



The incidence of congenital heart defects in the world regarding the severity of the defect

Incidencija urođenih srčanih mana u svetu prema težini mane

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Abstract

Background/Aim. Congenital heart defects (CHDs) are structural or functional abnormalities of the heart present at birth even if they are detected much later. Their importance lies in the fact that, depending on the severity, they change the quality of life, and may be life threatening. In addition, we should not ignore the high costs of treating people with congenital heart disease. The aim of this study was to analyze the incidence of congenital heart disease in relation to the severity in the world based on the available literature. **Methods.** All the available literature on the incidence of CHD cases regarding the severity of CHD published from 1955 to 2012 was analyzed. The researcher was able to read the titles and abstracts of 128 papers on the subject. Due to methodological inconsistency, 117 of the papers were rejected. Based on the criteria of reliability, availability and comparability, our analysis included 11 studies testing CHD incidence regarding the severity of the defect conducted all over the world. The Yates' χ^2 -test was used to compare the observed incidences. **Results.** The frequency of severe congenital heart defects, ranged from 0.414 to 2.3/1,000 live births, the incidence of moderate congenital heart defects from 0.43 to 2.6/1,000 live births while in the group of minor congenital heart defects the incidence ranged from 0.99 to 10.3/1000 live births. There were no statistically significant differences in the incidence of mild, moderate and severe CHDs. **Conclusion.** The results obtained studying of the available data suggest that no statistically significant difference in the incidence of mild, moderate and severe congenital heart defects. A universal methodological approach to the incidence of CHD is essential.

Key words:

heart defects, congenital; incidence; severity of illness index; epidemiology; statistics.

Apstrakt

Uvod/Cilj. Urođene srčane mane su strukturne ili funkcionalne anomalije srca prisutne na rođenju čak iako se otkriju mnogo kasnije. Njihov značaj leži u činjenici da zavisno od težine menjaju kvalitet života, ili ga ozbiljno ugrožavaju. Osim toga, ne treba zanemariti ni visoke troškove lečenja osoba sa urođenim srčanim manama. Cilj rada bio je da se analiziraju vrednosti incidencije urođenih srčanih mana u odnosu na njihovu težinu u svetu na osnovu dostupne literature. **Metode.** Analizirana je sva dostupna literatura koja se odnosi na incidencije urođenih srčanih mana prema težini objavljena u periodu od 1955. do 2012. godine. Analizirano je 128 naslova i apstrakata na ovu temu. Zbog metodološke nedosljednosti, 117 radova je odbačeno. Na osnovu kriterijuma dostupnosti i uporedivosti, u našu analizu uključeno je 11 studija u cilju proučavanja incidencije urođenih srčanih mana prema težini. Pri poređenju proučavanih incidencija korišten je Yates-ov χ^2 -test. **Rezultati.** Učestalost teških urođenih srčanih mana kreće se u rasponu od 0,414 do 2,3/1 000 živorođene dece, incidencija srednje teških urođenih srčanih mana je u intervalu od 0,43 do 2,6, dok je u grupi lakih mana incidencija u rasponu od 0,99 do 10,3/1 000 živorođene dece. Nije rađena statistički značajna razlika u incidenciji lakih, srednje teških i teških urođenih srčanih mana. **Zaključak.** Rezultati dobijeni na osnovu dostupnih podataka navode na zaključak da nema statistički značajne razlike u incidencijama lakih, srednje teških i teških urođenih srčanih mana kao i da je neophodan univerzalni metodološki pristup izučavanju incidencije urođenih srčanih mana.

Ključne reči:

srce, kongenitalne mane; incidenca; bolest, indeks težine; epidemiologija; statistika.

Introduction

Congenital heart defects (CHDs) are structural or functional abnormalities of the heart present at birth even if they are detected much later. CHDs are the most common birth defects that occur with an incidence of 4–10/1000 live

births¹. If one takes into account the fact that was recently published by the World Health Organization, that the incidence of CHDs is 10 per 1,000 live births, it is clear that each year 1.5 million children with CHDs are born in the world². The fact that CHDs cause death by 10% of children in the first year of life shows their impact on overall

mortality³. Not long ago all children with aortic atresia died in the first few months of life, 85% of children with transposition of the great arteries in the first few days after birth, and 78% with pulmonary atresia died during the first 6 months of life⁴. Children with CHDs occupy 25–30% of intensive care facilities.

