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An Assessment of the Impact of Patient Characteristics on Pediatric ECMO Outcome in the United States

Stanley C. Ibe
Medical University of South Carolina

AN ASSESSMENT OF THE IMPACT OF PATIENT CHARACTERISTICS ON PEDIATRIC ECMO OUTCOME IN THE UNITED STATES.

BY

Stanley Ibe

A doctoral project submitted to the faculty of the Medical University of South Carolina
in partial fulfillment of the requirements for the degree
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in the College of Health Professions

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Approved by:

Chair, Project Committee	Mary Dooley, Ph.D.	Date
Member, Project Committee	Kit Simpson, DrPH	Date
Member, Project Committee	David Fitzgerald, DHA	Date

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Abstract of Doctoral Project Presented to the
Medical University of South Carolina
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Chairperson: Mary Dooley, Ph.D.
Committee: Kit Simpson, DrPH
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Background. Extracorporeal membrane oxygenation (ECMO) is a critical life support mechanism in the intensive care of children with cardiopulmonary dysfunction. In this study, we aim to identify factors that impact ECMO outcome in pediatric population in the United States.

Methods. We conducted a retrospective cohort study of all ECMO admissions in the United States in years 2016, 2017 and 2019 using the National Inpatient sample (NIS) of the Healthcare Cost and Utilization Project (HCUP). The 2019 data was assessed to identify associations with the addition of ECMO type (VA vs VV).

Results. ECMO mortality rate was found to be 36.6%. Only pediatric chronic complex conditions (CCC) score and VA ECMO indication were associated with ECMO mortality. Age group, hospital region and CCC score were predictors of length of stay (LOS) for ECMO hospitalization. Hospital region and CCC score were predictors of total charges for ECMO hospitalization.

Conclusion. Age group, hospital region, VA ECMO type, and CCC score are predictors of ECMO outcome. Race, median household income and insurance type were not associated with ECMO outcome.

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CHAPTER I INTRODUCTION

1.1 Background.

Extracorporeal Membrane Oxygenation (ECMO) is an expensive yet critical procedure in the care of patients with cardiopulmonary dysfunction (Harvey et al 2015., Alizade et al 2023). ECMO is a procedure that serves as a cardiopulmonary life support mechanism used in cases of severe cardiac and/or pulmonary dysfunction that are non-responsive to conservative management (Makdisi & Wang 2015). Within the past decade, there has been a tremendous increase in the adoption and utilization of ECMO in various settings (Richardson et al 2023). Significant improvement has been made in the area of equipment and experience in ECMO use, leading to an expansion in the indications for the procedure (Makdisi and Wang, 2015). ECMO remains an expensive procedure globally even with improving technology and experience (Zhen et al 2022). For example, Zhen et al reported a total lifetime costs of $473,334, $654,771, and $1,007,476, for each congenital diaphragmatic hernia (CDH) infant who is placed on ECMO for ≤2 weeks, 2–3 weeks, and >3 weeks respectively in the United State (US) in 2022. Oude Lansink-Hartgring et al (2021) suggested that high-volume hospitals were not only associated with higher cost and length of stay for ECMO procedures, but also with higher ECMO-related inpatient mortality compared to low- and medium-volume hospitals.

Richardson et al (2023) conducted a retrospective cohort study using a national level dataset to evaluate the association between race and ECMO outcomes in the adult population. One of the compelling reasons the authors embarked on this study was to investigate racial disparities in outcomes for ECMO in the adult population. For the period 2016 to 2019, the authors discovered a significant decline in mortality among whites while other races remained stable. The odds of ECMO related mortality were reported to be higher for Asians/Pacific Islanders compared to whites. Black and Hispanic races were associated with higher complications of infection and pneumonia, as well as higher hospital length of stay (LOS) with a mean LOS of 19 days and 16days respectively compared to 14 days for Whites ($p = 0.001$). Blacks and Hispanics also had higher total hospitalization cost of $150,000 and $145,000 respectively compared to total hospitalization cost of $130,000 for whites ($p <0.001$). The findings of this study suggest race-based disparities in ECMO outcomes in adult populations. In one of the few studies to address racial disparities in the pediatric population, Brunetti et al (2022) reported reduced likelihood of ECMO use during surgical hospitalization for white children when compared with other races; this was found to be statistically significant. There is a dearth of evidence on the impact of social determinants of health on ECMO outcomes and utilization in pediatric population, utilizing representative national data (Alizadeh et al 2023). In this study, we seek to investigate further the association between race/ethnicity as well as other broader range of factors such as hospital type, insurance type, and US region, on ECMO outcomes (mortality, length of stay, and total costs) in Pediatric populations in the US.

1.2 Problem Statement.

ECMO is an expensive and critical procedure in intensive care. Understanding the factors that are associated with ECMO mortality, length of stay and hospital cost in the pediatric population is important for risk profiling and patient counseling. This knowledge would help physicians and other providers identify high risk candidates and modify their treatment plan and strategy accordingly.

1.3 Research Questions.

Is there an association between race, insurance type, hospital type (academic vs non-academic, Private vs public), and US region with ECMO outcomes in pediatric population in the US?

