Prevalence of Congenital Heart Disease among Infants from 2012 to 2014 in Langfang, China

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Abstract

Background: Congenital heart disease (CHD) is the most common congenital malformations with high mortality and morbidity. The prevalence of CHD reported previously ranged from 4 per 1000 live births to 50 per 1000 live births. In this cross-sectional study, we aimed to document the prevalence of CHD in Langfang district of Hebei Province, China by analyzing data collected by hospitals located in 11 the counties of the district, as supported by a public health campaign.

Methods: A total of 67,718 consecutive 3-month-old infants were included from July 19, 2012 to July 18, 2014. Structural abnormalities were diagnosed based on echocardiography findings, including two-dimensional and color Doppler echocardiography results.

Results: Of the 67,718 infants, 1554 were found to have cardiac structural abnormalities. The total prevalence of CHD was 22.9 per 1000 live births, a value significantly higher than the previously reported prevalence of 8 cases per 1000 live births. The top five most common cardiac abnormalities were as follows: atrial septal defect (ASD, 605 cases, 8.93‰); ventricular septal defect (550 cases, 8.12‰); patent ductus arteriosus (228 cases, 3.37‰); pulmonary stenosis (66 cases, 0.97‰); and tetralogy of Fallot (32 cases, 0.47‰). The CHD prevalence differed by gender in this study ($\chi^2 = 23.498$, $P < 0.001$), and the majority of ASD cases were females. Regional differences in prevalence were also found ($\chi^2 = 24.602$, $P < 0.001$); a higher prevalence was found in urban areas (32.2 cases per 1000 live births) than in rural areas (21.1 cases per 1000 live births). There was a significant difference in the prevalence of CHD in preterm versus full-term infants ($\chi^2 = 133.443$, $P < 0.001$). Prevalence of CHD in infants of maternal aged 35 years or over was significantly higher ($\chi^2 = 86.917$, $P < 0.001$).

Conclusions: The prevalence of CHD in Langfang district was within the range reported using echocardiography. Echocardiography can be used to early diagnose the CHD.

Key words: Congenital Heart Disease; Echocardiography; Infants; Prevalence

INTRODUCTION

In developing countries, congenital heart disease (CHD) is the most common congenital malformation, and it presents high mortality and morbidity. The prevalence of CHD has been reported to range from 4 to 50 cases per 1000 live births.[1] Most CHD prevalence data are based on population-based birth defect registries or clinical symptoms.[2] A few studies have assessed the prevalence of CHD at birth by the echocardiographic screening of an in-hospital population.[3,4] No large-sample, population-based study on CHD using echocardiography has been conducted in Langfang district.

Langfang district in Hebei province is one of the prefecture-level cities with an area of 6429 square kilometers, and the population is approximately 4.4 million, mainly to the Han nationality. The district governs 11 counties, namely Sanhe, Dachang, Yongqing, Yanjiao, Bazhou, Wen'an, Gu'an, Guangyang, Anci, Dacheng, Xianghe. In this cross-sectional study, we aimed to investigate the prevalence of CHD in Langfang district by analyzing data collected by hospitals located in the counties of the District, as supported a public health campaign focusing on CHD treatment.

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METHODS

Subjects

This cross-sectional study took place in the Langfang district's 11 maternal and child health certificate registries responsible for the diagnosis of CHD as commissioned by the Health Administrative Department of District. According to the schedule of the public health campaign, all 3-month-old infants in the district were encouraged to participate, but only those with willingness to undergo echocardiography in the outpatient department received an ultrasound examination. From July 19, 2012 to July 18, 2014, it is reported that there were totally 77,836 3-month-old infants in the district. Among those, 67,718 (87%) joined the campaign and had received an ultrasound examination, whereas the remaining 10,118 did not. The reasons for nonparticipating were not surveyed, but as speculated by the local health staff involved in the public health campaign, "feeling unnecessary" may be a key reason. Infants diagnosed with CHD were followed up at 1 year of age, and their parents were invited to complete a questionnaire then.

Ethical approval

The study was approved by the General Hospital of Beijing Military Region Ethics Committee (No. 2011-98), and written informed consent regarding the "the protocol of CHD screening in Langfang district" was signed by the parents of the infants.

