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Epidemiology of Congenital Heart Defects in Perinatal Infants in Guangxi, China

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Purpose: To explore the changing trends in the prevalence and epidemiological characteristics of congenital heart defects (CHDs) in perinatal infants (PIs) in Guangxi, China.

Patients and Methods: During 2016 and 2020, the Guangxi Birth Defects Monitoring Network (GXBDMN) monitored a total of 3627108 PIs in this study. The CHDs data for PIs can be obtained from the GXBDMN. The study analyzed the changing trends of total CHDs prevalence and each subtype of CHDs prevalence per year using prevalence-rate ratios (PRR). The correlation between characteristics (such as year, infant gender, maternal age, and quarter) and the prevalence of CHDs was also examined by the PRR.

Results: Between 2016 and 2020, 10817 PIs were diagnosed with CHDs, resulting in an overall CHDs prevalence of 29.82 [95% confidence intervals (CI): 29.26–30.38] per 10000 PIs. CHDs accounted for 24.50% of all types of BDs, making them the most common type of BDs. Atrial septal defect / patent foramen ovale (ASD/PFO), patent ductus arteriosus (PDA), ventricular septal defect (VSD), atrioventricular septal defect (AVSD), persistent left superior vena cava (PLSVC), and tetralogy of Fallot (TOF) were the 6 most common subtypes of CHDs. Together they accounted for 86.24% of all CHDs cases, with a total prevalence of 25.72 (95% CI: 25.20–26.24) per 10000 PIs. The study period saw a significant increase in the prevalence of CHDs (PRR = 1.300, 95% CI: 1.283–1.318), and the maternal age also played a significant role in this increase (PRR = 2.738, 95% CI: 2.428–3.087).

Conclusion: The prevalence of CHDs in Guangxi is rising and has an upward trend with maternal age. ASD/PFO, PDA, VSD, AVSD, PLSVC, and TOF were the top six subtypes of CHDs.

Keywords: congenital heart defects, perinatal infants, pregnant women, prevalence

Introduction

Congenital heart defects (CHDs) are problems with the heart structure that are present at birth.[1,2] The normal flow of blood through the heart can be altered by CHDs,[1,2] which are the most common type of birth defects (BDs).[2–4] CHDs represent for 36.63% of the total incident cases and 39.49% of the total deaths of BDs.[4] The global prevalence of CHDs was 230.52 per 10000 live births, and 69.12% of CHDs deaths occurred in infants under 1 year old.[5,6]

Infants with critical CHDs often require surgery or other treatments during their first year of life.[1] Though the rate of BDs deaths and years of life lost (YLLs) is consistently decreasing with the increasing socio-demographic index (SDI), the rate of CHDs prevalence and years lived with disability (YLDs) is on the rise.[7]

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The mean prevalence rate of CHDs at birth in China is 249.79/10,000.[8] Although there has been some progress in the prevention and control of CHDs in China, the disease burden in younger children remains high.[8] It is reported that 76.80% of CHDs deaths were found in children under 5 years old in China,[9] with a mortality rate of 101.67/10,0000.[8]

The Chinese Government has built a network system that includes prenatal screening, CHDs diagnosis, specialist consultations, and treatment centers using advanced international knowledge.[10] Routine screening can detect CHDs at birth or shortly thereafter, making it an important aspect of congenital defect registries. Monitoring the health of populations and identifying trends in congenital anomalies can be achieved through congenital defect registries,[10,11] which are a vital tool. The accuracy of CHDs diagnoses and overall coverage of prenatal and neonatal screening have gradually improved, contributing to significant decreases in neonate mortality rates.[10] However, China's efforts to prevent and treat CHDs still face several challenges, such as insufficient diagnostic capabilities and unqualified consultation services in some regions and rural areas.[10] Policy formulation is necessary to promote the graded management of CHDs.[12]

Guangxi is a province-level administrative region with 14 prefecture-level cities located in the southwest of China. Guangxi has consistently prioritized the health of women and children, continuously expanding comprehensive services throughout the childbearing process. With the aim of enhancing the quality of the newborn population, a series of people-oriented projects for the prevention and treatment of BDs have been implemented, including free CHDs screening for newborns. These initiatives have significantly promoted new developments in Guangxi's maternal and child health cause, and the health status of women and children has continued to improve.

The most common type of BDs in Guangxi is CHDs.[13] The prevalence of CHDs at birth in Guangxi has exceeded 30.00/10000, according to previous studies.[14,15] However, there has been limited reporting on the epidemiology of CHDs in perinatal infants (PIs) in Guangxi. It is necessary and important to investigate the epidemiology of CHDs in PIs in Guangxi. Therefore, this study aimed to explore the changing trends and the basic epidemiological characteristics of CHDs in PIs in Guangxi between 2016 and 2020 using congenital defect registries data, with a particular focus on temporal and spatial variations. The congenital defect registries data utilized in this study are robust and reliable, having undergone rigorous collection and validation processes. The data were sourced from a hospital-based BDs surveillance system, which in Guangxi has nearly 100% coverage of PIs delivered in hospitals. These data are of sufficient strength to meet the analytical requirements of this research and provide a fundamental representation of the CHDs prevalence among PIs. By leveraging this comprehensive dataset, it is able to draw meaningful conclusions regarding the prevalence and characteristics of CHDs in the study population. By examining prevalence, this study aimed to gain insights into the current state of CHDs in this study population and to identify any trends or patterns that may be useful for public health interventions and resource allocation. It is believed that this study will give the government constructive suggestions on how to prevent and control CHDs.

Materials and Methods

Study Population

The study population was the PIs between 28 weeks of gestation and 7 days after delivery who were diagnosed with CHDs and their mothers between 2016 and 2020. The prevalence of CHDs was defined as the number of PIs diagnosed with CHDs per 10000 PIs. In addition, the study did not separately list the prevalence of CHDs for PIs of unknown gender.

