

# Comparison of clinical prognosis between prenatal and postnatal diagnosis of fetuses with complex congenital heart disease

Shuyan Wu<sup>1</sup>, Le Chen<sup>1</sup>, Jianhui He<sup>1</sup>, Fengzhen Han<sup>1</sup>, Yanping Jiang<sup>1,\*</sup>

<sup>1</sup>Department of Obstetrics, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, 510080 Guangzhou, Guangdong, China

\*Correspondence: [yp34467@tom.com](mailto:yp34467@tom.com) (Yanping Jiang)

DOI: [10.31083/j.ceog4806215](https://doi.org/10.31083/j.ceog4806215)

This is an open access article under the CC BY 4.0 license (<https://creativecommons.org/licenses/by/4.0/>).

Submitted: 23 February 2021 Revised: 11 May 2021 Accepted: 7 June 2021 Published: 15 December 2021

**Background:** The purpose of this study was to explore the clinical value and prognosis of the "prenatal diagnosis-postnatal treatment" model for fetuses with complex congenital heart disease (CHD) by directly comparing the outcomes between prenatal and postnatal diagnosis. **Methods:** A total of 126 infants with complex CHD diagnosed by prenatal diagnosis and 160 infants with complex CHD diagnosed by postnatal diagnosis in Guangdong Provincial People's Hospital from January 2012 to December 2017 were enrolled in this retrospective study. The gestational age, birth weight, delivery mode, postpartum termination rate, qualified rate of follow-up assessment of pediatric heart surgery, postoperative complications, postoperative death, time of ventilator weaning, the length of postoperative hospital stay and prognosis were compared between the two groups. **Results:** There were no significant differences in delivery mode, premature birth rate, gestational age, birth weight, and mean maternal age between the two groups ( $p > 0.05$ ). However, frequencies of terminating treatment after birth and postoperative complications were significantly higher in postnatal diagnosis group compared with prenatal diagnosis group ( $p < 0.05$ ), while qualified rate of follow-up assessment of pediatric cardiac surgery was significantly lower in postnatal diagnosis group in comparison with prenatal diagnosis group ( $p < 0.05$ ). Moreover, postoperative complication rate was significantly higher in the postnatal diagnosis group than prenatal diagnosis group ( $p < 0.05$ ). **Conclusion:** Prenatal diagnosis can reduce postoperative complications after cardiac surgery and improve clinical prognosis for fetuses with complex CHD.

## Keywords

Fetus; Complex congenital heart disease; Prenatal diagnosis; Clinical prognosis

## 1. Introduction

Congenital heart disease (CHD) is the most frequent congenital disorder in newborns, and it is also the most common type of structural malformation of heart and large blood vessels [1]. Complex CHD refers to tetralogy of Fallot, pulmonary atresia, double outlet right ventricle, transposition of great arteries, left ventricular dysplasia, right ventricular dysplasia, complete anomalous pulmonary venous drainage, complete endocardial cushion defect, interrupted aortic arch and other complex cardiovascular malformations. There was an estimated incidence of 0.6% to 0.8% in China each year

[2]. According to the National Center for Birth Defects Monitoring in China, the incidence of CHD has a steep rise from the fifth to the most common birth defect from 2005 to 2009 [3, 4]. The phenotype of CHD is usually related to other cardiac and/or extracardiac malformations and genetic syndromes [5]. Patients with congenital heart disease require surgical intervention, intensive medical management, and multidisciplinary follow-up [6]. In addition, serious CHD is one of the main causes of the death or disability of the newborn and children, which seriously affects the quality of the born population and brings heavy mental and economic burden to the family and society.

With the wide application of prenatal diagnosis, such as echocardiography, many fetal complex CHD can be diagnosed earlier and more accurately. According to the results of echocardiography, doctors can make a prediction and evaluation of the outcome and prognosis of these fetuses with complex CHD, and provide professional guidance for pregnant women and their families [7]. Furthermore, it has been reported that the postnatally diagnosed neonates with CHD were much more likely to present with cardiovascular compromise and multi-organ dysfunction [8].

