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ORIGINAL ARTICLE

The Impact of Prenatal Diagnosis of Complex Congenital Heart Disease on Neonatal Outcomes

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Abstract Prenatal diagnosis of congenital heart disease (CHD) is increasingly common. However, the current impact of prenatal diagnosis on neonatal outcomes is unclear. Between January 2004 and January 2008, a retrospective chart review of infants who underwent surgical repair of CHD before discharge at our institution was conducted. Obstetric and perioperative variables were recorded. Of 439 neonates, 294 (67%) were diagnosed prenatally (PREdx). Infants with PREdx had a lower mean birth weight (3.0 ± 0.6 vs. 3.1 ± 0.6 kg, $p = 0.002$) and gestational age (37.9 ± 2.1 vs. 38.6 ± 2.4 wk, $p < 0.001$) than those with postnatal diagnosis (POSTdx). Severe lesions were more likely to be PREdx: Neonates with single-ventricle (SV) physiology ($n = 130$ patients [31.2%]) had increased odds of PREdx ($n = 113/130$, odds ratio [OR] 4.7; 95% confidence interval [CI] 2.7–8.2, $p < 0.001$). PREdx was associated with decreased preoperative intubation (OR 0.62; 95% CI 0.42–0.95, $p = 0.033$), administration of antibiotics (OR 0.23; 95% CI 0.15–0.36, $p < 0.001$), cardiac catheterization (OR 0.54; 95% CI 0.34–0.85, $p = 0.01$), and emergency surgery (OR 0.18; 95% CI 0.06–0.5, $p < 0.001$) compared with POSTdx infants. There was no difference in APGAR scores, preoperative pH, day of life of surgery, operative complications, hospital length of stay, or overall mortality in the PREdx versus POSTdx groups, even when controlling for lesion severity. PREdx was not independently associated with neonatal mortality, despite having included more severe cardiac lesions. PREdx was significantly associated with decreased neonatal morbidity in terms of decreased use of preoperative ventilator, administration of antibiotics, cardiac catheterization, and emergency surgery.

Keywords Congenital · Diagnosis · Echocardiography · Heart defects · Surgery

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Congenital malformations are a leading cause of infant mortality in the United States [6]. Heart defects comprise one quarter to one-third of all birth defects and are a large contributor to infant mortality. Prenatal diagnosis of congenital heart disease (CHD) by way of fetal echocardiography is increasingly common. Tworetsky et al. reported that from 1992 to 1999, 37% of hypoplastic left heart syndrome (HLHS) infants treated at Boston Children's Hospital were prenatally diagnosed (PREdx) [15], and Sivarajan et al., at the Royal Children's Hospital of Melbourne, reported that from 2001 and 2005, 77% of HLHS infants were PREdx [14].

Many infants with complex CHD require surgical intervention before hospital discharge. Previous studies investigating whether prenatal diagnosis of CHD favorably impacts survival have demonstrated inconsistent findings [9, 15]. Likewise, the impact on morbidity has been variably reported [3, 4, 16]. In light of these mixed reports, and with the knowledge that prenatal diagnosis is now more common than postnatal diagnosis, we sought to reassess the relations between prenatal diagnosis and various neonatal outcomes. First, we evaluated the effect of prenatal

diagnosis on birth characteristics, such as gestational age (GA) and birth weight (BW). Second, the differences in anatomic cardiac diagnoses between PREdx and postnatally diagnosed (POSTdx) infants were investigated. Third, we assessed the impact of prenatal diagnosis on neonatal morbidity, including the need for more aggressive preoperative measures, day of life (DOL) of surgery, and hospital length of stay (LOS). Fourth, the effect of prenatal diagnosis on mortality was determined. Finally, we investigated the trends in prenatal diagnosis and the impact of prenatal diagnosis on DOL of surgery and hospital LOS at our institution during the course of the study period.

