TRENDS IN THE INCIDENCE AND CHARACTERISTICS OF CONGENITAL HEART DISEASE IN LOPBURI PROVINCE, CENTRAL THAILAND, 2017-2021

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Abstract

Background: Congenital heart disease (CHD) is the newborn's most common congenital anomaly. Nevertheless, limited evidence is available of CHD incidence in Thailand. Therefore, we aimed to determine the trends in CHD incidence from 2017 to 2021.

Methods: A descriptive epidemiology study was conducted using data from 2017-2021. We collected data from the medical records of pediatric patients with CHD at the Pediatric Cardiology Clinic at Ananda Mahidol Hospital, central Thailand. The pediatric cardiologist reviewed medical records to obtain participants' characteristics and medical data, including CHD diagnosis, sex, child order and maternal risk factors during pregnancy.

Results: In total, 27,882 live births were recorded between 2017 and 2021 in Lopburi Province, Thailand. The study included 584 pediatric patients with CHD born between 2017 and 2021. Of these, 312 (53.4%) were males, and 89 (15.2%) presented cyanotic CHD. Sex-adjusted CHD incidence was 22.4 per 1000 live-births (95% CI: 17.6-34.5) in 2017; then rose to 25.7 per 1000 live-births (95% CI 21.7-30.2) in 2019 and dropped to 15.4 per 1000 live-births (95% CI 12.1-19.3) in 2021 (p for trend = 0.317). Two hundred and fourteen patients (36.6%) presented a ventricular septal defect. In 2017, the proportion of patients receiving a diagnosis of CHD before one year of age was 57.7% and continuously rose to 100% in 2021 (p-for trend <0.001). The proportion of alcohol consumption during pregnancy was consistently high, ranging from 61.6 to 74.8% (p for trend = 0.189). In addition, contraindicated drug use during the first trimester of pregnancy was also constantly high (73.1%) among study participants over five years (p for trend = 0.235).

Conclusion: CHD incidence in Lopburi Province has been persistently high from 2017 to 2021. The average age at diagnosis with CHD in this study population continuously declined over five years. Characteristics of CHD risk factors during pregnancy constituted a constantly high proportion among these study participants over one half decade.

Keywords: Congenital heart disease, Incidence, Maternal risk factors, Thailand, Trend

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Introduction

Congenital heart disease (CHD) is a newborn's most common congenital anomaly.[1, 2] Global CHD incidence was estimated at 17.2 per 1,000 live births in 1990 and stabilized at 17.9 per 1,000 live births in 2017. Regarding the global report 2017, CHD incidence tended to be higher among males (19.1 per 1,000 live births) than among females (16.6 per 1,000 live births).[1] CHD incidence differed in each global region; compared with a high sociodemographic index (SDI) region, the CHD incidence concerning low SDI was relatively high.[1] Regarding advances in cardiovascular medicine and cardiac surgery over the past decade [3], the global trends in CHD mortality continuously decreased from 1990 to 2017[1]; however, CHD remains a critical cause of morbidity and mortality from a congenital anomaly.[4, 5]

In Thailand, a related study in 2009 reported data on the prevalence of CHD among school children. For instance, a related study in western Thailand reported a CHD prevalence of 1.05 per 1000 children[6], while in 2010, another study in lower north Thailand showed a CHD prevalence of approximately 0.06 per 1000 healthy school children.[7] No evidence of CHD incidence in Thailand is available. Furthermore, maternal risk factors associated with CHD[8–10], including smoking, alcohol consumption and contraindicated drug use during pregnancy, were documented in related studies.[11–13] Therefore, understanding the epidemiology of CHD incidence and knowing the trends of the disease burden of CHD are essential for planning policies and managing CHD in the context of the Thai healthcare system, which has implemented universal health coverage (UHC) since 2002.[14]

In the present study, we aimed to determine the trends in CHD incidence from 2017 to 2021 in Lopburi Province, central Thailand. Furthermore, we also explored the characteristics of pediatric patients with CHD in this study area over five years.

Methods

Ethics approval and consent to participate

The study was reviewed and approved by the Institutional Review Board, RTA Medical Department, Bangkok, Thailand, in compliance with international guidelines such as the Declaration of Helsinki, the Belmont Report, CIOMS Guidelines and the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use—Good Clinical Practice (ICH—GCP) (approval number S040h/65). Because we used secondary data, the Institutional Review Board, RTA Medical Department granted a waiver of informed consent.

Study design and subjects

A descriptive epidemiology study was conducted using data from medical records from 2017 to 2021. We retrieved the data from the Pediatric Cardiology Clinic at Ananda Mahidol Hospital, a tertiary hospital in Lopburi Province. Since 2017, Lopburi Province has had only one pediatric cardiologist (N.N.) at Ananda Mahidol Hospital. Regarding the UHC scheme implemented in Thailand since 2002 [14, 15], all children who had been examined and were patients with suspected CHD from all hospitals in different areas of Lopburi Province would be directed through the coordination center and referred to the Pediatric Cardiology Clinic at Ananda Mahidol Hospital. Typically, clinically screened newborns by physical examination and measuring the oxygen saturation in the hands and feet were performed. [15] Then pediatric patients with suspected CHD would be referred to the Pediatric Cardiology Clinic for a definite diagnosis. All pediatric patients with suspected CHD would be physically examined and investigated at the Pediatric Cardiology Clinic; the pediatric cardiologist (N.N.) would make a definite diagnosis and collect those patients' data at the Pediatric Cardiology Clinic database.

