characterize associations between dichotomized CHD presence (outcome) and categorical age at hospitalization, sex, and history of asthma (exposure variables) with propensity scores included as a covariate in subsequent models. Therefore, multivariable mixed-effects log-binomial regression was used to estimate adjusted RRs for the associations between dichotomized CHD status and each outcome while including the propensity score and the hospital as a random effect term. Then utilizing CHD severity as a categorical variable, we repeated analyses to compute unadjusted and adjusted RRs separately for the associations between each outcome and CHD severity using patients with no CHDs as the referent while similarly including propensity score in the model.

Secondary analyses were performed to better understand the impact of concurrent diagnosis of a genetic condition, which may increase risk for adverse outcomes among children with CHDs [21–25]. Thus, analyses were repeated with four mutually exclusive exposure categories: 1) CHD and genetic condition, 2) CHD without genetic condition, 3) no CHD with genetic condition, or 4) neither (reference group). Across all analyses, comparisons with cell counts <5 were not performed. All measures of association were reported with a 95% confidence interval and reflect a two-sided p-value. A p-value <0.05 was considered to be statistically significant. Statistical analyses were performed using SAS (version 9.1 copyright 2002–2008, SAS, Cary, NC).

Results

A total of 55,161 patients were eligible for inclusion, 2369 of which had CHDs (4.3%, Table 1). A total of 30,754 were male (55.7%). Patients were predominantly of non-Hispanic White (41.2%), followed by non-Hispanic Black (23.7%), and Hispanic (22.0%) race/ethnicity. Median age at admission was 5.6 years (IQR 2.5–9.7 years), with admissions most frequently between 2016 and 2019 (41.2%). Among those with CHDs, 40.7% had minor biventricular disease, 39.6% had major biventricular disease, and the remaining 19.8% had single ventricle disease. Children with CHDs were more likely to have a diagnosis genetic condition compared to children without CHDs (25.2% vs. 3.3%, $p<0.0001$), but were less likely to have asthma compared to children without CHDs (25.8% vs. 29.2%, $p=0.0003$). All outcomes occurred more frequently among children with CHDs than without CHDs, including death (2.0% vs. 0.9%, $p<0.0001$; Table 1).

After propensity score adjustment in multivariable analysis, children with CHDs had 2.5-times the risk of dying while hospitalized compared to those without CHDs (RR 2.5, 95% CI 1.9–3.4; Table 2). In multivariable analysis, children with CHDs had 64% higher risk of being admitted to the ICU compared to those without CHDs (RR 1.6, 95% CI 1.6–1.7). Further, children with CHDs had approximately double the risk of undergoing mechanical ventilation (RR 1.9, 95% CI 1.8–2.1) or LOS > 12 days (RR 2.2, 95% CI 2.0–2.3) after controlling for propensity scores.

Similar associations were observed across all CHD categories for the association between CHD severity and death during hospitalization, with increasing magnitudes of association with increasing CHD severity (Table 3). For example, following propensity score adjustment, children with minor biventricular disease had 2.3-times the risk of dying compared to those without CHDs (RR 2.3, 95% CI 1.4–3.7), while those with more severe single ventricular disease had 3.2-times the risk of dying (95% CI 1.8–5.6). In multivariable analysis, patients stratified by CHD category had similar effect estimates (all statistically significant) when compared to those without CHD, with approximately 63% to 66% higher risk of ICU admission. Compared to those with no CHD, children with biventricular minor disease had the highest relative risk of receiving mechanical ventilation in multivariable analysis (RR 2.1, 95% CI 1.8–2.3).

Compared to children with neither a CHD nor genetic condition, those with either a CHD or genetic condition alone had 80% and 90% higher risk, respectively, of undergoing mechanical ventilation (genetic condition RR 1.8, 95% CI 1.6–2.0, CHD RR 1.9, 95% CI 1.8–2.1; Table 4). This effect estimate was magnified for patients with the combination of both a genetic condition and a CHD (RR 2.1, 95% CI 1.8–2.4). A similar trend was observed for LOS > 12 days (genetic condition RR 1.8, 95% CI 1.7–2.0; both RR 2.3, 95% CI 2.0–2.7).