Methods

Study Design and Procedures

A retrospective chart review of infants who underwent repair of CHD before hospital discharge between January 1, 2004 and January 1, 2008 at the Morgan Stanley Children's Hospital of New York (MSCHONY), a tertiary care center with a level IV neonatal intensive care unit, was conducted using the pediatric cardiothoracic surgical database and the Center for Prenatal Pediatrics database. Institutional Review Board approval was obtained. Patient data recorded included timing of diagnosis, type of congenital heart defect, BW, GA, and DOL of surgery. In addition, preoperative information such as use of antibiotics, pressor support, or mechanical ventilator, as well as cardiac catheterization and MRI was collected. Operative and postoperative information including DOL of surgery, bypass and cross-clamp time, and hospital LOS was also recorded. Lesions were categorized based on the surgical severity score described and validated by Jenkins et al., which ranks cardiac diagnoses based on the surgical repair performed before hospital discharge [7].

Univariate descriptive statistics are summarized as means and SDs for normal distributions and as medians and interquartile ranges (IQR) for nonparametric distributions. Differences in proportions between groups were analyzed using 2×2 tables and Pearson's χ^2 test statistic. Univariate relations were explored using Kaplan–Meier, and differences in medians were assessed using the log-rank test. In an effort to evaluate more fully the associations between prenatal diagnosis and DOL of surgery, hospital LOS, and neonatal mortality, multivariate models were constructed using both binary logistic regression and the Cox Proportional Hazards technique. Subject characteristics that showed a univariable association with DOL of surgery, hospital LOS, and mortality at the 0.1 level were eligible for inclusion in the multivariable models. All other alpha values were set at 0.05.

Results

During the 4-year study period, 439 infants underwent neonatal cardiothoracic surgery. Characteristics of the cohort are listed in Table 1. Prenatal diagnosis was made in 294 (67%) infants. Median DOL of surgery was 7 days

Table 1 Information on total cohort (total $n = 439$)

Variables		
Characteristic		*n* (%)
Catagoric variables		
PREdx		294 (67)
Born at MSCHONY		244 (55.6)
Preoperative MRI		26 (5.9)
Preoperative cardiac catheterization		100 (22.8)
Preoperative antibiotics		250 (56.9)
Preoperative mechanical ventilation		105 (23.9)
Preoperative ECMO		3 (0.7)
Preoperative pressor support		158 (36)
Severity score of surgery performed		
1		0 (0)
2		32 (7.3)
3		169 (38.5)
4		135 (30.8)
5		7 (1.6)
6		96 (21.9)
Surgery performed as emergency		18 (4.1)
Surgery postponed		84 (19)
Postoperative hospital mortality		22 (5)
Open chest		65 (14.8)
Characteristic	Mean ± SD	Median (IQR)
Continuous variables		
Maternal age (y)	30.3 ± 6.3	
GA (wk)	38.1 ± 2.1	
BW (kg)	3.04 ± 0.6	
Apgar score at 1 min	7.8 ± 1.5	
Apgar score at 5 min	8.6 ± 0.8	
WBC count (10^9/L)	16.3 ± 6	
Highest arterial lactate (mM/l)	4.2 ± 2.8	
Arterial pH DOL 1	7.34 ± 0.1	
Arterial pH DOL 2	7.34 ± 0.4	
Arterial pH DOL 3	7.37 ± 0.1	
Arterial pH DOL 4	7.38 ± 0.1	
DOL postnatal diagnosis	1.9 ± 2.2	
DOL preoperative cardiac catheterization	2.7 ± 2.9	
DOL preoperative MRI	5.4 ± 4.1	
DOL at surgery		7 (5–9)
LOS		17 (12–18)

ECMO extracorporeal membrane oxygenation

(IQR 5–9), and median length of hospital stay was 17 days (IQR 12–28). Postoperative mortality was 5% in the entire series.

Birth Characteristics

Differences between the prenatal and postnatal diagnosis group are listed in Tables 2, 3. The prenatal diagnosis group had a lower mean GA (37.9 ± 2.1 vs. 38.6 ± 2.4 wk, $p < 0.001$) and BW (3.0 ± 0.6 vs. 3.1 ± 0.6 kg, $p = 0.002$) and were more likely to be born at our tertiary care center where the surgery was performed (OR 156.7; 95% CI 55.6–441.8, $p < 0.001$) compared with infants diagnosed after birth.

