Congenital Heart Disease Prevalence in Portugal in 2015: Data from the National Register of Congenital Anomalies

Prevalência de Cardiopatias Congénitas em Portugal em 2015: Dados do Registo Nacional de Anomalias Congénitas

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ABSTRACT

Introduction: The prevalence at birth of congenital heart disease in Portugal is 8.3/1000 births; undetected critical congenital heart disease may result in adverse outcomes for the fetus/newborn infant. This study describes the reported cases of congenital heart disease in Portugal in 2015 regarding antenatal diagnosis, cardiac defect, and presence of other congenital anomalies/chromosomal abnormalities. These indicators are compared in live births and medical pregnancy terminations. Additionally, postnatal deaths were characterized.

Material and Methods: Congenital heart disease data derived from the 2015 Portuguese National Registry of Congenital Birth Defects were analyzed. The prevalence rates per 1000 births were assessed by the chi-square test of independence.

Results: The prevalence of congenital heart disease in this study was 5/1000 live-births (339 live-births, 20% with critical defects). The most common defects were ventricular septal defect (38%), atrial septal defect (15%), aortic coarctation (7%), tetralogy of Fallot (7%) and pulmonary stenosis (5%). One third of the live births had antenatal diagnosis of congenital heart disease. In the live-births with critical congenital heart disease, 54% had antenatal diagnosis and 14% were diagnosed at birth. There were records of 84 pregnancy terminations; 49% had critical defects, 75% had non-cardiac congenital anomalies and 40% had chromosomal abnormalities. There were 15 postnatal deaths recorded (3.4% mortality rate), associated with prematurity/low birthweight, critical congenital heart disease, other non-cardiac congenital anomalies and chromosomal abnormalities.

Discussion: The data analysis revealed a prevalence of congenital heart disease in this study of 5/1000 births (inferior to other international studies), with a distribution per type of anomaly similar to that reported in previously published work. There were significant regional differences that need further studying.

Conclusion: These results are paramount to characterize the Portuguese scenario and improve Healthcare planning. It is important to improve reporting in the Portuguese National Registry of Congenital Birth Defects.

Keywords: Heart Defects, Congenital / epidemiology; Portugal; Registries

RESUMO

Introdução: A prevalência de cardiopatias congénitas em Portugal é de 8,3/1000 nascimentos; cardiopatias congénitas críticas não detectadas podem resultar em graves consequências para o feto/recém-nascido. O objectivo deste trabalho é descrever os casos de cardiopatia congénita reportados em Portugal em 2015 quanto ao diagnóstico pré-natal, patologia cardíaca e à presença de outras malformações congénitas ou anomalias cromossómicas. Estas características são comparadas nos subgrupos dos nados-vivos e de interrupção médica da gravidez. Por último, caracterizam-se os óbitos.

Material e Métodos: Os dados de cardiopatias congénitas reportadas ao Registo Nacional de Anomalias Congénitas em 2015 foram analisados, e calculadas as taxas de prevalência por 1000 nascimentos, comparadas utilizando teste de independência do qui-quadrado.

Resultados: A prevalência de cardiopatias congénitas neste estudo foi de 5/1000, (339 nados-vivos, 20% com cardiopatias congénitas críticas). As cardiopatias mais frequentes foram as seguintes: comunicação interventricular (38%), comunicação interauricular (15%), coartação da aorta (7%), tetralogia de Fallot (7%) e estenose pulmonar (5%). Um terço dos nados-vivos teve diagnostico pré-natal de cardiopatia. Dos nados-vivos com cardiopatias congénitas críticas, 54% teve diagnostico pré-natal e 14% foi diagnosticado ao nascer. Foram identificados 84 registos de interrupção médica da gravidez; 49% apresentava cardiopatias congénitas críticas, 75% outras malformações associadas, e 40% cromossomopatias. Foram registados 15 óbitos (3,4% de mortalidade) associados a prematuridade e/ou baixo-peso ao nascer, cardiopatias congénitas críticas, outras malformações e anomalias cromossómicas.

