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ORIGINAL RESEARCH ARTICLE

Accuracy of fetal echocardiography diagnosis and anticipated perinatal and early postnatal care in congenital heart disease in mid-gestation

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Abstract

Introduction: The aim of this study was to determine discrepancies in fetal congenital heart disease (CHD) diagnoses and anticipated early postnatal care and outcomes.

Material and methods: A retrospective review of 462 randomly selected cases (23% of all cases) referred to a fetal cardiac assessment during the second trimester (mean 26 weeks) at the Children's Hospital in Helsinki between October 2010 and December 2020. Discrepancy between prenatal and postnatal CHD case evaluations was assessed with independently provided cardiac severity and surgical complexity scores.

Results: In all, 250 cases, 181 CHD and 69 normal, with complete prenatal and postnatal live birth data as well as seven fetal autopsy reports available were included in the analysis. There were 12 false normal and seven false abnormal prenatal assessments. The prenatally anticipated level of early neonatal care was actualized in 62% and prostaglandin infusion in 95%. In total, 32.7% (84/257) cardiac severity scores were discrepant and in 12,4% (32/257) cases the discrepancies were considered significant (≥ +/− 2 scores). Among significant discrepancies, CHD severity score was overestimated in 13 and underestimated in 19 in fetal assessment. Progression of CHD severity after mid-gestation and during early neonatal phase explained eight of 19 underestimated fetal assessments. The most common discrepant diagnostic categories included ventricular septal defects ($n = 7$), borderline ventricles ($n = 7$; 5 left heart, 1 right heart and 1 double outlet right ventricle/transposition of the great arteries), arch anomalies including coarctations ($n = 5$) and tricuspid valve dysplasias ($n = 4$) with a significant change in postnatal diagnoses and treatment.

Conclusions: Although fetal CHD diagnosis and counseling is accurate and reliable in general, the study elaborates specific areas of uncertainty in clinical fetal cardiology practice that may be important to consider in fetal CHD evaluation and counseling provided in mid-gestation.

Abbreviations: CHD, congenital heart disease; CoA, coarctation of the aorta; ICU, intensive care unit; PGE, prostaglandin E; TV, tricuspid valve; VSD, ventricular septal defects.

KEYWORDS
accuracy, aortic arch anomalies, congenital heart disease, fetal, postnatal care, tricuspid dysplasia, ventricular septal defects

1 | INTRODUCTION

Fetal ultrasound is a diagnostic tool commonly used to screen for congenital heart disease (CHD). Ultrasound is offered in Finland twice during pregnancy to determine gestational age and to detect karyotype defects, number of fetuses, malformations, etc. The heart is developed early during embryonic development and commonly CHD is detected during the obstetric anomaly ultrasound scan between 18 and 20 weeks.[1,2] In addition, first trimester early CHD screening may be applied for risk populations.

Prenatal detection and accurate delineation of fetal CHD morphology and function is essential for prenatal counseling as well as perinatal and early postnatal care planning. Prenatal diagnoses also allow targeted screening of CHD-associated chromosomal abnormalities and other associated malformations. Accurate CHD diagnosis is essential for CHD severity and likely prognosis assessments conveyed to parents during counseling. Key elements in postnatal care planning include anticipation of neonatal care and early intervention needs. Treatment outcomes and prognosis are also dependent on optimized early postnatal preintervention care.[3]

This study was inspired by previous studies evaluating fetal echocardiographic diagnostic accuracy of CHD,[4–7] and also by a few studies assessing accuracy of anticipated prognosis, early postnatal care and early intervention needs.[3,8] We hypothesized that the results would show more discrepancies in complex cases and more accurate prenatal diagnosis of simple cases. Our aim was to determine discrepancies in fetal CHD diagnoses and CHD severity at first fetal cardiology assessment in mid-gestation to compare the performance of our center with contemporary data from other centers. Secondary aims included assessment of discrepancies in anticipated early postnatal care level, prostaglandin infusion and complexity of early surgical intervention needs linked with outcome and prognosis. Diagnostic areas of uncertainty in fetal CHD diagnosis and counseling during the second trimester and potential predictors of prenatal diagnostic discrepancies were also elucidated.

