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# A post hoc analysis on the incidence of congenital heart disease in Baku-Azerbaijan calculated by a prospective epidemiology study

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## Abstract

**Background:** The incidence of Congenital Heart Disease (CHD)in Azerbaijan was firstly published following a prospective study, using Echo-2D as a study method, in 2019.

**Aim:** Of this post hoc analysis of the first ever prospective epidemiology study that calculated incidence and types of CHD in Baku, Azerbaijan, is to verify the forms of diseases that will have an early clinical impact on the patients and the health system of the country.

**Population-method:** From June 2016 to August 2018, 2570, term neonates were screened in 2 major state maternity hospitals in Baku. Their screening was randomized to equal females/males with not known previous obstetric alert regarding CHD. Scanning was done by two teams of pediatric cardiologists by using echo-2D. Each team was 'blinded' to the findings of each other. All scans were recorded, and a third senior physician reevaluated them.

**Results:** From 2570 term neonates of the general population, they detected 47 CHD's. From them, 17 were critical and severe-CHD and 7/47(14.9%) were of moderate complex. 17/47 (36.2%) were cyanotic and 30/47(63.8%) were non-cyanotic. The incidence of simple CHD was 25/47(53.2%). Analysis of the specific anatomy is presented in table1. The estimated incidence was 1.83%. As this incidence has been among the highest reported a post hoc analysis has clarified and presented an important clinical rate of 1.48% after redacting minimal defects without any clinical significance, as minor PDA's, ASD II, VSD's. A post hoc calculation of BAov, revealed an anatomical BAov incidence of 1.65% and a functional BAov incidence of 1.4%.

**Conclusions:** This first-ever prospective epidemiology study in Azerbaijan involving a cohort equal to 1.65% of the annual living births of the country, estimated a high incidence of CHD. This is among the highest reported globally. The amount of critical and severe CHD after the post hoc analysis increased from 46.8% to 55.3%. The incidence of cyanotic CHD after the post hoc analysis increased from 36.2% to 42.1%. These high numbers are possibly related to an isolated population and conjugated marriage customs of the country. As this represented a state population health burden a post hoc analysis based on clinical important CHD minimized the calculated index nearby 20%.

## Introduction

Congenital Heart Diseases (CHD) are usually defined as clinically significant structural heart disease present at birth[1]. The incidence of them in different studies varies from about 0.4% to 5% among the live births[2]. Previous estimates of CHD came from few data sources, were geographically narrow, and did not evaluate CHD throughout the life course[3]. Additional to the lack of worldwide data, the method and age spectrum when CHD are detected play a critical role on the calculated incidence[2,4]. For example, subaortic stenosis as well as valve lesions of Marfan's syndrome or obstruction due to hypertrophic cardiomyopathy and the clinical presentation of anatomical bicuspid valve almost always develops well after birth[4]. The use of echocardiography in the detection of CHD can "overestimate" the clinical importance of CHD. This can happen as rare and "self-treated" defects such as minimal alternations in the vena cava drainage, persistent left superior vena cava, draining in the coronary sinus or small muscular VSD's, ASD's II and silent PDA's can be included in an incidence or prevalence study of CHD[4]. These will not alternate the total burden of the disease as a state population health burden, so it will be better to exclude them from a national incidence study. These findings as well as the ability of the country to deal with a very sophisticated public health disease, lead or team to review our initial published data[5] by a post hoc analysis and clarify a number that presents to the public health facilities of the country a population of patients that will need to be treated and followed-up.

## Population - Method

In our initial paper[5], we included a cohort of 2570 term neonates (delivered after the 38th week of gestation) that represented 1.65% of live births of the country, to increase the strength of our findings. During the period from June 2016 to August 2018, our cohort was screened in 2 major state maternity hospitals in Baku. Their screening was randomized to equal females/males, age four to five days old with not known previous obstetric alerts regarding CHD. Scanning was done by two teams of pediatric cardiologists – each team was consisted by two experienced in echo-2D pediatric cardiologists, using the same echo-2D device. This was a General Electric Vivid i cardiac ultrasound system, using an 8C-RS microconvex ultrasound transducer probe, suitable for neonatal high-quality scanning. Each team was "blinded" to the findings of each other team. All scans were recorded, and a third senior physician reevaluated them to determine the exact anatomy. When a conflict of opinion existed a majority of the five major researchers prevailed.

## Results

From 2570 term neonates of the general population, they detected 47 CHD's. From them, 17 were cand s-CHD and 7/47(14.9%) were moderate complex CHD. 17/47 (36.2%) were cyanotic and 30/47(63.8%) were non-cyanotic. The incidence of simple CHD was 25/47(53.2%). Analysis of the specific anatomical types of CHD are presented in (**Table1**)[5]. The estimated incidence was 1.83%. As this incidence has been among the highest reported a post hoc analysis was undertaken aiming to clarify important clinical CHD that would receive a treatment in the first five years of life of the patient[2,4]. Taking in consideration the natural history and outcomes of specific types of CHD, such as small ASDII's, small muscular VSD's and silent PDA's, we revied our data and excluded all not important clinical defects[2,3,4]. So, 9 simple defects were reduced from the initial study. These represented 19.13% of the initial defects. Therefore, to that, the initial rate declined from 1.83% to 1.48 %. This represents a decline from the initial calculate incidence of 2019[5] by 19.3%. The new analysis of the specific types of CHD are presented in (**Table2**) Also, we specified an updated incidence of BAov by a post hoc calculation that revealed an anatomic BAov incidence of 1.65% and a functional BAov incidence of 1.4%[6].