1.4 Population.

This study will utilize archival data from the National inpatient sample (NIS) database of the Healthcare Cost and Utilization Project (HCUP) for the years 2016, 2017 and 2019.

CHAPTER II SCOPING LITERATURE REVIEW

2.1 ECMO Overview

ECMO is a critical component of intensive care for patients with several cardiopulmonary insufficiency. It is a life support procedure for patients with respiratory and/or cardiac failure (Song et al 2017). The ECMO mechanism sustains life while the heart and/or lungs are rested to enhance their recovery (Oyetunji et al 2013). Bokman et al (2015), classified ECMO indications in pediatric population into respiratory and cardiac ECMO. According to the authors, congenital diaphragmatic hernia, meconium aspiration and persistent pulmonary hypertension of newborn are the most common reasons for respiratory ECMO indications, whereas surgical correction of congenital heart defects, cardiogenic shock and cardiomyopathy are the major cardiac ECMO indications. Erdil et al (2019) added acute respiratory distress syndrome and pneumonia (including bacteria, viral and aspiration) as some of the common respiratory indications for ECMO in pediatric population.

2.2 ECMO in Pediatrics: Use and Indications

ECMO use in pediatrics has advanced in technology, indications and scale since the first successful use case in 1975 by Robert H. Bartlett (Bokman et al 2015). According to Oyetunji et al (2013), ECMO is a life-saving procedure in newborns, with a survival rate of greater than 80% in newborns who are in respiratory failure without a diagnosis of congenital diaphragmatic hernia. According to McCarthy et al (2015), ECMO is more readily adopted in neonates (0 – 30 days) and the pediatric population, demonstrating better outcomes in this population compared to adult population, with survival rate of 40 -80%. McCarthy et al (2015) also suggested that respiratory indications for ECMO are associated with better results and outcomes compared to other indications for ECMO.

In a study to determine factors that influence ECMO survival and resource utilization, Bokman et al (2015) analyzed the kids' inpatient Database (KID) for the years 1997 – 2009. The study explored the association between age group and ECMO survival in pediatric populations. Patients were grouped into neonates (<30 days), infant (≥30 days to 1 year), young child (1-5 years), and older child (5+ years). Following a multivariable logistic regression analysis, age group was found to be statistically significant ($p = 0.023$) as a predictor of ECMO survival in pediatric population, with increasing age associated lower survival rate. The neonatal survival rate was found to be 56%, while infants, young child and older child survival rates were 52%, 46% and 36% respectively. Bokman et al (2015) also found a statistically significant difference between ECMO indication and survival rate ($p<0.001$). Indication was classified into congenital diaphragmatic hernia (CDH), persistent pulmonary hypertension of newborn (PPHN), respiratory distress syndrome (RDS), and cardiac and circulatory congenital anomalies (CCCA). CDH (vs no CDH) had the lowest ECMO survival rate of 40%. Patients with PPHN (vs no PPHN) indication had the highest survival rate of 69%, whereas RDS (vs no RDS) and CCCA (vs no CCCA) both had a survival rate of 47%.

2.3 Outcomes

Caprarola et al (2022) reported an overall ECMO survival rate of 55% in the US. Using the National Inpatient Sample (NIS) data, Sanaiha et al (2019) explored the trend in ECMO mortality rate in adult population in the US from 2008 to 2014. The authors discovered a trend of decreasing mortality from about 62.4% to 42.7% ($p<0.001$) with ECMO admissions increasing by 361% ($p<0.001$) for the same period.

In a study to measure outcomes for ECMO in adult US population, Gill et al (2021) reported an overall in-hospital mortality of 60.4% among adult patients who underwent a Venoarterial (VA) ECMO for cardiac arrest. The primary outcome measurement was in-hospital mortality rate. According to the study, non-white race and lower household income were associated with higher mortality ($p=0.04$ and $p<0.01$ respectively). It is important to note that these rates were reported for patients whose indication for ECMO was cardiac arrest. As reported by Bokman et al (2015), ECMO indications are predictors of survival rate.

Shafi et al (2022) conducted a retrospective cohort study to assess ECMO outcomes in pediatric population in the US, using the HCUP National Readmission Database (NRD). The authors explored the HCUP NRD for index admissions in which ECMO was carried out in children aged 1 -18 years, for years 2012 -2018. The primary outcomes were rates for survival to hospital discharge and 30-day readmission rate following the index ECMO hospitalization. ECMO related complications were also studied as secondary measures of outcomes. The study reported an in-hospital mortality of 39.4% with a 30-day readmission of 17%. According to Shafi et al (2022), unplanned readmission rate for pediatric ECMO survivors in the US is about 35.5% with a readmission mortality rate of 3% within 1 year of index ECMO hospitalization. Acute kidney injury (AKI) was the most common ECMO related complication (51.5%). Disseminated intravascular coagulation (DIC) accounted for 22.5% of ECMO complications, while surgical site bleeding accounted for 12.7% of complications.