Cardiac Diagnosis Breakdown

The prenatal diagnosis group had higher surgical severity scores ($p < 0.001$) compared with the postnatal group in accordance with the higher prevalence of more severe forms of CHD among the prenatal group (Table 4). Infants with HLHS were more likely to be PREdx (OR 4.1; 95% CI 1.9–8.9), whereas infants with transposition of the great arteries (TGA) were less likely to have a prenatal diagnosis (OR 0.4; 95% CI 0.3–0.7). Infants with total anomalous pulmonary venous return (TAPVR) were also less likely to be diagnosed before birth (OR 0.02; 95% CI 0.0–0.1).

Neonatal Mortality

Prenatal diagnosis did not impact neonatal mortality. Independent factors associated with mortality are listed in Tables 5, 6. SV morphology ($p < 0.001$), surgical severity score ($p = 0.002$), postoperative open chest ($p < 0.001$), 1-min Apgar score ($p = 0.05$), and bypass time ($p < 0.001$) were significantly associated with mortality. Multivariate analysis demonstrated that postoperative open chest (OR 1.9; 95% CI, $p = 0.12$) was the only independent factor associated with mortality.

Preoperative Morbidity

PREdx infants were less likely to receive preoperative mechanical ventilation (OR 0.6; 95% CI 0.4–0.9), antibiotics (OR 0.2; 95% CI 0.1–0.4), cardiac catheterization (OR 0.5; 95% CI 0.3–0.9), or emergent surgery (OR 0.2; 95% CI 0.1–0.5) compared with POSTdx infants (Tables 2, 3).

DOL of Surgery

Prenatal diagnosis did not impact DOL of surgery (median DOL of surgery 7 days [IQR 5–8] for prenatal diagnosis vs. 6 days [IQR 5–9] for postnatal diagnosis, $p = 0.9$). There was no difference in DOL of surgery among groups even when stratified by cardiac lesion (Table 7). Univariate

Table 2 Catagoric variables

Perinatal characteristics	No. prenatal diagnosis (%)	No. postnatal diagnosis (%)	OR	95% CI	*p*
Total	294	145			
Born at MSCHONY	240 (81.6)	4 (2.7)	156.7	56–442	<0.001
Preoperative MRI	15 (5.1)	11 (7.6)	0.7	0.3–1.5	0.30
Preoperative cardiac catheterization	56 (19)	44 (30)	0.5	0.3–0.9	0.008
Preoperative antibiotics	136 (46)	114 (78.6)	0.2	0.1–0.4	<0.001
Preoperative mechanical ventilation	105 (35.7)	68 (46.9)	0.6	0.4–0.9	0.025
Preoperative ECMO	3 (1)	0 (0%)			0.22
Preoperative pressor support	102 (34.7)	56 (38.6)	0.8	0.6–1.3	0.42
Preoperative positive blood culture	11 (3.7)	5 (3.4)	1.1	0.4–3.2	0.87
Severity score of surgery performed			–	–	<0.001
2	16 (5.4)	16 (11)			
3	112 (38.1)	57 (39.3)			
4	80 (27.2)	55 (37.9)			
5	3 (1.0)	4 (2.8)			
6	83 (28.2)	13 (9.0)			
Surgery performed as emergency	5 (1.7)	13 (9)	0.2	0.1–0.5	<0.001
Surgery postponed	67 (22.8)	17 (11.7)	2	1.3–3.3	0.006
Postoperative hospital mortality	18 (6.1)	4 (2.8)	2.3	0.7–6.9	0.129
Patients with open chest	44 (15)	21 (14.5)	1.0	0.6–1.8	0.89