Inclusion and Exclusion Criteria

This study focused on infants who were in the perinatal period (between 28 weeks of gestation and 7 days after delivery), defined as the time around birth, including the antenatal (before birth) and early postnatal (immediately after birth) periods. Infants were confirmed to have CHDs through echocardiography, fetal magnetic resonance imaging (MRI), or postnatal cardiac catheterization. And infants with Down syndrome were excluded from the study. To ensure study homogeneity, infants with gestational ages outside the specified range will not be included.

Data Source and Collection

The Guangxi Birth Defects Monitoring Network (GXBDMN), a hospital-based BDs surveillance system, provided the CHDs data. The GXBDMN covers all hospitals in Guangxi. These hospitals consist of general hospitals, maternal and child health hospitals, and other medical institutions (excluding community hospitals). PIs born with CHDs between 28 weeks of gestation and 7 days after delivery in hospitals were monitored by GXBDMN. The "Medical Institution Birth Defects Fetus Registration Card" was used to record data about CHDs cases when PIs with CHDs were born or induced in the monitoring hospitals, regardless of their gestational age. The basic clinical information of PIs with CHDs and their mothers was recorded using GXBDMN.

Data Diagnostic Criteria, Primary Screening, and Diagnostic Methods

The International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) was the diagnostic criteria for CHDs. The primary screening and diagnostic methods for CHDs consisted of high-risk factor screening, clinical observation, physical examination, and auxiliary examinations. The screening for high-risk factors included family history, environmental teratogenic factors, and pregnancy history (early pregnancy, high-risk pregnancy, and high-risk neonatal history). The auxiliary examinations included ultrasound diagnosis, X-ray examination, autopsy and pathological section observation, chromosome abnormality detection, blood biochemical and immunological examinations, and more.

Data Quality Control

To ensure the quality and reliability of data on CHDs for this study. Each step in the surveillance of CHDs data was strictly controlled, including registration card filling, data collection and entry, data reduction and data clear-up, and data analysis. The completion rate of data entry was required to be 100% during quality control. The error rate of entry items and the underreporting rate of births and major subtypes of CHDs were all required to be less than 1%. The key components of quality control were checking gestation week, maternal age, subtypes of CHDs, and birth outcomes of fetuses with CHDs, and so on.

Statistics Analysis

The basic clinical characteristics of PIs with CHDs and their mothers were described. These include the gestational age, number of fetuses, clinical outcomes, induction of labor after diagnosis of defects, diagnostic methods, and diagnosis time of malformation. The mother's age, ethnic group, education level, family monthly income per capita (RMB), gravidity, and parity are taken into account.

The total prevalence of CHDs was calculated based on the year, infant gender, maternal age, and quarter. It needs to clarify that the definition of "quarter" refers specifically to the time of delivery for the PIs included in this analysis. In this study, the first quarter (Q1) includes January, February, and March; the second quarter (Q2) spans April, May, and June; the third quarter (Q3) comprises July, August, and September; the fourth quarter (Q4) encompasses October, November, and December.

The total prevalence of CHDs between 2016 and 2020 was geocoded using regionalism codes in the shapefile of Guangxi, which comprises of 14 prefecture-level city boundaries. This will be displayed on a map by ArcGIS 10.2 (ESRI, Redlands, USA). The geographical map data of Guangxi can be obtained from the National Platform for Common Geospatial Information Services.

Calculating the prevalence of one or more subtypes of CHDs should take into account the possibility that the fetus may be diagnosed with multiple subtypes of CHDs. The numerator was determined by specifying the frequency of subtypes of CHDs appearing in the PIs, and the denominator was the total number of PIs.

In this study, a total of the top 20 most common subtypes of CHDs were included. The prevalence of each major subtype of CHDs was also calculated separately by the year and ranked by the total prevalence in descending order. The 95% confidence intervals (CI) for the total prevalence of CHDs and for each major subtype of CHDs were calculated separately for each year.

The prevalence-rate ratios (PRR) were applied to explore the changing trends of CHDs prevalence by year and the correlation between the prevalence of CHDs and their characteristics (such as infant gender, maternal age, and quarter). The 95% CI for CHDs prevalence and PRR can be determined using univariate Poisson regression. Typically, calculating PPR does not require a single reference group when analyzing the overall trend in prevalence across different years. Instead, the PPR values are calculated relative to a baseline or reference point (implicitly or explicitly defined) within the dataset, which in this case represents the prevalence in a specific year or subtype serving as a comparator. The PPR values in this study will be presented in comparison to an implicit baseline (eg, the earliest year or a specified subtype) unless otherwise specified.

Stata MP 16.0 software (StataCorp LLC, Texas, USA) was utilized for all statistical analyses, with a significance level of $P < 0.05$.

Results

Clinical Characteristics of PIs with CHDs and Their Mothers, General Characteristics

Full-term infants were the majority of PIs with CHDs, accounting for 76.90%. Premature infants and extremely premature infants were followed by 17.09% and 5.72%, respectively. Post-term infants were the least, accounting for only 0.29%. Among these PIs, most of them were single births, accounting for 94.79%, while twins and multiple births only accounted for 5.19% and 0.03%, respectively. The majority of PIs with CHDs were born live, accounting for 93.22% of clinical outcomes. The next most common cause of death was fetal death, accounting for 6.24%. There were 0.44% of PIs with CHDs who died within 7 days after delivery, and stillbirths accounted for 0.09%. Furthermore, the induction of labor was performed by only 6.24% of PIs after diagnosis of CHDs. Prenatal ultrasound diagnosis was used by 86.65% of PIs to diagnose CHDs. In the diagnosis time of malformation, 86.11% and 13.89% of PIs were respectively diagnosed with CHDs within 7 days after delivery and in antenatal care. The clinical characteristics of PIs with CHDs are shown in Table 1.