In the present study, we intended to determine trends in CHD incidence per live birth from 2017 to 2021; therefore, the enrolled participants were pediatric patients receiving a diagnosis of

CHD and were born in Lopburi Province from January 1, 2017 to December 31, 2021. The number of live births in Lopburi Province from 2017 to 2021 was obtained from the National Statistical Office (NSO), Thailand.[16] Regarding the NSO data, the total number of live births in Lopburi Province accounted for 6353, 6007, 5486, 5299, and 4737 in 2017, 2018, 2019, 2020 and 2021, respectively.

Data collection

We collected the data from the medical records of pediatric patients with CHD at the Pediatric Cardiology Clinic, Ananda Mahidol Hospital, from 2017 to 2021. The pediatric cardiologist reviewed medical records to obtain participants' characteristics and medical data, for instance, sex, child order, maternal risk factors during pregnancy and signs and symptoms.

CHD diagnosis

We collected information on the symptoms presented to the doctor, CHD diagnosis and treatment plan. The International Statistical Classification of Disease and Related Health Problems, 10th Revision (ICD-10) defined the CHD diagnosis of pediatric patients. (**Supplementary 1**). Patients with innocent cardiac murmurs were excluded from the study.[11–13] Regarding CHD diagnosis, the pediatric cardiologist performed history taking, physical examination, a chest X-ray and electrocardiography. The gold standard for noninvasive imaging in CHD is echocardiography.[17] Based on the information of various procedures, when data were abnormal, an echocardiography examination would be performed for a definitive diagnosis of CHD. Furthermore, pediatric patients with CHD also received appropriate treatment, including medical and surgical treatment.

CHD classification

Regarding the study's aim to determine the characteristics of patients with CHD, we classified CHD lesions in two groups: cyanotic and acyanotic CHD. [22] Cyanotic heart disease is a congenital heart defect resulting when deoxygenated blood bypasses the lungs and enters the systemic circulation, or a mixture of oxygenated and deoxygenated blood enters the systemic circulation. The disease is caused by structural defects in the heart such as right-to-left shunts, bidi rectional shunts, malposition of the great arteries or any condition increasing pulmonary vascular resistance such as D-Transposition of the great arteries (D-TGA), pulmonary atresia; intact ventricular septum/with ventricular septal defect (VSD) and severe Tetralogy of Fallot, tricuspid atresia, single ventricle, double outlet right ventricle, truncus arteriosus, total anomalous pulmonary venous connection, critical pulmonary valve stenosis, hypoplastic left heart syndrome, aortic valve atresia and mitral valve atresia.

Acyanotic heart defect is one type of congenital heart defect. This condition diverts blood from the left to the right side of the heart, most often due to a structural defect in the interventricular septum. Oxyhemoglobin saturation in the patient's systemic circulation often remains at normal levels, such as atrioventricular septal defect, aortic stenosis, pulmonary stenosis, coarctation of the aorta, VSD and patent ductus arteriosus.

Maternal risk factors during pregnancy

Typically, the information on maternal antenatal care, including the history of exposure to occupational and environmental risks and contraindicated drug use, would be recorded in all pregnancy cases. Regarding a history of smoking and alcohol consumption during pregnancy, the data was recorded as yes or no. Other information including a history of exposure to occupational and environmental risks, history of contraindicated drug use, history of infection during pregnancy, and history of the underlying parental disease, would be noted in the medical records when positive findings were observed. The pediatric cardiologist reviewed and retrieved this information in medical records.

Occupations with a history or working environment characteristics of exposure to various chemicals such as pesticides and weed killers, mining dust industrial combustion, hydrocarbon

compounds and heavy metals define maternal occupational and environmental risks. [13] A history of contraindicated drug use during pregnancy included drug groups with a report from the study that could constitute a risk factor for congenital heart disease. Those drugs comprised amphetamines, cannabis and marijuana including anticonvulsant drugs, e.g., lithium and sodium valproate. Hormonal drugs included estrogen, progesterone or a combined oral contraceptive pill, isotretinoin. Antihypertensive drugs included angiotensin-converting enzyme inhibitors, beta blockers and renin-angiotensin system blockers. Nonsteroidal anti-inflammatory drugs (NSAIDs) included aspirin, ibuprofen, naproxen, diclofenac and indomethacin.[18–20]

In terms of maternal infection, we included viral infections during pregnancy in the first trimester, such as Hepatitis B virus (HBV), cytomegalovirus (CMV), herpes simplex virus (HSV) or coxsackie virus, which are diagnosed by physical examination with characteristic symptoms.[21] Parental underlying diseases included maternal diseases such as type 1 or type 2 diabetes mellitus, hypertension, CHD, diseases of connective tissue and immune deficiency and epilepsy, which by itself or having continued use of medications to treat that particular disease would have the opportunity to cause CHD in the child. In addition, information on a history of CHD among parents, which is related and unrelated to certain genetic diseases, was collected. [22]

