

Impacts of isomerism (heterotaxy) on birth hospitalization

Abstract

Isomerism, or heterotaxy, impacts 1 in 10,000 live births and can lead to anatomic and functional anomalies in any organ system. What isn't known is how isomerism affects characteristics of the initial birth hospitalization. Data from the Kids Inpatient Database was used to compare the birth hospitalization between those with and without isomerism. A total of 4,442,985 admissions were included in the analysis. Of these, 1,6624 (0.04%) had isomerism. Patients with isomerism had increased length and cost of hospital stay when compared to those without. Comorbidities were more likely in those with isomerism. Need for diagnostic procedures, surgeries, and extracorporeal membrane oxygenation was also greater in those with isomerism. Inpatient mortality was also found in a greater proportion of those with isomerism. Isomerism mediates differences in the birth admission.

Keywords: heterotaxy, isomerism, birth, prematurity

Introduction

Isomerism, also known as heterotaxy, is a rare clinical entity which affects approximately 1 in 10,000 live births.¹⁻³ The essence of isomerism has been demonstrated to be the mirror imaged findings in the thorax such that there are often two morphologically similar bronchuses, two morphologically similar lungs, and two morphologically similar atrial appendages. Abdominal arrangement in the setting of isomerism appears to be random. Nearly every organ system can be impacted in the setting of isomerism in an anatomic and/or functional manner. Isomerism can be segregated into the subsets of right and left based on the morphology of the atrial appendages. Those with right isomerism will often have eparterial bronchuses bilaterally, trilobed lungs bilaterally, and absence of a spleen. Those with left isomerism will often have hyparterial bronchuses bilaterally, bilobed lungs bilaterally, and presence of multiple spleens. Congenital malformations of the heart, intestinal malrotation, and arrhythmias are common in both right and left isomerism.⁴⁻⁸

Many patients with isomerism will require cardiac surgery, some requiring staged surgery as they proceed along the functionally univentricular pathway. Isomerism has been noted to impact postoperative outcomes and general morbidity and mortality.⁹⁻¹¹ What has not been previously described are the characteristics of the initial birth hospitalization in those with isomerism compared to those without. We used the Kids Inpatient Database to characterize and compare birth hospitalizations in those with and without isomerism. We hypothesized that isomerism would increase the neonatal admission's length, cost, and mortality.

Methods

A cross-sectional study was conducted using the Kids Inpatient Database maintained by the Agency for Healthcare Research and Quality and the Healthcare Cost and Utilization Project. Only in-hospital births were included in the final analysis. All in-hospital births were then separated by the presence or absence of isomerism. Comorbidities were then identified by international classification of diseases, ninth revision codes. Univariate analysis was conducted utilizing chi-square or fisher exact analysis for categorical variables and Mann-Whitney-U test for continuous variables. Linear regression

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Rohit S Loomba

Cincinnati Children's Hospital Medical Center, USA

Correspondence: Rohit S. Loomba, MD, Cincinnati Childrens Hospital Medical Center, 3333 Burnet Avenue, Cincinnati, OH, 45229, USA, Email loomba.rohit@gmail.com

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was then done to identify independent risk factors associated with greater length of stay as well as greater cost of hospitalization. Logistic regression was then conducted to identify independent risk factors associated with in-hospital mortality.

Results

A total of 4,442,984 in-hospital birth admissions were included in the analysis. Of these, 1,624 (0.04%) had isomerism. Characteristics and univariate analysis is outlined in Table 1. Prematurity was noted with less frequency in those with isomerism (odds ratio 0.871, 95% confidence interval 0.766 to 0.990). There was no statistically significant difference in the proportion of still births between the two groups. All congenital malformations of the heart were found to be more prevalence in those with isomerism when compared to those without. The most frequent was double outlet right ventricle found in 6.9% of those with isomerism followed by atrioventricular septal defect found in 6.0% of those with isomerism. Arrhythmia (0.7% of those with isomerism), heart failure (1.3% of those with isomerism), and cardiac arrest (0.5% of those with isomerism), were more frequent in those with isomerism as well. Noncardiac malformations were also noted with greater frequency in those with isomerism. Those with isomerism required a great number of procedures prior to discharge. They were more likely to require intubation and mechanical ventilation, require extracorporeal membrane oxygenation, undergo echocardiograms, and undergo cardiac magnetic resonance imaging (Table 1).

Regression analysis demonstrated that isomerism was an independent risk factor for greater length of stay, increasing the hospitalization by approximately 1.5 days ($p < 0.001$). Isomerism was also an independent risk factor for greater cost of hospitalization, increasing the cost of by approximately 42,088 US dollars ($p < 0.001$). Isomerism was also an independent risk factor for inpatient mortality (odds ratio 2.503, 95% confidence interval 1.898 to 3.300). The frequency of inpatient mortality in those with isomerism was 9.8%.