The past 5 decades have witnessed extraordinary advances in diagnostics and treatment of patients with CHDs from a puzzling curiosity to more or less solved problem. Today almost 85% of babies born with CHD can expect to reach adulthood⁵.

The importance of CHDs lies in the fact that, depending on the severity, they change the quality of life, or may be seriously life threatening requiring urgent measures in terms of organization of early diagnosis, well healthcare access and prompt medical care action.

Awareness of researchers on the incidence of CHDs is gradually maturing. First, the subject of the study was the incidence of CHDs itself, then the incidence of each CHD, then the focus of research was directed toward defects with the most severe clinical symptoms and the need for cardiac surgery treatment. CHD classification in the categories of severity (severe, moderate and mild CHDs) is not only a didactical issue, but a multidimensional approach including: use of health service, health related quality of life, as well as psychological state and social relationship. Mild (simple, trivial) CHDs do not significantly affect the life pattern of a patient or the quality of his/her life. Apparently innocent, harmless, minor CHDs need to be monitored as well. Studying of their incidence can point to some of the causes of CHDs or convince us of the sensitivity and specificity of new diagnostic tools.

However, there is a special interest in the study of the incidence of moderate (significant) and severe (complex) CHDs because they represent a very important health problem. The fact that the number of children and adults with CHDs is constantly increasing, generally raises medical attention. Huge advances in pediatric intensive care, echocardiography and cardiac surgery have provided an enormous growth in the number of surviving children and adults with CHDs, so that today there are more adults than children with CHDs. This continually growing population presents a big challenge for cardiologists and even more for the health system because of its unique issues and needs. Since a longer life does not necessarily mean a better life, there is a growing consensus that it is necessary to offer them specialized care facilities to meet their needs. The results of studies on

the incidence of CHDs regarding to their severity should be used to provide data to help in proper direction of resource allocation in CHDs.

Methods

All the available literature on the incidence of CHD regarding the severity of CHD published from 1955 to 2012 was analyzed. Following the example of Hoffman and Kaplan⁶, we took the year 1955 as the lower limit when cardiac catheterization was becoming a common diagnostic test. Thus, the researcher was able to read the titles and abstracts of 128 papers on the subject. Due to methodological inconsistency 117 of the papers were rejected. Based on the criteria of reliability, availability and comparability, our analysis included 11 studies testing the incidence of CHD conducted all over the world.

The following inclusion criteria were necessary to be fulfilled to be considered in this analysis: to have adopted the definition for CHDs by Mitchell⁷, to have adopted and applied the division of CHDs in relation to the severity to mild (simple, trivial), moderate (significant) and severe (complex); applied acceptable diagnostic hierarchy ("physiological" or "two-dimensional"); a clearly defined territory and population; that CHDs were diagnosed in the first 12 months of life; children with suspected CHD examined by pediatric cardiologist; the study lasted for at least 5 years (the only exception was a study in Beijing⁸).

The Yates' χ^2 -test was used to compare the observed incidences. The incidence was compared within each group separately (minor, moderate, severe), starting from the premise that there was no statistically significant difference among the analyzed samples. The arithmetic mean value of the incidence that is hypothetical and known in advance, was the value to the incidence that came in the "New England Regional Infant Cardiac Program," which is 1.5/1,000 live births for severe CHDs, 2.5/1,000 live births for moderate and 2.2/1,000 live births for minor CHDs⁹.

Results

Eleven studies included over more than 8 million live births and about 40,000 diagnosed CHDs were analyzed. The important characteristics of the studies are given in Table 1.