Key message

Although fetal congenital heart disease diagnosis and anticipated early neonatal care is accurate and reliable overall in mid-gestation, a significant change in diagnosis and early care was found in 12% of cases including borderline ventricles, ventricular septal defects, aortic arch anomalies and tricuspid dysplasia.

2 | MATERIAL AND METHODS

This retrospective review consisted of 462 pregnant women referred for a detailed fetal cardiology assessment with transabdominal ultrasound at the fetal cardiac outpatient clinic at the Children's Hospital in Helsinki, Finland, between October 2010 and December 2020. Women are referred to our tertiary care center from all hospital districts in Finland and the referral practice is in line with international fetal cardiology guidelines.[9] Our unit also provides telemedicine consultations. All pediatric cardiac surgery and catheter interventions in Finland are performed at the Children's Hospital in Helsinki. The random non-selected sample represents 23% of all 2011 fetal cardiology referrals during the time period.

The prenatal fetal cardiac diagnosis was based on fetal echocardiography performed and counseling provided by a fetal cardiologist during the randomly assigned initial visit as documented in the hospital charts during the second trimester. Anticipated level of early neonatal care, prostaglandin E (PGE) infusion, and early surgical intervention timing and type was documented from the latest antenatal fetal cardiology follow-up visit. Follow-up visits in the setting of significant fetal CHDs were arranged at 28–32 weeks and in late gestation prior to birth with anticipated level and type of neonatal care tuned during follow-up visits later in gestation. Descriptive maternal, gestational and neonatal background information was collected. Postnatal CHD diagnosis was defined as CHD diagnosis documented during the first early surgical intervention or, in the case of no early intervention, the CHD diagnosis documented by the pediatric cardiologist at first hospital discharge. Fetal autopsy reports were reviewed in the setting of terminations of pregnancy if parental consent had been obtained for fetal autopsy. Prenatal and postnatal information was independently collected by a medical student (MN) and based on hospital chart information only.

CHD diagnoses were categorized by cardiac severity score from zero to seven according to Davey et al., with zero indicating no heart malformation and seven indicating poor outcome and unexpected survival beyond early period of life despite attempted intervention.[10] The surgical interventions were given a basic cardiac surgery complexity score (SCS) between 3 and 14.5, with high scores indicating high complexity, mortality and complication risk as described in Lacour-Gayet et al.[11] These surgical complexity scores were also reported as level 1 (score 1–5.9), level 2 (score 6–7.9), level 3 (score 8–9.9) and level 4 (score 10–14.5). A fetal cardiologist (TS) independently provided prenatal cardiac severity score and SCS based on the data collected by MN. Postnatal scores were provided separately and independently by the same cardiologist based on collected postnatal data and blinded to prenatal diagnoses and scoring. Discrepancies between scores were quantified by subtracting prenatal scores from postnatal scores. A positive discrepancy was, thus,

consistent with a less severe prenatal CHD diagnosis, and a negative discrepancy with a more severe prenatal CHD diagnosis.

In all, 250 cases with complete pre- and postnatal information available and seven cases with fetal autopsy reports were included in the final analysis. Cases were excluded ($n = 205$) due to normal findings at fetal echocardiography combined with no documented need for postnatal intervention ($n = 56$), miscarriages ($n = 7$), and termination of pregnancies without fetal autopsy performed ($n = 46$). In addition, we excluded cases with arrhythmias but without CHD (bradycardia, tachyarrhythmia and extra systoles, $n = 76$) and mild CHDs on the fetal echocardiogram for which no follow-up information was available ($n = 20$). Excluded cases were screened for postnatal interventions (cath or surgery) performed within 3 months from birth in the nationally centralized interventional care of CHD at the Children's Hospital, Helsinki, Finland. No deaths among excluded cases were associated with CHD.

The data are presented in tables as *n* or proportions, mean or median with SD, or range. The results are summarized in tables, flow charts and figures. Associations between variables were analyzed with Pearson's correlation and relations between discrepancy and imaging quality were assessed using the Kruskal-Wallis H-test.