ECMO extracorporeal membrane oxygenation

Table 3 Continuous variables

Perinatal characteristics	PREdx (mean ± SD)[a]	POSTdx (mean ± SD)[a]	*p*
Maternal age (y)	30.6 ± 6.2	29.5 ± 6.5	0.098
GA (wk)	37.9 ± 2	38.6 ± 2	<0.001
BW (kg)	3 ± 0.6	3.1 ± 0.6	0.002
Apgar score at 1 min	7.8 ± 1.5	7.9 ± 1.6	0.47
Apgar score at 5 min	8.6 ± 0.7	8.6 ± 1.1	0.97
Highest arterial lactate (mM/l)	4.1 ± 2.5	4.5 ± 3.5	0.20
Arterial pH DOL 1	7.34 ± 0.07	7.33 ± 0.1	0.82
Arterial pH DOL 2	7.34 ± 0.45	7.37 ± 0.07	0.57
Arterial pH DOL 3	7.37 ± 0.06	7.38 ± 0.07	0.16
Arterial pH DOL 4	7.37 ± 0.08	7.39 ± 0.06	0.08
DOL of surgery (median)	7 (5–8)	6 (5–9)	0.88
Bypass time (min)	126.8 ± 46.1	119 ± 40.6	0.096
Cross-clamp time (min)	56 ± 29.6	54.6 ± 26.6	0.67
Circulatory arrest (min)	38.6 ± 19.0	31.2 ± 19.6	0.003
LOS (median d)	20 (13–33)	15 (11–25)	0.001

[a] Unless otherwise noted

Table 4 Diagnosis breakdown: PREdx versus POSTdx

Diagnosis	Total	No. PREdx (%)	No. POSTdx (%)	OR	95% CI	*p*
Total	439	294 (67)	145 (33)			
SV (total)	135	118 (87.4)	17 (12.6)	5.0	2.9–8.8	<0.001
HLHS	65	57 (89)	8 (11)	4.1	1.9–8.9	<0.001
Complex SV	60	53 (88)	7 (12)	4.3	1.9–9.8	<0.001
Heterotaxy	10	8 (80)	2 (20)	2	0.4–9.5	0.38
d–TGA (total)	89	46 (51.8)	43 (48.2)	0.4	0.3–0.7	0.001
d–TGA/IVS	51	22 (43.1)	29 (56.9)	0.3	0.2–0.6	<0.001
d–TGA/VSD	25	16 (64)	9 (36)	0.9	0.4–2.0	0.45
d–TGA/complex	13	8 (61.5)	5 (38.5)	0.8	0.3–2.4	0.44
Pulmonary atresia (non-SV)	10	7 (70)	3 (30)	1.2	0.3–4.5	0.84
DORV/MPGV	18	14 (77.8)	4 (22.2)	1.9	0.6–5.8	0.19
DORV, other	8	8 (100)	0	–	–	0.04
Tetralogy of Fallot	31	21 (67.8)	10 (32.2)	1.0	0.5–2.3	0.55
TAPVR, isolated	26	1 (3.8)	25 (96.2)	0.02	0.0–0.1	<0.001
IAA	16	10 (62.5)	6 (37.5)	0.8	0.3–2.3	0.44
Truncus arteriosus/IAA	4	1 (25)	3 (75)	0.2	0.0–1.6	1.1
Truncus arteriosus	11	7 (63.6)	4 (36.4)	0.9	0.2–3	0.52
Arch anomaly + intracardiac anomaly	41	32 (78)	9 (22)	1.8	0.9–4	0.076
Isolated arch anomaly	29	18 (62)	11 (38)	0.8	0.4–1.7	0.35
Intracardiac mass	7	5 (71)	2 (29)	1.2	0.2–6.5	0.58
Other	14	6 (42.8)	8 (57.2)	0.36	0.1–1.0	0.05