The average maternal age was 30.13 ± 5.55 years. Han and Zhuang nationalities made up 95.10% of pregnant women. 49.83% of pregnant women had a high-school education or below, and 50.17% had a college education or above. There were 30.29% of pregnant women with a monthly family income per capita of less than 4000 RMB. 26.87% of pregnant women had not been pregnant before and had given birth. The general characteristics of pregnant women whose PIs were diagnosed with CHDs are shown in Table 2.

Table 1 Clinical Characteristics of PIs with CHDs

Variables	Number of CHDs	Percentage (%)
Total number of CHDs	10817	100.00
Gestational age, weeks		
28~32 (extremely premature infant)	619	5.72
32~37 (premature infant)	1849	17.09
37~42 (full-term infant)	8318	76.90
≥42 (post-term infant)	31	0.29
Number of fetuses		
Single	10253	94.79
Twins	561	5.19
Multifetal	3	0.03
Clinical outcomes		
Live birth	10084	93.22
Dead fetus	675	6.24
Stillbirth	10	0.09
Death within 7 days	48	0.44

(*Continued*)

Table 1 (Continued).

Variables	Number of CHDs	Percentage (%)
Induction of labor after diagnosis of defects		
Yes	675	6.24
No	10142	93.76
Diagnostic method		
Clinical diagnosis after birth	520	4.81
Prenatal ultrasound diagnosis	9373	86.65
Clinical diagnosis after birth and Prenatal ultrasound diagnosis	825	7.63
Autopsy	8	0.07
Unknown	91	0.84
Diagnosis time of malformation		
Antenatal	1503	13.89
Within 7 days after delivery	9314	86.11

Abbreviations: CHDs, congenital heart defects; PIs, perinatal infants.

City-Level Map CHDs Prevalence

Nanning had the highest prevalence of CHDs among the 14 cities in Guangxi, followed by Liuzhou, Chongzuo, and Guilin. With a prevalence of 91.21 (95% CI: 88.82–93.60) per 10000 PIs, 55.72 (95% CI: 52.88–58.56) per 10000 PIs,

Table 2 General Characteristics of Pregnant Women Whose PIs Were Diagnosed with CHDs

Variables	Number of CHDs	Percentage (%)
Total number of CHDs	10817	100.00
Ethnic group		
Han	6927	64.04
Zhuang	3360	31.06
Yao	241	2.23
Miao	90	0.83
Others	199	1.84
Education level		
Illiteracy	104	0.96
Elementary school	431	3.98
Junior middle school	2989	27.63
Senior middle school	1866	17.25
College degree and above	5427	50.17

(*Continued*)

Table 2 (Continued).

Variables	Number of CHDs	Percentage (%)
Family monthly income per capita, RMB		
<1000	1347	12.45
1000~2000	228	2.11
2000~4000	1701	15.73
4000~8000	3389	31.33
≥8000	4152	38.38
Gravidity		
1	2907	26.87
2	3075	28.43
3	2401	22.20
4	1358	12.55
≥5	1076	9.95
Parity		
0	2907	26.87
1	3075	28.43
2	2401	22.20
3	1358	12.55
≥4	1076	9.95

Abbreviations: CHDs, congenital heart defects; PIs, perinatal infants.

23.38 (95% CI: 20.77–26.00) per 10000 PIs, and 23.25 (95% CI: 21.54–24.97) per 10000 PIs, respectively. While the CHDs prevalence in Fangchenggang was the lowest, with a prevalence of 4.44 (95% CI: 2.93–5.96) per 10000 PIs. The city-level map of CHDs prevalence in Guangxi between 2016 and 2020 is shown in Figure 1.

Prevalence and Trends of Each Major Subtype of CHDs

In this study, a total of the top 20 most common subtypes of CHDs were included, collectively representing 88.76% (9601/10817) of all CHDs cases, and their overall prevalence rate was 26.47 (95% CI: 25.94–27.00) per 10000 PIs. Atrial septal defect / patent foramen ovale (ASD/PFO), patent ductus arteriosus (PDA), ventricular septal defect (VSD), atrioventricular septal defect (AVSD), persistent left superior vena cava (PLSVC), and tetralogy of Fallot (TOF) were the six most common subtypes of CHDs during the five-year study period. With a prevalence of 17.13 (95% CI: 16.71–17.56), 12.22 (95% CI: 11.86–12.58), 5.61 (95% CI: 5.37–5.85), 1.54 (95% CI: 1.42–1.67), 0.54 (95% CI: 0.46–0.62), and 0.51 (95% CI: 0.43–0.58) per 10000 PIs, respectively. The six most prevalent subtypes of CHDs constitute 57.45% (6214/10,817), 40.98% (4433/10,817), 18.81% (2035/10,817), 5.18% (560/10,817), 1.81% (196/10,817), and 1.70% (184/10,817), respectively, of all CHDs cases. Together, these 6 most common subtypes of CHDs made up 86.24% (9329/10817) of all CHDs cases, with a total prevalence of 25.72 (95% CI: 25.20–26.24) per 10000 PIs.

Between 2016 and 2020, AVSD was the only subtype of the six most common CHDs to exhibit a declining trend over time, with a PRR of 0.977 (95% CI: 0.920–1.037), albeit not statistically significant. Conversely, other prevalent CHDs subtypes such as ASD/PFO, PDA, VSD, PLSVC, TOF, pulmonary valve stenosis (PVS), coarctation of the aorta (CoA),