Table 1

Important characteristics of the studies included in the analysis				
Country	Duration (years)	Live births (n)	Cases with CHDs	Incidence of CHD per 1,000 live births
Massachusetts, USA	6	1,528,964	8,071	6.2
Cleveland, USA	13	477,960	2,671	5.59
Montenegro	10	88,098	1,004	8.8
Taiwan	6	238,143	3,115	13.08
Tuzla, Bosnia	6	39,699	234	6.12
Beijing, China	1	84,062	686	8.2
Anatolia, Turkey	8	219,870	1,693	7.77
Quebec, Canada	15			5.78
Island	10	44,013	740	9.2
Atlanta, USA	20	937,195	5,813	5.8
France	10	4,400,000	12,932	2.85

The incidence of CHDs in dependence on their severity is given in Table 2.

The results showed that the incidence of severe CHDs was in the range of 0.414 to 2.3/1,000 live births. The highest frequency was in the range of 1.4–1.6/1,000 live births. The incidence of moderate CHD is in the range of 0.43–2.6, but even 9 studies reported the frequency interval 1.97–2.6, while in the minor group CHD incidence ranged from 0.99–10.3/1,000 live births. The percentage of different categories of CHD severity relative to the total incidence for severe CHDs was found to be from 5.38% to 50.2%, while the minor and moderate ranged from 15.6% to 38.6% and from 34.5% to 74.64% (Table 2).

the severity of the defect. Despite the large number of studies that have reviewed, only a small number of them ($n = 11$) met the criteria for inclusion in the study. Nevertheless, we believe that the applied methodological procedure for conducting the research upon which we drew the conclusions is more important than the number of studies included to the analysis. Of course, all provided that the survey covers the population large enough to make conclusions that are considered reliable. A meta-analysis published in 2011 assures us that our presumptions are accurate. The authors that drew their study's conclusions based on 114 papers published on the topic of the prevalence of CHDs, when

Table 2

Incidence of congenital heart defects (CHDs) per 1,000 live births regarding the severity in 11 different studies

Place of study	Minor CHDs		Moderate CHDs		Severe CHDs	
Massachusetts, USA,	2.2		2.5		1.5	
Cleveland, USA,	3.136		2.04		0.414	
Montenegro	5.59		2.6		0.61	
Taiwan	10.3	$\chi^2 = 11.698^*$	1.99	$\chi^2 = 1.367^*$	1.5	$\chi^2 = 0.718^*$
Tuzla, Bosnia	2.4	$p = 0.2309$	2.26	$p = 0.9980$	1.46	$p = 0.9998$
Beijing, China	4.96		2.34		0.9	
Anatolia, Turkey	4.63		1.97		1.1	
Quebec, Canada	2.23		2.1		1.45	
Island	9.2		4.6		2.3	
Atlanta, USA	3.05		2.11		0.64	
France	0.99		0.43		1.43	

*Statistically insignificant difference ($p > 0.05$, Yates' χ^2 -test); Incidence – number of new cases of CHD per 1,000 live births.

Based on the hypothesis that most of research authors on the incidence expressed the view that the incidence of CHDs is predictable in relation to the severity of defects, in fixed ranges, we found it reasonable for our hypothesis to be based on this presumption. Using the Yates' χ^2 -test we came to the result that supports the hypothesis of no statistically significant differences among the incidence of minor ($\chi^2 = 11.698$; $p = 0.2309$), moderate ($\chi^2 = 1.367$; $p = 0.9980$) and severe ($\chi^2 = 0.718$; $p = 0.9998$) CHDs (Table 2).

Discussion

Studying of the incidence of CHD requires a series of complex procedures that are tailored to the specific phenomena investigated: some CHDs are very rare, others have special natural evolution, and the third group shows sometimes variations of clinical manifestations. On the other hand, the reliability of each epidemiological study depends on a clear set of definitions, including population, methods used and applied, ethical principles, inclusion of rigorous criteria is mandatory for each study, time of diagnosis, classification, diagnoses faults, their clustering in relation to severity. Comparison of the data is only possible if there is a methodological compliance of each listed segment.