Discussão: A prevalência de cardiopatias congénitas neste estudo (5/1000 nascimentos) foi inferior ao descrito noutros estudos internacionais, não obstante uma distribuição por tipo de anomalia semelhante ao previamente reportado. Observaram-se assimetrias regionais significativas que necessitam de mais investigação.

Conclusão: Este estudo é relevante para melhor conhecimento da realidade nacional e organização dos Cuidados de Saúde. É importante uma maior adesão ao Registo Nacional de Anomalias Congénitas.

Palavras-chave: Cardiopatias Congénitas/epidemiologia; Portugal; Registos

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INTRODUCTION

Congenital heart diseases are the most frequently diagnosed congenital disorders in Portugal and worldwide,[1] with a commonly quoted prevalence of eight per 1,000 live births[1–3] and the latest data based on the 2014-2015 Portuguese Registry of Congenital Anomalies (*Registo Nacional de Anomalias Congénitas*) (RENAC) with a prevalence of 8.3 per 1,000 live births throughout that period.[3]

It is estimated that one in four congenital heart diseases is a critical heart defect, defined as one in which surgery or percutaneous intervention are required within the first year of life.[4] Potentially life-threatening ductal-dependent congenital heart diseases are included in a narrower definition of critical congenital heart diseases (CCHD) with death as the outcome or in which surgery or percutaneous intervention are required within the first month of life.[5,6]

Despite the advances in prenatal diagnosis (PND), not all CCHD can be detected in utero; on the other hand, appropriate antenatal care is not provided to all pregnant mothers.[7,8] Additionally, considering the significant changes in cardiovascular physiology during the adaptation to extrauterine life, some forms of heart disease only become symptomatic at the end of the first week of life, following spontaneous closure of the ductus arteriosus.[4,6] A cardiogenic shock or sudden death can arise as initial presentations of CCHD within the neonatal period.[8,9]

Pulse oximetry pre-discharge CHD screening is aimed at the early identification of cases that were not detected both antenatally or postnatally, with early presentations of CCHD, before a cardiac decompensation emerges.[6,10] Newborns diagnosed by this screening can be immediately referred for an adequate treatment (surgery and/or percutaneous intervention) under more favourable clinical conditions, with better immediate and long-term outcomes.[4,11]

An improved survival of newborns and infants with CCHD has relevant implications on healthcare delivery and organisation.[12,13] These children, young people and adult patients should remain under follow-up with a cardiologist (often interdisciplinary) and even with an indication for multiple reinterventions.[13]

An improved epidemiological knowledge of the national reality will allow for adequate and organised resources aimed at broader coverage of antenatal and/or postnatal diagnosis, with adequate healthcare delivery to newborns, infants, children and adults with CHDs.

The study's primary goal was to estimate the 2015 CHD prevalence in Portugal. A secondary goal was to estimate the prevalence of CCHD within the same period, according to the moment of diagnosis (pre, peri or postnatal), pregnancy outcome (live birth, miscarriage, stillbirth or termination of pregnancy), type of heart disease, cardiac diagnosis, associated anomalies and presence of chromosomal abnormalities. CCHD were analysed for regional distribution, main diagnoses, PND, presence of other congenital anomalies and chromosomal abnormalities. A comparison has been made between medical terminations of pregnancy *vs.* live births of newborns presenting with CHD in terms of gender of the foetus, presence of CCHD, CHD type, presence of other congenital anomalies and chromosomal abnormalities. Finally, death registered cases were characterised according to age at death, PND, gestational age, birth weight, heart disease and associated non-cardiac anomalies.

MATERIAL AND METHODS

This was a cross-sectional study including all cases of CHD that were notified to the RENAC in 2015.

Registo Nacional de Anomalias Congénitas

The Portuguese *Registo Nacional de Anomalias Congénitas* (RENAC) is a population-based record of all cases of congenital anomalies that were reported in Mainland Portugal and Autonomous Regions of Azores and Madeira from 1997 onwards. Notifications are voluntary, filled in by healthcare professionals with the parents, based on a questionnaire with information regarding pregnancy, maternal consumption habits, family history, prenatal diagnosis, delivery type and autopsy diagnosis. Link staff to the RENAC currently exist at all the Portuguese maternity hospitals (at the departments of Obstetrics and Paediatrics/Neonatology).