2.1 | Ethical approval

The study conforms to the ethical guidelines of the 1975 Declaration of Helsinki and the review of hospital charts was approved by the Helsinki University Hospital (August 25, 2020; HUS180/2020).

3 | RESULTS

Maternal and perinatal data are presented in Table 1. The obstetric charts showed a normal first trimester screening in 157/250 cases. A cardiac abnormality on the anatomic scan at mid-gestation was documented in 174 cases and was the most common reason for a referral to a fetal cardiology assessment. Termination of pregnancy was performed prior to 24 weeks in 53 cases due to severe fetal abnormalities, with fetal autopsy reports available in seven cases (Table S1).

Of the 250 liveborn cases, 181 were abnormal and 69 normal postnatally. Among 181 postnatally abnormal, 169 were abnormal in the prenatal assessment. Among 69 postnatally normal, 62 were normal in the prenatal assessment. In all, there were then 12 false normal and seven false abnormal prenatal assessments performed. The accuracy of the assessment was 97%. False prenatal abnormal cases included two suspected coarctations of the aorta (CoA), two small ventricular septal defects (VSD), one cardiomyopathy with congenital complete heart block and ventricular tachycardia (cardiomyopathy not confirmed postnatally), one case with tricuspid valve (TV) dysplasia (insignificant TV regurgitation), left superior vena cava and mild hypoplasia of the aortic arch (not confirmed) and one case with right aortic arch without aberrant left subclavian artery.

TABLE 1 Data at fetal echocardiographic examination and early neonatal care

		Mean + SD
n		250
Maternal age, years		31.1 ± 5.9
Gestations	G1	73
	G2	67
	G3 or more	85
	Missing information	25
Parity	P0	94
	P1	74
	P2 or more	63
	Missing information	19
Gestational age at fetal assessment, weeks		25.8 ± 5.5
Screening 1	Normal	157
	Abnormal	40
	Missing information	53
Screening 2	Normal	41
	Abnormal	174
	Missing information	35
Indication for fetal	No information	14
cardiology referral	Suspected CHD	170
	Arrhythmia	9
	Other malformation	23
	Maternal disease	3
	CHD in family	21
	Other	10
Prenatal genetic	Yes, normal	46
testing of fetus performed	Yes, abnormal	27
	No	177
Fetal echocardiography imaging quality	Good	210
	Poor	34
	Very poor	6
CPAP or respirator		114
PGE infusion started		91
Early intervention (<6 months)		81
Early repeat intervention		18
Early death (<30 days)		26

Abbreviations: CHD, congenital heart disease; CPAP, continuous airway pressure, PGE, prostaglandin E.

False prenatal normal cases included five cases with isolated VSDs, one operated right atrial Chiari network malformation, one combined secundum atrial septal defect (ASD) and VSD, one hypoplasia of the aortic arch, one Noonan syndrome with hypertrophic cardiomyopathy, one VSD with left superior vena cava, and one primum ASD. Distributions of postnatal diagnostic CHD groups are provided in Table 2.

TABLE 2 Postnatal diagnostic congenital heart disease (CHD) groups

CHD group	*n*	Autopsy reports	Discrepancies[a]
Transposition of the great arteries and variants	31	1	
Interrupted aortic arch, coarctation of the aorta and variants	10		5
Hypoplastic left heart single ventricle	18	2	
Pulmonary atresia with intact ventricular septum and variants	6		1
Other single ventricle and functionally univentricular hearts (eg TA, DILV, unbalanced AVSD, complex ccTGA and DORV/TGA)	17	1	2
Tetralogy of Fallot and variants including PA + VSD	24		1
Atrioventricular septal defect and variants	9	1	2
Isolated VSD	19		4
Congenitally corrected transposition and variants	5		
Heterotaxy and isomerism	6	2	2
Ebstein's anomaly, tricuspid dysplasia and variants	6		3
Aortic stenosis	1		
Common arterial trunk	3		1
Tumors	3		1
Cardiomyopathies	4		1
Other abnormal hearts	19		4
Normal heart	69		5

Abbreviations: AVSD, atrioventricular septal defect; ccTGA, congenitally corrected transposition of the great arteries; DILV, double inlet left ventricle; DORV, double outlet right ventricle; PA, pulmonary atresia; TA, tricuspid valve atresia; VSD, ventricular septal defect.

