Delayed diagnosis of critical congenital heart defects predicting risk factors and survival rate in newborns in Beijing: a retrospective study

Wen Zhang, Hong-Yan Xu, Yan-Chun Zhang and Kai-Bo Liu 🔾

Abstract

Objective: To assess the prevalence and survival rate of newborns with a delayed diagnosis of critical congenital heart defects (CCHD) in Beijing.

Methods: This retrospective study analysed data from births between 2010 and 2017 from the Birth Defects Monitoring Network in Beijing. Newborns with CCHD were analysed according to seven categories. Statistical analyses were used to calculate the mortality rate within the first week (days 0–6) after live birth. Multivariate logistic regression analysis of survival was performed to analyse the potential risk factors for newborn mortality.

Results: A total of 1 773 935 perinatal newborns were screened in Beijing and 1851 newborns were diagnosed with CCHD, showing a prevalence of 10.43 per 10 000. Among the total 1851 CCHD patients, the majority (1692 of 1851; 91.41%) were identified through prenatal diagnosis, 104 of 1851 (5.62%) were diagnosed before obstetric discharge/transfer and 55 of 1851 (2.97%) were identified through delayed diagnosis. The prevalence of CCHD in newborns was 1.96 per 10 000 births. Multivariate logistic regression analysis of survival demonstrated that gestational age at delivery was the only risk factor for death within the first week after birth.

Conclusions: Within the first week after birth, gestational age was the only risk factor for death in newborns with CCHD.

Keywords

Critical congenital heart defects, delayed diagnosis, neonatal mortality

Beijing Obstetrics and Gynaecology Hospital, Capital
Medical University, Beijing, China

Corresponding author:
Kai-Bo Liu, Beijing Obstetrics and Gynaecology Hospital,
Capital Medical University, 251 Yaojiayuan Road,
Chaoyang District, Beijing 100026, China.
Email: kaibo1021@163.com

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative
Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits
non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed
as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).

Introduction

Critical congenital heart defects (CCHD), one type of the birth defect, are major causes of neonatal death.[1] In this current study, CCHD were defined as structural malformations of the heart that were present at birth and required intervention in the first year of life, which included the seven categories of CCHD that were considered by the Secretary of Health and Human Service's Advisory Committee on Heritable Disorders in Newborns and Children.[2] These seven categories of CCHD are as follows: (i) tetralogy of Fallot; (ii) complete transposition of the great arteries; (iii) persistent truncus arteriosus; (iv) left ventricular dysplasia; (v) pulmonary atresia; (vi) tricuspid atresia; and (vii) total anomalous pulmonary venous return.[2] Thirty percent of new-borns suffering from CCHD die within 1 month after birth without treatment.[3] The timely treatment of CCHD in newborns requires the precise diagnosis either during the prenatal process or after birth. Some newborns with CCHD will have obvious clinical signs in the nursery, but since a subset of affected infants depend on circulation through the ductus arteriosus, physical examination might not detect cyanosis or other clinical signs before transitions from fetal circulation are completed, closure of the ductus after discharge can be catastrophic and responsible for unexpected deaths.[4]

Diagnosis of CCHD after birth is called delayed diagnosis, which is regarded as one of the risk factors for newborn death.[5] Understanding the correlation between a CCHD diagnosis at different stages and newborn mortality is critical in order to guide staged CCHD screening, with the aim of increasing the survival rate of newborns suffering from CCHD. Systematic statistical analysis of CCHD diagnosis and outcomes has been undertaken in the US and other countries.[2,3,6–9] In the US,

suspected CCHD cases are usually screened out from newborns within 24–48 h of birth through the combination of percutaneous oximetry and prenatal ultrasound.[6,7] Neonatal percutaneous oximetry provides a reliable approach for the precise diagnosis of CCHD, which eventually decreases the risk of newborn mortality.[4] The prevalence of CCHD among newborns in the US was reported as 10.2/10 000.[4,10] However, these clinically significant results may not be directly applicable to China, due to different clinical settings. Therefore, a comparable study to assess the prevalence rate of CCHD with a delayed diagnosis and non-delayed diagnosis at China is required.