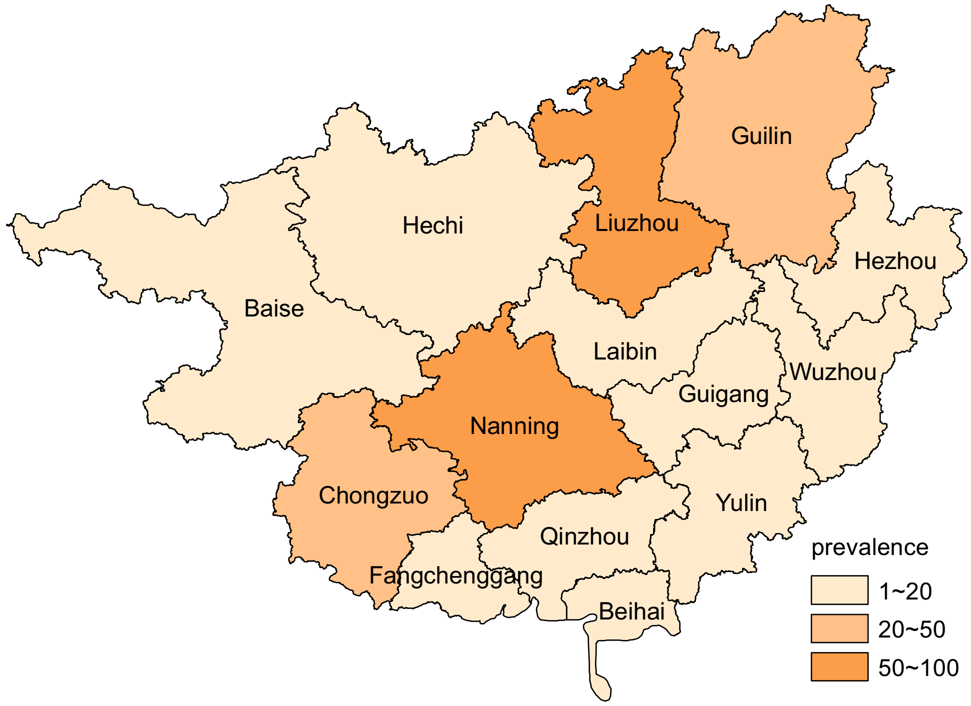

Figure 1 City-level map of CHDs prevalence in Guangxi between 2016 and 2020 (per 10000 PIs).
Abbreviations: CHDs, congenital heart defects; PIs, perinatal infants.

and pulmonary artery stenosis (PAS) all demonstrated significant increasing trends over time, with their respective PRR values being 1.491 (95% CI: 1.464–1.519), 1.498 (95% CI: 1.466–1.532), 1.312 (95% CI: 1.272–1.354), 1.644 (95% CI: 1.474–1.834), 1.173 (95% CI: 1.059–1.301), 1.190 (95% CI: 1.015–1.394), 1.220 (95% CI: 1.030–1.447), and 1.766 (95% CI: 1.341–2.327). Table 3 displays the prevalence and trends of each major subtype of CHDs in Guangxi from 2016 to 2020.

Table 3 Prevalence and Trends of Each Major Subtype of CHDs in Guangxi, 2016–2020 (per 10000 PIs)

Subtypes of CHDs	Rank	Total Prevalence	Annual Prevalence Rates					PRR (95% CI)		
			2016	2017	2018	2019	2020	PRR	95% CI	*P-value*
Atrial septal defect / Patent foramen ovale	1	17.13	8.32	9.60	15.18	23.06	36.67	1.491	1.464~1.519	< 0.001
Patent ductus arteriosus	2	12.22	5.42	7.19	11.39	16.03	26.20	1.498	1.466~1.532	< 0.001
Ventricular septal defect	3	5.61	3.37	4.32	5.07	6.85	10.04	1.312	1.272~1.354	< 0.001
Atrioventricular septal defect	4	1.54	1.32	1.32	2.55	1.76	0.71	0.977	0.920~1.037	> 0.05
Persistent left superior vena cava	5	0.54	0.25	0.15	0.38	1.13	1.07	1.644	1.474~1.834	< 0.001
Tetralogy of Fallot	6	0.51	0.42	0.42	0.43	0.55	0.80	1.173	1.059~1.301	< 0.01
Malcoordination of ventricular-arterial connection / Rightward displacement of aorta / Complete transposition of the great arteries	7	0.25	0.35	0.19	0.22	0.29	0.17	0.898	0.773~1.044	> 0.05
Pulmonary valve stenosis	8	0.22	0.11	0.22	0.28	0.23	0.28	1.190	1.015~1.394	< 0.05
Double outlet right ventricle	9	0.19	0.21	0.18	0.14	0.26	0.17	1.000	0.846~1.183	> 0.05
Coarctation of the aorta	10	0.19	0.13	0.16	0.14	0.31	0.24	1.220	1.030~1.447	< 0.05
Dextrocardia	11	0.14	0.14	0.10	0.13	0.12	0.26	1.174	0.967~1.425	> 0.05

(*Continued*)

Table 3 (Continued).

Subtypes of CHDs	Rank	Total Prevalence	Annual Prevalence Rates					PRR (95% CI)		
			2016	2017	2018	2019	2020	PRR	95% CI	*P-value*
Hypoplastic left heart syndrome	12	0.14	0.11	0.17	0.10	0.12	0.19	1.085	0.889~1.324	> 0.05
Mitral valve insufficiency	13	0.13	0.08	0.16	0.11	0.12	0.17	1.120	0.912~1.375	> 0.05
Pulmonary valve atresia	14	0.12	0.06	0.13	0.20	0.09	0.10	1.068	0.861~1.325	> 0.05
Double inlet ventricle / Common ventricle / Single ventricle	15	0.11	0.13	0.12	0.07	0.12	0.09	0.921	0.733~1.157	> 0.05
Pulmonary artery stenosis	16	0.09	0.02	0.04	0.07	0.17	0.21	1.766	1.341~2.327	< 0.001
Pulmonary valve insufficiency / Pulmonary regurgitation	17	0.06	0.02	0.07	0.07	0.05	0.10	1.243	0.921~1.677	> 0.05
Aortopulmonary Septal Defect / Aortic septal defect / Aortopulmonary window	18	0.06	0.05	0.04	0.06	0.06	0.10	1.250	0.920~1.699	> 0.05
Aortic valve stenosis	19	0.06	0.06	0.05	0.04	0.09	0.05	1.055	0.778~1.431	> 0.05
Aortic valve insufficiency	20	0.06	0.09	0.05	0.00	0.03	0.10	0.950	0.692~1.304	> 0.05

Notes: The PPR values are presented relative to an implicit baseline (the earliest year).
Abbreviations: CHDs, congenital heart defects; PIs, perinatal infants; PRR, prevalence-rate ratios; CI, confidence intervals.