Statistical analysis

Characteristics of participants were analyzed using descriptive statistics and presented categorical variables as percentages. Continuous variables like age were presented as mean and standard deviation (SD). The study's outcome was the cumulative CHD incidence each year from 2017 to 2021, presented as incidence per 1000 live births and 95% confidence interval (CI). Sex-adjusted CHD incidence was standardized by sex distribution of live births in the 2017 Thailand census. Sex-specific CHD incidence each year was also calculated. The *Cochran–Armitage* trend test was employed for CHD incidence to test the statistical significance of trends from 2017 to 2021. The *chi*-squared test was used to compare the different distributions of categorical data. All statistical tests were two-sided, and a *p*-value less than 0.05 was considered statistically significant. All statistics were analyzed using Stata Corp. 2021 *Stata Statistical Software: Release 17*. College Station, TX: Stata Corp LLC.

Results

Characteristics of study participants

Between 2017 and 2021, 27,882 live births were recorded in Lopburi Province, Thailand. Of those, 14,217 (51.1%) were males. The present study included 584 pediatric patients with CHD born from 2017 to 2021. In all, 312 (53.4%) were males, and 294 (50.3%) were first-child orders (**Table 1**).

Incidence of CHD in Lopburi Province, central Thailand, 2017 to 2021

Table 1 shows CHD incidence per 1000 live births from 2017 to 2021. Sex-adjusted CHD incidence was 22.4 per 1000 live-births (95% CI: 17.6 to 34.5) in 2017, then rose to 25.7 per 1000 live-births (95% CI 21.7-30.2) in 2019 and dropped to 15.4 per 1000 live-births (95% CI 12.1-19.3) in 2021 (*p* for trend = 0.317). Among males, CHD incidence was 26.3 per 1000 live births (95% CI: 21.1 to 32.4) in 2017, then dropped to 18.1 per 1000 live births (95% CI: 13.7 to 23.5) in 2018. After that, it rose to 24.5 and 23.7 per 1,000 live births in 2019 and 2020, respectively. In 2021, the CHD incidence among males declined to 16 per 1000 live births (95% CI 11.4 to 21.8), *p* for trend = 0.104 (**Figure 1**). Likewise, the CHD incidence among females also fluctuated. It totaled 18.3 per 1000 live births (13.9 to 23.6) in 2017, then rose to 26.9 per 1000 live births (21.1 to 33.8) in 2019 and dropped to 14.8 per 1000 live births (10.3 to 20.6) in 2021, *p* for trend = 0.759. However, in 2017, a significant difference was observed in CHD incidence between males and females, $p = 0.03$.

CHD diagnosis among pediatric patients with CHD in central Thailand

Table 2 shows the diagnosis of CHD from 2017 to 2021. Of 584 pediatric patients with CHD, VSD and atrial septal defect (ASD) were

Table 1. Incidence of Congenital Heart Disease/1000 live births in central Thailand from 2017 to 2021

		2017	2018	2019	2020	2021	*p* for trend
Overall							
Number of live birth	27,882	6,353	6,007	5,486	5,299	4,737	
CHD cases	584	142	103	141	125	73	
Incidence (case/1,000 live births)	20.9	22.4	17.1	25.7	23.6	15.4	0.329
95% CI	19.3-22.7	18.9-26.3	14.0-20.8	21.7-30.2	19.7-28.0	12.1-19.3	
Sex-adjusted incidence* (case/1000 live births)	20.9	22.4	17.2	25.7	23.6	15.4	0.317
95% CI	19.3-22.7	17.6-34.5	14.2-20.8	21.7-30.2	19.7-28.0	12.1-19.3	
Male							
Number of live birth	14,217	3,232	3,035	2,813	2,698	2,439	
CHD cases	312	85	55	69	64	39	
Incidence (case/1,000 live births)	21.9	26.3	8.1	24.5	23.7	16	0.104
95% CI	19.6-24.5	21.1-32.4	13.7-23.5	19.1-30.9	18.3-30.2	11.4-21.8	
Female							
Number of live-birth	13,665	3,121	2,972	2,673	2,601	2,298	
CHD cases	272	57	48	72	61	34	
Incidence (case/1,000 live births)	19.9	18.3	16.2	6.9	23.5	14.8	0.759
95% CI	17.6-22.4	13.9-23.6	11.9-21.4	21.1-33.8	18.0-30.0	10.3-20.6	
***p*-value (male vs. female)**	0.234	0.03	0.556	0.573	0.949	0.739	

* Sex-adjusted CHD incidence was standardized by sex distribution of live births in the 2017 Thailand census