2.4 Factors in ECMO outcome.

Several authors have examined the predictors of outcomes for extracorporeal membrane oxygenation in the United States (Bokman et al 2015). Race and ethnicity are among factors that have been reported to impact outcomes among adult ECMO patients (Chan et al 2018). However, there is limited evidence generated from national level data, making it difficult to establish an association between these sociodemographic variables and ECMO outcomes among pediatric patients. In order to understand the trend in ECMO utilization in the United States, Stentz et al (2019) examined the Healthcare Cost and Utilization project (HCUP) in-patient data for 34 states for the years 2011 to 2014. The authors used the international classification of diseases (ICD)-9 code 39.65 for ECMO, and were able to capture ECMO utilization in the inpatient service without including those in the operating room.

The study included patient characteristics (pediatrics and adults), hospital characteristics (region, ownership, bed size, and academic status), and insurance type (private, Medicaid, Medicare, uninsured and others). Due to differences in population distribution among states, ECMO utilization per state was calculated as ECMO patients per 100,000 persons.
One of the key findings of the study was an increasing trend in ECMO utilization from 2011 to 2014 driven by its use in the adult population. Whereas all regions showed increasing utilization, regional variations were still evident. The study also showed a significant difference in utilization between insured and uninsured patients ($p < 0.0005$). Large hospitals~~,~~ and academic centers (both private and not-for-profit) cared for most ECMO patients. The HCUP data utilized in the study came from 34 out of 50 states which limits the generalizability of the findings of this study.

In another study assessing the impact of race and ethnicity on ECMO use and outcome, Brunetti et al (2022) conducted a multicenter retrospective cohort study. Data was obtained from the clinical registry of the pediatric cardiac critical care consortium (PC^4). The PC^4 is a consortium of about 73 hospitals in the United States. A total of 50,552 hospitalizations between August of 2014 and January 2019 from 34 participating hospitals were studied. About 2.9% of all hospitalizations (n = 1467) involved ECMO use. Race/ethnicity was stratified into White, Black, Asian, Hispanic and other race which included Native American, Pacific Islander and mixed race. For the purpose of analysis, ECMO hospitalizations were grouped into medical vs surgical. A multivariable logistic regression analysis was conducted to evaluate the association between race/ethnicity and ECMO use, failure to rescue and mortality. Associations between insurance type, and socioeconomic status were also explored in secondary analysis.

The study did not find any significant association between race/ethnicity and ECMO use for medical hospitalization. Other race was associated with higher adjusted odds for failure to rescue (FTR): (adjusted odd ratio [aOR] 1.69, 95%, CI 1.06 – 2.70, P =0.03) and mortality (aOR 1.61, 95%, CI 1.22 – 2.12, P = 0.001) for medical hospitalization. Black (aOR 1.24, 95%, CI 1.02 – 1.50, P = 0.03) and other race (aOR 1.50, 95%, CI 1.17 – 1.93, P = 0.001) were associated with higher adjusted odds for ECMO use in surgical hospitalizations compared to whites. Hispanic race was associated with higher adjusted odds of mortality (aOR 1.31, 95%, CI 1.03 – 1.68, P=0.03) in surgical ECMO hospitalizations. No association was found between race and FTR in surgical ECMO hospitalizations. The study did not show any significant association between race/ethnicity and indicators of socioeconomic status with ECMO utilization or outcome.

Richardson et al (2023) conducted a retrospective cohort study using national level data, to investigate the impact of race on ECMO outcomes in adult population. The authors analyzed the National Inpatient Sample (NIS) data for the years 2016 – 2019. Adult patients aged 18 years and above were identified using the ICD-10 code. Patients undergoing heart/lung transplantation or receiving preoperative ECMO were excluded. Other exclusion criteria included missing key data such as gender, age, race/ethnicity and mortality. Patients were classified into four groups based on the indications for ECMO; respiratory failure, cardiopulmonary failure, cardiogenic shock and postcardiotomy. Variables of interest included gender, age, self-reported race/ethnicity, insurance status, income quartile and hospital teaching status. All variables were defined using the NIS data dictionary. The Elixhauser comorbidity index was used to account for comorbidities. This index corrects for about 30 listed disease conditions.

2.5 Social determinants of health

According to Singu et al (2020), social determinants of health (SDoH) comprise of five variables that describe social and economic conditions of a population, which are considerable predictors of health outcome for the given population. The five variables described by Singu et al include health and healthcare, economic stability, education, neighborhood and built environment, and social and community context. Health and healthcare factors include access to healthcare including primary care, health literacy and access to health insurance coverage. Economic stability includes factors like employment, poverty level, food security and housing stability. Built environment assesses factors like neighborhoods, transportation, housing, access to healthy foods, air and water quality, access to recreational facilities etc. According to the authors, these factors affect other aspects of health. For example, the presence of safety and recreational facilities in neighborhoods could encourage healthy lifestyle like exercise. On the other hand, air pollution has been associated with higher incident of asthma and related diseases.

Furthermore, level of education also impacts health outcome (Singu et al., 2020). Factors considered under this theme include graduation from high school, enrollment in higher education, literacy and language. The last factor considered by the authors is community context. Here the authors argue that the level of community support available to members of a community also impacts mortality rate and health outcome.