Protocol

In this study, diagnosis was made by echocardiography, and in all of the 11 hospitals, the SonoSite M-Turbo ultrasonic diagnostic instrument equipped with a pediatric probe (frequency 4–8 MHz) was used for the examination. Cardiac structure and function were observed along the standard parasternal long-axis, short-axis, suprasternal, subcostal, and apical four-chamber views. All infants were scanned by a senior echocardiographic doctor with more than 5 years of echocardiographic experience to ensure quality. Meanwhile, a self-administered standard questionnaire was designed to investigate socio-demographic characteristics, including maternal age, residence, infant gender, birth weight, gestational age, etc.

The screening group comprised a pediatrician who was responsible for the clinical examination, an echocardiographic doctor who conducted the echo-diagnosis and a cardiologist who explained the abnormality or outcome.

Diagnosis criteria of congenital heart disease

CHD was classified on the basis of the International Classification of Diseases, Ninth Revision, and the Clinical Modification code. Patent foramen oval and atrial septal defect (ASD) (defect <4 mm in diameter) were excluded from CHD to avoid overestimation.

Quality control

To improve the participation rate, half of the cost of echocardiography (approximately RMB 245 Yuan) was supported by the local government, and the maternity and child care institutions prescribed an echocardiography application form for every infant while distributing birth certificates or at the time of vaccination or physical examination. Along with the echocardiography application form, a data collection form was also provided to infants' parents. The data collection form was used to collect the demographic information and to record the echocardiography result and referral information. Once the echocardiography was completed, the data will be entered into an online data collection system designed specifically for this public health campaign by trained staff from the maternity and child healthcare institutions. To standardize the diagnosis, echocardiography expert from General Hospital of Beijing Military Region are in charge of confirmation of CHD and providing technical support. To facilitate reassessment of echocardiography diagnosis, all image graphs were required to be stored in the computer. To avoid misdiagnosis and omissions, health-care professionals examined the reports from surveillance hospitals. Questionable reports must be correct or supplementation.

Statistical analysis

The data used in this study were directly exported from the data collection system in the form of an Excel spreadsheet. Statistical analyses were performed using SPSS version 17.0 software package (SPSS Inc., Chicago Illinois, USA). The Chi-square test was used to compare rates. The value of $P < 0.05$ was considered statistically significant.

RESULTS

Study population

Of the 77,836 3-month-old infants who were born during the study, 67,718 were examined by echocardiography (coverage rate: 67,718/77, 836 = 87%), including 61,505 full-term infants and 6213 preterm infants (<37 weeks). Thirteen percent were reported to have a failed screening result. The population included 32,918 (48.6%) males and 34,800 (51.4%) females.

Echocardiography findings

A total of 1554 infants were diagnosed with CHD during the 2-year (42.5% boys, 57.5% girls). The prevalence of CHD was 22.9 cases per 1000 live births. The top five most common cardiac abnormalities were the following: ASD (605 cases, 8.93‰); ventricular septal defect (VSD, 550 cases, 8.12‰); patent ductus arteriosus (PDA, 228 cases, 3.37‰); pulmonary stenosis (PS, 66 cases, 0.97‰); and tetralogy of Fallot (TOF, 32 cases, 0.47‰). The CHD prevalence differed by gender in this study ($\chi^2 = 23.498$, $P < 0.001$), and there were more females with ASD ($\chi^2 = 56.62$); however, this was not true of VSD ($\chi^2 = 0.01$) or PDA ($\chi^2 = 0.86$) [Table 1]. Regional differences in prevalence were also found ($\chi^2 = 24.602$, $P < 0.001$); a higher prevalence was found in urban areas (32.2 cases per 1000 live births) than in rural areas (21.1 cases per 1000 live births). There was a significant difference in the prevalence of CHD in preterm versus full-term infants ($\chi^2 = 133.443$, $P < 0.001$). Prevalence of CHD in infants of maternal aged 35 years or over was significantly higher ($\chi^2 = 86.917$, $P < 0.001$).