Since 2003, hospitals in Beijing, China began to screen and monitor CCHD through the combination of prenatal ultrasound with neonatal physical examination and auscultation, which provides a reliable database for the evaluation of the impact of a delayed diagnosis of CCHD. This current study used this disease database collected in Beijing between 2010 and 2017 to evaluate the prevalence of CCHD and to determine the correlation between CCHD diagnosed at different stages with the outcome of newborns during their first week after birth.

Patients and methods

Data collection

This retrospective study collected data from consecutive newborns through the Birth Defects Monitoring Network in Beijing between January 2010 and December 2017. All cases were extracted from a province-wide hospital-based surveillance programme in Beijing, China, with a monitoring period from 13 weeks of gestation to 7 days after birth. A three-level (hospital, district and province) surveillance network and corresponding expert groups were established to perform routine data assessment. Information regarding individual

birth defect cases ($\geq$13 weeks of gestation) and summary of all births (live or stillbirths $\geq$28 weeks of gestation) was collected by the hospital staff and checked by the expert groups at each level. In addition, underreported cases of birth defects were identified through an independent retrospective survey.

The diagnosis of CCHD was targeted to the seven categories as follows: (i) tetralogy of Fallot; (ii) complete transposition of the great arteries; (iii) persistent truncus arteriosus; (iv) left ventricular dysplasia; (v) pulmonary atresia; (vi) tricuspid atresia; and (vii) total anomalous pulmonary venous return.[2] Multiple diagnostic sources, including birth defects and neonatal death monitoring data from medical institutions in Beijing, were used to confirm the cases of CCHD. All individual cases were subjected to tertiary review and information quality control by specialists.

This study was approved by the Ethics Committee of Beijing Maternal and Child Health Care hospital, Beijing, China (no. 2019-KY-025-01). Informed consent was not required as this was a retrospective study.

Diagnostic and classification criteria

For each CCHD case, the collected data included information regarding the primary extra-cardiac symptoms, specific type of heart defects, diagnostic basis, time to diagnosis, delivery date, location of maternity wards and outcomes during the monitoring period. For all CCHD cases, their echocardiography results were used as the diagnostic basis.

The CCHD cases were classified into three groups as follows: (i) isolated CCHD; (ii) CCHD with extra-cardiac malformation; and (iii) CCHD with syndrome. The isolated CCHD cases were defined as those with no extra-cardiac defects or identifiable syndromes. CCHD with extra-cardiac malformation were defined as those cases with concomitant extra-cardiac malformations or without identifiable syndromes. CCHD with syndrome were those newborns with concomitant syndromes.

The timing of diagnosis in this study was divided into three time-points as follows: (i) prenatal diagnosis; (ii) diagnosis before obstetric discharge or transfer; and (ii) diagnosis after obstetric discharge or transfer. Diagnosis after obstetric discharge/transfer was defined as a delayed diagnosis.

Statistical analyses

All statistical analyses were performed using the SPSS® statistical package, version 12.0 (SPSS Inc., Chicago, IL, USA) for Windows®. χ^2-test was used to evaluate the mortality rate of newborns within the first 7 days after birth. Multivariate logistic regression was undertaken to identify the number of live births. The cases with therapeutic labour induction, trisomy 18, trisomy 13, gestational age < 24 weeks and body weight $< 1000\,\mathrm{g}$ were excluded from the multivariate logistic regression analysis. A P-value < 0.05 was considered statistically significant.

Results

This retrospective study recorded that between 2010 and 2017, 1 773 935 perinatal newborns were screened in Beijing and 1851 were diagnosed with CCHD, showing a prevalence of 10.43 per 10 000. The newborns diagnosed with CCHD were grouped into seven CCHD categories and the prevalence (per 10 000 births) of these subtypes from high to low was 4.41 for tetralogy of Fallot, 2.56 for complete transposition of the great arteries, 1.18 for persistent truncus arteriosus, 1.23 for left ventricular dysplasia, 0.78 for pulmonary atresia, 0.52 for total anomalous pulmonary venous return and 0.37 for tricuspid atresia.