## Discussion

CHD's are a major cause of serious morbidity and mortality, among all age groups, worldwide; additional to that they are quite common and their - in many cases lifelong - management involves multidisciplinary teams of specialists leading to sophisticated services with a high cost[3,4]. The incidence of congenital heart disease at birth

**Table 1.** Classification of CHD

| | | |
|---|---|---|
| 1 | BAov (functional/anatomic) no additional disease | 3.035% |
| 2 | VSD (isolated/all types) | 16.8% |
| 3 | ASD (isolated/all types) | 8..4% |
| 4 | PDA (isolated) | 6.3% |
| 5 | c-AVSD | 4.2% |
| 6 | A-P window | 2.1% |
| 7 | Coronary artery abnormalities | 4.2% |
| 8 | PA valve stenosis | 4.2% |
| 9 | Ao valve stenosis | 4.2% |
| 10 | Mitral valve disease | 2.1% |
| 11 | CoA (isolated/all types) | 4.2% |
| 12 | IAA (isolated/all types) | 2.1% |
| 13 | ToF (all types) | 6.3% |
| 14 | d-TGA (all types) | 4.2% |
| 15 | PAv atresia with IVS | 4.2% |
| 16 | DORV (all types) | 4.2% |
| 17 | TAPVD (all types) | 4.2% |
| 18 | Tricuspid valve atresia | 2.1% |
| 19 | HLHS | 2.1% |
| 20 | c-c-TGA | 2.1% |
| 21 | Trancus Arteriosus | 2.1% |
| 22 | Ebstein Anomaly | 2.1% |
| 23 | Univentricular Anatomy | 2.1% |
| 24 | Heterotaxia Syndromes | 2.1% |
| 25 | Shone's Complex | 2.1% |
| 26 | Core triatriatum | 2.1% |

**Table 2.** Classification of CHD after post hoc analysis

| | | |
|---|---|---|
| 1 | BAov: [Functional 1.4%] & [True 1.65%] no additional disease | 3.035% |
| 2 | VSD (isolated/all types) | 7.9% |
| 3 | ASD (isolated/all types) | 5..4% |
| 4 | PDA (isolated) | 2.6% |
| 5 | c-AVSD | 5.3% |
| 6 | A-P window | 2.6% |
| 7 | Coronary artery abnormalities | 2.6% |
| 8 | PA valve stenosis | 5.3% |
| 9 | Ao valve stenosis | 5.3% |
| 10 | Mitral valve disease | 2.6% |
| 11 | CoA (isolated/all types) | 5.3% |
| 12 | IAA (isolated/all types) | 2.6% |
| 13 | ToF (all types) | 7.9% |
| 14 | d-TGA (all types) | 5.3% |
| 15 | PAv atresia with IVS | 5.3% |
| 16 | DORV (all types) | 5.3% |
| 17 | TAPVD (all types) | 5.3% |
| 18 | Tricuspid valve atresia | 2.6% |
| 19 | HLHS | 2.6% |
| 20 | c-c-TGA | 2.6% |
| 21 | Trancus Arteriosus | 2.6 % |
| 22 | Ebstein Anomaly | 2.6% |
| 23 | Univentricular Anatomy | 2.6% |
| 24 | Heterotaxia Syndromes | 2.6% |
| 25 | Shone's Complex | 2.6% |
| 26 | Core triatriatum | 2.6% |

(sometimes referred to as birth prevalence) depends on how a population is studied[2,7]. Many incidence studies conclude now days to a figure close to 1.2% of live births. To this we need to add another 1.2% approximately of neonates that suffer from a BAov that at birth shows no pathology[4]. These seldom cause problems in childhood but account for many adult patients who require treatment for late-onset aortic stenosis or regurgitation. Any consideration of the burden of CHD must take these into account[4]. More, resent studies have shown a shift of the incidence of adults and median age of patients with severe CHD in the general population from the traditional pediatric age group, since 1985 to 2000. In 2000, there were nearly equal numbers of adults and children with severe CHD. This shift in figures is continues creating a larger adult than pediatric population of patients suffering from CHD[8]. So, this is the essence of CHD: a growing population worldwide of severe and critical forms of the diseases that will need a long-life follow-up and multiple interventional and surgical treatment. On the level of State Health Services, we need to take in consideration that resources to treat CHD are both inadequate and seriously maldistributed worldwide[4]. The 2007–2009 World Society for Paediatric Heart Surgery Manpower Survey noted that about

75% of the world's population has no access to cardiac surgery, and that the distribution of cardiac surgeons as well as the was distribution of cardiovascular centers are very uneven, towards the needs of the bulk of the patients suffering from CHD[9].