In response, a CHD network has been established in our institution based on the integrated "prenatal diagnosis-postnatal treatment" model. Therefore, in the present study, we aimed to explore the clinical value and prognosis of the "prenatal diagnosis-postnatal treatment" model for fetuses with CHD by directly comparing the outcomes between prenatal and postnatal diagnosis.

## 2. Subjects and methods

### 2.1 Study subjects and grouping

A total of 126 infants with complex CHD diagnosed by prenatal diagnosis (prenatal diagnosis group) and 160 infants with complex CHD diagnosed by postnatal diagnosis (postnatal diagnosis group) in Guangdong Provincial People's Hospital from January 2012 to December 2017 were enrolled in this retrospective study. All infants in the prenatal diagnosis group were delivered at our hospital and their mothers

had received prenatal diagnosis and decided to protect the fetus after prenatal consultation. After delivery, the infants were transferred to the neonatal intensive care unit (NICU) for further diagnosis and treatment. Infants in the postnatal diagnosis group were tentatively diagnosed after delivery at local hospitals and transferred to the NICU of our hospital within 72 h. This retrospective study was approved by the ethics committee of Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences. All subjects or their families provided informed written consent.

### 2.2 Data collection

Some infants in the two groups were received cardiac surgery if they were advised to undergo surgical treatment because of the severe life-threatening congenital heart disease. The clinical data of infants and their mothers, including general characteristics, medical records of surgical operation, postoperative complications and follow-up (6 months) were collected.

### 2.3 Evaluation indexes

The gestational age, birth weight, delivery mode, postpartum termination rate, qualified rate of follow-up assessment of pediatric heart surgery, postoperative complications, postoperative death, time of ventilator weaning, the length of postoperative hospital stay and prognosis were compared between the two groups.

### 2.4 Statistical analysis

All data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 23.0 (IBM; Chicago, IL, USA). Univariate descriptive statistics are expressed as means  $\pm$  standard deviation (SD). The differences between the two groups of continuous variables were evaluated by Student *t* test, and the differences between the two groups of classified variables were evaluated by Pearson's  $\chi^2$  test or Fisher's exact test.  $p < 0.05$  (two-tailed) was considered statistically significant.

## 3. Results

### 3.1 Comparison of delivery mode and CHD type between the two groups

A total of 182 pregnancies with CHD fetus occurred in our hospital. However, there were only 126 live births and they were considered as the prenatal diagnosis group. Moreover, 160 infants which were transferred from local hospitals to our hospital constituted the postnatal diagnosis group. The delivery modes and CHD types in the two groups were shown in Table 1. Complex CHD types in fetuses included single ventricle, complex single ventricle, hypoplastic left heart syndrome (HLHS), dextro-transposition of the great arteries (D-TGA), tetralogy of Fallot (TOF), isolated arch anomaly, arch anomaly with additional anomaly, interrupted aortic arch, total anomalous pulmonary venous return (TAPVR), pulmonary valve stenosis, double-outlet right ventricle and tricuspid valve dysplasia. After prenatal consultation at our institution, 56 mothers chose induced labor to the termi-

nation of pregnancy in the 4–5 months of pregnancy, and the types of CHD included nine single ventricle, eight complex single ventricle, one HLHS, five D-TGA, twelve TOF, one arch anomaly with additional anomaly, one interrupted aortic arch, eleven pulmonary valve stenosis, seven double-outlet right ventricle, and one double-outlet right ventricle with malposed great vessels case. The remaining 126 women determined to plan the birth in our hospital. After birth, the infants were transferred to the NICU for subsequent treatment. In the postnatal diagnosis group, 160 infants were delivered at local hospitals, tentatively diagnosed with complex CHD, and transferred to our NICU within 72 h after birth. The number of infants who had D-TGA was notably decreased in prenatal diagnosis group than those in postnatal diagnosis group ( $p < 0.01$ ), while the number of infants who had TOF was markedly increased in prenatal diagnosis group than that in postnatal diagnosis group ( $p < 0.01$ ). The other types of CHD between the two groups were not significantly different ( $p > 0.01$ ). Moreover, the number of abortions in the prenatal diagnosis group was 56 (30.76%).