[a]Discrepancy cardiac severity score equal to or more than +/−2; there were no discrepant autopsy reports.

High cardiac severity scores were prevalent among prenatal and postnatal CHD cardiac severity scores. The numbers of discrepant cases for each CHD group are provided in Table 2. There were 173 cases with no discrepancy, 43 cases with higher and 41 cases with a lower prenatal cardiac severity score compared with the postnatal. The distribution of discrepancies between postnatal and prenatal cardiac severity score assessments among discrepant cases, and discrepancy in relation to postnatal score is shown in Figure 2A and 2B. In total, 32.7% (84/257) scores showed a discrepancy (score difference > +/−0); in 12,4% (32/257) the discrepancies were equal or more than +/− 2 (Table S3). Among those significantly discrepant 32 cases, the CHD cardiac severity score was higher among 13 and lower among 19 cases in the fetal assessment compared with the postnatal assessment. The most common diagnostic categories among these 32 cases included seven cases with VSDs (four isolated and three complex), five cases with aortic arch anomalies including coarctations, and four cases with tricuspid valve dysplasia and later evolving severe regurgitation in three. Significantly discrepant cases also included seven borderline ventricles (five left heart, one right heart and one double outlet right ventricle/transposition of the great artery [DORV/TGA]) with a major change in postnatal diagnoses, treatment and outcomes following biventricular or univentricular repair. Progression of cardiac severity after mid-gestation and during the early neonatal stage explained 8/19 cases (three evolving TV regurgitation, two cardiomyopathy, one pulmonary atresia with intact ventricular septum single ventricle, one DORV/TGA single ventricle, and one hypoplasia of the aortic arch) with underestimated cardiac severity score in the fetal assessment. The mean difference between postnatal and prenatal cardiac severity scores was 0.09 ± 1.14.

Of 178 abnormal postnatal cases, 136 cases required a surgical intervention, including 81 interventions required within 30 days after birth. Eighteen cases required a repeat surgical intervention within 6 months after the first intervention and 26 cases died within 30 days from birth. Intensive care unit (ICU) duration was a median of 10 days (IQR 14 days) from birth, and age at hospital discharge was a median of 19 days (IQR 22 days). High surgical complexity scores were prevalent among prenatal and postnatal scores (Figure 3). Distribution of discrepancies between postnatal and prenatal surgical intervention complexity score assessments among discrepant cases, and discrepancy in relation to postnatal score is shown in Figure 4A and 4B. There were 81 cases with no discrepancy, 36 cases with higher prenatal scores and 19 cases with lower prenatal scores compared with the postnatal scores. In total, 40.4% (55/136) of the scores were

