EURASIAN JOURNAL OF CLINICAL SCIENCES

EJCS, Vol 1, No 4 (2018)
Review Article

Prevention and Early Detection of Congenital Heart Defects. Where do we stand?

A.C. Petropoulos*[1,2] MD

[1] *Mərkezi Klinika*

[2] *Azerbaijan Medical University, Baku, Azerbaijan.*

***Corresponding author**: * Dr Andreas C Petropoulos, andrepetropoulos@gmail.com*

Abstract

Introduction: Since the origin of Medicine in 4th BC. Century research has taught us that learning and practicing preventive medicine is properly the best method to prevent disease from happening in the first place. Preventive health care must be planned and executed ahead of time, even when illness/ disease, is absent, especially for those that are common and fetal. Among neonates and infants, congenital heart disease (CHD) is responsible for the largest proportion of mortality caused by birth defects. Actual numbers of patients and mortality resulting from CHD reportedly is increasing. In the developed world the treatment of CHD has escalating costs for health care systems and private covered patients, while in low-income countries it is not always available. Prevention is urgently needed to tackle the increasing needs.

Aim: To present the current practice in preventing/early detecting CHD and justify why pulse oximetry is the best available, early detecting postnatal screening test we currently have.

Methods: The existing in use preventing/early detecting methods for avoiding or early diagnosing CHD are: 1. Eliminate the maternal risk factors by obtaining a good level of health and medical surveillance during pregnancy. 2. Avoiding teratogenic agents, 3. Detecting risk factors from Family History, 4. Delivering a balanced Nutrition during Pregnancy 5. Obtaining at least an experienced 4-chamber view and outflow tracts imaging during the 20-weeks anomaly scan. 6. Fetal Echocardiography when indicated 7. Postnatal evaluation by experienced Pediatricians. 8. Pulse Oximetry, screening test after 72 hours post-delivery in term babies. 9. Hyperoxia test when indicated.

Conclusion: Although CHD's are the most common, high morbidity and mortality, congenital malformations, we still lack a single, easy to apply, non-invasive and low-cost screening test, for prevention/early detection. The current preventive methods must be combined to counterbalance the CHD prevalence. Meanwhile, they are costly and partially accessible. The most advantageous method for minimizing CHD deaths worldwide seems to be currently, pulse oximetry combined with clinical assessment.

Keywords: Prevention/early detection of Congenital Heart Diseases; Fetal Echocardiography; Pulse oximetry screening; Critical Congenital Heart Disease

Abbreviations: CHD: Congenital Heart Disease; NT: Nuchal Translucency; echo-2D: Echocardiography; DV-flow: Ductus Venosus; PAPP-A: Pregnancy-Associated Plasma Protein-A; free–hCG: Free Beta-Human Chorionic Gonadotropin; 1st TST: First Trimester Screening Test; c-CHD: Critical-CHD; DA: Ductus Arteriosus.

Introduction. Hippocrates first stated, in the 4th century b. C. that prevention is the best medical action to address any Sickness. From his days until know the value of his statement "Prevention is better than cure" -if and when possible- has been tested numerous times and has been adopted as the golden standard of care. Any prevention method used in clinical practice, ought following specific qualities. It must be reliable in detecting a common and/or even lethal disease under its scope, with a high level of sensitivity and specificity. It needs to be as less as invasively, easy to apply and inexpensively around the globe [1]. It is also self evident that the more preventive methods are used, the less accurate they are and therefore a combination of them is needed. CHD fall under these circumstances [2-4]. Where any combination of prevention is better than none. This has also been proved and supported by efficiency and cost effectiveness studies [6]. CHD, are not only commonly found but also a major cause of serious morbidity and mortality. They are usually defined

as clinically significant structural heart disease present at birth [2,6]. The incidence of CHD at birth (birth prevalence) depends on how a population has been studied. Before the introduction of echocardiography, incidence diagnosis was ranging from 8 -12 /1 000 live births [7]. Much depends on how early and how intensively the diagnosis was made. The best current figure to use is 10–12 per 1 000 live births [8]. Some caveats apply when calculating the prevalence in neonatal age. Few CHD, for example: valve lesions of Marfan's or Ehlers - Danlos syndromes, left ventricular (LV) obstruction due to hypertrophic Cardiomyopathy [8], and late presenters of moderate size atrial septal defects or coarctation of the aorta that can be found in any stage of life masquerading as hypertension [9]. Not to forget the very common bicuspid aortic valves that can present later in life with stenosis and/or regurgitation [8,9]. Another important issue is the relation incident-birth rates: Is the incident number universal or do countries with higher births by year having a higher incidence? In 2012, the Ministry of Health of the People's Republic of China reported a prevalence of 1.512% of CHD in China, with the comment of an even higher number when a national study of all age-all CHD will have been completed [10]. Furthermore, the important fact is not the prevalence of CHD per country but how many children suffering from CHD are born per million populations in each country. This information is given knowing the fertility rate (the number of children born per woman) in different countries. Open sources such as Wikipedia, United Nations reports and the CIA World Factbook, indicate that low income and lower middle-income countries of sub-Saharan Africa, Middle East, Islamic states of the Indian peninsular and Southeast Asia present the higher fertility rates from more than 4 to 8 children per woman. So, in these particular countries we will find more children suffering from CHD [8]. Finally, children with CHD have additional morbidity. These can be associated genetic syndromes (most common Down's syndrome), defects in several other systems, and neuro developmental problems [3]. Many studies have showed moderate to severe neuro developmental disabilities in over 50% of children with severe or palliated surgically as neonate's CHD. Even in those with less severe anomalies, 25% will have a degree of cognitive impairment [11].