### 3.2 Comparison of pregnancy outcomes and clinical prognosis between the two groups

There were no significant differences in delivery mode, premature birth rate, gestational age, birth weight, gestational age, death rate after birth and the numbers of infants scheduled for cardiac surgery during and after the neonatal period between the two groups ( $p > 0.05$ ). However, the number of cases in which treatment was terminated by mothers after birth was significantly higher and the number of infants eligible for follow-up was significantly lower in postnatal diagnosis group in comparison with those in prenatal diagnosis group, respectively ( $p < 0.05$ ) (Tables 2,3).

### 3.3 Comparison of clinical prognosis after cardiac surgery between the two groups

There were 73 infants in the prenatal diagnosis group and 84 in the postnatal group who needed to receive urgent postnatal surgery. The postoperative death rate, postoperative survival rate, postoperative time of ventilator weaning, and length of postoperative hospital stay did not differ significantly between the two groups ( $p > 0.05$ ), whereas postoperative complication rate was significantly higher in the postnatal diagnosis group than prenatal diagnosis group ( $p < 0.05$ ) (Table 4). Postoperative complications included pulmonary infection, septicemia, poor healing, infection of the surgical incision, necrotizing enteritis, pericardial tamponade, and pneumothorax.

## 4. Discussion

As the most common birth defect in China, complex CHD is a major public health concern. It severely affects physical health, mental health, and quality of life of infants. It is also a major complication for family planning in China. Pregnancies in which the fetuses present a CHD have higher rates of preclampsia, small for gestational age (SGA) and preterm birth [9]. Early diagnosis and treatment can reduce the mor-

**Table 1. The types of CHD between the two groups [n (%)].**

CHD types	Prenatal diagnosis (n = 182)	Postnatal diagnosis (n = 160)	OR (95% CI)	p value
Single ventricle (all)	21 (11.54)	20 (12.50)	1.10 (0.57–2.10)	0.79
Complex single ventricle	11 (6.04)	19 (11.88)	2.10 (0.27–1.20)	0.06
HLHS	2 (1.10)	0 (0.00)	0.99 (0.97–1.01)	0.50
D-TGA (all)	41 (22.53)	60 (37.50)	2.06 (1.29–3.31)	<0.01
D-TGA (intact ventricular septum)	19 (10.44)	43 (26.88)	3.15 (1.75–5.69)	<0.01
D-TGA (ventricular septal defect)	22 (12.09)	17 (10.63)	0.87 (0.44–1.69)	0.67
TOF	32 (17.58)	8 (5.00)	0.25 (0.11–0.55)	<0.01
Isolated arch anomaly	4 (2.20)	2 (1.25)	0.56 (0.10–3.12)	0.69
Arch anomaly with additional anomaly	14 (7.69)	6 (3.75)	0.47 (0.18–1.25)	0.12
Interrupted aortic arch	6 (3.30)	5 (3.13)	0.95 (0.28–3.16)	0.93
TAPVR	7 (3.85)	12 (7.50)	2.03 (0.78–5.28)	0.14
Pulmonary valve stenosis	35 (19.23)	39 (24.38)	1.35 (0.81–2.27)	0.25
Double-outlet right ventricle	13 (7.14)	4 (2.50)	0.33 (0.11–1.04)	0.08
Double-outlet right ventricle with malposed great vessels	4 (2.20)	1 (0.63)	0.28 (0.3–2.53)	0.38
Tricuspid valve dysplasia	3 (1.65)	3 (1.88)	1.14 (0.23–5.73)	0.87
The number of abortions	56 (30.76)	0 (0.00)	0.19 (0.13–0.34)	<0.01

OR, odds ratio; CI, confidence interval; HLHS, hypoplastic left heart syndrome; D-TGA, dextro-transposition of the great arteries; TOF, tetralogy of Fallot; TAPVR, total anomalous pulmonary venous return.