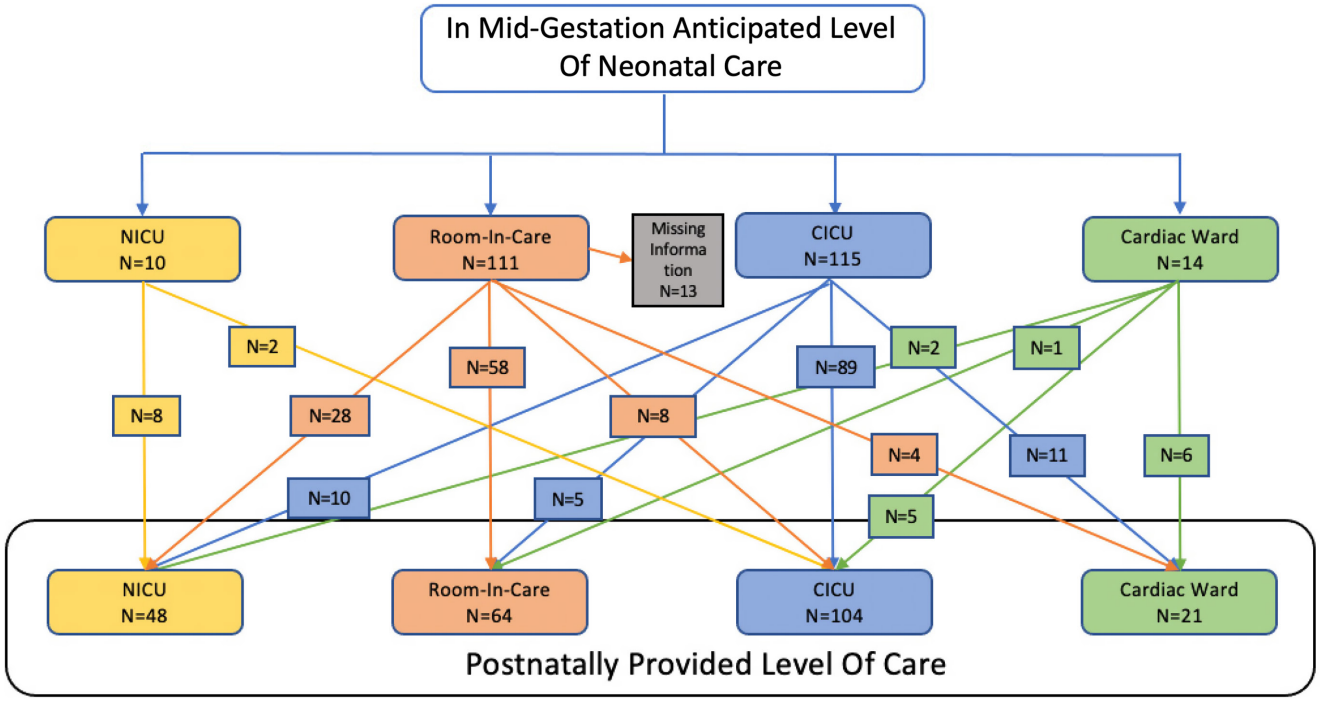

FIGURE 1 Anticipated level of neonatal care recommended by the fetal cardiologist in relation to postnatally provided level of care. CICU, cardiac intensive care unit; NICU, neonatal intensive care unit.

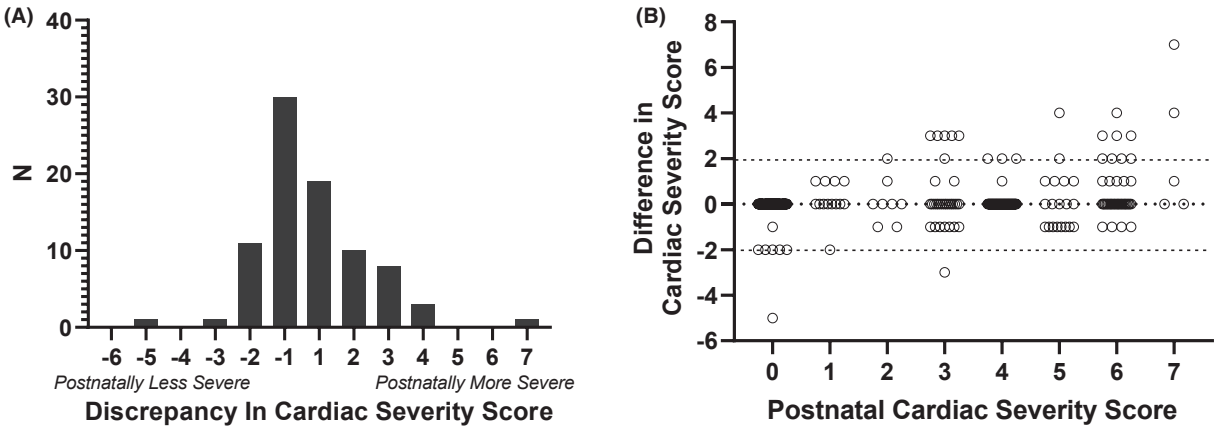

FIGURE 2 Distribution of discrepancies between postnatal and prenatal cardiac severity score assessments among discrepant cases (A), and discrepancy in relation to postnatal score (B).

discrepant. The mean difference between postnatal and prenatal surgical complexity scores was −0.31 ± 2.39.