Trends in the Prevalence of Total CHDs and the Perspective of Maternal Characteristics

From 2016 to 2020, 3627108 PIs and 3607929 live birth infants were monitored by GXBDMN. Of which, 10817 PIs were diagnosed with CHDs, resulting in an overall CHDs prevalence of 29.82 (95% CI: 29.26–30.38) per 10000 PIs. General hospitals, maternal and child health hospitals, and other medical institutions monitored 1659275, 1022554, and 926100 live birth infants, respectively. During the period of 2016 to 2020, CHDs were the most common types of BDs, accounting for 24.50% (10,817/44146) of all types of BDs. The study period saw a significant increase in the prevalence of CHDs, as demonstrated by the univariate Poisson regression results (PRR = 1.300, 95% CI: 1.283–1.318). Male PIs did not have a higher prevalence of CHDs than female PIs (PRR = 1.016, 95% CI: 0.978–1.055). The age of mothers had a positive impact on the prevalence of CHDs. CHDs had a rise in prevalence from 15.56 per 10000 PIs in mothers under the age of 20 to 42.59 per 10000 PIs in mothers aged 35 or above. In the four quarters, CHDs were prevalent at 29.14 per 10000 PIs to 30.50 per 10000 PIs. However, the univariate Poisson regression results indicated that the PRR was not

Table 4 Prevalence of Total CHDs Analyzed Over the Years and the Perspective of Maternal Characteristics (per 10000 PIs)

Variables	Prevalence (95% CI)		PRR (95% CI)		
	Prevalence	95% CI	PRR	95% CI	*P*-value
Total prevalence	29.82	29.26~30.38	—	—	—
Years					
2016	20.67	19.71~21.63	1.300	1.283~1.318	< 0.001
2017	19.97	19.01~20.93			
2018	27.13	25.92~28.34			
2019	35.82	34.37~37.27			
2020	54.01	52.12~55.90			
Infant gender					
Male	30.04	29.26~30.81	1.016	0.978~1.055	> 0.05
Female	29.56	28.74~30.38	Reference	—	—

(*Continued*)

Table 4 (Continued).

Variables	Prevalence (95% CI)		PRR (95% CI)		
	Prevalence	95% CI	PRR	95% CI	*P*-value
Maternal age, years					
<20	15.56	13.80~17.31	Reference	—	—
20–24	19.86	18.81~20.92	1.277	1.127~1.447	< 0.001
25–29	27.83	26.89~28.78	1.789	1.590~2.014	< 0.001
30–34	34.82	33.66~35.97	2.238	1.989~2.518	< 0.001
≥35	42.59	40.86~44.31	2.738	2.428~3.087	< 0.001
Quarter					
The first quarter	29.3	28.17~30.43	1.006	0.954~1.060	> 0.05
The second quarter	30.5	29.31~31.69	1.047	0.993~1.104	> 0.05
The third quarter	30.49	29.35~31.62	1.046	0.993~1.102	> 0.05
The fourth quarter	29.14	28.09~30.18	Reference	—	—

Notes: The PPR value of years is presented relative to an implicit baseline (the earliest year); the first quarter includes January, February, March; the second quarter includes April, May, June; the third quarter includes July, August, September; the fourth quarter includes October, November, December.
Abbreviations: CHDs, congenital heart defects; PIs, perinatal infants; PRR, prevalence-rate ratios; CI, Confidence intervals.

significant in every quarter. The perspective of maternal characteristics and the prevalence of total CHDs evaluated over the years are depicted in Table 4.

Discussion

CHDs have become a serious public health problem in the world in recent years. It's a problem that affects not just developed countries but also developing countries; not only among adults but also among children and infants. The burden of CHDs is evident due to differences in race and gender, with low-SDI regions facing significant differences from high-income regions.[16] Between 1990 and 2017, though the prevalence of CHDs was relatively low in most developed countries, it still increased in some developed countries, such as Germany and France.[17] China, India, Pakistan, and Nigeria were the four developing countries with the highest CHDs mortality in 2019, accounting for 39.7% of CHDs deaths globally.[6] Though the global death rate of CHDs in infants under 1 year decreased from 180624 deaths in 2017[18] to 150000 deaths in 2019.[5] The CHDs were still the underlying cause of infant deaths.[5]

In this study, the subtypes of CHDs were identified by the criteria of ICD-10 from the CHDs cases obtained from GXBDMN Guangxi in southwestern China between 2016 and 2020. This is the first study to perform univariate Poisson regression to calculate the PRR to explore the changing trends of CHDs prevalence in Guangxi. The results suggested 5 epidemiological characteristics of CHDs in Guangxi.

Firstly, Guangxi had a lower prevalence of CHDs than China, with an average level, and much lower than other provinces of China. Between 2016 and 2020, there was a total prevalence of CHDs in Guangxi of 29.82 per 10000 PIs in this study. This was considerably lower than that of the world in 2019 (230.52 per 10000 live births),[5] and was also lower than that of China in 2015–2019 (49.05 per 10000 PIs).[19] In comparison with other provinces, autonomous regions, or municipalities directly under the Central Government in China. The total prevalence of CHDs in Guangxi between 2016 and 2020 was much lower than that in Beijing in 2018–2020 (114.00 per 10000 births),[20] in Zhejiang between 2014 and 2018 (160.00 per 10000 births),[21] and in Hunan between 2012 and 2020 (74.17 per 10000 PIs).[22] But it was less than that in Shanghai during 2014–2017 (42.01 per 10000 live births).[23] These above differences in the prevalence of CHDs might be due to the different monitored periods. The monitored period in this study was from 28 gestation weeks to 7 days after birth. The meta-analysis of CHDs prevalence in China[19] and epidemiology research in Hunan[22] showed that the monitored period was the same. But in the world, it is from birth to 1 year old,[5] and in Shanghai it is from early fetuses (< 28 weeks of gestation) to 42 days after birth.[23] And in Beijing and Zhejiang, from early fetuses (< 28 weeks of gestation) to 7 days after birth.[20,21] Table 5 displays the comparison of the prevalence of CHDs between Guangxi and other regions. Therefore, according to publicly available data, it has been concluded that the total prevalence of CHDs in Guangxi was lower than that in China at an average level. It is much lower than in other provinces of China, such as Hunan. But it cannot be concluded that it was lower than that in the world and all other provinces, autonomous regions, or municipalities directly under the Central Government in China. Because the monitoring period for pregnant women in this study was not all identical to that of other provinces in reporting the prevalence of CHDs. Despite this, screening and diagnostic capabilities are constantly being improved.[8] The current ultrasound diagnostic techniques and the expertise of ultrasound doctors may still result in a relatively low prenatal diagnosis rate for CHDs.