DORV/MPGV double–outlet right ventricle/malposed great vessels, *TAPVR* total anomalous pulmonary venous return, *IAA* interrupted aortic arch, *SV* single ventricle, *d–TGA (total)* dextro-TGA of the great arteries, *d–TGA/IVS* dextro-TGA of the great arteries/intact ventricular septum, *d–TGA/VSD* dextro-TGA of the great arteries/ventricular septal defect

associations between subject characteristics and DOL of surgery are listed in Table 8. Multivariate Cox-proportional hazard modeling demonstrated that the use of preoperative antibiotics (hazard ratio [HR] 0.7; 95% CI 0.6–0.9, $p = 0.002$) and additional fetal anomalies (HR 0.5; 95% CI 0.4–0.7, $p < 0.001$) were independently

Table 5 Univariate associations with mortality

Catagoric variables	Total (*n*)	Mortality (*n*)	OR	95% CI	*p*
Timing of diagnosis			2.3	0.7–6.9	0.13
Prenatal	294	18			
Postnatal	145	4			
Born at MSCHONY			0.96	0.4–2.2	0.92
Yes	244	12			
No	195	10			
SV anatomy			4.5	1.9–11.1	<0.001
Yes	135	14			
No	304	8			
Other fetal anomalies			1.8	0.58–5.5	0.304
Yes	50	4			
No	389	18			
Preoperative pressor support			2.23	0.94–5.3	0.063
Yes	158	12			
No	281	10			
Preoperative antibiotic use			1.1	0.46–2.6	0.85
Yes	250	13			
No	188	9			
Preoperative positive blood culture			1.2	0.16–9.7	0.84
Yes	16	1			
No	409	21			
Preoperative ventilation			1.8	0.7–4.4	0.20
Yes	173	11			
No	246	9			
Severity of surgery performed			–	–	0.002
2	32	0			
3	169	1			
4	135	11			
5	7	1			
6	96	9			
Emergency surgery			1.1	0.14–8.8	0.91
Yes	18	1			
No	421	21			
Postoperative open chest			4.46	1.8–10.9	<0.001
Yes	65	9			
No	374	13			

Table 6 Continuous variables associated with mortality

Variable	Mortality	No mortality	*p*
GA at birth (wk)	37.5 ($n = 22$)	38.1 ($n = 410$)	0.19
BW (kg)	2.842 ± 0.67 ($n = 21$)	3.045 ± 0.62 ($n = 407$)	0.15
Apgar score at 1 min	7.2 ± 1.6 ($n = 20$)	7.9 ± 1.5 ($n = 389$)	0.05
Apgar score at 5 min	8.4 ± 0.7 ($n = 20$)	8.6 ± 0.8 ($n = 389$)	0.27
Highest arterial preoperative lactate (mM/L)	3.5 ± 1.4 ($n = 17$)	4.3 ± 2.8 ($n = 299$)	0.29
DOL at surgery	6 (5–9) ($n = 22$)	7 (5–9) ($n = 417$)	0.86
Bypass time (min)	168 ± 40.9 ($n = 15$)	122 ± 43.7 ($n = 353$)	<0.001

All data reported as means with SD, except for DOL at surgery, which is reported as median with interquartile range

Table 7 Median DOL of surgery by cardiac diagnosis and diagnosis timing

Lesion	PREdx	POSTdx	*p*
SV	7 (5–8)	8 (5–15)	0.17
HLHS	7 (5–8)	5 (5–7)	0.6
d–TGA	7 (5–8)	6 (4–7)	0.07

d–TGA dextro-TPA of the great arteries

Data reported as medians with interquartile ranges

associated with a longer time to surgery when controlling for timing of diagnosis, prematurity, and low BW.