**Table 2. Patient characteristics and demographics.**

Items	Prenatal diagnosis (n = 126)	Postnatal diagnosis (n = 160)	OR (95% CI)	p value
Male sex [n (%)]	80 (63.49)	119 (74.38)	1.67 (1.01–2.77)	0.03
Mode of delivery: cesarean section [n (%)]	50 (39.68)	57 (35.63)	1.19 (0.734–1.93)	0.48
Preterm birth (GA <37 wk) [n(%)]	14 (11.11)	18 (11.25)	1.01 (0.48–2.13)	0.97
GA at birth (week)	37.99 ± 2.03	38.46 ± 1.70		0.97
Birth weight (g)	28829.76 ± 502.21	3033.78 ± 535.61		0.41
Mean maternal age (years)	29.87 ± 4.72	30.04 ± 4.51		0.54

GA, gestational age.

idity and mortality rates of CHD in fetuses. In developed countries, the diagnostic rate of fetal CHD is as high as 90% and the cure rate with early intervention has reached 80% [2, 10]. In the past 8 years, a CHD network has been established in our hospital according to the integrated “prenatal diagnosis-postnatal treatment” model. Pregnancy termination should be considered for severe and untreatable cardiac defects to reduce the birth rate and postnatal death rate of infants with complex CHD. Almost half of infants with complex CHD can be diagnosed within 28 weeks of pregnancy. For certain complex CHD cases, the decision to induce labor or perform scheduled cardiac surgery is determined after comprehensive consultation between the mother and her physicians [11]. For CHD infants scheduled to receive treatment, the delivery mode can be chosen according to the physician’s advice, and vaginal delivery is usually the safest option [12].

In this study, 56 pregnant women whose fetuses was diagnosed as CHD by prenatal diagnosis chose induced labor to the termination of pregnancy in the 4–5 months of pregnancy, which eliminated the births of fetuses with severe life-threatening CHD, while postnatal diagnosis failed to avert the birth of infants with severe or untreatable complex CHD. However, early screening and treatment of CHD cannot be performed in many Chinese hospitals, especially

primary hospitals. Thus, effective approaches for early prevention and treatment are urgently required.

In China, prenatal screening of fetal CHD mainly depends on fetal echocardiography. In recent years, new technologies, including three-dimensional and four-dimensional echocardiography, magnetic resonance imaging, and fetal magnetocardiography, have been adopted to improve the prenatal diagnosis rate [13]. In primary Chinese hospitals, many infants with complex CHD die soon after birth due to lack of expertise and medical technologies, and the surviving CHD infants must be referred to major centers for subsequent treatment. However, an array of issues may disrupt the efficient referral, including unclear referral pathways, lack of a referral network between large and primary hospitals, insufficient staff, and poor transportation equipment. Lack of accesses of diagnostic and therapeutic technologies for complex CHD leads many physicians in primary hospitals to abandon therapy for treatable CHD. In the present study, the diagnosis was not confirmed in the postnatal diagnosis group before admission to our institution. After diagnosis of complex CHD was validated, subsequent treatment was abandoned in 45 cases. While in the prenatal diagnosis group, treatment was terminated in only 10 of 126 (7.94%) cases. In addition, the number of infants eligible for follow-up was significantly higher in the

**Table 3. Postnatal outcome in the two groups [n (%)].**

Items	Prenatal diagnosis (n = 126)	Postnatal diagnosis (n = 160)	OR (95% CI)	p value
Death after birth	4 (3.17)	4 (2.50)	0.78 (0.19–3.19)	0.74
Give up treatment	10 (7.94)	45 (28.13)	4.54 (2.18–9.44)	<0.01
Surgical treatment in neonatal period	73 (57.94)	84 (52.50)	0.80 (0.50–1.29)	0.36
Percutaneous therapy	1 (0.79)	1 (0.63)	0.79 (0.05–12.69)	0.69
Surgical treatment after neonatal period	9 (7.14)	10 (6.25)	0.87 (0.34–2.20)	0.76
Follow up	29 (23.02)	16 (10.00)	0.37 (0.19–0.72)	<0.01

**Table 4. Postoperative outcomes in the two groups.**

Items	Prenatal diagnosis (n = 73)	Postnatal diagnosis (n = 84)	OR (95% CI)	p value
Survival, all patients [n (%)]	62 (84.93)	77 (91.67)	1.96 (0.71–5.33)	0.19
Surgical complications [n (%)]	44 (60.27)	68 (80.95)	2.28 (1.37–5.75)	<0.01
Postoperative mortality [n (%)]	11 (15.07)	7 (8.33)	1.96 (0.71–5.33)	0.19
Median length of hospital stay (day)	29.28 ± 14.82	26.18 ± 11.83		0.12
Time of ventilator weaning (h)	5.73 ± 4.07	4.88 ± 3.91		0.24

prenatal diagnosis group than that in the postnatal diagnosis group ( $p < 0.05$ ), suggesting that accurate prenatal diagnosis and timely pregnancy termination can mitigate the harm to the mother and family and enhance the clinical prognosis of delivered infants.