CHD = congenital heart disease

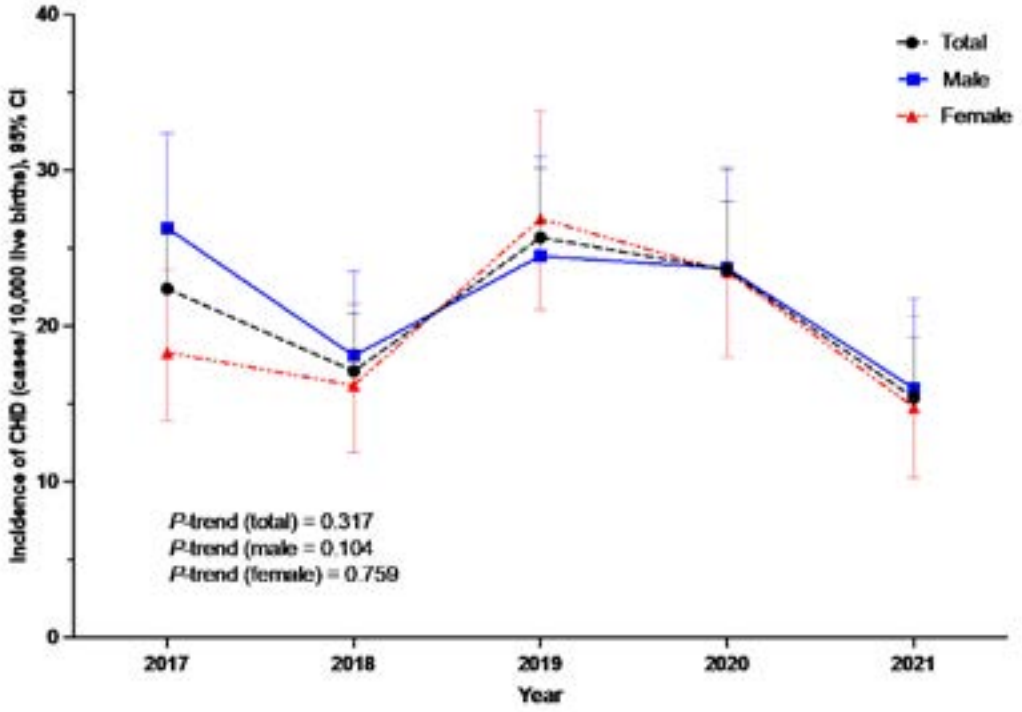

Figure 1. Incidence of Congenital Heart Disease/1000 live births (95% CI) in central Thailand from 2017 to 2021; the error bar demonstrates the 95% CI of the incidence (case/1000 live births)

the most common diagnoses among this study's participants. In all, 214 (36.6%) and 124 (21.2%) pediatric patients with CHD had VSD and ASD, respectively. At the same time, pediatric CHD patients were diagnosed with congenital pulmonary valve stenosis and patent ductus arteriosus, accounting for 11.1% and 7.5%, respectively.

Characteristics of pediatric patients with CHD in central Thailand

Table 3 shows the characteristics of pediatric patients with CHD from 2017 to 2021. The average age at diagnosis with CHD in this study population continuously decreased over five years (*p* for trend <0.001) and 69.9% of study participants received a diagnosis of CHD at <1 year old. In 2017, the proportion of pediatric patients receiving a diagnosis of CHD before one year of age totaled 57.7% and continuously rose to 61.2% in 2018, 66% in 2019, 77.6% in 2020 and 100% in 2021 (*p* for trend <0.001).

Regarding symptoms related to CHD, most pediatric patients with CHD presented cardiac murmur, accounting for 92% over five years. Furthermore, 78.3% of study participants presented growth delay. In all, 84.8% of pediatric patients with CHD exhibited acyanosis. In this group of patients, all individuals reported experiencing palpitations and dyspnea, followed by lower respiratory tract infections (90.8%), cardiac murmurs (85.1%) and growth delays (84.7%) (**Table 4**).

Regarding surgical or interventional treatment, 392 (76.1%) pediatric patients with CHD received surgical or interventional treatment. With CHD classification, pediatric patients with acyanotic CHD received definitive or palliative surgical or interventional treatment, accounting for 82.1%, while 17.9% of those with cyanotic CHD received surgical or interventional treatment (**Table 4**).

Characteristics of CHD risk factors during pregnancy

Risk factors for CHD during pregnancy among this study's participants are presented in **Table 3.** From 2017 to 2021, the proportion of maternal alcohol consumption during pregnancy

Table 2. CHD diagnosis among pediatric patients with CHD in central Thailand, from 2017 to 2021