Discussion

Using 16 years of multicenter data available in PHIS, this study found that children with CHDs hospitalized for influenza are at significantly higher risk of adverse outcomes compared to children without CHDs hospitalized for influenza, including death during hospitalization. We additionally found that children with CHDs are at significantly higher risk of ICU admission, undergoing mechanical ventilation, and prolonged length of hospital stay, regardless of age at admission, sex, and history of asthma. Further, findings suggested that risk may be modified by concurrent genetic diagnoses. Altogether, this study adds to the base

Table 1 Cohort characteristics

Variable	CHD ($n=2369$)	No CHD ($n=52,792$)	p-value[a]
Sex			0.20
Male	1291 (54.5%)	29,463 (55.8%)	
Female	1078 (45.5%)	23,320 (44.2%)	
Unknown	0 (–)	9 (0.02%)	
Race and ethnicity			**< 0.0001**
Non-Hispanic White	1025 (43.3%)	21,710 (41.1%)	
Non-Hispanic Black	409 (17.3%)	12,669 (24.0%)	
Hispanic	645 (27.7%)	11,490 (21.8%)	
Non-Hispanic Asian	75 (3.2%)	1600 (3.0%)	
Non-Hispanic Other	176 (7.4%)	3846 (7.3%)	
Unknown	39 (1.7%)	1477 (2.8%)	
Year of admission			**< 0.0001**
2004–2010	592 (25.0%)	15,465 (29.3%)	
2011–2015	730 (30.8%)	15,672 (29.7%)	
2016–2019	1047 (44.2%)	21,655 (41.0%)	
Age at admission, years (IQR)	3.5 (1.7–7.1)	5.6 (2.6–9.8)	**< 0.0001**
CHD severity			–
Single ventricle	468 (19.8%)	–	
Major, biventricular	938 (39.6%)	–	
Minor, biventricular	963 (40.7%)	–	
No CHD	–	52,792 (100.0%)	
Asthma	610 (25.8%)	15,393 (29.2%)	**0.0003**
Genetic condition	598 (25.2%)	1747 (3.3%)	**< 0.0001**
Outcomes			
Death During hospitalization	47 (2.0%)	471 (0.9%)	**< 0.0001**
ICU admission	952 (40.2%)	12,641 (24.0%)	**< 0.0001**
Mechanical ventilation	533 (22.5%)	6002 (11.4%)	**< 0.0001**
LOS > 12 days	493 (20.8%)	5049 (9.6%)	**< 0.0001**

Categorical variables are reported in counts and frequencies (%). Continuous variables are reported in median and interquartile range (IQR)

CHD congenital heart defect, *CI* confidence interval, *ICU* Intensive care unit

[a]Statistics are presented prior to propensity score matching. Bolded p-values represent statistical significance at a 95% confidence level

Table 2 Unadjusted and adjusted risk ratios of CHD status by outcome

Outcome	Unadjusted analysis RR (95% CI)	Adjusted analysis[a] RR (95% CI)
Death during hospitalization	2.22 (1.65–2.99)	2.51 (1.85–3.42)
ICU admission	1.67 (1.59–1.76)	1.64 (1.56–1.73)
Mechanical ventilation	1.98 (1.83–2.14)	1.90 (1.75–2.06)
LOS > 12 days	2.18 (2.00–2.36)	2.16 (1.97–2.34)

RR risk ratio, *CI* confidence interval, *ICU* intensive care unit

[a]Adjusted analyses included propensity score in the model and hospital as a random effect

of literature elucidating the risk associated with CHDs and inpatient adverse outcomes in the setting of influenza infection. Findings may be helpful to further investigations identifying additional characteristics contributing to this increased risk among children with CHDs.

To date, there is one prior large published study evaluating the association between CHD and inpatient outcomes among children hospitalized for influenza [12]. Using data available from 2003 to 2016 in the Kids' Inpatient Database (KID), Ghimire et al. found that inpatient mortality was significantly more frequent among children with CHDs hospitalized for influenza compared to those without CHDs (2.0% vs. 0.5%), as children with CHDs had nearly 4-times the risk of dying while admitted compared to their non-CHD counterparts [12]. Given children with CHDs in PHIS had more than 2.5-times the risk of dying while hospitalized for