The mean cardiac severity score discrepancy for good imaging quality was 0.05 ± 1.10 (n = 210), poor image quality 0.15 ± 1.11 (n = 34) and very poor image quality 1.83 ± 1.72 (n = 6). The positive association between image quality and discrepancy was statistically significant (R^2 = 0.058; P = 0.0011; n = 250; Figure S1). Postnatal cardiac severity score correlated significantly with surgical complexity score (r = 0.44; P < 0.001; n = 134).

Information on prenatal recommendations on anticipated level of neonatal care was available in 237 case charts. The anticipated level of neonatal care was actualized in 146/237 (61.6%) of cases (Figure 1). Of 125 planned intensive care (cardiac and neonatal ICU combined) in mid-gestation, 16 were later in gestation or were downgraded at birth to cardiac ward or room-in-care levels. Of the 138 cases with no anticipated need of intensive care, 43 cases were later upgraded to cardiac or neonatal ICU care levels. Of the 91 postnatally provided PGE infusions, eight were not prenatally planned and five were anticipated prenatally but not provided based on the early not anticipated postnatal CHD assessment (Table S2). Among the PGE infusions not anticipated prenatally, four cases were associated with obstructed pulmonary outflows. Among the prenatally anticipated but postnatally not administered PGE infusions, two cases were associated with pulmonary outflow, two to systemic outflow and one to cardiomyopathy.

4 | DISCUSSION

This retrospective review of pregnant women referred to a fetal cardiac assessment outlines challenges in prenatal CHD assessment and counseling performed in mid-gestation in a tertiary care setting. Overall, we found that fetal cardiac assessments are in general accurate, specific and reliable (specificity 92.6%, no discrepancy in 167 of 257 cases). However, a significant discrepancy in fetal CHD diagnosis compared with the postnatal evaluation was still found in one of eight cases, with a major change in diagnostic severity and postnatal management. Of these, the cardiac condition was considered more severe postnatally in two of three cases than anticipated during the mid-gestation fetal assessment. Among cases with more severe CHD postnatally, a significant proportion was explained by natural CHD severity progression that was not disclosed in the initial mid-gestation fetal counseling process. The prenatally anticipated neonatal care levels were actualized in two of three cases, and the need for PGE infusion correctly anticipated in most cases. The study highlights areas of uncertainty in fetal CHD assessment that may be important to consider in planning of care and counseling during mid-gestation.

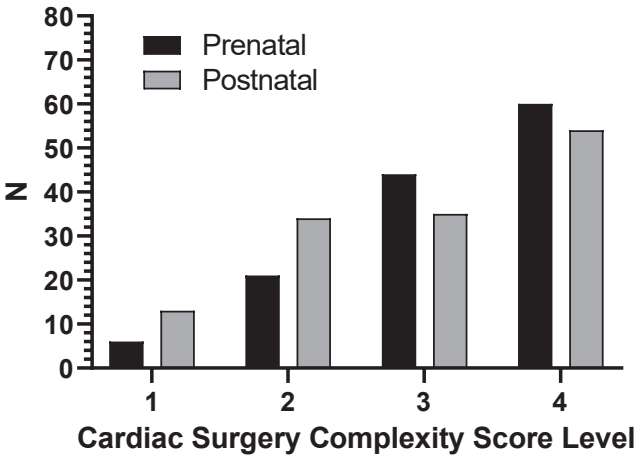

FIGURE 3 Distribution of cardiac surgery complexity score levels for prenatal and postnatal assessments.