Table 1: CHD distribution by gender

CHD	Male (n)	Female (n)	Total (n)	Prevalence (‰)
ASD	202	403	605	8.93
VSD	266	284	550	8.12
PDA	103	125	228	3.37
PS	32	34	66	0.97
TOF	17	15	32	0.47
ASD + VSD	11	9	20	0.29
Endocardium cushion defect	6	5	11	0.16
VSD + PDA	2	9	11	0.16
ASD + PDA	3	3	6	0.09
Anomalous pulmonary venous drainage	2	3	5	0.07
Cardiac tumor	3	1	4	0.06
Transposition of the great arteries	1	1	2	0.03
Persistent left superior vena cava	2	0	2	0.01
Aortic arch abnormalities	2	0	2	0.01
Diverticulum of the left ventricle	2	0	2	0.01
Dextrocardia	2	0	2	0.01
Pulmonary atresia with intactventricular septum	1	0	1	0.01
Pulmonary atresia with VSD	1	0	1	0.01
Pulmonary artery sling	0	1	1	0.01
DORV	1	0	1	0.01
SV	1	0	1	0.01
IAA	1	0	1	0.01
Total	661	893	1554	22.90

ASD: Atrial septal defect; VSD: Ventricular septal defect; PDA: Patent ductus arteriosus; PS: Pulmonary stenosis; TOF: Tetralogy of Fallot; DORV: Double-outlet right ventricle; SV: Single ventricle; IAA: Interrupted aortic arch; CHD: Congenital heart disease.

DISCUSSION

A total of 67,718 3-month-old infants were diagnosed using echocardiography in Langfang district during 2012–2014, and 1554 infants were found to have CHD. The total prevalence of CHD was 22.9‰, which higher than the previously reported 8‰, but within the range reported using echocardiography. The order of CHD in Langfang district as follow: ASD, VSD, PDA, PA, and TOF. The CHD prevalence differed by gender, regional, gestational, and maternal age.

In this study, we used echocardiography as a diagnosis tool to investigate the prevalence of CHD in Langfang district in China; the overall prevalence of CHD was found to be 22.9 cases per 1000 live births. This result is similar to those found in Shanghai (26.6 cases per 1000 live births) and Japan (50.3 cases per 1000 live births)[3,4] but is significantly higher than that found in other reports. The similar findings in the former two studies might be a result of the use of echocardiography as a diagnosis tool. Similarly, some of the differences in results might be caused by differences in methodology (i.e., in the US, assessment might be more accurate because of the assessment of intracardiac deformity rather than auscultation), data source (birth defect registration or clinical assessment), and subject age at time of diagnosis (small muscular VSD; PDA has a high spontaneous closure rate, which might decrease the detection rate). The CHD prevalence found here (22.9‰) was determined by echocardiographic diagnosis and is higher than the internationally accepted level of 8 cases per

1000 live births and the published domestic rate (6.64 cases per 1000 live births).[5] To some extent, this result occurred because of more complete supervision by local public health authorities, better monitoring and greater standardization, and the wide application of echocardiography diagnosis. However, this finding also reflects the heavy responsibility of diagnosis for CHD and the need for long-term follow-up and observation. Further study is necessary to reduce the overall prevalence of CHD.

Our data indicate that ASD is the most frequent type of CHD, followed by VSD, PDA, PS, and TOF, in that order. This result is consistent with a previous report from India,[6] which indicated that ASD was the most frequent lesion. However, some researchers[7] have found VSD to be the most frequent type of CHD. This difference might be age-related. Some small VSDs might close spontaneously, and large VSDs present symptoms early, prompting treatment. Many asymptomatic infants with ASD were diagnosed for the first time during the screening; this might also be responsible for the higher ASD prevalence found in our study. In general, the top five types of CHD were similar between the studies.

The difference in the prevalence between males and females was significant in this study ($\chi^2 = 23.498$, $P < 0.001$); there were more female cases of ASD. At present, the cause of heart malformation in infants remains unclear and is perhaps related to gestational age, family history, radiation exposure, the use of medication, etc. Previous studies have shown that the prevalence of CHD in males and females

is approximately the same;[8,9] however, the prevalence of artery stenosis, TOF, and transposition of the great artery is higher in males than in females. By contrast, ASD is more common in females.