Hospital LOS

Univariate associations between subject characteristics and hospital LOS are listed in Table 9. The prenatal diagnosis group had longer median hospital LOS (20 [range 13–33] vs. 15 days [range 11–25], $p = 0.001$) than the postnatal

Table 8 Univariate associations with DOL at surgery

Variable	Total (*n*)	Median DOL	IQR	*p*
Timing of diagnosis				0.88
Prenatal	294	7	5–8	
Postnatal	145	6	5–9	
Born at MSCHONY				0.43
Yes	244	6	4–8	
No	195	7	5–9	
SV anatomy				0.19
Yes	135	7	5–9	
No	304	6	4–9	
Other fetal anomalies				<0.001
Yes	50	9	6–16	
No	389	6	4–8	
Premature[a]				0.003
Yes	139	7	5–9	
No	300	6	4–8	
Low BW[b]				0.001
Yes	84	8	6–10	
No	355	6	4–8	
Peak preoperative arterial lactate (mM/l)				0.125
≤2.6	89	7	5–8	
2.7–3.5	73	6	5–8	
3.6–5.1	73	6	4–8	
>5.1	77	6	4–10	
Preoperative pressor support				0.053
Yes	158	7	5–9	
No	281	6	4–8	
Preoperative antibiotic use				0.001
Yes	250	7	5–9	
No	188	6	4–8	
Preoperative positive blood culture				<0.001
Yes	16	13	8–16	
No	409	6	5–8	
Preoperative cardiac catheterization				0.25
Yes	100	7	5–9	
No	339	6	4–9	
Preoperative MRI				0.12
Yes	26	8	7–10	
No	413	6	4–9	

Table 8 continued

Variable	Total (*n*)	Median DOL	IQR	*p*
Preoperative ventilation				0.71
Yes	173	6	4–9	
No	246	7	5–9	
Severity of surgery performed				0.22
2	32	7	4–10	
3	169	7	5–10	
4	135	6	4–8	
5	7	6	5–8	
6	96	7	5–8	
Surgery postponed				<0.001
Yes	84	11	8–16	
No	355	6	4–8	
Emergent surgery				<0.001
Yes	18	2	2–2	
No	421	7	5–9	

[a] GA <38 weeks

[b] BW <2,500 g

diagnosis group. Multivariate Cox-proportional hazard modeling demonstrated that surgical severity score (HR 0.9; 95% CI 0.8–0.9, $p < 0.001$), other fetal anomalies (HR 0.7; 95% CI 0.5–0.9, $p = 0.03$), prematurity (HR 0.8; 95% CI 0.6–0.9, $p = 0.036$), and DOL of surgery (HR 0.9; 95% CI 09–1, $p < 0.001$) were independently associated with a longer hospital LOS when controlling for prenatal diagnosis and low BW. Prenatal diagnosis was not associated with hospital LOS in this multivariate model.

Prenatal Diagnosis Trends

Trends in prenatal diagnosis, DOL of surgery, and hospital LOS across the 4-year study period are listed in Table 10. Although there was no significant difference in the rate of prenatal diagnosis, median DOL of surgery and hospital LOS decreased significantly from 2004 to 2007.

Discussion

This study demonstrates that the prevalence of prenatal diagnosis of CHD in the current era is higher than previously reported, reaching as high as 88% for certain defects at our center. There are various explanations for the increase in prenatal detection of CHD. First, standard of care of obstetrical screening for fetal anomalies has expanded to include first-trimester nuchal fold measurements. Abnormalities in these early scans typically result in referral for fetal echocardiography. Second, modern technology has improved image resolution, thus making it easier to detect anomalies during routine obstetric ultrasound screening.

Our study demonstrated an association between prenatal diagnosis and lower GA and BW. This has been reported previously [3]. This finding may be explained in part by institutional practices of scheduling delivery, especially among women who live far from the medical center, to assure availability of maximal neonatal medical support. The differences in BW and GA are small and are unlikely to be of clinical significance, as evidenced by the decrease in neonatal morbidity among the prenatal diagnosis group.

We found that the more severe cardiac anatomic lesions are likely to be PREdx. This finding has been reported previously [3] and can be explained by advances in obstetrical screening methods. The most common indication for referral for fetal echocardiography is a cardiac abnormality seen on the routine obstetrical anatomic scan [5, 12]. Guidelines from the American Institute of Ultrasound in Medicine recommend a complete second-trimester anatomic scan of the fetal chest, including a four-chamber view of the fetal heart and, if technically feasible, views of the two outflow tracts [1]. Therefore, the more grossly abnormal the appearance of the heart in the four-chamber view, the more likely the lesion is to be recognized on routine ultrasound. Conversely, lesions such as TAPVR and TGA that do not significantly change the appearance of the four-chamber view are more likely to be missed. TGA is likely to be overlooked because views of the outflow tracts are not always obtained. The same is true for anomalous pulmonary venous connections because pulmonary veins are not often discerned on fetal studies.