Flanagan et al (2018) explored the concept of social vulnerability index (SVI) as a measure of community resilience or the ability of a community or individuals to withstand or overcome adverse events including those related to health. The SVI model for assessing community vulnerability includes four major variables each with sub-themes. These include socioeconomic status, household composition and disability, minority status and language, and housing and transportation. Sub-themes considered under socioeconomic status include below poverty level, unemployed, income, and no high school diploma. Household composition and disability includes age 65 or older, age 17 or younger, older than 5 with a disability, and single-parent households. Sub-themes for minority status and language includes minority, and speaks English “less than well”. Finally, housing and transportation is described under the sub-themes of multiunit structures, mobile homes, crowding, no vehicle, and group quarters.

The SVI as a replacement for the SDoH framework, categorizes communities into their relative resilience to both social and anthropogenic hazards. Communities with higher SVI are considered more vulnerable to both natural and man-made disasters including health related hazards. The SVI framework comes preloaded with the socioeconomic and sociodemographic variables that have been implicated as determinants of health, and therefore could be applied in healthcare studies evaluating the impact of these factors on established outcomes.

Alizade et al (2022) conducted a single center study to explore the impact of SDoH on ECMO outcomes in pediatric population. The authors conducted a single-center retrospective cohort study of all patients aged 18 years or less, who had ECMO hospitalization for the years 2010 – 2021. SDoH variables were classified into race, interpreter requirement, insurance status and socioeconomic status (SES) which was defined by child opportunity index (COI) quintiles and SVI. The COI quintiles classified patients into very-low, low, moderate, high and very-high SES, whereas SVI described the patient’s percentile vulnerability based on census tract data. Multivariable regression analysis was conducted to evaluate the impact SDoH on outcome.

Alizadeh et al (2022) found no difference in ECMO in-hospital mortality across COI quintiles, interpreter requirement, race, insurance status, rural residence and travel distance from home address to hospital.

In another study, Alizadeh et al (2023) examined variations in pediatric ECMO utilization by socioeconomic status. The authors conducted a retrospective cohort study using data from 49 hospitals in the Pediatric Health Information Systems (PHIS) database from 2015 to 2021. The authors utilized the COI as a predictor of SES. The COI framework contains about 29 neighborhood-level parameters that are used as markers for SES. Neighborhoods are assigned a COI value ranging from 0-100 with 0 representing the lowest SES.

Children aged 18 years or less who were born at term (>35 weeks), and who were hospitalized in the intensive care for "high" and "very high" severity of illness between 1st of October 2015 and 1st of March 2021 were included in the study. Patients were grouped into three outcome categories: died without ECMO (DWE), survival without ECMO, and supported on ECMO. Patient variables were compared across these three outcomes. A multivariable analysis was conducted to compare the DWE outcome group and those supported on ECMO, while correcting for clinical covariates.

Patients in the DWE cohort had a lower SES (median COI[IQR] 41 [19, 66]) compared with those who survived without ECMO (44 [20, 70]) or were supported on ECMO (47 [22, 72]; p<0.001). Non-white races were more in the DWE cohort (45%), than in those that survived without ECMO (42%) or supported on ECMO (39%; P<0.001). The authors concluded that SES influence ECMO utilization, and lower SES as predicted by the COI, is independently associated with greater odds of DWE.

The findings from this literature review demonstrate the need to further investigate the potential impact of patient and hospital characteristics (such as race/ethnicity, income level, insurance type and hospital type) on ECMO outcome and utilization in pediatric population for two reasons. Firstly, there is no consensus in the literature on the nature of impact of these variables on ECMO outcome and utilization. Secondly, there are limited number of studies evaluating these variables of interest using national level data. The objective of this study therefore is to explore a broader range of factors that may be associated with ECMO utilization and outcomes in pediatric population, including race/ethnicity, insurance type, income level of parents, hospital characteristics (academic vs non-academic), and US region.

CHAPTER III METHODOLOGY

3.1 Research Design/Method

This study shall adopt a quantitative research design. This retrospective cohort study design method is appropriate for testing the association between factors and outcomes in a secondary dataset.

3.2 Data Set Description

This study shall adopt a retrospective cohort approach using national level data. Data shall be collected from the National inpatient sample (NIS) database of the Healthcare Cost and Utilization Project (HCUP) for the years 2016, 2017 and 2019. Using national level data, we shall study the association of race, insurance type, and hospital region (US region) on outcome. ECMO admissions for years 2016 and 2017 will be identified using the ICD-10 code: 5A15223, extracorporeal membrane oxygenation, continuous. There was a change in ICD-10 procedure codes used to identify ECMO in October of 2018, therefore, we utilized 2019 hospital admission data, the first full year of the new procedure codes, to include ECMO cannulation type (The Society of Thoracic Surgeons). For 2019, ECMO admissions will be identified using ICD-10 codes: 5A1522G, extracorporeal membrane oxygenation, peripheral Veno-arterial and 5A1522H, extracorporeal membrane oxygenation, peripheral Veno-venous.