Until now, researchers have reported a higher prevalence in urban areas than in rural areas,[10] but the potential risk factors for CHD in urban areas are unknown. Regional differences in prevalence were also found in our study; the prevalence was higher in urban areas (32.2 cases per 1000 live births) and lower in rural areas (21.9 cases per 1000 live births). Although urban areas have the advantage over rural areas in terms of size, population, the economy and other aspects, there might be more environmental risk factors in urban environments, such as extensive applications of lead and other heavy metals in industrial and agricultural production[11] or the emission of toxic pollutant gases,[12] all of which increase the prevalence of CHD. Second, in rural areas, birth asphyxia, CHDs, premature birth/low birth weight, pneumonia, and drowning were the five leading causes of death in 1997. The death rate was also lower in urban areas than in rural areas at that time.[13] Thus, the prevalence of CHD in urban areas was high.[10] In addition, Mahle *et al*.[14] and Hunte *et al*.[15] suggest that a prenatal diagnosis has a favorable effect on the treatment of patients undergoing staged palliation, reduces early morbidity, and improves the child survival rate. The prevalence of CHD in Dachang Hui Autonomous County (19.5 cases per 1000 live births) was below average (22.9 cases per 1000 live births); further large-sample studies are necessary to clarify differences between races. Unfortunately, the number of ethnicities in the current study was too small to yield significant results.

Langfang district is mainly rural, reflects the diagnosis of CHD at the grass-roots level in China. The treatment of CHD has made great progress in recent years. The surgical survival of part of the CHD has reached a higher level, but the understanding and diagnosis of CHD remain to be improved at the grass-roots level in China, especially in rural areas and basic-level hospitals. The study is given priority to with the rural population, the data showed that train the doctor of community and township hospitals on CHD diagnosis is very important.

This study indicated a significant difference in preterm versus full-term infants. Previous studies have showed the prevalence of CHD to correlate with the preterm. Researchers have pointed out that in very preterm/low birth weight infants CHD are more prevalent than in the general liveborn population, and confer an increased risk of death and serious morbidities independently of other risk factors.[16,17] Tanner *et al*. showed that preterm infants have more than twice as many cardiovascular malformations as do infants born at term and that 16% of all infants with cardiovascular malformations are preterm.[18] Pappas *et al*. reported that extremely preterm infants (<1000 g) with congenital heart defect were 0.8%.[19] The date came from the National Institute of Child Health and Human Development Neonatal Research Network.

In this study, we found that prevalence of CHD in infants of maternal aged 35 years or over were significantly higher. Advanced maternal age is proposed to be a risk factor of the heart malformation in some studies; Miller *et al*.[20] found that advanced maternal age ≥35 years was associated with increased prevalence of several CHD. The reason might be caused by increased mutations in the germ cell line because of cumulated cell replications. Similar to maternal age, advanced paternal age is proposed to be a risk factor of CHD in the offspring, but the biological mechanism is not clear.[21]

The screening team comprised 3 doctors: a pediatrician who was responsible for clinical examination, an echocardiographer who was responsible for screening the CHD, and a cardiologist who was responsible for explaining any abnormality or the outcome. Our multidisciplinary clinical practice model consolidated different experts into one team, which directly communicated comprehensive treatment recommendations to parents with CHD infants to improve the quality of the infants' lives. Early screening not only helps reduce undetected CHD but also can provide accurate data for improving the management of CHD.

This study had some limitations. First, as a cross-sectional and single center study, the results only reflect the prevalence of CHD in Langfang District, providing the up-to-date in this geographical region. Second, since not all infants underwent echocardiography, 13% of infants have been missed. Therefore, missing data might have affected the actual prevalence of CHD. Third, we included only live births, and some infants with CHD who died before screening were not included. Long-term follow-up is necessary to determine the temporal trends of the prevalence of CHD.

In conclusions, the prevalence of CHD in Langfang district within the range reported using echocardiography. Echocardiography is a reliable and simple imaging examination method that can be used in the diagnosis of CHD, particularly for measuring intracardiac structure and blood flow. Currently, echocardiography has become the most important, noninvasive and standard diagnostic method for CHD and is helpful in early diagnosis and in reducing mortality.

Conflicts of interest
There are no conflicts of interest.

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