Congenital Heart Disease (CHD)	n (%)	2017 n (%)	2018 n (%)	2019 n (%)	2020 n (%)	2021 n (%)
Total	**584**	**142**	**103**	**141**	**125**	**73**
Diagnosis						
Ventricular septal defect	214 (36.6)	56 (39.4)	40 (38.8)	57 (40.4)	41 (32.8)	20 (27.4)
Atrial septal defect	124 (21.2)	21 (14.8)	26 (25.2)	27 (19.1)	31 (24.8)	19 (26)
Congenital pulmonary valve stenosis	65 (11.1)	18 (12.7)	14 (13.6)	9 (6.4)	12 (9.6)	12 (16.4)
Patent ductus arteriosus	44 (7.5)	9 (6.3)	6 (5.8)	13 (9.2)	12 (9.6)	4 (5.5)
Tetralogy of Fallot	39 (6.7)	11 (7.7)	5 (4.9)	10 (7.1)	6 (4.8)	7 (9.6)
Atrioventricular septal defect	17 (2.9)	5 (3.5)	1 (1)	6 (4.3)	5 (4)	N/A
Double outlet right ventricle	13 (2.2)	6 (4.2)	1 (1)	4 (2.8)	N/A	2 (2.7)
Stenosis of pulmonary artery	12 (2.1)	3 (2.1)	2 (1.9)	4 (2.8)	2 (1.6)	1 (1.4)
Congenital malformation of great arteries, unspecified	10 (1.7)	1 (0.7)	2 (1.9)	3 (2.1)	4 (3.2)	N/A
Coarctation of aorta	6 (1)	1 (0.7)	2 (1.9)	N/A	2 (1.6)	1 (1.4)
Congenital stenosis of aortic valve	5 (0.9)	2 (1.4)	N/A	1 (0.7)	1 (0.8)	1 (1.4)
Pulmonary infundibular stenosis	5 (0.9)	N/A	1 (1)	1 (0.7)	1 (0.8)	2 (2.7)
Congenital insufficiency of aortic valve	4 (0.7)	1 (0.7)	1 (1)	N/A	1 (0.8)	1 (1.4)
Atresia of pulmonary artery	3 (0.5)	N/A	1 (1)	1 (0.7)	1 (0.8)	N/A
Primary pulmonary hypertension	3 (0.5)	2 (1.4)	N/A	1 (0.7)	N/A	N/A
Pulmonary valve atresia	3 (0.5)	N/A	N/A	2 (1.4)	N/A	1 (1.4)
Aortopulmonary septal defect	2 (0.3)	N/A	N/A	N/A	2 (1.6)	N/A
Congenital malformation of cardiac septum, unspecified	2 (0.3)	2 (1.4)	N/A	N/A	N/A	N/A
Dextrocardia	2 (0.3)	1 (0.7)	N/A	1 (0.7)	N/A	N/A
Mitral insufficiency	1 (0.2)	N/A	N/A	N/A	1 (0.8)	N/A
Anomalous portal venous connection	1 (0.2)	N/A	N/A	N/A	1 (0.8)	N/A
Aortic (valve) insufficiency	1 (0.2)	1 (0.7)	N/A	N/A	N/A	N/A
Aortic (valve) stenosis with insufficiency	1 (0.2)	N/A	N/A	N/A	N/A	1 (1.4)

Table 2. CHD diagnosis among pediatric patients with CHD in central Thailand from 2017 to 2021 (Cont.)

Congenital Heart Disease (CHD)	n (%)	2017 n (%)	2018 n (%)	2019 n (%)	2020 n (%)	2021 n (%)
Dilated cardiomyopathy	1 (0.2)	N/A	1 (1)	N/A	N/A	N/A
Ebstein's anomaly	1 (0.2)	1 (0.7)	N/A	N/A	N/A	N/A
Mitral (valve) insufficiency	1 (0.2)	N/A	N/A	1 (0.7)	N/A	N/A
Mitral valve disease, unspecified	1 (0.2)	N/A	N/A	N/A	1 (0.8)	N/A
Non-rheumatic mitral valve disorder, unspecified	1 (0.2)	N/A	N/A	N/A	N/A	1(1.4)
Hypertrophic cardiomyopathy	1 (0.2)	1 (0.7)	N/A	N/A	N/A	N/A
Tricuspid insufficiency	1 (0.2)	N/A	N/A	N/A	1 (0.8)	N/A

CHD = congenital heart disease

Table 3. Characteristics of pediatric patients with congenital heart disease in central Thailand from 2017 to 2021

Year		2017	2018	2019	2020	2021	*p* for trend
Characteristics	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	
Sex							0.196
Male	312 (53.4)	85 (59.9)	55 (53.4)	69 (48.9)	64 (51.2)	39 (53.4)	
Female	272 (46.6)	57 (40.1)	48 (46.6)	72 (51.1)	61 (48.8)	34 (46.6)	
Child order							0.166
1st order	294 (50.3)	81 (57)	51 (49.5)	67 (47.5)	58 (46.4)	37 (50.7)	
2nd order	290 (49.7)	61 (43)	52 (50.5)	74 (52.5)	67 (53.6)	36 (49.3)	
Age at a definite diagnosis							<0.0001
<1 year	408 (69.9)	82 (57.7)	63 (61.2)	93 (66)	97 (77.6)	73 (100)	
≥1 years	176 (30.1)	60 (42.3)	40 (38.8)	48 (34)	28 (22.4)	0 (0)	
Mean (95% CI)	0.6 (0.5-0.7)	0.8 (0.6-1.0)	0.8 (0.6-1.0)	0.7 (0.5-0.8)	0.4 (0.3-0.6)	0 (0-0)	<0.0001
Surgical/ interventional treatment							0.323
No	192 (32.9)	39 (27.5)	38 (36.9)	49 (34.8)	39 (31.2)	27 (37)	
Yes	392 (67.1)	103 (72.5)	65 (63.1)	92 (65.2)	86 (68.8)	46 (63)	
Symptoms							
Growth delay							0.591
No	127 (21.7)	28 (19.7)	22 (21.4)	34 (24.1)	26 (20.8)	17 (23.3)	
Yes	457 (78.3)	114 (80.3)	81 (78.6)	107 (75.9)	99 (79.2)	56 (76.7)	
Lower respiratory tract infection							0.703
No	519 (88.9)	128 (90.1)	91 (88.3)	123 (87.2)	114 (91.2)	63 (86.3)	
Yes	65 (11.1)	14 (9.9)	12 (11.7)	18 (12.8)	11 (8.8)	10 (13.7)	
Murmur							0.409
No	47 (8)	8 (5.6)	9 (8.7)	13 (9.2)	11 (8.8)	6 (8.2)	
Yes	537 (92)	134 (94.4)	94 (91.3)	128 (90.8)	114 (91.2)	67 (91.8)	
Palpitation							0.464
No	582 (99.7)	142 (100)	102 (99)	141 (100)	125 (100)	72 (98.6)	
Yes	2 (0.3)	0 (0)	1 (1)	0 (0)	0 (0)	1 (1.4)	

