RESEARCH PAPER

Prevalence of Congenital Heart Disease Amongst Schoolchildren in Southwest China

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Objective: To investigate the prevalence and risk factors of congenital heart disease in Yunnan, China which has diverse ethnic groups. **Methods:** This cross-sectional study enrolled 244,023 children from 2010 to 2015. To diagnose CHD, a conventional physical examination was used to screen suspicious cases, which were further confirmed by echocardiography. **Results:** A total of 1695 children were diagnosed with CHD. The estimated prevalence was 6.94%. Atrial septal defects were the most common cardiac abnormalities. A higher prevalence of CHD was observed with preterm birth, low birth weight, maternal age ≥35 years, and high-altitude regions. The prevalence also showed differences between diverse ethnic groups. **Conclusion:** The prevalence of CHD in China may have ethnic differences.

Keywords: *Altitude, Epidemiology, Ethnic group, Risk factor.*

Congenital heart disease (CHD) is a major cause of non-infectious death among children [1]. CHD is a result of alterations of multifactorial origin that include genetic and environmental factors [2]. Since 2012, CHD has become the most frequent type of birth defect in China [3]. Yunnan is a remote and underdeveloped southwestern province of China with an area of 394,000 km2. Furthermore, it is one of the most geographically and ethnically diverse places in the world, with over 26 different ethnic groups, and approximately 90% of the area is mountainous with altitudes ranging from 40 to 6000 m. The study was conducted to collect epidemiological data and risk factors of CHD in schoolchildren (aged 3-18 years) in Yunnan.

METHODS

The study was conducted by Yan'an Affiliated Hospital of Kunming Medical University. We used a cluster sampling method to recruit children aged from 3 to 18 years in Yunnan. From October 2010 to March 2015, all the children in the 1309 schools and kindergartens of Yunnan were recruited in this study. The altitude of each school was measured to evaluate the altitude at which those children lived. This study was carried out after permission from the Ethics Committee of Yan'an Affiliated Hospital of Kunming Medical University (Yunnan, China), and informed written consent was obtained from the parents or legal guardians of each child.

Each participant completed a questionnaire, which included information such as birth date, gender, gestational age, birth weight, parent age, and the ethnic group. We used a two-step method to diagnose CHD. First, a primary screen consisting of a physical examination was performed on all participants, and children with signs of cyanosis, cardiac murmur, and splitting of the second heart sound were suspected as patients with CHD. Second, the subjects suspected to have CHD were further screened by echocardiography (Philips, CX50) to assess their parasternal long-axis, short-axis, apical four-chamber, and subcostal views (2D and Doppler) to confirm CHD by an expert in pediatric senior echocardiography. The classification of CHD was based on the International Classification of Diseases, Ninth Revision, and the Clinical Modification code. However, patent foramen ovale (defects <4 mm in diameter) was excluded from the inclusion criteria.

Statistical analyses: Analysis were done with SPSS version 17.0 software package (SPSS, Chicago, Illinois). Chi-square and Fisher's exact test were used compare rates. For the comparison of the prevalence of CHD in different altitude level regions, a Cochran-Armitage Trend Test was used. Odds ratios and 95% Confidence intervals were calculated. A *P* value <0.05 was considered statistically significant.

RESULTS

A total of 244,023 children (127, 295 boys) participated in the primary physical examination with a mean (SD) age of 9.8 (2.1) years. Furthermore, 24,646 children [13,122 girls, mean age of 9.2 (2.7) years] suspected to have CHD were further screened by echocardiography.

A total of 1695 children (877 girls) were diagnosed with CHD, giving an estimated prevalence of CHD of 6.9 (95% CI, 1.78-12.11) per 1000 live births in Yunnan. There was a clear sex difference in prevalence of CHD, with 7.5 per 1000 live births among 116,728 girls compared to 6.4 per 1000 live births among 127,295 boys (OR, 1.17; 95% CI, 1.06-1.29; $P<0.01$) higher prevalence of CHD was found in mothers aged over 35 years (OR, 1.36; 95% CI; 1.23-1.51; $P<0.001$), children with gestational age <37 weeks (OR, 1.74; 95% CI; 1.52-1.99; $P<0.001$), and birthweight <2500 g (OR: 2.23, 95% CI; 1.98-2.51; $P<0.001$) (***Table* I**).There was a significant difference between different altitudes ($P<0.001$), prevalence of CHD increasing with elevation.

Atrial septal defect was the most common acyanotic congenital heart lesions (***Table* II**). Fifteen diverse ethnic groups were enrolled. Compared with the Chinese Han population, many other ethnic groups, including Tibetan, Hani, Yi, Naxi, Lisu, Jingpo, and Achang ethnic groups showed a higher prevalence of confirmed CHD ($P<0.05$) (***Table* III**).

DISCUSSION

Our study observed that Yunnan has a higher CHD prevalence than other areas of China, and ASD is the most common subtype. The higher prevalence of CHD was found among children who were born in high-altitude regions. The prevalence of CHD in most of the minority ethnic groups was higher than that in Han Chinese. Meanwhile, some other risk factors such as advanced maternal age, low birth weight, and premature birth were associated with CHD.