Data collection is anonymous and only the liaison at each institution could associate the patient's clinical record with the information in the RENAC database. A formal request for access to data was made and approved in November 2017.

According to the study's inclusion criteria, all cases diagnosed with CHD (ICD-10 codes Q20 to Q26) extracted from the 2015 database were included. The following variables were obtained: date and place of birth, gender, pregnancy outcome, birth weight, gestational age (in weeks), date of the first identification of a congenital anomaly (antenatal, at birth, first week of life, between one and four weeks of life, autopsy or unknown), foetal/newborn status, first prenatal examination with abnormalities, cardiac morphology, survival beyond the first week, date of death, autopsy, description of the anomalies. Diagnoses of other (non-cardiac) anomalies and the presence of associated chromosomal abnormalities were also included.

This study corresponds to a secondary data analysis of the *Registo Nacional de Anomalias Congénitas* data. The RENAC provides anonymous data for epidemiological studies and specific data are requested in writing by the researcher. Anonymity implies the removal of any personal data. According to the Ethics Committee for Clinical Research, "personal data that have been rendered anonymous so that people are not or no longer identifiable are no longer considered personal data and therefore are not covered by General Data Protection Regulation".[15]

Medical coding

All medical cases were coded by each hospital, based on eight different Regional Health Administrations (*Administrações Regionais de Saúde*) (ARS): Northern, Central,

Lisbon and Tagus Valley (LVT), Alentejo, Algarve and the Autonomous Regions of Azores and Madeira. Ultrasound monitoring of pregnancy was considered adequate in compliance with the *Direção Geral da Saúde* (Directorate-General of Health) criteria[7]: first-trimester ultrasound scan at 11-13 weeks of gestation and second-trimester ultrasound scan at 20-22 weeks, if it had exceeded this duration.

According to each diagnosis, the cases were recoded as critical or non-critical CHD. CCHD were defined as primary and secondary goals of pulse oximetry screening in patients presenting with the following pathologies: pulmonary artery atresia, tricuspid valve atresia, total anomalous pulmonary venous return, hypoplastic left heart syndrome, tetralogy of Fallot, d-transposition of the great arteries, truncus arteriosus, Ebstein's anomaly, coarctation of the aorta, aortic arch interruption, double-outlet right ventricle and single ventricle (Table 1).[9]

Heart diseases were also classified as: left-to-right shunts, left outflow obstruction, right outflow obstruction, transposition physiology, complex congenital heart anomalies and others (Table 2).

Statistical analysis

The prevalence rates were based on the number of live births, medical terminations of pregnancy (MTP) and CHD-related foetal deaths reported by the Regional Health Administration to the RENAC in 2015 as numerator, the total number of births (live births and stillbirths) as national denominator and the sum of live births and stillbirths by the residence of the mother in the different health regions as regional denominator, according to the 2015 data published by the National Institute of Statistics.[16,17]

Chi-square ($\chi 2$) test of independence has been used in frequency and contingency tables as the first approach to an analysis of the results. Cross-frequency tables and chi-square test of independence were used to compare both groups (live births *vs.* MTP), based on (i) ARS of each registration hospital, (ii) gender, (iii) obstetric monitoring and PND, (iv) presence of CCHD and (v) other associated anomalies and chromosomal abnormalities. Regions were compared by using tests of proportions, assuming a 5% level of statistical significance. The frequencies of the different diagnoses and CHD types were also compared (live births *vs.* MTPs). Both groups (critical *vs.* non-critical congenital heart diseases) were compared as regards any recorded PND in pregnancy.

The software IBM SPSS v. 24 was used for statistical analysis and a significance level of 0.05 was considered.