3.2.1 Independent and Dependent Variables

The primary outcome is in-hospital mortality. Secondary measures of outcome include hospital length of stay and total cost. Patients will be grouped by age (Infants: < 1-year, young children: 1-5 years and older children: 6-18 years) and controlling for comorbidities using the

Pediatric complex chronic conditions classification system (Feudtner et al., 2014). Independent variables of interest include race, insurance type, median income of the zip code where the patients reside (0-25th percentile vs 26-100th percentile), and US region (Northeast, South, Midwest, West). Hospital type was not assessed as > 98% of cases occurred in teaching hospitals.

3.3 Data Analysis

Data was analyzed using both descriptive (frequency, mean, and standard deviation) and inferential statistics (regression analysis). Multivariable logistic regression analysis was conducted to measure the association between the independent variables of interest and mortality. Generalized linear models were used to evaluate continuous outcomes (LOS and cost). Results with 2019 data were assessed separately to identify possible associations on ECMO type (Veno-venous vs Veno-arterial). All potential factors with p-values < 0.20 in bivariate models were assessed in the multivariable models to evaluate their significance while controlling for other significant factors. Results were presented using tables.

CHAPTER IV RESULTS

4.1 Results/Findings

Table 1 shows the demographic description of patients who underwent ECMO procedure for years 2016, 2017, and 2019. A total of 890 patients underwent ECMO cannulation for years 2016 and 2017 compared to 364 patients in 2019. The demographic characteristics of ECMO patients in 2016/2017 are descriptively similar to 2019 apart from slight variation in age group where 68.31%, 13.03% and 18.65% were <1 year, 1-5 years and 6+ years respectively for 2016/2017 compared to 60.71%, 17.03% and 22.25% respectively for 2019. One-third of patients in both groups were from zip codes with median household income below 25th percentile. The majority of patients were seen in hospitals within the Southern region (42.8% and 43.7%, for 2016/2017 and 2019, respectively). The Northeast had the least population of ECMO admissions.

Gender was almost evenly split between males and females.

A total of 1093 patients had their race documented, with 171 patients missing data on their racial background. Approximately half of the patients were White, whereas Black and other race accounted for the remaining half. Almost half of patients had private insurance (40.6% and 37.1% for 2016/2017 and 2019, respectively).

Combined pediatric ECMO mortality rate was found to be 36.6%. Pediatric ECMO mortality was similar across age groups (see appendix 1). Combined mean length of stay (LOS) was 48.4 days, hospital length of stay decreased as age groups increased (55.1, 43.3 and 29.9 days for age group <1 year, 1-5 years and 6+ years respectively; see appendix 1). Combined mean pediatric complex chronic conditions (CCC) was 2.4 while combined mean total hospitalization cost was $1,340,836 US dollars (USD).

Table 1 Demographic Characteristics of patients who received ECMO for years 2016, 2017 and 2019.

Characteristics		
	2016/2017	**2019**
n	890	364
Gender (%)		
Male	495(55.6)	187(51.4)
Female	395(44.4)	177(48.6)
Race (%)		
White	408(53.9)	162(49.4)
Black	125(16.5)	79(24.1)
Other	224(29.6)	87(26.5)
Insurance Type (%)		
Private	361(40.6)	135(37.1)
Other/Uninsured	529(59.4)	229(62.9)
US Region (%)		
Northeast	128(14.38)	49(13.46)
Midwest	189(21.24)	87(23.90)
South	381(42.8)	159(43.7)
West	192(21.6)	69(19.0)
Median Household Income (%)		
0-25th percentile	269(30.8)	114(31.6)
26th - 100th percentile	604(69.2)	247(68.4)
Age group in years (%)		
<1	608(68.3)	221(60.7)
1 - 5	116(13.0)	62(17.0)
6+	166(18.7)	81(22.3)
In-hospital Mortality		
Survival (rate)	535(60.1)	243(66.8)
Mortality (rate)	355(39.9)	121(33.2)
Length of Stay (LOS)		
Mean LOS(SD)	48.2(52)	48.6(49.3)
Hospitalization Cost		
Mean total hosp. cost in USD	$1,320,966($1,312,713)	$1,360,706($1,515,665)
Mean Feudtner CCC score (SD)	2.3(1.3)	2.4(1.4)

4.2 Statistical model results.

MORTALITY

Table 2. Association of patient and hospital characteristics on mortality among pediatric patients receiving ECMO, p-values from bivariate and multivariable logistic regression for years 2016 and 2017. (N=890)

Model Variable	Univariate	Multivariable
Age Group[1]	0.9750	*NA*
Race[2]	0.4375	*NA*
Private Insurance	0.4025	*NA*
Hospital Region[3]	0.2739	*NA*
Low Income Quartile[4]	0.2793	*NA*
Number of CCC[5]	**0.0004***	*NA*

1 Groups: < 1 year, 1-5 years, ≥ 6 years

2 Groups: White, Black, Other

3 Regions: Northeast, Midwest, South, West.

4 Income quartiles based on patient's zip code, Low is 0-25th percentile.

5 Pediatric complex chronic conditions

** Statistically significant characteristic*

NA = Not applicable

Among children receiving ECMO in 2016-2017, only the number of pediatric complex chronic conditions was statistically significantly associated with death (p = 0.0004).