Table 3 Unadjusted and adjusted risk ratios of CHD severity by outcome

Outcome	Unadjusted analysis	Adjusted analysis[a]	
	RR (95% CI)	RR (95% CI)	*p*-value[b]
Death during hospitalization			
No CHD	Ref	Ref	
Biventricular, minor	1.86 (1.14–3.05)	2.25 (1.36–3.71)	**0.0018**
Biventricular, major	2.27 (1.44–3.58)	2.42 (1.53–3.84)	**0.0002**
Single ventricle	2.87 (1.63–5.06)	3.18 (1.80–5.62)	**< 0.0001**
ICU admission			
No CHD	Ref		
Biventricular, minor	1.67 (1.55–1.81)	1.66 (1.53–1.79)	**< 0.0001**
Biventricular, major	1.69 (1.56–1.82)	1.64 (1.51–1.78)	**< 0.0001**
Single ventricle	1.64 (1.47–1.84)	1.63 (1.45–1.82)	**< 0.0001**
Mechanical ventilation			
No CHD	Ref	Ref	
Biventricular, minor	2.17 (1.94–2.43)	2.06 (1.84–2.31)	**< 0.0001**
Biventricular, major	2.02 (1.79–2.27)	1.93 (1.72–2.18)	**< 0.0001**
Single ventricle	1.50 (1.23–1.84)	1.47 (1.20–1.80)	**0.0003**
LOS > 12 days			
No CHD	Ref	Ref	
Biventricular, minor	2.29 (2.03–2.59)	2.31 (2.05–2.62)	**< 0.0001**
Biventricular, major	2.13 (1.87–2.42)	2.09 (1.83–2.38)	**< 0.0001**
Single ventricle	2.03 (1.69–2.45)	1.96 (1.62–2.36)	**< 0.0001**

CHD congenital heart defect, *CI* confidence interval, *ICU* intensive care unit, *LOS* length of stay, *RR* risk ratio

[a]Adjusted analyses included propensity score and hospital as fixed random effect, respectively

[b]Bolded *p*-values represent statistical significance at a 95% confidence level

influenza compared to those without CHDs, our conclusions are generally consistent with Ghimire's prior conclusions [12]. Notably, children with CHDs were less frequent in their cohort (1.7%) compared to the 4.3% with CHDs in our PHIS cohort [12]. Given the fact that Ghimire et al. investigated the KID, a cross-sectional database of approximately 80% of pediatric discharges in the United States, we posit this difference may be due to their potential inclusion of general hospitals and other centers in addition to the tertiary centers that comprise the PHIS database [12]. Therefore, it is possible that our findings evaluating solely tertiary centers comprising PHIS may reflect outcomes of more medically complex children or those who inherently have worse prognoses.

In addition to death during hospitalization, risk for undergoing mechanical ventilation was elevated (e.g., 1.9-times higher) among those with CHDs compared to those without CHDs, which was observed across all CHD categories. Given the fact that mechanical ventilation is typically administered in the case of impaired oxygen levels or high carbon dioxide levels and that children with CHDs already have impaired cardiac, pulmonary, and systemic blood flow, these affected patients with a concurrent influenza infection may have even more impaired cardiac reserve and therefore demonstrate higher morbidity and mortality [26]. Such findings have already been implicated in other studies of patients with CHDs and other respiratory infections [27–30]. For example, a retrospective cohort study of adults with CHDs and SARS-CoV-2 infection hospitalization found that prevalence of invasive mechanical ventilation among children and adults with CHDs was 40% higher compared to that of those without CHDs, which persisted even after restriction to younger patients and those without comorbidities such as heart failure or pulmonary hypertension [28].

When evaluating mortality risk, children with even minor biventricular disease, such as an isolated ventricular or atrial septal defect, had more than double the risk of dying while admitted compared to those without CHDs. As severity of the CHD increased, this risk increased, whereby children with major biventricular and single ventricle disease had 2.5-times and 3.3-times the risk of dying on propensity-adjusted analyses, respectively, compared to those without CHDs. For the remaining outcomes, however, effect estimates for patients with minor and major biventricular disease were relatively similar. Investigators hypothesize this to be related to increased frequency of pulmonary overcirculation among patients with ventricular septal defects, whereby pulmonary overcirculation may be associated with particularly high risk of mechanical ventilation, which in turn may necessitate an ICU admission and longer length of stay. Alternatively, given the fact that infants were not included on analyses, patients with single ventricle disease will likely be post-Glenn or Fontan surgery and therefore may have well-balanced pulmonary circulation. Taken altogether, findings suggest that the especially high mortality risk associated with more severe lesions may operate through other mechanisms, and more work is needed to consider additional intermediate outcomes that may contribute to mortality risk. Analytically, while diagnosis-related groups (DRGs) theoretically may be helpful for model inclusion to control for clinical features, DRGs also incorporate diagnoses classified as outcomes on this analysis, such as respiratory failure or discharge status (e.g., mortality), and subsequently may bias results toward the null via model overadjustment if included as a covariate [31].