RESULTS

Global data

A total of 435 cases of CHD out of 85,797 births (live births, stillbirths and MTPs) were notified in 2015 to the RENAC.[3] Most cases were related to live births (78%) and 19% to MTPs; six spontaneous abortions (before 20 weeks of gestation) and six stillbirths (1.4%) were also notified. A CHD prevalence rate of 5.1 per 1,000 live births has been found in Portugal in 2015 (Table 3).

A significant regional asymmetry has been found, with statistically significant differences in CHD prevalence: 3/1,000 in Alentejo and Lisbon and Tagus Valley, 4/1,000 in the Northern region and Azores, 5/1,000 in Madeira, 6/1,000 in the Central region and 7/1,000 in the Algarve (Table 3). Statistically significant regional differences ($p < 0.001$) were also found regarding CHD prenatal diagnosis (including all cases), when Northern, LVT and Algarve regions (55% of the cases were on average prenatally diagnosed, above the 47% national average) were compared to Central, Algarve, Azores and Madeira regions (29% of the cases). MTP rate was also asymmetric within the different regions: no MTP cases were notified in the Azores and Madeira, 26% in Lisbon and Tagus Valley, 45% in Central, 47% in the Algarve and 49% in the Northern region and the only statistically significant differences were found between the Northern region and the national average, Central, LVT and Alentejo regions.

Table 1 – Congenital heart diseases classified as critical9; ICD-10 – 10th update – International Classification of Diseases

Primary goal of newborn pulse oximetry screening (ICD-10 code):
• Pulmonary valve atresia (Q22.0)
• Tricuspid valve atresia (Q22.4)
• Total anomalous pulmonary venous connection (Q26.2)
• Hypoplastic left heart syndrome (Q23.4)
• Tetralogy of Fallot (Q21.3)
• dextro-Transposition of the great arteries (Q20.3)
• Common arterial trunk (Q20.0)
Secondary goal of newborn pulse oximetry screening:
• Ebstein's anomaly (Q22.5)
• Coarctation of aorta (Q25.1)
• Interrupted aortic arch (Q25.2)
• Double outlet right ventricle (Q20.2)
• Double inlet ventricle (Q 20.4)

Table 2 – Pathophysiological classification of the cases of CHD. ICD-10 – 10th update – International Classification of Diseases

Type	Diagnoses (ICD-10 code)
Left-to-right shunts	1. Interatrial communication - IAC / Patent foramen ovale PFO (Q21.1) 2. Interventricular communication – IVC (Q21.0) 3. Patent ductus arteriosus – PDA (Q25.0) 4. Atrioventricular septal defect AVSD (Q21.2) 5. Single ventricle (Q20.4) 6. *Truncus arteriosus* (Q20.0)
Left outflow obstruction	1. Aortic stenosis (Q23.0) 2. Coarctation of the aorta (Q25.1) 3. Mitral stenosis (Q.23.2) 4. Interrupted aortic arch (Q25.2)
Right outflow obstruction	1. Pulmonary stenosis (Q22.1) 2. Tricuspid stenosis (Q22.4) 3. Ebstein's anomaly (Q22.5)
Transposition physiology	1. dextro-Transposition of the great arteries (Q 20.3)
Complex congenital heart anomalies	1. Tetralogy of Fallot (Q21.3) 2. Pulmonary artery atresia (Q22.0) 3. Hypoplastic left heart syndrome – HLHS (Q23.4) 4. Total anomalous pulmonary venous return – TAPVR (Q26.2) 5. Double-outlet right ventricle (Q20.1)
Other	1. Left superior vena cava syndrome (Q26.1) 2. Right aortic arch (Q25.41) 3. Dextrocardia (Q24.0) 4. levo-Transposition of the great arteries (Q20.5) 5. Other

No gender predominance was found; one case of sexual ambiguity was notified, associated with malposition of the great arteries, interventricular communication (IVC) and other associated congenital anomalies (agenesis of the corpus callosum, micrognathia and talipes equinovarus).