Table 3. Association of VA ECMO, patient, and hospital characteristics on mortality among pediatric patients receiving ECMO, p-values from bivariate and multivariable logistic regression for year 2019. (N = 325)

Model Variable	Univariate	Multivariable
VA ECMO (vs. VV)	**0.0005***	**0.0017***
Age Group[1]	0.7388	*NA*
Race[2]	0.2200	*NA*
Private Insurance	**0.0417***	0.0585
Hospital Region[3]	0.9886	*NA*
Low Income Quartile[4]	0.6129	*NA*
Number of CCC[5]	**0.0012***	**0.0067***

1 Groups: < 1 year, 1-5 years, ≥ 6 years

2 Groups: White, Black, Other

3 Regions: Northeast, Midwest, South, West

4 Income quartiles based on patient's zip code, Low is 0-25th percentile

5 Pediatric complex chronic conditions

** Statistically significant characteristic*

NA = Not applicable

Among patients in 2019, age group, race, hospital region, and income quartile were not statistically associated with death in the bivariate models. Similarly to children in assessed in 2016-2017, the number of pediatric complex chronic conditions was statistically significantly associated with death (p = 0.0012). However, for patients in 2019, receiving VA ECMO (p =

0.0005) and not having private insurance status (p = 0.0417) were also statistically significantly associated with mortality. In the multivariable model, not having private insurance did not remain statistically significant (p = 0.0585) when controlling for VA ECMO status and the number of pediatric complex chronic conditions. Both VA ECMO status and the number of pediatric complex chronic conditions remained significantly associated with death in the multivariable model (p = 0.0017 and 0.0069, respectively).

LENGTH OF STAY

Table 4. Association of patient and hospital characteristics on length of stay among pediatric patients receiving ECMO, p-values from bivariate and multivariable generalized linear model regression for years 2016 and 2017. (N=890)

Model Variable	Univariate	Multivariable
Age Group[1]	**<0.0001***	**<0.0001***
Race[2]	0.7715	NA
Private Insurance	**0.0401***	0.2092
Hospital Region[3]	0.2147	NA
Low Income Quartile[4]	0.3045	NA
Number of CCC[5]	**<0.0001***	**<0.0001***

1 Groups: < 1 year, 1-5 years, ≥ 6 years

2 Groups: White, Black, Other

3 Regions: Northeast, Midwest, South, West

4 Income quartiles based on patient's zip code, Low is 0-25th percentile

5 Pediatric complex chronic conditions

** Statistically significant characteristic*

NA = Not applicable

For patients receiving care in 2016-2017, race, hospital region, and income quartile were not statistically associated with LOS. However, there was a statistically significant association with LOS in the bivariate models for age group (p <0.0001), private insurance status (p = 0.0401) and the number of pediatric complex chronic conditions (p <0.0001). In the multivariable model, private insurance status did not remain statistically significant (p = 0.2092) when controlling for age group and the number of pediatric complex chronic conditions. Both age group and the number of pediatric complex chronic conditions remained highly significantly associated with LOS in the multivariable model (Table 4).

Table 5. Association of VA ECMO, patient, and hospital characteristics on length of stay among pediatric patients receiving ECMO, p-values from bivariate and multivariable generalized linear model regression for year 2019. (N = 362)

Model Variable	Bivariate	Multivariable
VA ECMO (vs. VV)	0.0708	0.6048
Age Group[1]	**<0.0001***	**0.0002***
Race[2]	0.1843	*NA*
Private Insurance	0.9323	*NA*
Hospital Region[3]	**0.0106***	**0.0286***
Low Income Quartile[4]	0.6230	*NA*
Number of CCC[5]	**<0.0001***	**<0.0001***

1 Groups: < 1 year, 1-5 years, ≥ 6 years

2 Groups: White, Black, Other

3 Regions: Northeast, Midwest, South, West

4 Income quartiles based on patient's zip code, Low is 0-25th percentile

5 Pediatric complex chronic conditions

** Statistically significant characteristic*

NA = Not applicable

For patients with episodes of care in 2019, VA ECMO status, race, private insurance status, and income quartile were not statistically associated with LOS among children receiving ECMO. Among children on ECMO in 2019, age group (p <0.0001), hospital region (p = 0.0106), and the number of pediatric complex chronic conditions was statistically significant associated with LOS in bivariate models. In the multivariable model, when also controlling for VA ECMO status (p = 0.0708 in bivariate model), all variables that were statistically significant in the bivariate models remained statistically significant (Table 5).

Total Charges

Table 6. Association of patient and hospital characteristics on total charges among pediatric patients receiving ECMO, p-values from bivariate and multivariable generalized linear model regression for years 2016 and 2017.