The newborns with CCHD were analysed according to the different classification criteria. Specifically, 1094 of 1851 (59.10%) were male, 719 of 1851 (38.84%) were female; with the sex being unknown in 38 (2.05%) patients. According to the diagnosis standard, 1518 of 1851 (82.01%) of CCHD patients belonged to the isolated CCHD, 260 of 1851 (14.05%) had CCHD with extra-cardiac malformation and 73 of 1851 (3.94%) had CCHD with syndrome.

Among the identified 1851 newborns with CCHD, the majority (1692 of 1851; 91.41%) were identified through prenatal diagnosis, 104 of 1851 (5.62%) were diagnosed before obstetric discharge/transfer and 55 of 1851 (2.97%) were identified through delayed diagnosis. Analysis of the newborns with CCHD based on the year (2010–2017) clearly demonstrated that the proportion of newborns being diagnosed at the three time-points varied from year to year (Figure 1). Specifically, approximately 5% of patients had a delayed diagnosis in the years 2010–2012, but this population decreased to approximately 2% during the years 2014–2017.

When the overall study cohort of patients with CCHD were categorized according to their CCHD category from the 2010 to 2017, the data showed the following: (i) the majority of patients with CCHD were identified through prenatal diagnosis; and (ii) the CCHD population identified as a result of delayed diagnosis varied from 0% (none of 210 patients) to 15.05% (14 of 93 patients) (Figure 2). Specifically, a delayed diagnosis did not identify any of the patients with persistent truncus arteriosus, while a delayed diagnosis was observed in 15.05% (14 of 93 patients) of the patients with total anomalous pulmonary venous return.

Among the overall study cohort of newborns with CCHD ($n = 1851$), 1505 died

before birth, including 1337 therapeutic labour induction and 168 intrauterine deaths; the remaining 346 newborns were born alive (prevalence, 1.96/10 000 births [346 of 1 768 138 of monitored live births]). Of these live births, 34 died within the first week (i.e. days 0–6) after birth (mortality, 0.02/1000 [34 of 1 768 138 of monitored live births]).

The prevalence and mortality rate of CCHD live births were analysed according to the timing of the diagnosis. Among the 346 CCHD live births, 55 patients (15.90%) were identified through delayed diagnosis; with 189 and 102 patients undergoing prenatal diagnosis or diagnosis before obstetric and transfer, respectively (Table 1). Of these live births, 34 died within the first week (i.e. days 0–6) after birth: seven of 55 patients in the delayed diagnosis group, 21 of 189 patients in the prenatal diagnosis group and six of 102 patients in the diagnosis before obstetric discharge and transfer group. There were no significant differences in the case fatality rates for the three groups.

Of the 55 CCHD newborns identified through delayed diagnosis, seven had CCHD with extra-cardiac malformation and they were still alive after the first week of birth (Table 2). The remaining 48 patients had isolated CCHD and seven of them died within the first week after birth. In addition, data analysis showed that the distribution of these 55 CCHD patients among the seven categories of CCHD varied from 0% (none of 14 patients) to 43.75% (14 of 32 patients).