Table 3. Characteristics of pediatric patients with congenital heart disease in central Thailand from 2017 to 2021 (Cont.)

Year		2017	2018	2019	2020	2021	*p* for trend
Characteristics	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	
Chest pain							N/A
No	584 (100)	142 (100)	103 (100)	141 (100)	125 (100)	73 (100)	
Yes	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Cyanosis							0.954
No	495 (84.8)	119 (83.8)	91 (88.3)	115 (81.6)	110 (88)	60 (82.2)	
Yes	89 (15.2)	23 (16.2)	12 (11.7)	26 (18.4)	15 (12)	13 (17.8)	
Dyspnea							0.552
No	583 (99.8)	142 (100)	102 (99)	141 (100)	125 (100)	73 (100)	
Yes	1 (0.2)	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)	
Syncope							N/A
No	584 (100)	142 (100)	103 (100)	141 (100)	125 (100)	73 (100)	
Yes	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Risk Factors							
Infection during pregnancy							0.364
No	562 (96.2)	136 (95.8)	99 (96.1)	133 (94.3)	123 (98.4)	71 (97.3)	
Yes	22 (3.8)	6 (4.2)	4 (3.9)	8 (5.7)	2 (1.6)	2 (2.7)	
Drug use during pregnancy							0.235
No	157 (26.9)	38 (26.8)	23 (22.3)	38 (27)	31 (24.8)	27 (37)	
Yes	427 (73.1)	104 (73.2)	80 (77.7)	103 (73)	94 (75.2)	46 (63)	
Alcohol use during pregnancy							0.189
No	168 (28.8)	38 (26.8)	26 (25.2)	44 (31.2)	32 (25.6)	28 (38.4)	
Yes	416 (71.2)	104 (73.2)	77 (74.8)	97 (68.8)	93 (74.4)	45 (61.6)	

Table 3. Characteristics of pediatric patients with congenital heart disease in central Thailand from 2017 to 2021 (Cont.)

Year		2017	2018	2019	2020	2021	*p* for trend
Characteristics	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	
Smoking during pregnancy							0.993
No	519 (88.9)	127 (89.4)	91 (88.3)	123 (87.2)	114 (91.2)	64 (87.7)	
Yes	65 (11.1)	15 (10.6)	12 (11.7)	18 (12.8)	11 (8.8)	9 (12.3)	
Occupational and environmental risks							0.819
No	121 (20.7)	28 (19.7)	20 (19.4)	34 (24.1)	23 (18.4)	16 (21.9)	
Yes	463 (79.3)	114 (80.3)	83 (80.6)	107 (75.9)	102 (81.6)	57 (78.1)	
Parents having CHD							0.184
No	579 (99.1)	141 (99.3)	103 (100)	141 (100)	122 (97.6)	72 (98.6)	
Yes	5 (0.9)	1 (0.7)	0 (0)	0 (0)	3 (2.4)	1 (1.4)	
Parents having comorbidities							0.897
No	538 (92.1)	131 (92.3)	94 (91.3)	129 (91.5)	120 (96)	64 (87.7)	
Yes	46 (7.9)	11 (7.7)	9 (8.7)	12 (8.5)	5 (4)	9 (12.3)	

CHD = congenital heart disease

Table 4. Characteristics of pediatric patients with congenital heart disease in central Thailand by cyanosis