Infants with CHD must be closely monitored during the neonatal period. Therefore, these infants should be delivered in the monitoring center of a tertiary hospital if possible to reduce the incidence of complications and ventilator time, and lower the risks conferred by antibiotics use and emergency surgery [14]. In this study, prenatal diagnosis of CHD was not associated with reduced preoperative or pre-discharge mortality, which was consistent with a previous finding [15]. Furthermore, the time to ventilator weaning after cardiac surgery and the length of postoperative hospital stay did not differ between the two groups. However, the number of infants with postoperative complications was significantly higher in the postnatal diagnosis group, which confirmed the certain safety advantages of “prenatal diagnosis-postnatal treatment”. The apparent discrepancy between actual complication rate and other complication indices may be due to the limited sample size and warrants further investigation. The outcome of fetuses with CHD shows and increase rate of SGA, particularly with small head circumference [16].

The results of this study are consistent with the previous findings that prenatal diagnosis of left ventricular dysplasia syndrome can significantly improve right ventricular function after birth and reduce the risk of metabolic acidosis and terminal organ dysfunction [17]. Prenatal counseling involves providing an accurate diagnosis of CHD, clearly explaining complex medical information to parents in crisis, including management options and outcomes, preparing parents for the delivery and disease course after birth, which supports them through the process of decision-making and throughout the pregnancy. Improved prenatal detection of CHD is needed in order to provide parents important oppor-

tunity for counseling and education to optimize outcomes in infants with CHD [18]. For newborns who were likely to benefit from treatment for critical CHD, such as the absence of additional risk factors and/or the family who was committed to treatment, prenatal diagnosis reduced the risk of death prior to planned cardiac surgery in comparison with infants with a comparable postnatal diagnosis [19]. Due to lack of prenatal diagnosis, some newborns with untreatable CHD are inevitably delivered, while others may not receive proper treatment during the neonatal period, especially if delivered at local hospitals. Therefore, the integrated model of “prenatal diagnosis-postnatal treatment” is highly recommended and deserves widespread application. In addition, the establishment of a monitoring network for complex CHD, including a standardized prenatal screening and diagnostic system, are key to improving coverage rate and postnatal outcomes.

## 5. Conclusions

In conclusion, integrated “prenatal diagnosis-postnatal treatment” model can confirm prenatal diagnosis, reduce complications after cardiac surgery, improve clinical prognosis, and decrease the birth rate of infants with untreatable complex CHD, thereby alleviating economic and emotional burdens on families.

## Author contributions

SW and YJ contributed to the collection of data and writing the manuscript. LC, JH and FH contributed to analysis of the data and writing the manuscript. All authors approved the final version of the manuscript.

## Ethics approval and consent to participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the research was approved by the Guangdong Provincial People’s Hospital Ethics Committee (No. GDREC2019657H).

## Acknowledgment

Not applicable.

## Funding

This study was supported by Guangzhou Science and Technology plan Major Project of Collaborative Innovation (NO. 201604020008) and Medical Science and Technology Research Fund Project of Guangdong Province (NO. A2020623).

## Conflict of interest

The authors declare no conflict of interest.