Most pregnant women were submitted to adequate prenatal follow-up and ultrasound monitoring (85%); no obstetric ultrasound scan was notified in 10% of the cases. Half of the cases were prenatally diagnosed (n = 203; 46%) and 33% of live births. Foetal ultrasound was notified in only 47 cases, having been considered as normal (false negative) in 30% of the cases (14), two of which with a critical defect (aortic coarctation).

The most frequent diagnoses are shown in Table 4.

A prenatal diagnosis was established in most cases (46%), 29% (126 cases) within the first week of life, 16% (71 cases) at birth, 6% (25 cases) between the first and fourth week of life and 1% (four cases) at autopsy; the moment of diagnosis was unavailable in 1% (six cases). Three of the four cases that were diagnosed at autopsy corresponded to stillbirths of the second trimester (gestational ages between 15 and 16 weeks) and the fourth case to a stillbirth at 36 weeks of gestational age, presenting with coarctation of the aorta.

Critical congenital heart diseases

Twenty-five percent (109) of the cases corresponded to CCHD, corresponding to a 1.3/1,000 prevalence rate of CCHD in Portugal in 2015. Most cases were notified in the Northern region (54 cases; 47%), followed by Lisbon and Tagus Valley (32 cases; 28%) and the Central region (16 cases; 14%); no cases of CCHD were notified in Alentejo; these regional differences were statistically significant (*p*-value = 0.002) and no gender predominance has been found. The presence of other congenital anomalies in 36% of the cases and chromosomal anomalies in 11% did not show any statistically significant differences when compared to what was found in the group of cases with non-critical heart diseases. Aortic coarctation was the most frequently notified CCHD (32 cases), followed by tetralogy of Fallot (28 cases) and pulmonary artery atresia (16 cases) (Table 4).

Most (72%) cases of CCHD (82 cases) were diagnosed before birth and 54% of live births had been submitted to PND, a statistically significant difference when compared to non-critical heart diseases (27%). CCHD were mostly diagnosed before birth (live births and MTP included): hypoplastic left heart syndrome (12/12), dextro-transposition of the great arteries (8/11), pulmonary artery atresia (11/16), aortic coarctation (19/32; 59%), while 9% of CCHD were diagnosed at birth, 15% within the first week of life and 4% throughout the remaining neonatal period (three cases of aortic coarctation and one of pulmonary artery atresia).

Medical termination of pregnancy *versus* live births

All cases of MTP in this study (n = 84) regarded CHD that were prenatally diagnosed: 49% were diagnosed as CCHD (compared with 20% in the group of cases that were not related to MTP); 37% of cases with CCHD were submitted to MTP, compared with 13% of non-CCHD cases. Other congenital anomalies were found in 75% of the cases related to MTP, while these were only found in ¼ of the cases that were not related to MTP (Table 4). Finally, chromosomal abnormalities were found in 40% (n = 34) of those that

Table 3 – Global data

Total births – Portugal (live-birth and stillbirth)	85,797	
Congenital heart diseases:	435 (prevalence of 5 per 1,000 live births)	
Gender		
- Male	- 226 (52%)	
- Female	- 207 (48%)	
- Ambiguous gender	- 1 (0.2%)	
- Unavailable	- 1 (0.2%)	
ARS (births per maternal residence):		Prevalence
1. Northern region (27,342)	156 (36%)	4/1,000
2. Central region (16,146)	113 (26%)	6/1,000
3. Lisboa/Vale Tejo (30,366)	101 (23%)	3/1,000
4. Alentejo (3,633)	11 (3%)	3/1,000
5. Algarve (4,090)	37 (9%)	7/1,000
6. Azores (2,267)	8 (2%)	4/1,000
7. Madeira (1,954)	9 (2%)	5/1,000
		($p \leq 0.05$)
Obstetric monitoring (%):		
a) Adequate	368 (85%)	
b) Suboptimal	64 (15%)	
i. With no prenatal ultrasound imaging	42 (10%)	
c) Foetal ultrasound	47	
Pregnancy outcome:		
a) Spontaneous abortion	6 (1%)	
b) MTP	84 (19%)	
c) Stillbirth	6 (1%)	
d) Live birth	339 (78%)	
→ prevalence	→ 4.0/1,000 live births	