Characteristics	No Cyanosis n (%)	Cyanosis n (%)	*p*-value
Sex			0.413
Male	268 (85.9)	44 (14.1)	
Female	227 (83.5)	45 (16.5)	
Child order			0.783
1st order	248 (84.4)	46 (15.6)	
2nd order	247 (85.2)	43 (14.8)	
Age at a definite diagnosis			0.011
<1 year	356 (87.3)	52 (12.7)	
≥1 years	139 (79)	37 (21)	
Surgical/ interventional treatment			0.012
No	173 (90.1)	19 (9.9)	
Yes	322 (82.1)	70 (17.9)	
Symptoms			
Growth delay			0.921
No	108 (85)	19 (15)	
Yes	387 (84.7)	70 (15.3)	
Lower respiratory tract infection			0.153
No	436 (84)	83 (16)	
Yes	59 (90.8)	6 (9.2)	
Murmur			0.437
No	38 (80.9)	9 (19.1)	
Yes	457 (85.1)	80 (14.9)	
Palpitation			0.548
No	493 (84.7)	89 (15.3)	
Yes	2 (100)	0 (0)	
Chest pain			N/A
No	495 (84.8)	89 (15.2)	
Yes	0 (0)	0 (0)	
Dyspnea			0.671
No	494 (84.7)	89 (15.3)	
Yes	1 (100)	0 (0)	
Syncope			N/A
No	495 (84.8)	89 (15.2)	
Yes	0 (0)	0 (0)	
Infection during pregnancy			0.696
No	477 (84.9)	85 (15.1)	
Yes	18 (81.8)	4 (18.2)	
Drug use during pregnancy			0.81
No	134 (85.4)	23 (14.6)	
Yes	361 (84.5)	66 (15.5)	

Table 4. Characteristics of pediatric patients with congenital heart disease in central Thailand by cyanosis (Cont.)

Characteristics	No Cyanosis n (%)	Cyanosis n (%)	*p*-value
Alcohol use during pregnancy			0.878
No	143 (85.1)	25 (14.9)	
Yes	352 (84.6)	64 (15.4)	
Smoking during pregnancy			0.153
No	436 (84)	83 (16)	
Yes	59 (90.8)	6 (9.2)	
Occupational and environmental risks			0.874
No	102 (84.3)	19 (15.7)	
Yes	393 (84.9)	70 (15.1)	
Parents having CHD			0.766
No	491 (84.8)	88 (15.2)	
Yes	4 (80)	1 (20)	
Parents having comorbidities			0.39
No	454 (84.4)	84 (15.6)	
Yes	41 (89.1)	5 (10.9)	

CHD = congenital heart disease

among pediatric patients with CHD was consistently high, ranging from 61.6 to 74.8% (*p* for trend 0.189). In addition, maternal contraindicated drug use during the first-trimester pregnancy was also constantly high (73.1%) among study participants over five years (*p* for trend 0.235). Furthermore, among pediatric patients with acyanotic CHD, approximately 84% reported maternal alcohol consumption during pregnancy and contraindicated drug use (**Table 4**).

Regarding occupational and environmental risks, from 2017 to 2021, 79.3% of pediatric patients with CHD reported maternal exposure to occupational and environmental risks during pregnancy. The constantly high proportion of occupational and environmental risks over five years was also observed (*p* for trend 0.819). Among pediatric patients with acyanotic CHD, approximately 85% experienced maternal exposure to occupational and environmental risks during pregnancy (**Table 4**). For infection during pregnancy, the proportion of pediatric patients with CHD presented a maternal infection, accounting for 4.2% in 2017, and dropping to 2.7% in 2021.

Discussion

The current study successfully included 584 pediatric patients with CHD in Lopburi Province, central Thailand, from 2017 to 2021. To our knowledge, this constitutes the first and updated report on trends in CHD incidence and characteristics in Thailand. CHD incidence in the present study has been constantly high over five years. Males were more likely to have CHD than females, and VSD and ASD were the most common CHD diagnoses among study participants. The average age at diagnosis with CHD in this study population continuously decreased over five years; moreover, the proportion of pediatric patients receiving a diagnosis of CHD before one year of age significantly rose from 2017 to 2021. Characteristics of CHD risk factors during pregnancy, including alcohol consumption, contraindicated drug use and occupational and environmental risks, comprised a constantly large proportion among these study participants over one half decade.

A global report indicated that the CHD incidence rate remained stable between 1990 and 2017. [1] Likewise, our study demonstrated stable trends in CHD incidence in central Thailand from 2017 to 2020 but declined in 2021. The reduced fertility rate may explain this phenomenon with better pregnancy screening and antenatal planning during the COVID-19 pandemic. [23] Therefore, revealing the information on CHD in the long run after the COVID-19 pandemic will be necessary.

In the present study, we reported that overall CHD incidence was 20.9 per 1,000 live births, which had been constantly high between 2017 and 2021. It indicated that CHD incidence in the current study was relatively high compared with the global CHD incidence in 2017, which was estimated at 17.9 per 1,000 live births.[8] Our study indicated that CHD incidence in Thailand was far higher than in countries with a high middle sociodemographic index, reporting 11.8 CHD cases per 1,000 live births in 2017.[8] In Thailand, a few related studies reported data on the prevalence of CHD among school children and adults. For instance, a related study in Tak Province, Thailand, reported a CHD prevalence of 1.05 per 1000 elementary school children in 2009 [6], while in 2010, another study in lower northern Thailand demonstrated a prevalence of CHD of approximately 0.06 per 1000 healthy school children.[7] Furthermore, a study from a university hospital in Bangkok was conducted among adult patients, showing that the CHD prevalence between 2003 and 2013 was approximately 4%. [24] Unfortunately, the results of these studies are difficult to compare because of different study populations and designs. However, our results indicated that CHD in central Thailand remains an essential health issue among children.