All the above-mentioned facts underline the need of an incidence that will be mostly orientated towards a clinical use than a rather academic one. These reasons led to the need of a post hoc analysis of our initial prospective epidemiology analysis, that still has a few weaknesses as it doesn't calculate a nationwide incidence of CHD and doesn't include data from fetal cardiol-

ogy that would represent a more accurate risk of CHD in the total population of the country.

Meanwhile the exception of tiny muscular VSD's with a diameter after birth of less than 1.0 mm,[2,10,11]; ASD II's less than 5.0 mm[2,12] and PDA's less than 1.0 mm in diameter[2,13], that can either spontaneously resolved or have none-specific clinical risk, amalgamates our calculated incidence to a more robust clinical index of 1.48 % regarding the exact index of CHD's that will need medical management.

In summary, the initial study[5] showed a high incidence that has been reduced after our post hoc analysis, but still, a figure of 1.48% is higher than the mean worldwide reporter figure of 1.2%[4,14]. The important message from the initial epidemiology study[5] and its post hoc analysis is that when comparing to the standard western Europe -North Americas data both the critical and severe CHD as well as the percentage of the cyanotic forms of CHD are higher in Azerbaijan. Specifically, the average of critical and severe CHD in western Europe-North Americas is 25-30% and in both of our studies this number is between 46.8-55.3% and for the cyanotic forms of CHD from 20% in western Europe-North Americas, raised from 36.2-41.1%[14]. These data as well as the high incidence of functional BAov 1.65%, clearly indicate a specific spectrum of critical and severe forms of CHD, many of them cyanotic forms of CHD, that are not found in the standard epidemiology of western Europe -North Americas. Our personal explanation to these findings is a possibly related isolated population with a specific genotype in which a high-frequency conjugated marriage custom of the country owns this high and interesting phenotype of CHD's. These findings represent a state population health burden that will be addressed by specific policies in the nearby future.

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## References

1. Mitchell SC, Korones SB, Berendes HW. Congenital heart disease in 56,109 births. Incidence and natural history; (1971); Circulation; 43:323–332.
2. Hoffman J I E, Kaplan S; The Incidence of Congenital Heart Disease; (2002); JACC Vol. 39, No. 12
3. Zimmerman MS, Carswell Smith AG, Sable GA, et.al for the Global Burden of Diseases, Injuries, and Risk Factors Study 2017; Global, regional, and national burden of congenital heart disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017; (2020); Lancet Child Adolesc Health; 4: 185–200
4. Hoffman J I E; The global burden of congenital heart disease;(2013); Cardiovascular Journ. of Africa; Vol 24, No 4
5. Petropoulos AC, Hudiyeva A, Behbudov V, Mustafayeva G, Guliyev N, Huseynov R, Seyidov N; The incidence of congenital heart disease in Baku-Azerbaijan. prospective epidemiology study; (2019); ADC 2019;104(Suppl 3): A1–A428
6. Petropoulos AC; The Bicuspid Aortic Valve Syndrome: A Multifaceted Challenge: Do We Know Enough; J Cardiol 2018, 2(4): 00012 9
7. Wren C. The epidemiology of cardiovascular malformations. In: Moller JH, Hoffman JIE, Benson DW, van Hare GF, Wren C, eds. Pediatric Cardiovascular Medicine; (2012); Oxford, England: Wiley-Blackwell :268–275
8. Marelli AJ, Mackie AS, Ionescu-Ittu R, Rahme E, Pilote L. Congenital heart disease in the general population: changing prevalence and age distribution;(2007); Circulation;115:163–72
9. Bernier PL, Stefanescu A, Samoukovic G, et al. The challenge of congenital heart disease worldwide: epidemiologic and demographic facts; (2010); Sem thorac cardiovasc surg. Pediatr Card Surg A; 13:26–34.
10. Du ZD, Roguin N, Wu XJ. Spontaneous closure of muscular ventricular septal defect identified by echocardiography in neonates;(1998) Cardiol Young; 8:500–5.
11. Wolfenden J.L, Petropoulos AC, Carvalho JS; Apical and mid-muscular ventricular septal defects in the fetus: prenatal characteristics and outcome; (2007); Ultrasound in Obstetrics & Gynecology; 30: 456–546
12. Brassard M, Fouron JC, van Doesburg NH, Mercier LA, De Guise P. Outcome of children with atrial septal defect considered too small for surgical closure; (1999); Am J Cardiol ;83:1552–5.
13. Lloyd TR, Beekman RH, 3rd. Clinically silent patent ductus arteriosus (letter);(1994); Am Heart; 127:1664–5
14. Petropoulos A C, Daskalakis G, Anatolitou F, Eleftheriadis M, Antsaklis P, Moutafi A, Petropoulos P, Varvarigou A, Charitou A; The importance of screening for critical and severe congenital cardiac diseases by pulse oximetry in the early neonatal age; Position statement of the Hellenic Society of Perinatal Medicine; Journal of Pediatric and Neonatal Individualized Medicine 2021;10(2):e100211