MTP: medical termination of pregnancy

Table 4 – Critical congenital heart diseases: frequencies and prenatal diagnosis (PND)

Diagnosis	n (%)	PND
Coarctation of the aorta	32 (28%)	19/32
Tetralogy of Fallot	28 (25%)	19/28
Pulmonary artery atresia	16 (14%)	11/11
Hypoplastic left heart syndrome	12 (10%)	12/12
Transposition of the great arteries	11 (10%)	8/11
Truncus arteriosus	5 (4%)	5/5
Double-outlet of the right ventricle	5 (4%)	5/5
Total anomalous pulmonary venous return	4 (3,5%)	2/4
Anomalia de Ebstein	1 (1%)	0/1
TOTAL	114	82 (72%)

were related to MTP compared with only 6% in the group of non-MTP cases (Table 4). All these differences were statistically significant (Table 5).

Most cases of hypoplastic left heart syndrome in this study were referred for MTP (8/11), as these were all diagnosed with double-outlet right ventricle (5/5). The highest number of MTP was found in the Northern region, with a statistically significant difference when compared to the other regions (Table 5).

Postnatal deaths

In this study, 15 deaths were notified in a total of 339 live births: eight within a PND, six diagnosed at birth and one case diagnosed within the first week of life (transposition of the great arteries) (Table 6). Four of the six deaths that occurred within the first week of life were not diagnosed before birth; cases 1, 2 and 3 were notified in the Autonomous Regions of Azores and Madeira.

DISCUSSION

The national CHD prevalence of 5 / 1,000 births that was found in this study was lower than what has been published in literature[1] with estimates of 9,4:1,000 or even higher[18-20]; it was also lower than data previously described by the RENAC and on the island of S. Miguel in the Azores.[3,20] Interventricular communications (IVC) were most

frequently found (38% of the cases, corresponding to 42% of live births), followed by interatrial communications (IAC) with 14% of the cases (corresponding to 15% of live births), as described in all large studies.[2,18-20] However, patent ductus arteriosus (PDA), usually described as the third most frequent diagnosis, was the seventh most frequent in this study with only 3% of all cases (*vs.* the usual 10%).[2,18,20,21] Aortic coarctation, tetralogy of Fallot and pulmonary valve stenosis were the next most frequent diagnoses, with most cases of aortic coarctation than what has been usually described.[1,2,18-20]

This lower CHD prevalence may be due to the voluntary nature of the notification and to some asymmetry between institutions as regards case notification. Some cases of left-to-right shunts (ventricular septal defect - VSD, atrial septal defect - ASD, patent ductus arteriosus - PDA) have been diagnosed after the neonatal period, due to the decrease in pulmonary vascular resistances at the end of the first month of life. The prevalence of CCHD that was found in this study was also in line with the literature (around 20%), as well as a 20% failed CCHD diagnoses before discharge from hospital.[22]

The regional asymmetries found in the study may be explained not only by different levels of adherence to the notification, but also by the asymmetry of highly differentiated resources, such as foetal ultrasound and the referral of