Our study did not demonstrate an association between prenatal diagnosis and surgical mortality. Other studies similarly did not demonstrate a positive impact of prenatal diagnosis on the survival of infants with HLHS and other forms of CHD [8–11]. In 2001, Tworetsky et al. demonstrated a survival advantage to prenatal diagnosis among HLHS infants. In this study, 37.5% of the HLHS infants

Table 9 Univariate associations with LOS

Variable	Total (*n*)	Median LOS	IQR	*p*
Timing of diagnosis				0.001
Prenatal	294	20	13–33	
Postnatal	145	15	11–25	
Born at MSCHONY				<0.001
Yes	244	20	13–34	
No	195	15	11–25	
SV anatomy				<0.001
Yes	135	22	14–39	
No	304	16	12–26	
Other fetal anomalies				<0.001
Yes	50	28	18–45	
No	389	16	12–27	
Premature[a]				0.007
Yes	139	21	14–34	
No	300	16	12–27	
Low BW[b]				0.087
Yes	84	21	14–30	
No	355	17	12–28	
Peak preoperative arterial lactate (mM/l)				0.030
≤2.6	89	17	12–34	
2.7–3.5	73	16	12–22	
3.6–5.1	73	20	12–28	
>5.1	77	19	13–33	
Preoperative pressor support				0.47
Yes	158	18	12–32	
No	281	17	12–28	
Preoperative antibiotic use				0.99
Yes	250	17	13–28	
No	188	18	11–30	
Preoperative positive blood culture				0.31
Yes	15	20	16–45	
No	409	17	12–28	
Preoperative cardiac catheterization				0.18
Yes	100	16	11–26	
No	339	18	12–29	
Preoperative MRI				0.86
Yes	26	22	14–32	
No	413	17	12–28	
Preoperative ventilation				0.47
Yes	173	18	12–31	
No	246	17	12–28	
Severity of surgery performed				0.072
2	32	14	9–25	
3	169	17	12–26	
4	135	16	12–27	
5	7	22	8–59	
6	96	25	14–39	

Table 9 continued

Variable	Total (*n*)	Median LOS	IQR	*p*
Surgery postponed				<0.001
Yes	84	26	16–45	
No	355	16	12–26	
Emergent surgery				<0.001
Yes	18	11	10–14	
No	421	18	12–29	
Surgery at DOL < 7				<0.001
Yes	216	14	10–22	
No	223	22	15–37	
Open chest				0.002
Yes	65	28	17–39	
No	374	16	12–26	

[a] GA <38 weeks

[b] BW <2,500 g

Table 10 Outcomes over the years

Timing of diagnosis	Year of surgery (% total)				
	2004 ($n = 107$)	2005 ($n = 101$)	2006 ($n = 123$)	2007 ($n = 108$)	*p* comparing 2004 and 2007
Prenatal	70 (65.4)	63 (62.4)	80 (65)	81 (75)	0.166
DOL at surgery (median)					
Prenatal	8 (5–9)	7 (5–9)	6 (5–8)	6 (4–8)	0.036
Postnatal	6 (5–8)	7 (4–12)	7 (6–9)	6 (4–9)	
All patients	7 (5–9)	7 (5–10)	6 (5–8)	6 (4–8)	
LOS (median d)					
Prenatal	21 (15–35)	22 (15–43)	17 (12–26)	17 (10–17)	0.002
Postnatal	16 (12–28)	15 (12–26)	15 (11–27)	14 (12–28)	
All patients	20 (14–34)	20 (13–34)	16 (12–27)	16 (11–26)	

were PREdx, whereas in our study 88% of HLHS infants were PREdx and 88% survived neonatal surgery. This change in the prevalence of prenatal diagnosis and in the prevalence of survival may partially explain the differences in findings. Although it is true that for some infants prenatal diagnosis is life saving, there are others for whom immediate delivery of targeted cardiac support may not be as crucial. If 88% of HLHS infants are PREdx indiscriminately, which includes a mix of the above phenotypes, then the association between prenatal diagnosis and survival may be difficult to discern.