Similar to prior research published by Ghimire et al., children with CHDs were less frequently diagnosed with

Table 4 Risk of select outcomes associated with concurrent diagnoses of CHD and genetic condition

Outcome	Unadjusted RR (95% CI)	Adjusted RR (95% CI)[a]	*p*-value[b]
Death during hospitalization			
Neither	Ref	Ref	
Genetic condition only	1.99 (1.37–2.87)	1.96 (1.35–2.84)	**0.0005**
CHD only	2.42 (1.73–3.37)	2.38 (1.18–3.33)	**< 0.0001**
CHD with genetic condition	1.94 (1.04–3.60)	1.90 (1.01–3.56)	**0.045**
ICU admission			
Neither	Ref	Ref	
Genetic condition only	1.42 (1.32–1.52)	1.40 (1.31–1.50)	**< 0.0001**
CHD only	1.74 (1.64–1.84)	1.70 (1.61–1.80)	**< 0.0001**
CHD with genetic condition	1.56 (1.41–1.74)	1.52 (1.37–1.69)	**< 0.0001**
Mechanical ventilation			
Neither	Ref	Ref	
Genetic condition only	1.79 (1.62–1.97)	1.77 (1.61–1.95)	**< 0.0001**
CHD only	1.98 (1.81–2.17)	1.92 (1.75–2.10)	**< 0.0001**
CHD with genetic condition	1.27 (1.88–2.51)	2.09 (1.81–2.41)	**< 0.0001**
LOS > 12 days			
Neither	Ref	Ref	
Genetic condition only	1.88 (1.69–2.09)	1.84 (1.65–2.04)	**< 0.0001**
CHD only	2.21 (2.00–2.43)	2.11 (1.92–2.32)	**< 0.0001**
CHD with genetic condition	2.34 (2.00–2.73)	2.28 (1.95–2.66)	**< 0.0001**

Reference group is patients with CHD without a genetic syndrome or chromosomal anomaly

CHD congenital heart defect, *CI* confidence interval, *ICU* intensive care unit, *LOS* length of stay, *RR* risk ratio

[a]Adjusted analyses included propensity score and hospital as fixed random effect, respectively

[b]Bolded p-values represent statistical significance at a 95% confidence level

asthma compared to those without CHDs [12]. Conversely, children with CHDs were more frequently diagnosed with a genetic condition compared to children without CHDs. Compared to patients with neither CHD nor genetic condition, children with 1 of these conditions (either CHD or genetic condition) had significantly higher risk of all outcomes. Further, for children who had both CHD and a genetic condition, their risk for specifically mechanical ventilation and prolonged LOS was magnified.

Overall, there also may be different levels of influenza disease acuity at initial presentation between those with varying CHD severity levels, as children with more severe CHDs presenting with influenza may be more or less sick compared to those with those with influenza harboring more mild or no CHDs. It is possible that there are differences in seasonal influenza vaccination across the population, whereas those with more complex CHDs may be the most likely to be vaccinated [32]. Further, in considering the H1N1 influenza pandemic in 2009, frequency of admissions for influenza infection among children may vary by year, warranting longitudinal trend analyses.

Lastly, PHIS is comprised of tertiary centers across the United States; given this, it is possible that children with more minor CHDs are admitted to these centers when they have a poor prognosis. Further investigation of additional markers of overall health, CHD and influenza disease severity, and vaccination status may contribute further toward understanding observed associations.

A key strength of this study was the large sample size enabled by use of PHIS data, which allowed for a statistically well-powered assessment of children with and without CHDs hospitalized for influenza. However, the administrative nature of the data evaluated in this study limited our ability to evaluate more granular characteristics beyond diagnostic codes, including influenza vaccination data or comorbidity indices, which were not available and may be confounders. There are also inherent limitations of relying on diagnostic codes, as these may not accurately reflect the true clinical diagnoses or subtle differences in CHD physiology that may change arbitrary CHD categorizations within this study, may not be inclusive of all diagnoses, and depend on accurate coding by discharge providers. It is possible that a surgically repaired CHD may have a differential

impact on outcomes than the same unrepaired CHD, which may not be reflected within PHIS data. We were unable to determine the method of influenza diagnosis (e.g., antigen-based, symptoms-based, or diagnosis by polymerase chain reaction) using available diagnostic codes alone. Further, there is possible selection bias if patients evaluated at tertiary centers included in the PHIS database possess different characteristics than that of all children with CHDs, including if medically complex children are overrepresented within this database. Children less than 1 year of age at admission were not included on analyses, and therefore findings cannot be generalized to this age group. Lastly, we were unable to assess for outcomes following their hospital discharge.

Conclusion

Overall, this study further elucidates on outcomes associated with a CHD diagnosis among children hospitalized for influenza infection. Consistent with prior literature, children with CHDs are at significantly higher risk of death during hospitalization and other adverse inpatient outcomes. Concurrent diagnoses including genetic conditions may impact the association between CHD and adverse outcomes in the setting of influenza hospitalization. Additional investigations evaluating more granular clinical data, including influenza vaccination by CHD severity, are needed. Findings may be instrumental for development of public health interventions designed to reduce morbidity and mortality associated with influenza infection among children with CHDs.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

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