This analysis is the result of extensive research that has led us to the conclusion that we must not succumb to the imperative of including in the study just any article that concerns the problems of the incidence of CHD in relation to

commenting critically on their study limitations expressed a degree of doubt in their performance. They state that it is very hard to determine whether the detected differences in CHD birth prevalence are real or merely methodological¹⁰.

We felt it reasonable to include in the analysis those studies that covered the period of 5 years or longer. The study should last for many years to measure the level of occasional high or low values of incidence. The only exception was made in a research conducted in Beijing, given the large number of live births in that city on annual basis and a very small amount of data on this subject from the Far East⁸.

In this analysis older studies^{9, 11}, and recent studies^{8, 12–18} are equally represented because this was an opportunity for confronting old and new diagnostics and testing their impact on the incidence of CHD regarding the severity of the defect. The result showed that no substantial, statistically significant difference was found in the groups of CHD, and the right opportunity to realistically define the impact of echocardiography on epidemiological aspect of severe, moderate and mild CHD. There is a general agreement that echocardiography fundamentally affected the content of the research of CHD incidence results. Modern studies (from around 1985 to nowadays), using echocardiography have improved the knowledge of the frequency of CHDs. But Hoffman and Kaplan⁶, with the authority of great researchers in this area, conclude that the incidence of severe and moderate CHD has not changed substantially in the last

50 years anywhere in the world. They believe that echocardiography does not contribute significantly to the diagnosis of severe and moderate CHDs, but the influence on the growth of minor CHDs, especially in the identification of small muscular ventricular septal defects (VSDs) is important. They said that the frequency of clinical examination from previous studies was high and when combined with catheterization, many children with severe and moderate CHDs were identified with great certainty.

Confirmation of these claims is the fact that the estimated number of adults with severe, moderate or mild CHD in USA was based on the results from the New England Regional Infant Cardiac Program, which is mainly carried out in the time before the invention of echocardiography⁹. Use of echocardiography has influenced the identification of the non-categorized defects that are commonly found at the end of the list of diagnosed CHD called "all others", "mixed group" by reducing their share from 28%¹⁹ to 3.2%¹³. Its noninvasive nature and availability, sensitivity and specificity are the recommendations for widespread use.

The results of our study showed that the prevalence of severe CHD is in the range from 0.414 to 2.3/1,000 live births with the highest frequency in the range of 1.4–1.6/1,000 live births. The incidence of moderate CHD is much more balanced. Even 9 studies reported the frequency interval of 1.97–2.6. Highest diversity is expected to be in the mild CHD group (from 0.99–10.3/1,000 live births), and yet not distinct enough to be statistically significant.

Analyzing the results of statistical processing and the fact that we found no statistically significant difference in the incidence in none of the three groups of CHD, we have focused on the examination of the reasons for this to happen in several directions. First, previous studies that are part of our analysis are not burdened by a large number of harmless, clinically asymptomatic VSDs. Part of recent researches in the incidence analysis included only those VSDs which required more than three clinical examinations of the cardiologist during the first year of life. This way, the incidence of VSD reduced to a reasonable level, and indirectly influenced the minor incidence of CHD.

Share of different severity categories of CHD in relation to the overall incidence has shown a high degree of diversity primarily in the category of severe CHD (from 5.38% to 50.2%). Such a high percentage of severe CHD is attributed to studies that have reported an overall low incidence of CHD, mainly on account of minor CHD, so the percentage share of severe CHD reached high values.

We were faced with several problems while comparing the available studies. The first one was an attitude to the classification of CHD. We had a dilemma about the classification used in analyzed studies to define the criteria for inclusion in the analysis. "New England Regional Infant Cardiac Program" offered a classification based on anatomical significance of CHD⁹. "Baltimore-Washington study" in the classification, gives priority to the components of the earliest embryonic malformation disorder²⁰, but in practice, however, the most commonly used model takes into account

the physiological hierarchy (considers the most significant impediment, the earliest lesion that requires intervention, or that causes the greatest hemodynamic disturbances). For classifying children with CHD in Montenegro, we used a two-dimensional approach for the model applied in the metropolitan Atlanta²¹ and Wren et al.¹³ from New Castle, United Kingdom, which published the results of their work and offered this kind of diagnostic hierarchy as a standard in 2000. It consolidates and defines the major structural anomalies, and abnormalities that contribute to the clinical recognition of cardiovascular malformations. We considered that the inclusion of those studies that have incorporated the "physiological" or "two-dimensional" approaches in the analysis lead to the most accurate data.