Multivariate logistic regression analysis of survival was performed for 346 live births (excluding patients with therapeutic labour induction, trisomy 18, trisomy 13, gestational age < 24 weeks or body weight < 1000 g) (Table 3). Gestational age at delivery was the only risk factor for death at 0–6 days after live birth ($P < 0.001$). The
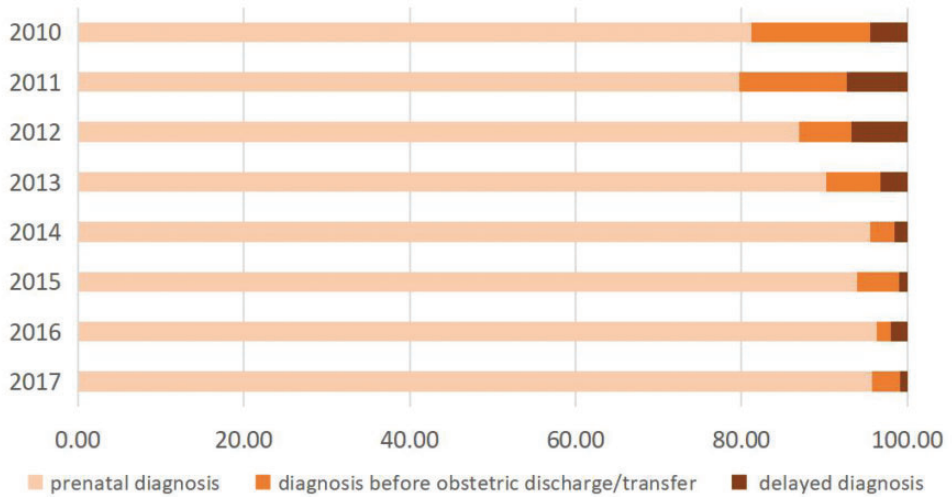
Figure 1. The proportion of newborns being diagnosed with critical congenital heart defects at the three stages of diagnosis stratified according to the year of diagnosis. The colour version of this figure is available at: http://imr.sagepub.com.
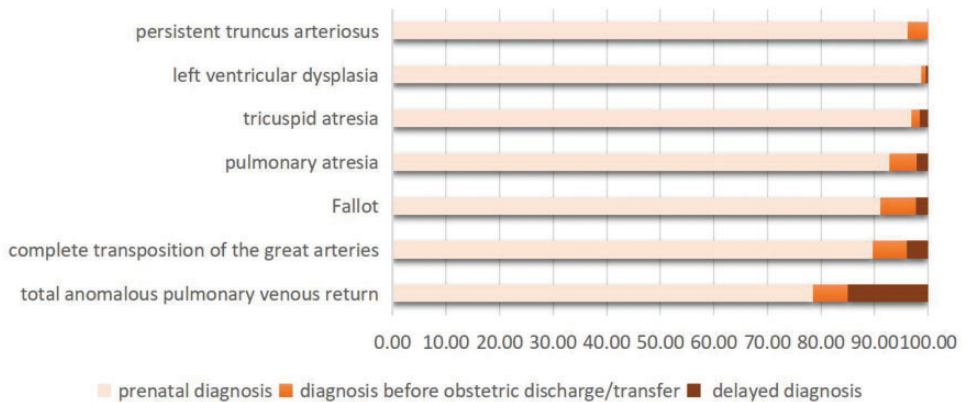

Figure 2. The proportion of newborns being diagnosed at the three stages of diagnosis stratified according to the categories of critical congenital heart. The colour version of this figure is available at: http://imr. sagepub.com.

Table 1. The timing of diagnosis and mortality outcomes at 0–6 days after the live birth of newborns ($n = 346$) diagnosed with critical congenital heart defects.

Time of diagnosis	Alive	Dead	Total	Case fatality rate
Prenatal diagnosis	168	21	189	11.11%
Diagnosis before obstetric discharge/transfer	96	6	102	5.88%
Delayed diagnosis	48	7	55	12.73%
Total	312	34	346	9.83%

Table 2. The mortality outcomes at 0–6 days after the live birth of newborns with a delayed diagnosis (n = 55) of isolated critical congenital heart disease (CCHD) or CCHD with extra-cardiac malformation stratified according to the categories of CCHD.

| | | Newborns with a delayed diagnosis n = 55 | | | | | |
| | Live birth cohort n = 346[a] | CCHD with extra-cardiac malformation n = 7 | | Isolated CCHD n = 48 | | Total | |
CCHD category		Alive	Dead	Alive	Dead	n	%[b]
Total anomalous pulmonary venous return	32	0	0	11	3	14	43.75
Tricuspid atresia	5	0	0	0	1	1	20.00
Pulmonary atresia	17	0	0	3	0	3	17.65
Complete transposition of the great arteries	103	2	0	13	3	18	17.48
Tetralogy of Fallot	165	5	0	13	0	18	10.91
Left ventricular dysplasia	14	0	0	1	0	1	7.14
Persistent truncus arteriosus	14	0	0	0	0	0	0.00
Total	346	7	0	41	7	55	15.90

[a]The total number of subtypes was 350 because four newborns had two categories of CCHD.
[b]Proportion of newborns with a delayed diagnosis with the CCHD category compared with the overall cohort of live births.