The accuracy of fetal CHD assessments and parental counseling regarding CHD severity, perinatal and early postnatal care at our fetal cardiac clinic seems comparable to previous contemporary studies.[3,8] On a normal vs abnormal fetal cardiac assessment level, most false-positive (mostly VSDs and CoA suspicions) and false-negative assessments (mostly VSDs) were only mildly discrepant, with limited impact on postnatal CHD management or outcomes. However, among cases with cardiac abnormalities detected, 12% showed a significant change or refinement in postnatal CDH severity. Changes were found within diagnostic groups including borderline ventricles, isolated VSDs, aortic arch anomalies including hypoplastic arch and coarctations, as well as among cases with tricuspid valve dysplasia or Ebstein's anomaly with evolving severe tricuspid valve regurgitation over time. Among these, borderline ventricles are, per definition, challenging to assess and counsel, as there is a lack of solid predictors for postnatal one or two ventricle treatment tracks.[12] The detection of VSDs is challenged by VSD size, location and fetal hemodynamics,[7] although in our study, most of the significant isolated VSDs not detected were small to moderate. Small VSDs typically do not need surgery, and isolated VSDs usually have no impact on care during the neonatal phase, low operative mortality, and good long-term prognosis when treated in a timely manner. Aortic arch hypoplasia and local coarctations are notably difficult to diagnose accurately, prenatally due to changes in aortic arch structure and hemodynamics during early postnatal adaptation.[13] Disclosure of known limitations of fetal echocardiography including the possibility of not detecting small to moderate VSDs and isolated CoAs should be standard procedure in the fetal counseling process. Postnatally documented significant tricuspid valve dysplasia and Ebstein's anomaly-related tricuspid regurgitation may be overlooked during mid-gestation as these typically progress later in gestation with a significant negative impact on fetal and neonatal outcomes.[14]

Overall, our fetal CHD diagnostic accuracy is similar to contemporary data reported in France,[8] USA,[3,7] Netherlands,[6] Japan,[15] and China,[16] although minor differences may exist associated with sample case severity distribution, case exclusion criteria and definition

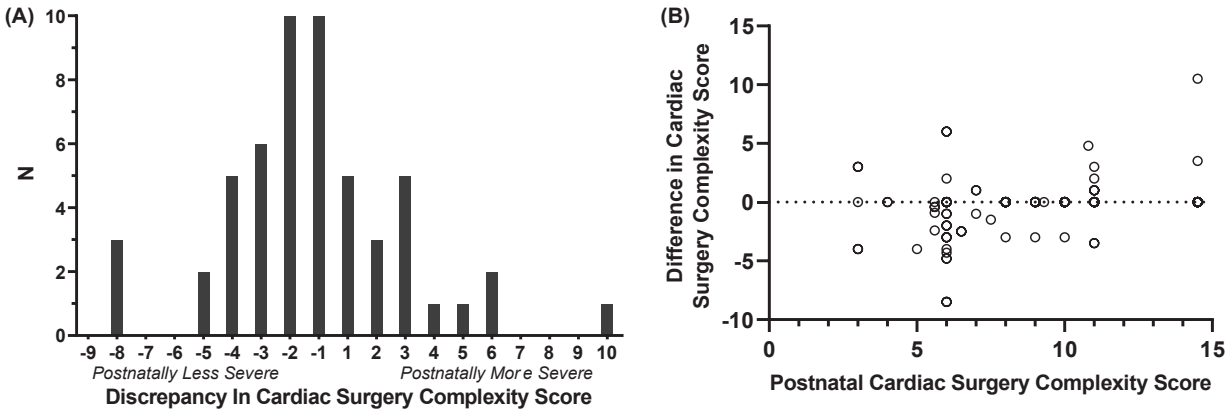

FIGURE 4 Distribution of discrepancies between postnatal and prenatal surgical intervention complexity score assessments among discrepant cases (A), and discrepancy in relation to postnatal score (B).

of discrepancy applied in the different studies. Kurosaki et al. reported a discrepancy rate of 12% but did not include cases with fetal cardiologist evaluation prenatally.[15] Qiu et al. reported discrepancies in 23.8% of diagnoses when assigned to four groups based on simple or complex CHD with or without extracardiac malformations.[16] Van Velzen et al. reported discrepancies in 17.9% cases but did not include VSD or smaller defects.[6] Bensemlali et al. used similar scoring to scoring in the present study and reported discrepancies of any kind in 29.2% and a significant change in neonatal management in 10.6% of cases.[8] Mozumdar et al. reported discrepancies in 13.5% of all diagnoses.[7] Our diagnostic accuracy of 97% was as previously reported.[15] In common with previous studies, high anatomical complexity and valvular disease was associated with discrepancies, but CHDs with less complex anatomy (eg VSDs and CoAs) were difficult to rule out antenatally. The comparison of our fetal cardiology performance of CHD diagnostics and early care anticipation assessment with that in other centers is challenged by differences in samples, metrics and the definitions applied.