The prevalence of CHDs among PIs in Guangxi is notably lower than the global or national averages. This phenomenon can be attributed to several factors, including favorable policies and healthy lifestyles prevalent in the region. Firstly, Guangxi has implemented a series of effective health policies aimed at reducing the prevalence of CHDs. The Guangxi government has prioritized maternal and child health, leading to the implementation of various preventive measures and health promotion campaigns. These initiatives have been crucial in raising awareness about CHDs and encouraging early diagnosis and treatment. Additionally, the Guangxi government has provided financial support for CHDs treatment, reducing the economic burden on families and encouraging more individuals to seek medical care. Secondly, the lifestyle of residents in Guangxi may also contribute to the lower incidence of CHDs. Guangxi is known for its rich natural resources and beautiful scenery, which promote outdoor activities and physical exercise. This active lifestyle is beneficial for cardiovascular health and may reduce the risk of CHDs. Furthermore, the traditional diet in Guangxi, which often includes fresh fruits, vegetables, and whole grains, is rich in nutrients that support heart health. Several studies have investigated the prevalence of CHDs in Guangxi and adjacent provinces. For instance, a study by Xu et al reviewed and prospected of the prevention and treatment of CHDs in Guangxi and emphasized the importance of prenatal screening and diagnosis in reducing the prevalence of the disease.[26] In conclusion, the lower prevalence of CHDs among PIs in Guangxi can be attributed to effective health policies, a healthy lifestyle, and the availability of medical resources. These factors have collectively contributed to a favorable environment for maternal and child health, leading to a reduced risk of CHDs in the region.

Secondly, the total prevalence of CHDs in Nanning, Guangxi was much higher than that in China at an average level and some other cities in China. The 2 most prevalent CHDs in prefecture-level cities in Guangxi between 2016 and 2020 were Nanning and Liuzhou. They had a prevalence of 91.21 per 10000 PIs and 55.72 per 10000 PIs, respectively. Which were 3.06 and 1.87 times higher than the prevalence of CHDs in Guangxi during the same study period, respectively. Compared to other prefecture-level cities in China, the total prevalence of CHDs in Nanning, Guangxi between 2016 and 2020 was roughly equivalent to that in Qingdao between 2018 and 2019 (93.80 per 10000 live births).[24] This is much higher than in Jinan between 2016 and 2020 (52.10 per 10000 births).[25] However, the monitored periods in Qingdao and Jinan were all different from that in this study, which were all from early fetuses (< 28 weeks of gestation) to 7 days after birth.[24,25] Table 5 displays the comparison of the prevalence of CHDs between Guangxi and other regions. Therefore,

Table 5 Comparison of the Prevalence of CHDs Between Guangxi and Other Regions

Author (year)	Study period	Region	Monitoring population	Monitored period	Prevalence (per 10000)
In this study					
Peng et al	2016–2020	Guangxi	Perinatal infants	From 28 gestation weeks to 7 days after birth	29.82
Peng et al	2016–2020	Nanning	Perinatal infants	From 28 gestation weeks to 7 days after birth	91.21
Peng et al	2016–2020	Liuzhou	Perinatal infants	From 28 gestation weeks to 7 days after birth	55.72
Other studies					
Roth et al (2020)[5]	2019	World	Under 1 year old infants	From birth to 1 year old	230.52
Zhao et al (2020)[19]	2015–2019	China	Perinatal infants	From 28 gestation weeks to 7 days after birth	49.05
Xie et al (2018)[22]	2012–2020	Hunan	Perinatal infants	From 28 gestation weeks to 7 days after birth	74.17

(*Continued*)

Table 5 (Continued).

Author (year)	Study period	Region	Monitoring population	Monitored period	Prevalence (per 10000)
Zhang et al (2021)[20]	2018–2020	Beijing	Early fetuses and perinatal infants	From early fetuses (< 28 weeks of gestation) to 7 days after birth	114.00
Zhang et al (2020)[21]	2014–2018	Zhejiang	Early fetuses and perinatal infants	From early fetuses (< 28 weeks of gestation) to 7 days after birth	160.00
Che et al (2023)[23]	2014–2017	Shanghai	Live birth infants	From early fetuses (< 28 weeks of gestation) to 42 days after birth	42.01
Jin et al (2021)[24]	2018–2019	Qingdao	Live birth infants	From early fetuses (< 28 weeks of gestation) to 7 days after birth	93.80
Zhang et al (2022)[25]	2016–2020	Jinan	Birth infants	From early fetuses (< 28 weeks of gestation) to 7 days after birth	52.10

Abbreviations: CHDs, congenital heart defects; PIs, perinatal infants.

Nanning of Guangxi had a much higher prevalence of CHDs than China at an average level and some other cities in China, like Jinan. It is also higher than that in Qingdao. The high prevalence of CHDs in Nanning of Guangxi may be due to the fact that it is the provincial capital of Guangxi in China. Compared to other prefecture-level cities in Guangxi, its economy is developed and its medical conditions are better. Doctors may have a greater amount of expertise in diagnosing CHDs, and fetuses with CHDs are more likely to be diagnosed during the perinatal period.