Table 3. Multivariate logistic regression analysis of potential risk factors for death at 0–6 days after the live birth of newborns (n = 346) with a diagnosis of critical congenital heart disease.

| | | | | Exp (B) 95% confidence interval | |
Risk factors		P-value	Exp (B)	Lower limit	Upper limit
The timing of diagnosis	Prenatal diagnosis				
	Diagnosis before obstetric discharge/transfer				
	Delayed diagnosis	P = 0.347	0.607	0.214	1.719
Birth weight	1000–2499 g				
	>2500 g	P = 0.774	1.233	0.295	5.156
Gestational age	>34 weeks				
	25–33 weeks	P < 0.001	0.031	0.006	0.155
Maternity ward level	Two-level				
	Three-level	P = 0.162	0.499	0.188	1.321
Extra-cardiac malformation	No				
	Yes	P = 0.844	0.861	0.194	3.821
Twins	No				
	Yes	P = 0.193	2.688	0.606	11.925

timing of diagnosis, birth weight, maternity ward level and occurrence of concomitant extra-cardiac malformation were not significant parameters.

Discussion

This retrospective study analysed data from a large database of 1 773 935 perinatal

newborns that included diagnostic information collected from Beijing between 2010 and 2017 in order to: (i) systematically analyse the prevalence of CCHD; (ii) investigate the correlation between the diagnosis of CCHD at different time-points and mortality outcomes in the first week of life; (iii) evaluate the risk factors contributing to newborn death in the first week of life.

This current study showed that the prevalence of CCHD (including therapeutic labour induction and intrauterine death) was 10.43/10 000 in Beijing, which was comparable to the CCHD prevalence (10.2/10,000) identified in the US.[4,10] Although China and the US have different clinical settings and monitoring techniques, the comparable results indicate that these current data from Beijing are reliable; having been dependent upon the improvement in diagnostic techniques, management policies and a province-wide hospital-based monitoring programme. Specifically, prenatal ultrasound screening for CHD was introduced to Beijing in 2003, which was followed by the initiation of physician training for ultrasound screening in 2007 and the introduction of foetal echocardiography in 2009.[11] In addition, expedited referral of suspicious cases identified from screening has improved access to prenatal diagnostic services.[11] Moreover, the professional quality control of screening has improved each year since the addition of outflow tracts to the screening views in 2014.[12]

Although the overall identified CCHD prevalence in Beijing between 2010 and 2017 was 10.43/10 000, the CCHD prevalence among newborns was 1.96/10 000, which was much lower than that identified in the US (10.2/10 000).[4,10] This current study also observed 91.41% of CCHD patients were identified through prenatal diagnosis. Such a high prenatal diagnosis rate might explain the low newborn CCHD prevalence in Beijing. Low newborn

CCHD prevalence appears to be associated with the widespread implementation of the prenatal diagnosis service, which was promoted by the National Regulation on the Administration of Prenatal Diagnosis Techniques since 2003 in mainland China.[13] According to the National Regulation, pregnant women are recommended to have systematic ultrasound examinations to screen for birth defects in the second trimester and a pregnancy affected by severe birth defects is legally allowed to be terminated through a standardized process.[13] As a consequence of the widespread use of prenatal sonography, a proportion of fetuses with CCHD could be diagnosed prenatally and terminated before 28 weeks of gestation, which might, in part, result in the decrease in the newborn CCHD prevalence. The increased prenatal diagnosis rate also appeared to lower the number of newborns with a postnatal diagnosis. The green channels between local institutions and CHD centres have increased the survival rate of newborns suffering from CCHD, which eventually decreased the mortality rate within the first week after birth.[14] Moreover, the newly initiated 'perinatal integrated diagnosis and treatment programme' shortens the postnatal transit interval, reduces the emergency operation rate of neonatal CCHD and provides better preoperative status for surgery.[15]