## References

- [1] van der Bom T, Zomer AC, Zwinderman AH, Meijboom FJ, Bouma BJ, Mulder BJM. The changing epidemiology of congenital heart disease. *Nature Reviews. Cardiology*. 2011; 8: 50–60.
- [2] Tegnander E, Williams W, Johansen OJ, Blaas H-K, Eik-Nes SH. Prenatal detection of heart defects in a non-selected population of 30 149 fetuses-detection rates and outcome. *Ultrasound in Obstetrics & Gynecology*. 2006; 27: 252–265.
- [3] Pradat P, Francannet C, Harris JA, Robert E. The epidemiology of cardiovascular defects. Part I: A study based on data from three large registries of congenital malformations. *Pediatric Cardiology*. 2003; 24: 195–221.
- [4] Hoffman JIE, Kaplan S. The incidence of congenital heart disease. *Journal of the American College of Cardiology*. 2002; 39: 1890–1900.
- [5] Gilboa SM, Devine OJ, Kucik JE, Oster ME, Riehle-Colarusso T, Nembhard WN, *et al*. Congenital Heart Defects in the United States: Estimating the Magnitude of the Affected Population in 2010. *Circulation*. 2016; 134: 101–109.
- [6] Xia Y, Yang Y, Huang S, Wu Y, Li P, Zhuang J. Clinical application of chromosomal microarray analysis for the prenatal diagnosis of chromosomal abnormalities and copy number variations in fetuses with congenital heart disease. *Prenatal Diagnosis*. 2018; 38: 406–413.
- [7] Krishna MR, Kumar RK. Diagnosis and Management of Critical Congenital Heart Diseases in the Newborn. *The Indian Journal of Pediatrics*. 2020; 87: 365–371.
- [8] Brown KL, Ridout DA, Hoskote A, Verhulst L, Ricci M, Bull C. Delayed diagnosis of congenital heart disease worsens preoperative condition and outcome of surgery in neonates. *Heart*. 2006; 92: 1298–1302.
- [9] Giorgione V, Fesslova V, Boveri S, Candiani M, Khalil A, Cavoretto P. Adverse perinatal outcome and placental abnormalities in pregnancies with major fetal congenital heart defects: a retrospective case-control study. *Prenatal Diagnosis*. 2020; 40: 1390–1397.
- [10] Allan L. Antenatal diagnosis of heart disease. *Heart*. 2000; 83: 367–370.
- [11] Han FZ, Jiang YP, Zhou CB, Pan W, Zhuang J. Perinatal outcome and prognosis analysis of the 151 fetal congenital heart diseases. *Journal of Practical Obstetrics and Gynecology*. 2012; 28: 760–764.
- [12] Walsh CA, MacTiernan A, Farrell S, Mulcahy C, McMahon CJ, Franklin O, *et al*. Mode of delivery in pregnancies complicated by major fetal congenital heart disease: a retrospective cohort study. *Journal of Perinatology*. 2014; 34: 901–905.
- [13] Donofrio MT, Moon-Grady AJ, Hornberger LK, Copel JA, Sklansky MS, Abuhamad A, *et al*. Diagnosis and treatment of fetal cardiac disease: a scientific statement from the American Heart Association. *Circulation*. 2014; 129: 2183–2242.
- [14] Levey A, Glickstein JS, Kleinman CS, Levasseur SM, Chen J, Gersony WM, *et al*. The impact of prenatal diagnosis of complex congenital heart disease on neonatal outcomes. *Pediatric Cardiology*. 2010; 31: 587–597.
- [15] Landis BJ, Levey A, Levasseur SM, Glickstein JS, Kleinman CS, Simpson LL, *et al*. Prenatal diagnosis of congenital heart disease and birth outcomes. *Pediatric Cardiology*. 2013; 34: 597–605.
- [16] Inversetti A, Fesslova V, Deprest J, Candiani M, Giorgione V, Cavoretto P. Prenatal Growth in Fetuses with Isolated Cyanotic and Non-Cyanotic Congenital Heart Defects. *Fetal Diagnosis and Therapy*. 2020; 47: 411–419.
- [17] Markkanen HK, Pihkala JI, Salminen JT, Saarinen MM, Hornberger LK, Ojala TH. Prenatal diagnosis improves the postnatal cardiac function in a population-based cohort of infants with hypoplastic left heart syndrome. *Journal of the American Society of Echocardiography*. 2013; 26: 1073–1079.
- [18] Lee CK. Prenatal Counseling of Fetal Congenital Heart Disease. *Current Treatment Options in Cardiovascular Medicine*. 2019; 19: 5.
- [19] Holland BJ, Myers JA, Woods CR. Prenatal diagnosis of critical congenital heart disease reduces risk of death from cardiovascular compromise prior to planned neonatal cardiac surgery: a meta-analysis. *Ultrasound in Obstetrics & Gynecology*. 2015; 45: 631–638.