Table 5 – Global data: comparison MTP *vs.* live birth

	Total	Termination of pregnancy	Live birth (%)	
	423	84 (20%)	339 (80%)	***p***
ARS (%):				
1. Northern	149 (35%)	43 (29%)	106 (71%)	
2. Central	113 (27%)	17 (15%)	96 (85%)	
3. Lisboa/Vale Tejo	98 (23%)	15 (15%)	83 (85%)	
4. Alentejo	11 (3%)	0 (0%)	11 (100%)	
5. Algarve	35 (8%)	9 (25%)	26 (75%)	
6. Azores	8 (2%)	0 (0%)	8 (100%)	
7. Madeira	9 (2%)	0 (0%)	9 (100%)	
Gender:				
- Male	221 (52%)	41 (49%)	180 (53%)	= 0.62
- Female	201 (48%)	42 (51%)	159 (47%)	
Obstetric monitoring (%):				
- Adequate	339 (81%)	78 (96%)	279 (78%)	**= 0.001**
- PND	195 (46%)	84 (100%)	111 (33%)	**< 0.001**
Other anomalies	148 (35%)	63 (75%)	85 (25%)	**< 0.001**
Chromosomal abnormalities	53 (13%)	34 (40%)	19 (6%)	**< 0.001**
CCHD	109 (26%)	41 (49%)	68 (20%)	**< 0.001**
Type of heart disease:				
1. Left-to-right shunts:	251 (59%)	29 (35%)	222 (65%)	
i. IAC/FOP	56 (14%)	4 (5%)	52 (15%)	
ii. IVC	161 (38%)	18 (21%)	43 (42%)	
iii. DSAV	17 (4%)	4 (5%)	13 (4%)	
iv. PDA	11 (3%)	0 (0%)	11 (3%)	
v. *Truncus arteriosus*	5 (1%)	1 (1%)	4 (1%)	
2. Left outflow obstruction:	45 (11%)	9 (11%)	36 (11%)	
i. Coarctation of the aorta	30 (7%)	8 (10%)	22 (7%)	
ii. Aortic stenosis	10 (2%)	1 (1%)	9 (3%)	
3. Right outflow obstruction	22 (5%)	3 (4%)	19 (6%)	**< 0.001**
i. Pulmonary stenosis	20 (5%)	3 (4%)	17 (5%)	
4. Transposition	11 (3%)	6 (7%)	5 (2%)	
5. Complex congenital heart anomalies:	65 (15%)	25 (30%)	40 (12%)	
i. HLHS	11 (3%)	8 (10%)	3 (1%)	
ii. TOF	28 (7%)	7 (8%)	21 (6%)	
iii. Pulmonary atresia	14 (3%)	5 (6%)	9 (3%)	
iv. TAPVR	4 (1%)	0 (0%)	4 (1%)	
v. DORV	5 (1%)	5 (6%)	0 (0%)	
6. Other	29 (8%)	12 (14%)	17 (5%)	

IAC: interatrial communication; IVC: interventricular communication; AVSD: atrioventricular septal defect; PDA: patent ductus arteriosus; HLHS: hypoplastic left heart syndrome; TOF: tetralogy of Fallot; TAPVR: total anomalous pulmonary venous return; DORV: Double-outlet right ventricle

Table 6 – Characteristics of the CHD cases notified as deceased as regards the age at death, prenatal diagnosis (PND), gestational age, birth weight, cardiac diagnosis, presence of genetic abnormalities and other associated anomalies

Case	Age at death	PND	Gestational age (weeks)	Birth weight (g)	Diagnosis	Genetic abnormalities	Other anomalies
1	< 8 days	No*	38	2,300	Pulmonary stenosis	No	No
2	< 8 days	No*	38	2,760	Pulmonary stenosis	No	No
3	< 8 days	No*	39	3,200	Aortic stenosis	No	No
4	< 8 days	No	26	570	IVC**	No	No
5	2 days	Yes	42	2,155	Tetralogy of Fallot, PDA	Trisomy 18	Yes
6	5 days	Yes	26	570	IVC**	No	No
7	8 days	Yes	37	2,643	d-Transposition of the great arteries	No	No
8	9 days	Yes	37	2,620	AVSD, coronary anomaly, others	No	No
9	10 days	Yes	38	3,095	Hypoplastic aortic arch, IVC	DiGeorge Syndrome	No
10	22 days	Yes	38	2,795	Pulmonary atresia	DiGeorge Syndrome	No
11	1 month	Yes	39	3,035	TAPVR, IVC	No	Yes
12	1 month	No*	37	1,940	TAPVR	Trisomy 18	Yes
13	1 month	No	38	2,950	d-Transposition of the great arteries	No	No
14	4 months	No*	38	2,800	AVSD	Trisomy 18	No
15	9 months	Yes	32	1,855	Unavailable	No	No

*: Diagnosed at birth; **: Of a twin pregnancy
IVC: interventricular communication; PDA: patent ductus arteriosus; AVSD: atrioventricular septal defect; TAPVR: total anomalous pulmonary venous return

prenatally-diagnosed cases to Paediatric Cardiology (in the Northern, LVT or Coimbra regions).[23] In addition to a lower number of births, lower access to these medical resources and therefore a lower number of prenatally-diagnosed heart diseases could explain what has been found in regions with a lower population density, such as the Alentejo or in most remote regions, such as the Autonomous Region.