The second problem was source of data: secondary or tertiary health center. In small countries such as Montenegro, Island, Bosnia-Herzegovina it means that diagnosis, registration, and follow-up are conducted by only a few cardiologists, and take place at a single center for pediatric cardiology. In big countries the access to a pediatric cardiologist is possible even on secondary level, but cardiac surgery, cardiac intensive care units are part of tertiary health care. So, there is a high possibility of dissipation of patient data in the way from secondary to tertiary level. For example, studies conducted in Korea in the institution of secondary level, we can see that results are unrepresentative and meaningless²². For these reasons, we have included projects that contain detailed description of how the data was collected from the base to the top of the health care system, which has convinced us in the greater coverage of patients with CHD.

The third problem was counting or estimation of patients with CHDs. One major dilemma was whether to include in the analysis those studies whose data is based on statistical methods for estimating the number of patients with different types of CHD. Large health care systems like USA²³, Germany²⁴, and Great Britain²⁵ chose the method of extrapolating to estimate the prevalence of severe, moderate and mild CHD based on the results of "New England Regional Infant Cardiac Program." They used a documented incidence of 1.5/1,000 live births for severe, 2.5/1,000 live births for significant, and 2.2/1,000 live births for simple CHD. Considering that the base of each estimate was a certain serious study, methodological impeccably formulated, we have included the results of these studies in the analysis.

It is obvious that awareness of researchers in the incidence of CHD has been maturing gradually: the first subject of study was the incidence of CHD itself, then each individual CHD, and finally the focus of the research was directed towards the defects with the most severe clinical symptoms and cardiac surgery treatment (moderate and severe). After the invention of echocardiography attention was concentrated on a small VSD that previously could not be diagnosed.

The first organized, conceptually arranged approach to examine the incidence of CHDs was "New England Regional Infant Cardiac Program," which includes a number of

hospitals in New England that began to work on improving the quality health services to children with CHD in 1968 and still continues⁹. In this study, we can recognize only remarks of necessity to allocate significant and severe CHD in the group of interest. Of course, the criteria for inclusion in this category correspond to time and former level of knowledge: children with CHD who required cardiac catheterization or cardiac surgery or died with CHD in the first year of life. Several other studies deserve attention because of the introduction of useful innovations in the study of the incidence of CHDs. These studies were conducted in Blackpool in the period from 1957 to 1971¹¹ and in Liverpool²⁶. A set of CHD diagnoses on the basis of clinical examination time ranges from 52%¹³, 44%²⁶, 32%⁹ to 26%¹⁴. That is the reason that the data collected for more than 30–40 years is less accurate and complete than nowadays, but the approach to the patient was more clinical, less technological.

Hoffman²⁷ is the most consistent cardiologist in the study of the epidemiological aspects of CHDs. After a great experience in this field he has suggested the introduction of a

standard set for the diagnosis of CHDs and standard methods of implementation of studies aimed at determining the incidence of CHDs which would allow data comparability. All important studies after the introduction of echocardiography agree on one thing: there is no change in the incidence of severe and moderate CHDs, but there is a significant increase in mild defects^{13,28}. A study conducted in Montenegro on a sample of 88,098 live births revealed that the incidence of moderate to severe defects in the analyzed period of ten years is without oscillations, while easier defects show temporal variation (increase sharply, then maintain the same high-level and then a lower drop)²⁹.

Conclusion

The results obtained on the basis of the available data support the hypothesis that there is no statistically significant difference in the incidence of mild, moderate and severe congenital heart defects.

A universal methodological approach to the study of incidence of congenital heart defects is essential.

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