To date, there have been no clinical reports investigating the impact of a delayed diagnosis of CCHD on newborn mortality in China. In this current study, the proportion of CCHD newborns identified as the result of a delayed diagnosis was 2.97% (55 of 1851 patients), which was lower than that reported in the US and other countries (4.3–22.9%).[2,3,6–9] The multivariate logistic regression analysis of the potential risk factors associated with mortality in live birth newborns (considering the exclusion criteria) showed that the

gestational age of premature infants was the only risk factors for newborn death within the first week after birth. It was reported that the gestational age of premature infants, with a weight of < 2500 g, was a risk factor for CCHD-related death.[16] However, previous studies demonstrated that a delayed diagnosis of isolated CCHD was a risk factor for CCHD-related death.[5,17] These discrepancies between the studies might be due to several possible reasons. First, different definitions of a delayed diagnosis have been used. In previous studies, the diagnosis of CCHD at 3 days after birth was defined as a delayed diagnosis.[4] However, in this current study, a delayed diagnosis was defined as a diagnosis that was made after obstetric discharge/ transfer. This was because that the data specific to postnatal diagnosis 3 days after birth were not collected by the obstetric birth defect monitoring system in Beijing. Secondly, the high rate of prenatal diagnosis and therapeutic labour induction in Beijing, which might produce a bias in the severity of malformations in affected newborns, decreased perioperative deaths. Thirdly, the studies had different postnatal CCHD screening methods, monitoring of mortality and rates of autopsy. In the US, a delayed diagnosis was performed in maternity wards within 24–48 h of birth with percutaneous oximetry;[7,8] while in Beijing, the combination of neonatal physical examination, auscultation and echocardiography was used to perform the delayed diagnosis of suspicious cases, which was followed-up by community physicians using percutaneous oximetry at 3–7 days after obstetric discharge.[18] The endpoint of the hospital-based birth defects surveillance system is 7 days after birth in China.[19] This might have resulted in an underestimation of the prevalence and mortality rate of CCHD in China. In addition, some other factors may contribute to an underestimation of the prevalence of CCHD and mortality rate in Beijing, including the difference in the diagnosis rates between different hospitals, different definitions of target cases for CCHD, short monitoring periods and changes in the monitoring policy (including implementing foetal echocardiography and hospital monitoring of birth defects in paediatric institutions from 2009). To improve this situation, the performance of expensive neonatal percutaneous oximetry in maternity wards in Beijing is a possible solution, but further health and economic evaluations are required. In addition to screening costs, future healthcare and educational costs for children with CCHD and health sector expenses for supporting and monitoring CCHD screening policies must be considered.

In conclusion, this retrospective study systematically analysed the prevalence of CCHD, as well as investigating the correlation between the timing of the diagnosis and the resulting mortality rate, based on a very large database over an 8-year collection period in Beijing. This current study demonstrated the latest status of CCHD patients in Beijing, which may provide valuable reference for future interventions in China and other countries that have a high prenatal diagnosis rate and therapeutic labour induction rate.

Contributors' statement

Wen Zhang performed a literature search, analysed data and wrote the manuscript. Hong-Yan Xu and Yan-Chun Zhang performed a literature search and analysed data. Kai-Bo Liu designed the study, analysed data and critically reviewed the manuscript.

Declaration of conflicting interest

ORCID iD

Kai-Bo Liu https://orcid.org/0000-0001-9540-024X

References

1. Wren C, Reinhardt Z and Khawaja K. Twenty-year trends in diagnosis of life-threatening neonatal cardiovascular malformations. *Arch Dis Child Fetal Neonatal Ed* 2008; 93: F33–F35. doi: 10.1136/adc.2007.119032.

2. Kemper AR, Mahle WT, Martin GR, et al. Strategies for implementing screening for critical congenital heart disease. *Pediatrics* 2011; 128: 1259–1267. doi: 10.1542/peds.2011-1317.

3. Glidewell J, Grosse SD, Riehle-Colarusso T, et al. Actions in Support of Newborn Screening for Critical Congenital Heart Disease – United States, 2011-2018. *MMWR Morb Mortal Wkly Rep* 2019; 68: 107–111. doi: 10.15585/mmwr.mm6805a3.