Discussion

This analysis demonstrates that isomerism impacts the characteristics of in-hospital birth admissions, increasing the length of stay, cost of hospitalization, and risk of mortality. This

is not unexpected as those with isomerism often have congenital malformations in multiple organ systems. Functional complications are also present in several organ systems. As such, these patients require additional diagnostic evaluation and intervention. Interestingly, neither premature birth nor still birth was noted in greater proportion in those with isomerism. The proportion of cardiac and noncardiac malformations and procedures such as echocardiograms noted in this analysis are not representative of the true proportion noted in

isomerism overall as not all patients are diagnosed with isomerism prenatally or during their birth admission. Comparison to previous studies cannot be really done as characteristics of neonatal admissions in those with isomerism have not really been investigated as such. This data characterizes birth admissions for those with isomerism, highlighting increased morbidity and mortality which highlights the need for increased vigilance in these patients during this early period of life.

Table I Categorical data presented as absolute frequency and percentage. Continuous data presented as median and range

	No Isomerism (N=4,441,342)	Isomerism (N=1,642)	Odds Ratio (95% Confidence Interval)	P-Value
Race				
White	1,855,090 (51.5)	631 (47.0)		
Black	579,739 (16.1)	207 (15.4)		
Hispanic	770,152 (21.4)	339 (25.2)	--	0.001
Asian or Pacific Islander	165,333 (4.6)	71 (5.3)		
Native American	24,386 (0.7)	15 (1.1)		
Other	206,286 (5.7)	80 (6.0)		
Heart failure	2,462 (0.1)	22 (1.3)	24.485 (16.047 to 37.360)	< 0.001
Acute kidney injury	4,744 (0.1)	25 (1.5)	14.459 (9.731 to 21.485)	< 0.001
Cardiac lesion				
Double outlet right ventricle	1,308 (0.01)	114 (6.9)	253.256 (202.793 to 308.667)	< 0.001
Atrioventricular septal defect	2,706 (0.1)	98 (6.0)	104.112 (84.592 to 128.136)	< 0.001
Partial anomalous pulmonary venous connection	105 (0.01)	5 (0.3)	129.192 (52.607 to 317.271)	< 0.001
Total anomalous pulmonary venous connection	471 (0.01)	33 (2.0)	193.377 (135.414 to 276.150)	< 0.001
Coronary artery anomaly	537 (0.01)	10 (0.6)	50.672 (27.057 to 94.897)	< 0.001
Tetralogy of Fallot	4,299 (0.1)	40 (2.4)	25.771 (18.804 to 35.318)	< 0.001
Transposition of the great arteries	1,763 (0.01)	59 (3.6)	93.856 (72.076 to 122.217)	< 0.001
Congenitally corrected transposition	81 (0.01)	5 (0.3)	167.472 (67.785 to 413.760)	< 0.001
Pulmonary atresia	1,063 (0.01)	47 (2.9)	123.088 (91.529 to 165.527)	< 0.001
Tricuspid atresia	942 (0.01)	18 (1.1)	52.247 (32.690 to 83.502)	< 0.001
Ebstein anomaly	741 (0.01)	5 (0.3)	18.304 (7.586 to 44.165)	< 0.001
Hypoplastic left heart syndrome	2,530 (0.1)	32 (1.9)	34.871 (24.523 to 49.587)	< 0.001
Truncus arteriosus	720 (0.01)	4 (0.2)	15.081 (5.631 to 40.286)	< 0.001
Arrhythmia	1,976 (0.01)	11 (0.7)	15.152 (8.361 to 27.460)	< 0.001
Pancreatic anomaly	207 (0.01)	5 (0.3)	65.531 (26.955 to 159.316)	< 0.001
Atresia of the small intestine	4,690 (0.1)	14 (0.9)	8.135 (4.803 to 13.777)	< 0.001
Atresia of the large intestine	5,021 (0.1)	43 (2.6)	23.760 (17.529 to 32.206)	< 0.001
Biliary atresia	224 (0.01)	4 (0.2)	48.416 (17.992 to 130.283)	< 0.001
Intestinal malrotation	1,630 (0.01)	49 (3.0)	83.781 (62.792 to 111.787)	< 0.001
Cardiac arrest	681 (0.01)	8 (0.5)	31.926 (15.874 to 64.206)	< 0.001
Extracorporeal membrane oxygenation	719 (0.01)	23 (2.0)	75.684 (49.770 to 115.091)	< 0.001
Still birth	2,813 (0.1)	3 (0.2)	2.888 (0.930 to 8.969)	0.055
Premature birth (Prior to 37 weeks gestation)	851,413 (19.2)	281 (17.1)	0.871 (0.766 to 0.990)	0.034
Length of hospital stay (days)	3 (0 to 656)	3 (0 to 276)	--	0.002
Cost of hospitalization (US dollars)	3,223 (1 to 5,522,992)	11,153 (73 to 4,176,035)	--	< 0.001
Number of procedures prior to discharge	1 (0 to 34)	2 (0 to 30)	--	< 0.001
Intubation with mechanical ventilation	497,430 (11.2)	566 (34.5)	4.186 (3.712 to 4.721)	< 0.001
Echocardiogram	66,620 (1.5)	189 (11.5)	8.413 (7.034 to 10.061)	< 0.001
Cardiac magnetic resonance imaging	443 (0.01)	7 (0.4)	153.303 (61.912 to 379.601)	< 0.001
Inpatient mortality	45,858 (1.0)	161 (9.8)	10.417 (8.851 to 12.260)	< 0.001

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Conflicts of interest

The authors declare no conflicts of interest.

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