Model Variable	Bivariate	Multivariable
Age Group[1]	**0.0042***	0.1068
Race[2]	0.0775	0.5339
Private Insurance	0.1766	0.4354
Hospital Region[3]	**0.0065***	**0.0040***
Low Income Quartile[4]	0.7756	NA
Number of CCC[5]	**<0.0001***	**<0.0001***

1 Groups: < 1 year, 1-5 years, ≥ 6 years

2 Groups: White, Black, Other

3 Regions: Northeast, Midwest, South, West

4 Income quartiles based on patient's zip code, Low is 0-25^{th} percentile.

5 Pediatric complex chronic conditions

** Statistically significant characteristic*

NA = Not applicable

For ECMO patients in 2016-2017, race, private insurance status, and income quartile were not statistically associated with total charges in bivariate models. However, there was a statistically significant association with total charges in the bivariate models for age group (p =0.0042), hospital region (p = 0.0065) and the number of pediatric complex chronic conditions (p <0.0001). In the multivariable model, only hospital region and the number of pediatric complex chronic conditions remained highly significantly associated with total charges when controlling for age group, race, and private insurance status (Table 6).

Table 7. Association of VA ECMO, patient, and hospital characteristics on total charges among pediatric patients receiving ECMO, p-values from bivariate and multivariable generalized linear model regression for year 2019. (N = 323)

Model Variable	Bivariate	Multivariable
VA ECMO (vs. VV)	**0.0044***	0.1049
Age Group[1]	0.1435	0.4875
Race[2]	0.0740	0.0707
Private Insurance	0.6001	*NA*
Hospital Region[3]	**<0.0001***	**0.0028***
Low Income Quartile[4]	0.1591	0.3043
Number of CCC[5]	**<0.0001***	**0.0004***

1 Groups: < 1 year, 1-5 years, ≥ 6 years

2 Groups: White, Black, Other

3 Regions: Northeast, Midwest, South, West.

4 Income quartiles based on patient's zip code, Low is 0-25th percentile.

5 Pediatric complex chronic conditions

** Statistically significant characteristic*

NA = Not applicable

For ECMO patients in 2019, age, race, private insurance status, and income quartile were not statistically associated with total charges in bivariate models. However, there was a statistically significant association with total charges in the bivariate models for VA ECMO (p =0.0044), hospital region ($p < 0.0001$) and the number of pediatric complex chronic conditions ($p < 0.0001$). In the multivariable model, VA ECMO status did not remain statistically significant when controlling for age group, race, hospital region, income quartile, and the number of pediatric complex chronic conditions. However, both hospital region and number of pediatric complex chronic conditions remained highly significantly associated with total charges when controlling for VA ECMO, age group, race, and income quartile (Table 7).

5 CHAPTER V DISCUSSION

5.1 Discussion of Results

In this study, we set out to explore possible association between patient and hospital characteristics and ECMO outcome in pediatric population in the United States. We looked at how patients' characteristics such as race, median household income based on zip code, insurance type, age group and pediatric complex chronic conditions (CCC) impact ECMO outcomes. We also looked at the impact of hospital characteristics such as region where the hospital is located, on ECMO outcome. Lastly, we looked at how ECMO indication (VA vs VV) impacts outcome using 2019 HCUP data.

For years 2016 and 2017, only CCC score was found to be significantly associated with mortality ($p = 0.0004$). This implies that sicker patients are more likely to die during an ECMO hospitalization than patients who are less sick prior to ECMO. This agrees with Olson et al (2021) who indicated that greater comorbidity burden is associated with poorer ECMO outcome in pediatric population. Race, median household income based on zip code, insurance type, and age group were not significantly associated with ECMO mortality among pediatric patients. Compared to the 2019 data, bivariate model indicates that CCC score ($p = 0.0012$), receiving VA ECMO ($p = 0.0005$) and not having a private insurance ($p = 0.0417$) are significantly associated with ECMO mortality. However, having a private insurance was not statistically significantly associated ($p = 0.0585$) with ECMO mortality in the multivariable model when controlling for VA ECMO and CCC score. Receiving VA ECMO ($p = 0.0017$) and CCC score ($p = 0.0069$) both remained statistically significant in the multivariable model. These findings agree with Mistry et al (2018) who also found that VA ECMO is associated with higher morbidity and mortality. Race, low household income based on zip code, hospital region and age group were not found to be significantly associated with ECMO Mortality. This agrees with the findings of Brunetti et al (2022), who found no association between race/ethnicity and other indicators of socioeconomic status with ECMO outcome, and disagrees with the findings of Gill et al (2021) who reported that non-white race and lower household income were associated with higher ECMO mortality. Although the study by Gill et al (2021) was conducted in adult population.

Bokman et al (2015) also reported a significant association between ECMO indication and survival rate, however, the authors also reported an association between age group and ECMO survival rate which differs from the findings of this study. In the study by Bokman et al (2015), patients were grouped into neonates (<30 days), infant (≥30 days to 1 year), young child (1-5 years), and older child (5+ years). In this study, neonates (<30 days), and infants (>30days to 1 year) are combined into one group due to small sample size. This may not have impacted the overall result of the study especially given that Bokman et al (2015) reported a decreasing survival rate with increasing age. It is important to note that the authors utilized datasets from 1997 to 2009, so, it is possible that the difference in the findings of this study with that of Bokman et al (2015) could be attributable to improvement in pediatric ECMO practices in the United States both from advancement in professional expertise and technology.