Our study has some limitations. We did not perform echocardiography in all children; thus, some minor lesions without cardiac murmurs such as very small ASD, tiny PDA, and uncomplicated bicuspid aortic valve might have been missed on physical examination. Furthermore, some children with severe or complex malformations might have died at a younger age, so the prevalence of

TABLE I Characteristics of 244023 Schoolchildren With Congenital Heart Disease in Yunnan, China

Variable	*CHD*	*Prevalence*
*Sex**		
Boys (*n*=127295)	818	6.426
Girls (*n*=116728)	877	7.513
Maternal age (*y*)#		
<35 (*n*=183018)	1165	6.36
≥35 (*n*=61005)	530	8.69
Gestation age (*wk*)#		
<37 (*n*=22430)	253	11.3
≥37 (*n*=221593)	1442	6.51
Birthweight (*g*)#		
<2500 (*n*=24591)	337	13.7
≥2500 (*n*=219432)	1358	6.19

*CHD: Congenital heart disease; Prevalence: per 1000 live births; *P<0.01; #P<0.001.*

TABLE II Subtypes of Congenital Heart Disease Among Schoolchildren in Yunnan, China

Type of	*Male*		*Female*		*Total*	
CHD	*No.*	*Prevalence*	*No.*	*Prevalence*	*No.*	*Prevalence*
ASD	346 (42.2)	2.718	370	3.170	716	2.893
VSD	227 (27.6)	1.783	241	2.065	468	1.918
PDA	135 (16.9)	1.061	151	1.293	286	1.213
BAV	36 (4.1)	0.283	34	0.291	70	0.287
TOF	16 (1.8)	0.126	15	0.129	31	0.127
PS	15 (1.6)	0.118	13	0.111	28	0.115
AVSD	11 (1.5)	0.086	14	0.120	25	0.102
TGA	3 (0.3)	0.024	3	0.026	6	0.025
Ebstein	2 (0.3)	0.016	4	0.034	6	0.025
others	27 (3.5)	0.212	32	0.274	59	0.242

CHD: Congenital heart disease; Prevalence: per 1000 live births; ASD: atrial septal defect, VSD: ventricular septal defect, PDA: patent ductus arteriosus BAV: bicuspid aortic valve, TOF: Tetralogy of Fallot, PS: pulmonary valvular stenosis; AVSD: Atrioventricular septal defect; TGA: Transposition of the great arteries.

What This Study Adds?

- High-altitude levels, maternal age prematurity and ethnicity were associated with the prevalence of congenital heart disease in Southwest China.

CHD in our investigation may be underestimated. Secondly, we use the altitude of each school to represent the altitude at which the children were born and lived in, which may not be very accurate. Furthermore, the physical examination, such as auscultation to screen CHD, may differ depending on the doctor even though their medical training may be similar.

Some previous studies in China have shown that the prevalence of CHD to vary from 1.5 to more than 20 per 1000 live birth [4-6]; which might have been due to the varying use of echocardiography as a diagnosis tool. Our data indicated that ASD was the most frequent lesion, which was consistent with some previous reports [7]; though others found VSD to be the most common type [8]. Some altitude correlation studies have indicated that a higher prevalence of CHD is found in high-altitude regions [9,10], which was consistent with our results. Furthermore, decreased oxygen tension has been implicated as an extrinsic factor for the formation of CHD in high-altitude areas [11]. Previous authors have also shown that maternal age ≥35 years, preterm birth, and low birth weight are risk factors for CHD [12,13]. Meanwhile, these results were also consistent with some studies conducted in China [14], but the biological mechanism for these risk factors needs further exploration. As a multi-ethnic country, some previous studies have shown that the different ethnic groups in China have different a prevalence of CHD [14,15]. This may be associated with a unique genetic background, consanguineous marriage, or bad living environment.

Through this school-based, multiple-ethnic, and multiple altitude study with an enormous number of participants, we can conclude that a physical examination combined with echocardiography is a reliable, economical, and efficient method to screen CHD in remote areas. We obtained data on risk factors and the prevalence of CHD in Yunnan, which provides additional information on the epidemiology of CHD as well as additional support for the development of diagnostic and treatment plans in many high-altitude and poor minority areas of Yunnan, China.

TABLE III Prevalence of Congenital Heart Diseases by Different Ethnic Groups in Yunnan, China

Ethnic group	*No.*	*CHD*	*Prevalence*
Han	144132	890	6.17
Tibetan*	9443	85	9.00
Bai	37300	263	7.05
Dai	15590	98	6.2
Hani*	5570	54	9.69
Yi*	14383	123	8.55
Zhuang	3564	15	4.2
Lisu*	3219	58	18.0
Wa	2094	20	9.55
Jingpo*	1630	22	13.49
Jino	1172	8	6.83
Miao	851	8	9.40
Hui	1063	7	6.58
Achang*	323	5	15.48
Others	419	2	4.78

*CHD: Congenital heart disease; Prevalence: per 1000 live births; *P value<0.05 compared with Chinese Han population.*

Contributors: SH: drafting the work and revising it critically; CW: agreement to be accountable for all aspects; ZH: design of the work; YL: acquisition of data; YD: acquisition of data; XG: acquisition of data; DH: analysis of data; ZhN: analysis of data; WC: interpretation of data. LJ: final approval of the version to be published. All authors approved the final version of manuscript, and are accountable for all aspects related to the study.
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