4. Olney RS, Ailes EC and Sontag MK. Detection of critical congenital heart defects: Review of contributions from prenatal and newborn screening. *Semin Perinatol* 2015; 39: 230–237. doi: 10.1053/j.semperi.2015.03.007.

5. Liberman RF, Getz KD, Lin AE, et al. Delayed diagnosis of critical congenital heart defects: trends and associated factors. *Pediatrics* 2014; 134: e373–e381. doi: 1542/peds.2013-3949.

6. Ewer AK, Middleton LJ, Furmston AT, et al. Pulse oximetry screening for critical congenital heart defects in newborn infants (PulseOx): a test accuracy study. *Lancet* 2011; 378: 785–794. DOI: 10.1016/S0140-6736(11)60753-8.

7. Centers for Disease Control and Prevention. Newborn screening for critical congenital heart disease: potential roles of birth defects surveillance programs – United States, 2010-2011. *MMWR Morb Mortal Wkly Rep* 2012; 61: 849–853.

8. Peterson C, Ailes E, Riehle-Colarusso T, et al. Late detection of critical congenital heart disease among US infants: estimation of the potential impact of proposed universal screening using pulse oximetry. *JAMA Pediatr* 2014; 168: 361–370. doi: 10.1001/jamapediatrics.2013.4779.

9. Wacker-Gussmann A, Ehringer-Schetitska D, Herceg-Cavrak V, et al. Prevention of delayed diagnosis in congenital heart disease. *Cardiol Young* 2019; 29: 730–731. doi: 10.1017/S1047951119000064.

10. Van Naarden Braun K, Grazel R, Koppel R, et al. Evaluation of critical congenital heart defects screening using pulse oximetry in the neonatal intensive care unit. *J Perinatol* 2017; 37: 1117–1123. doi: 10.1038/jp.2017.105.

11. The prenatal diagnosis and prenatal screening work norms in Beijing, Beijing Municipal Health and Family Planning Commission, http://wjw.beijing.gov.cn/zwgk_20040/fgwj/wjwfw/201912/t20191219_1306079.html (2011, accessed 24 June 2021).

12. Zhang L, Xu HY, Zhang W, et al. Effect of ultrasound screening strategy for fetal congenital heart disease in Beijing. *Chinese Journal of Birth Health Heredity* 2019; 9: 1116–1118.

13. Bian XM, Guo Q and Qi QW. Current situation and development of prenatal diagnosis in China. *Front Med China* 2010; 4: 271–274. doi: 10.1007/s11684-010-0100-z.

14. Jin M, Lv ZY and Gu Y. The development and application of the heart disease screening and treatment monitoring network over the past decade in Beijing. *China Medicine* 2017; 12: 1765–1767.

15. Liu X, Hong HF, Zhang HB, et al. Neonatal surgical outcomes after prenatal diagnosis of complex congenital heart disease: experiences of a perinatal integrated diagnosis and treatment program. *World J Pediatr* 2020; 16: 494–501. doi: 10.1007/s12519-020-00383-z.

16. Lopes SAVDA, Guimarães ICB, Costa SFO, et al. Mortality for Critical Congenital Heart Diseases and Associated

Risk Factors in Newborns. A Cohort Study. *Arq Bras Cardiol* 2018; 111: 666–673. doi: 10.5935/abc.20180175.

17. Eckersley L, Sadler L, Parry E, et al. Timing of diagnosis affects mortality in critical congenital heart disease. *Arch Dis Child* 2016; 101: 516–520. doi: 10.1136/archdischild-2014-307691.

18. Administrative Measures for the Screening of Congenital Heart Diseases for Children Aged 0–6 in Beijing, Beijing Municipal Health Bureau, http://wjw.beijing.gov.cn/zwgk_20040/fgwj/gfxwj/201912/t20191216_1239785.html (2009, accessed 24 June 2021).

19. Chinese Maternal and Child Health Statistical Survey System, National Bureau of Statistics of China, http://www.stats.gov.cn/tjfw/bmdcxmsp/bmzd/201808/t20180806_1614259.html (2018, accessed 24 June 2021).