Regarding characteristics of pediatric patients with CHD, our study found that CHD incidence among males was more likely than among females, which was compatible with the global report.[1] A related study also emphasized that compared with females, mortality was more significant among males with CHD.[25] In line with the related literature[7, 26], approximately 90% of CHD cases were acyanotic CHD, and VSD was the most common lesion of CHD, followed by ASD. Our findings agreed with the related evidence[7, 26] that only one tenth of CHD involved cyan is related to severe CHD; moreover, we also found that approximately one third and one fifth of study participants presented VSD and ASD, respectively.

Our results demonstrated that the average age at diagnosis with CHD constantly decreased since 2017, and in 2021, 100% of pediatric patients with CHD received a definite diagnosis before one year. This finding reflects the advantages of Thailand's health system, especially in this study area, including the universal health coverage scheme implemented since 2002, the seamless referral system, advancements in the CHD screening process and the availability of pediatric cardiologists in Lopburi Province leading to reduced waiting times for diagnosis.

Our study reported that two fifths of pediatric patients with CHD received surgical or interventional treatment regarding CHD severity. Of those receiving the surgical treatment, 17.9% were cyanotic CHD, while one to ten patients without surgical treatment had acyanotic CHD. To date, according to the advancement of treatment technology, pediatric patients with minor lesions of CHD receive the current treatment as a cardiac catheter and a closed device instead of open-heart surgery, bringing significant benefits to patients in alleviating complications after surgery and reducing hospital stays. [21, 22] On the other hand, in cases of severe symptoms, patients with CHD would be sent for open heart surgery, which could only be performed in university and regional hospitals.

Related evidence documented various maternal risk factors associated with CHD, including smoking, alcohol consumption and contraindicated drug use during pregnancy. [11–13] In the present study, we did not obtain an opportunity to measure an association between maternal risk factors during pregnancy and CHD because only CHD cases were included. However, we found a large proportion of these maternal risk factors among pediatric patients with CHD, which were constantly high over

five years. These findings may explain the high CHD incidence in this area and reflect this population's health literacy problems and health risk behaviors. Therefore, our study suggested that maternal health literacy should be improved. For instance, evidence supporting group antenatal care can improve maternal health literacy, increase healthy behaviors, improve the quality of care and improve maternal and newborn outcomes. [29]

Many industrial factories and agricultural industries are distributed in this study site; early pregnant women may be exposed to occupational and environmental risks such as chemical substances throughout their living areas or working careers, affecting the newborn's development.[12] Thus, other than improving maternal health literacy, community participation, including local authorities, employers and community members, should be aware of these health risks and collaborate to solve these health challenges. [30,31]

This study encountered several limitations. Firstly, this constituted a descriptive epidemiology study in which we collected data from the Pediatric Cardiology Clinic at Ananda Mahidol Hospital; consequently, suspected pediatric patients with CHD attending other hospitals outside Lopburi Province would be excluded from the present study. Therefore, the incidence of CHD in the present study may have been underestimated. However, regarding implementing the UHC scheme in Thailand, between 2017 and 2021, all CHD cases in Lopburi Province should have received a diagnosis at this Pediatric Cardiology Clinic. Secondly, regarding the variability of healthcare facilities in different hospitals in Lopburi Province, the screening process to detect pediatric patients with suspected CHD to receive a definite diagnosis at the Pediatric Cardiology Clinic could have underestimated CHD incidence in the present study. Thirdly, although at present, echocardiography is the gold standard for noninvasive imaging in CHD, the existing literature demonstrated that diagnostic errors in pediatric echocardiography could occur, especially among patients weighing less than 5 kg.[32] Fourthly, we lacked the opportunity to collect data on exposure among individuals without CHD; hence, in the present study, the association between exposure and incidence of CHD was not evaluated. However, we could report characteristics of CHD risk factors in only the proportion and trend of maternal risk factors among pediatric patients with CHD. Consequently, further study using a case-control design may be helpful to explore the association between exposures and CHD. Fifth, regarding the retrospective data, the information on maternal risk factors was recorded in the medical records as positive findings, and we cannot guarantee that if the information did not appear in medical records, it would remain unexposed; accordingly, misclassification may have occurred. Finally, the study was conducted in Lopburi Province, so the results may not be generalized to the whole country. However, it may reflect the actual situation in this province in central Thailand, where a pediatric cardiologist is available.

Conclusion

CHD incidence in central Thailand remained persistently high from 2017 to 2021, and VSD and ASD were the most common CHD diagnoses among study participants. The average age at diagnosis with CHD in this study population continuously declined over five years. Maternal risk factors for CHD during pregnancy including alcohol consumption, contraindicated drug use and occupational and environmental risks in the first trimester of pregnancy, revealed a constantly large proportion among these study participants.

Availability of data and materials

The datasets generated or analyzed during the current study are not publicly available; the data sets are available from the author on reasonable request (contact Nutthaporn Narknok via guide-18cardioped@gmail.com)

Competing interests

The authors declare they have no competing interests.

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Authors' contributions

NN and BS developed the concept for the study. NN collected the data. BS analyzed the data. NN and BS wrote the first draft; all authors contributed and approved the final version.

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