The mortality rate of 17.5 / 100,000 births that was found in this study is in line with international data.[11] However, this may have been underestimated, considering that no notifications were received from three of the four national surgical centres. Extreme prematurity, presence of genetic anomalies, other associated malformations and more peripheral geographical locations (cases 1, 2 and 3 in Table 6) were associated with a poorer outcome.

Medical coding was based on ICD-10 and reviewed by researchers at the INSA (*National Health Institute Doutor Ricardo Jorge)*, improving data homogeneity. The results found in this study are an important contribution to the knowledge of the national reality and may contribute to planning and organisation strategies of prenatal diagnosis and CCHD screening in newborns.

As regards pulse oximetry CHD screening, it is estimated that up to 20% of patients with CCHD will still be discharged from the maternity hospital without a pre or postnatal diagnosis.[22] As a compensation for these undiagnosed discharges, pulse oximetry has been studied and implemented within the last decade as a newborn universal CCHD screening method before discharge from the maternity hospital (ideally after 24 hours of life).[5,24-26] This is a quick and easy method to be used at patient's bedside, in addition to its high sensitivity in the identification of cyanotic CCHD,[4] considered to be the screening's primary goal (Table 1). However, pulse oximetry screening has relevant limitations in CCHD, including false positive results and lower sensitivity for acyanotic heart diseases such as aortic coarctation.[8,27]

For example, this screening method has been implemented in the United States of America (USA) and in the Nordic countries, with a decrease in mortality and in the diagnostic gap.[11] However, a British prospective multicentric study (32,836 screenings) has found 239 newborns with hypoxaemia, eight with CCHD and two false negatives; a decision was made not to implement an universal screening, given that most positive results had no heart disease, diverting resources from newborns in need of greater care.[28]

This pre-discharge screening has been implemented by different Portuguese maternity hospitals, both public and private,[29] even though the Portuguese reality is quite different from the abovementioned countries: newborns are usually discharged from hospital on the second day of life (or beyond) and are always examined by a paediatrician, unlike in the USA and Nordic countries, where they are assessed by nurses. From the authors' point of view, this type of screening could only be implemented at a population level based on a more extensive survey of the national reality, namely the potential health gains that could be obtained.

The voluntary nature of RENAC notifications is the main limitation of this study, with a likely undervaluation. There may also be asymmetries in the way diagnoses are notified by the different institutions. The analysis of data from several consecutive years or from different cohorts could lead to a better understanding of the trends of the evolution of the indicators. A medical recoding by more than one physician

would also be relevant in further studies. It is worth mentioning that, as far as we know from literature, this is the first nationwide study with estimates of the prevalence of the different CHD and including contributions from all maternity hospitals.

CONCLUSION

A CHD prevalence of 5 / 1,000 births was described in 2015 in Portugal (RENAC), showing relevant regional asymmetries. A critical heart defect has been found in 20% of live births. Only one of the 15 deaths found in this study had a late diagnosis of CHD (post-discharge). This study is relevant to know the Portuguese reality and to better healthcare planning. An improved adherence to the *Registo Nacional de Anomalias Congénitas* (RENAC) and monitoring, in conjunction with the medical societies of the specialties involved is crucial to a more comprehensive knowledge in the area of congenital heart diseases, adequate healthcare planning and implementation of universal screening and outcome monitoring.

HUMAN AND ANIMAL PROTECTION

The authors declare that the followed procedures were according to regulations established by the Ethics and Clinical Research Committee and according to the Helsinki Declaration of the World Medical Association.

DATA CONFIDENTIALITY

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in writing this manuscript.

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