Bivariate model for 2016 and 2017 data shows a significant association between age group ($p<0.0001$), having private insurance ($p = 0.0401$) and CCC score ($p<0.0001$) with LOS. Controlling for age group and CCC score in the multivariable model, private insurance status was not significantly associated with LOS ($p = 0.2092$), while age group ($p<0.0001$) and CCC score ($p<0.0001$) remained statistically significantly associated with LOS. Race, hospital region and household income were not statistically associated with LOS. In the 2019 data, both bivariate and multivariable model showed significant association between age group ($p<0.0001$ and $p = 0.0002$, respectively), hospital region ($p = 0.0106$ and $p = 0.0286$, respectively) and CCC score ($p<0.0001$ and $p<0.0001$, respectively) with LOS even after controlling for VA ECMO status. The mechanism of association between CCC score and LOS could be more easily deduced; sicker kids are likely going to have poorer outcomes and also longer hospitalization. However, the exact nature of impact of hospital region and Age group on LOS require further scrutiny. One explanation could come from the findings by Bokman et al (2015) which suggested an association between increasing age and decreasing ECMO survival rate. Improvement in ECMO practice could possibly account for improvement in survival rate among older kids at the expense of a longer course of hospitalization. This remains a good area for further studies.

Age group ($p = 0.0042$), hospital region ($p = 0.0065$) and CCC score ($p<0.0001$) were significantly associated with total charges in the bivariate model for 2016-2017 and 2019. Only hospital region ($p = 0.0040$) and CCC score ($p<0.0001$) were statistically significantly associated with total charges in the multivariable model. The bivariate and multivariable models for 2019 mirrors the 2016 and 2017 findings. Race, private insurance status and household income quartile were not statistically associated with total charges for ECMO hospitalizations for 2016, 2017 and 2019. Patients with higher CCC score have more comorbidities which could influence the number of diagnostic investigations, the length of stay and as such, total charges associated with ECMO hospitalization. The association between Hospital region and total charges could be explained by differences in cost of living per region which could impact several cost factors in hospital operations such as staffing and fixed asset cost. Although beyond the scope of this study, It would be interesting to know what regions are associated with greater cost and also understand the spread of patients per region based on CCC score. This would give more insight into how much region alone influences total charges for ECMO hospitalization, and what regions are associated with higher costs.

5.2 Implications for Policy and Practice

The findings of this study suggest that race, household income quartile and insurance type do not impact ECMO outcome in pediatric population in the United States. Policy initiatives should be targeted towards programs that would improve access to ECMO services.

5.3 Limitations

This study is partly limited by the sample size. As mentioned, neonates and infants were grouped together when classifying patients into age group. Although this is not believed to impact the final results, it does constitute a limitation.

5.4 Future Research

Further research is encouraged to explore significant drivers of variation in mortality, LOS, and total ECMO charges.

5.5 Conclusions

This study sets out to explore the impact of patient and hospital characteristics on pediatric ECMO outcome. Among the patient characteristics explored, the findings indicate that pediatric complex chronic conditions score is the major driver of mortality in ECMO hospitalizations. Age group and pediatric complex chronic conditions score were found to impact LOS. Major drivers of cost for ECMO hospitalizations are Hospital region and pediatric complex chronic conditions score. Race, household income quartile and insurance type were not statistically associated with ECMO outcomes. Regional variations in total charges for ECMO hospitalizations should be explored further. The concept of social vulnerability index and its impact on ECMO outcome should also be explored as well.

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Appendices

Appendix 1. **Demographic characteristics per Age group of patients who underwent an ECMO procedure for years 2016, 2017 and 2019.**

(N = 1264)

Characteristics	**AGE GROUP**		
	<1 yr.	**1 – 5 yrs.**	**6+ yrs.**
n	832	180	252
Gender			
Male (%)	451(54.21)	101(56.11)	135(53.57)
Female (%)	381(45.79)	79(43.89)	117(46.43)
Race			
White (%)	373(52.68)	76(48.10)	122(53.74)
Black (%)	119(16.81)	35(22.15)	51(22.47)
Other (%)	216(30.51)	47(29.75)	54(23.79)
Insurance Type			
Private (%)	314(37.74)	70(38.89)	115(45.63)
Other/Uninsured (%)	518(62.26)	110(61.11)	137(54.37)
US Region			
Northeast	116(13.94)	28(15.56)	36(14.29)
Midwest	184(22.12)	45(25.00)	50(19.84)
South	357(42.91)	69(38.33)	116(46.03)
West	175(21.03)	38(21.11)	50(19.84)
Median Household Income (%)			
0-25th percentile	256(31.18)	52(29.71)	78(31.45)
26th50th percentile(median)	227(27.65)	39(22.29)	57(22.98)
51st to 75th percentile	187(22.78)	54(30.86)	52(20.97)
76th to 100th percentile	151(18.39)	30(17.14)	61(24.60)
In-hospital Mortality			
Survival (rate)	515(61.90)	114(63.33)	155(61.51)
Mortality (rate)	317(38.10)	66(36.67)	97(38.49)
Length of Stay (LOS)			
Mean LOS(SD)	55.1(55.7)	43.3(42.9)	29.9(32)
Hospitalization Cost			
Mean total hosp. cost in USD	1414370.	1278632	1148443.
Mean CCC score (SD)	2.4(1.3)	2.1(1.3)	2.0(1.2)