The prevalence of CHDs among PIs in Nanning and Liuzhou, Guangxi, exceeds the national and regional averages in China. This elevated prevalence can be attributed to a combination of genetic, environmental, and socioeconomic factors. Firstly, genetic predisposition plays a significant role in the occurrence of CHDs. Guangxi, including Nanning and Liuzhou, has a diverse ethnic composition, which may contribute to the genetic variability and susceptibility to CHDs. Studies have shown that certain genetic mutations and syndromes are associated with an increased risk of CHDs.[27] In this context, the genetic background of the population in Nanning and Liuzhou may explain the higher incidence of CHDs. Secondly, environmental factors contribute to the high prevalence of CHDs in these cities. Air pollution, particularly from industrial emissions and traffic, has been linked to an increased risk of CHDs. Liuzhou, as industrial cities, may have higher levels of air pollutants, which can affect fetal development and increase the likelihood of CHDs.[28] Furthermore, socioeconomic factors play a crucial role in the prevalence of CHDs. Nanning and Liuzhou, while economically developing, may still have disparities in healthcare access and quality. Limited access to prenatal care, diagnostic facilities, and specialized treatment can delay the detection and management of CHDs, leading to higher prevalence rates. Additionally, socioeconomic status can influence maternal health behaviors, such as nutrition, smoking, and alcohol consumption, which are known risk factors for CHDs. Several studies have investigated the prevalence and risk factors of CHDs in Guangxi, including Nanning and Liuzhou. For instance, a study by Jing et al analyzed the monitoring results of CHDs among PIs in Guangxi from 2011 to 2015 and found an average prevalence rate of 17.00 per 10000 PIs, with an upward trend.[29] Another study by Peng et al examined the data on CHDs among PIs in Guangxi, and observed a similar trend of increasing prevalence.[14] These studies highlight the need for comprehensive prevention and intervention measures to reduce the burden of CHDs in the region. In conclusion, the higher prevalence of CHDs among PIs in Nanning and Liuzhou, Guangxi, is due to a combination of genetic, environmental, and socioeconomic factors. Addressing these factors through targeted interventions, such as improving air quality, enhancing access to healthcare, and promoting healthy lifestyles, is crucial for reducing the prevalence of CHDs in the region.

Thirdly, the prevalence of CHDs increased significantly year by year during the study period in Guangxi. The prevalence of CHDs in Guangxi significantly increased from 20.67 per 10000 PIs in 2016 to 54.01 per 10000 PIs in 2020 in Guangxi, with an average annual growth rate of 27.13%. This phenomenon might be explained by the following two reasons. On the one hand, GXBDMN was a hospital-based surveillance system for BDs. The information of fetuses who were born with CHDs and their mothers was recorded exactly in it, including basic clinical information and diagnosis information for CHDs. The GXBDMN is the most accurate source of information for all CHDs fetuses and their mothers since 2016. On the other hand, the gradual improvement of integrated prenatal and postpartum screening and diagnostic networks for BDs, as well as the continual improvement of screening and diagnostic capabilities.[8] This has enabled the diagnosis of patients with asymptomatic and mild CHDs.[8] The prevalence of CHDs in the world remained largely unchanged from 1990 to 2019.[5] The global level experienced a slight increase from 171.61 per 10000 births in 1990 to 178.76 per 10000 births in 2017.[17,18] The prevalence of CHDs in newborns (≤ 28 days) in China has slightly decreased from about 238.00 per 10000 births in 1990 to about 235.00 per 10000 births in 2019.[8] However, the prevalence of CHDs was increasing in some other provinces of China, such as Beijing, where the prevalence increased by 30.70% from 2018 to 2020.[20] The prevalence of CHDs in Zhejiang increased by 62.20% from 2014 to 2018.[21] In conclusion, specifically, the increasing prevalence of CHDs in Guangxi can be attributed to several factors. Firstly, genetic mutations play a crucial role, which may lead to structural abnormalities of the heart.[30] Secondly, maternal infections during pregnancy can interfere with the normal development of the fetal cardiovascular system, resulting in congenital heart disease.[31,32] Furthermore, maternal malnutrition can also affect fetal heart development.[33] Pregnant women should maintain a balanced diet during pregnancy to ensure adequate intake of vitamins and minerals to support fetal health.

Fourthly, the prevalence of CHDs in Guangxi had a significant upward trend with maternal age. The increase in CHDs prevalence may be partly attributed to the increase in the number of high-risk pregnant women.[8] In particular, the universal two-child policy (implemented since 2016) has been associated with an increase in maternal age.[34,35] For another, notable sex disparities persisted.[16] There is a higher susceptibility to specific diseases on the Y chromosome than on the X chromosome.[36] The sex bias in gene expression may be caused by differences in the dosage of X-linked genes.[36] In 2017, the global prevalence of CHDs was higher in males (191.00 per 10000 births) than in females (166.00 per 10000 births), which precisely confirms this theory.[17] However, some other research showed that the prevalence of CHDs in females was significantly higher than that in males.[37,38] While some others showed that CHDs were equally distributed between males and females.[39] In this study, regarding gender, CHDs were roughly equally distributed between males and females. Moreover, different maternal delivery seasons might result in a significant difference in the prevalence of CHDs.[25] However, this study did not find a seasonal trend in the prevalence of CHDs, despite calculating the prevalence based on the birth time of fetuses.