Upgrading to intensive care was relatively common (36/111; cardiac ICU 8 and neonatal ICU 28) and mostly ($n = 22$) associated with early neonatal respiratory postnatal adaptation. Other reasons for upgrading included premature birth and some cases were upgraded due to suspicion of extracardiac problems. A few cases were upgraded due to progression in fetal CHD severity later in gestation (eg evolving TV regurgitation). PGE infusion recommendations provided in mid-gestation were actualized in most cases.

The anticipated timing and surgical complexity of intervention for CHD was largely determined by CHD diagnostic severity in our sample including a relatively high proportion of higher surgical complexity score levels. This is due to the higher detection and referral of more complex fetal CHD in the study sample. The highest discrepancies in the surgical complexity scores were found among cases with borderline ventricles, as expected. Complex CHDs may also include cases with valvular problems that progress later in gestation or during the neonatal period (eg pulmonary outflow obstruction and TV regurgitation), with a significant change in the timing and complexity of the surgical procedure needed compared with that anticipated in mid-gestation.

Our relatively small sample size but high proportion of abnormalities among cases reflects screening and referral practice in our institution and is explained by refinement of fetal assessments and diagnoses by perinatologists impacting final referral indications. The nationally centralized sample as well as the comprehensive and combined accuracy evaluation of both antenatal CHD diagnosis and anticipated perinatal and detailed early postnatal care needs are considered significant strengths as previous studies accounting for these aspects are rare.[3,5] The unselected sample was representative of case evaluations performed at our fetal cardiac assessment unit during the 2010–2020 study period. A significant proportion (74%) of excluded cases represented normal fetal assessments (27%) and mild abnormalities (10%) without follow-up in our center, as well as isolated fetal arrythmias (37%). The proportion of major CHDs excluded from analyses represented only 11.5% of the total sample and included miscarriages and terminations of pregnancy without postmortem verification available. Terminations were performed for severe CHDs only and we were unable to detect discrepancies with a significant impact on counseling and outcomes among available autopsy reports. Cases lost to follow-up and a relatively low fetal autopsy rate may, nevertheless, have impacted the present results. There were no early deaths associated with CHD or surgical interventions performed within 3 months from birth among excluded cases. We may, nevertheless, have missed non-critical CHD cases typically diagnosed later in life, such as cases with ASD, partial anomalous pulmonary venous drainage, isolated aortic coarctation, cardiomyopathy, connective tissue disorder or leaking bicuspid aortic valve. We also acknowledge that although our purpose was to elaborate factors associated with discrepancies in the fetal evaluation, we were only able to assess this in terms of the imaging quality documented in the charts in addition to the diagnostic groups highlighted above.

5 | CONCLUSION

We present the performance of our fetal cardiac outpatient clinic CHD diagnostic and anticipated perinatal and early neonatal care planning during mid-gestation that is comparable to contemporary international data. Although fetal CHD diagnosis and counseling is accurate and reliable in general, this study elaborates specific areas of uncertainty and pitfalls that may be important to consider in the fetal CHD evaluation and counseling process provided in mid-gestation.

AUTHOR CONTRIBUTIONS

This retrospective study was initially conceived and designed by TS. All authors participated in the study protocol, MN collected all the data and made analyses under the supervision of TS. MN wrote the first draft and all authors participated in the writing of the manuscript and approved the final version.

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

DATA AVAILABILITY STATEMENT

Data were gathered from patient charts and thus are not openly available. Data that support the findings in this article are available upon a reasonable request from the corresponding author (TS).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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