We have demonstrated that prenatal diagnosis improves certain measures of neonatal morbidity. Others have reported that prenatal diagnosis decreases neonatal metabolic acidosis [2, 4, 13, 16]. Although we found no statistically significant impact of prenatal diagnosis on neonatal acid–base status, we did see decreased use of ventilators, antibiotics, and cardiac catheterization, and fewer emergent surgeries among the prenatal diagnosis group. These findings can be attributed in part to the anticipation of medical needs of patients with a fetal diagnosis of CHD and the institution of medical support before clinical status deterioration, avoiding the poor status that is the usual presentation of the POSTdx infant. The majority of our PREdx cohort (82%) was born at our institution, thus allowing the immediate delivery of medical support, including prostaglandin, which is vital for the maintenance of ductal patency in a ductal-dependent lesion. In addition, the development of cyanosis and respiratory distress in an infant without a prenatal CHD diagnosis often prompts intubation and a sepsis workup, further explaining the higher prevalence of these findings in the postnatal diagnosis group. Furthermore, infants born at outside institutions may have been intubated for the purposes of transportation to our center. The decreased use of cardiac catheterization in the prenatal diagnosis group may be accounted for by the high proportion of POSTdx infants with TGA, who often require balloon atrial septostomy, and those with TAPVR, who may undergo diagnostic cardiac catheterizations to delineate the anatomic pathways of the anomalous pulmonary veins. Similarly, the association with emergent surgery may be explained by the TAPVR anatomic subgroup, many of whom present in distress and are urgently repaired.

We found no association between prenatal diagnosis and DOL of surgery or hospital LOS, even when controlling for lesion severity. Although median hospital LOS was longer in the prenatal diagnosis group in a univariate analysis, the association was no longer significant in multivariate analysis. Copel et al. demonstrated that prenatal diagnosis was associated with an overall increase in neonatal hospital LOS and hospital expenses for live-born infants and postulated that this might be due to increased illness severity in the PREdx cohort [3].

Limitations

Our study consisted of a retrospective review of data. Only infants who survived to cardiac surgery were captured in this analysis; therefore, the effect of prenatal diagnosis on overall neonatal mortality cannot be assessed with the present data. In addition, our sample does not include pregnancies that were terminated. It has been our experience that few fetuses with a prenatal diagnosis of CHD seen at our institution are terminated, which is likely due to selection bias: patients who have decided to continue the pregnancy seek care at a tertiary-level referral center, whereas patients wishing to terminate the pregnancy may do so locally. One could postulate that prenatal diagnosis of CHD may lead to increased terminations of pregnancy, especially among fetuses with more severe lesions and with additional significant anomalies. All of these factors may confound our ability to establish a causal relation between prenatal diagnosis and neonatal outcomes.

Conclusion

Prenatal diagnosis of complex CHD is now more common than postnatal diagnosis; levels were as high as 75% overall in the final year of our study. Prenatal diagnosis is more likely to occur in lesions of higher severity. Despite representing more severe lesions, prenatal diagnosis was associated with decreased neonatal morbidity, including decreased use of mechanical ventilation, antibiotics, and emergent surgery. Prenatal diagnosis did not impact DOL of surgery, hospital LOS, or mortality. Further investigation into the impact of prenatal diagnosis on DOL of surgery and hospital LOS is needed. The positive economic impact of more efficient management of these patients is also an important consideration. Advanced prenatal knowledge of an indication for cardiac surgery may allow for the optimization of factors beyond immediate neonatal resuscitation that affect neonate survival, including labor, delivery, and operative repair.

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