Fifthly, ASD/PFO, PDA, VSD, AVSD, PLSVC, and TOF were the top six subtypes of CHDs in Guangxi, China. Among the top six subtypes of CHDs, except for AVSD, an increase in the prevalence of others was found. However, although the above results of this study differ from those of the world, China, and other regions of China, CHDs patients are mainly asymptomatic or mild. VSD and ASD were the two most common subtypes of CHDs worldwide. They had a total prevalence of 52.90 per 10000 births and accounted for approximately 29.6% of all CHDs cases.[17] The change in the global birth prevalence of VSD, ASD, and PDA explained 93.40% of the increased overall prevalence of CHDs between 1970 and 2017.[40] From 1995 to 2015, there was a significant increase in the prevalence of AVSD and ASD according to the European Surveillance of Congenital Anomalies (EUROCAT) network.[41] From 1990 to 2018, there was a total prevalence of AVSD in Denmark of 3.9 per 10000 births.[42] Between 2011 and 2012, a Chinese multicenter prospective screening study revealed that VSD, ASD, PDA, pulmonary stenosis (PS), TOF, and transposition of the great arteries (TGA).[38] They have a prevalence of 33.00, 17.00, 7.80, 7.30, 4.70, and 3.50 per 10000 live births respectively.[38] In Zhejiang province of China, ASD, PDA, and VSD were the three most prevalent subtypes of CHDs during 2014–2018.[21] Which account for 67.9%, 34.7%, and 6.4% of all CHDs cases respectively.[21] A hospital-based CHDs surveillance data from 2012 to 2016 in Hunan province of China showed that the 3 most common subtypes of CHDs of fetuses were VSD, TOF, and AVSD.[22] Which account for 22.06%, 9.43%, and 6.69% of all CHDs cases respectively.[22] While among PIs, ASD, PDA, and VSD were the three most common subtypes of CHDs, accounting for 42.81%, 16.07%, and 15.21% of all CHDs cases, respectively.[22] This phenomenon may be caused by the gradual improvement of integrated prenatal and postpartum screening and diagnostic networks for BDs and the continual improvement of screening and diagnostic capabilities.[8] This causes the likelihood of diagnosing asymptomatic and mild CHDs patients to increase.[8] The major role of improving postnatal screening and detecting less severe CHDs lesions is consistent with this.[40] Despite this, screening and diagnostic capabilities are constantly being improved. The study found that only 13.89% of PIs were diagnosed with CHDs during their antenatal care. CHDs had a lower prenatal diagnosis rate than total BDs (19.84%) in the previous study.[43] The previous study only had 32.78% of PIs diagnosed with prenatal ultrasound,[43] but in this study, 86.65% of PIs used prenatal ultrasound to diagnose CHDs. Even though CHDs is a structural BDs. The current ultrasound diagnostic techniques and the expertise of ultrasound doctors may still result in a relatively low prenatal diagnosis rate for CHDs.

The prevention and treatment of CHDs is a complex and systematic endeavor. Based on this study, the authors propose the following public health recommendations for the prevention and management of CHDs in Guangxi. (1) Strengthening prenatal screening programs: Expanding and enhancing prenatal screening programs to detect CHDs early, allowing for timely interventions and improved outcomes. (2) Promoting awareness and education: Increasing public awareness about CHDs, its symptoms, and the importance of early diagnosis through educational campaigns and workshops targeted at pregnant women and their families. (3) Improving access to healthcare: Ensuring equitable access to specialized pediatric cardiac care by expanding healthcare facilities and training more specialists in the region. (4) Implementing genetic counseling services: Offering genetic counseling to families with a history of CHDs to inform reproductive choices and provide support. (5) Advocating for policy changes: Encouraging policymakers to allocate more resources towards CHDs prevention and management programs, including funding for research, treatment, and patient support services. These recommendations are grounded in the evidence presented in this study and align with the current public health landscape in Guangxi. It is believed that these measures will contribute significantly to reducing the burden of CHDs in the region.

Strengths and Improvements

This study presented two major strengths. Firstly, GXBDMN was the source of the CHDs data, which was based on all CHDs monitoring hospitals throughout Guangxi. So that the epidemiological characteristics of CHDs during the study period can be presented accurately. Secondly, this study was the first to examine the changing trends in the prevalence of CHDs and the major subtypes of CHDs in Guangxi using a Poisson regression model. As a result, it provides strong evidence for the government to comprehend the epidemiological characteristics of CHDs when they formulate CHDs prevention and control policies.

However, the GXBDMN, a hospital-based BDs surveillance system, was used to collect the CHDs data for this study. Furthermore, since the GXBDMN only monitors fetuses within 7 days after birth. Currently, this study is incapable of tracking and following up infants with physiological CHDs (like PDA and PFO). As a result, there may be a slight deviation in the epidemiological characteristics of CHDs in this study. The best solution could be to establish a population-based CHDs birth cohort in the future.

For another, multivariate analyses were not employed in this study due to the nature of this surveillance data, which may not have sufficient granularity or completeness to support them. Instead, this study focused on PRR as a measure of association between exposure and outcome, recognizing its limitations as a univariate analysis. Future studies need to use more comprehensive data sources to conduct multivariate analyses.

Conclusion

In conclusion, this study provides important insights into a time trend analysis and epidemiological exploration for CHDs. The results indicate that the prevalence of CHDs in Guangxi is rising and has an upward trend with maternal age. ASD/PFO, PDA, VSD, AVSD, PLSVC, and TOF were the top six subtypes of CHDs. These findings have significant implications for the government in the policy-making process of CHDs prevention and control, as they suggest that CHDs constitutes the majority of BDs and is a major public health issue.

Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Ethical Statement

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Maternal and Child Health Hospital of Guangxi Zhuang Autonomous Region (No. 2021-3-24). In addition, the authors have taken all necessary steps to ensure that the individuals involved in this research were informed about the research aims and procedures. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements. Furthermore, the authors affirm that the data accessed and utilized in this study strictly adhered to all relevant data protection and privacy regulations. Specific measures were implemented to safeguard the confidentiality and anonymity of individuals whose data were included in the analysis, ensuring that no personal information could be traced back to any individual participant. The study protocol adhered to the guidelines established by the journal.

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Author Contributions
All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure
The authors report no conflicts of interest in this work.

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