Finally, the resources to treat CHD both in a matter of Human and finance are inadequate and seriously mal distributed around the world, not allowing these patients the quality of care needed that involves a long-life follow-up by specialists in the field as well as an amount of additional interventional and/or surgical procedures as they age [8,12,13].

Methods

The methods used historically in preventing / early detecting CHD were close linked to the evolution of many fields of medicine. These included biochemistry embryology, epidemiology, pediatrics, obstetrics, radiology, in combination with the evolution of ultrasonography and genetics. The first published agent linked to CHD was maternal infection from rubella virus in 1941 [14]. Since then, we have advanced in detecting several risk factors for CHDs such as family history of a sibling suffering from CHD or of many spontaneous unexplained miscarriages, exposure to teratogenic medications or radiation, and parenteral CHDs. Unfortunately most causes leading to CHDs remain still unexplained [14]. Regarding the maternal element of the pregnancy, preventing CVD was historical focused on the maternal age (less risky if under 35 years old), avoiding during pregnancy viral infections, having a balanced diet rich in iron, calcium, vitamins and folic acid and avoid pregestational diabetes [15,16]. A regular physician's follow-up during the pregnancy and a balanced increase of the maternal weight aiming to avoid obesity and diabetes, was the only prevention/early detection methods until the era of advanced ultrasonography and biochemistry. In recent years three more indications have been added. Multiple pregnancy, In-vitro fertilized fetuses and increased nuchal translucency (NT) [17].

Since the first reported use of echocardiography (echo-2D) for prenatal diagnosis of CHD in 1980 by pediatric cardiologists [18] this technique has been used worldwide to detect prenatally CHDs. The evaluation is mostly done between the 18-22

weeks of pregnancy. It remains one of the most challenging methods of prenatal diagnosis and many studies have focused on its effectiveness in detecting fetal CHDs, and provided convincing evidence about its reliability and high diagnostic efficiency [19]. Recent studies have proved efficiency in early detection of CHD by echo-2D delivered in the end of the first and the beginning of the second trimester. Early fetal echocardiography in high risk pregnancies have been reported as diagnostic in 96% of cases -in the hands of specialist Pediatric Cardiologists- detecting isolated defects in 48% and major CHD in 67%. This allows early possible termination of pregnancy or planning strategies for delivering the best treatment. Additional benefit exists when the scan is normal, allowing family reassurance [20].

A new era in prenatal diagnosis of CHD has started with the combination of biochemical tests and imaging indexes in the first trimester of pregnancy. Today we can offer in 11-13 weeks of gestation age a combination of a measurement of the NT, the doppler flow pattern in the ductus venosus (DV-flow) combined with maternal serum pregnancy-associated plasma protein-A (PAPP-A), and free beta-human chorionic gonadotropin (free -hCG). This test - also known as first trimester screening test(1stTST) provides an independent contribution in the prediction of chromosomal abnormalities that are very common related to CHD as Down's syndrome (40-50% will suffer from CHD). It increases the detection rate to 96% at a cost of a 2.6% false-positive rate. In twin pregnancies, abnormal DV-flow is associated with chromosomal abnormalities and CHD [21,22].

The most resent advancement in early postnatal detection of CHD is the use of pulse oximetry to screen term newborns for critical-CHD(c-CHD). With this term we are indicating a subcategory of CHD in which early diagnosis and interventional/surgical treatment must be offered in the first month of life to avoid serious morbidity or death. In this group we in cloud all the complex cyanotic defects, the systemic and pulmonary ductus arteriosus depending circulations and the severe LV outflow tract obstruction conditions [2,4,9]. Table 1 summarizes all current methods of Prevention/Early detection of CHD in a chronological order.

Discussion

As aforementioned, CHD carry a high incidence rate and actual number of children worldwide suffering - mostly in countries with high fertility rate- is dramatical increasing. The 2007–2009 World Society for Pediatric 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 was very unbalanced worldwide [8-13]. We have demonstrated above the variety of available methods. These start from low cost and easy to apply measures, such as avoidance of teratogenic elements or conditions, continue with screening family history for CHD risk factors and reach to a good surveillance of the pregnancy - avoiding under or over nutrition- and delivering a diet rich in folic acid, minerals and vitamins [5-16]. In the early 1980's the introduction of fetal echo-2D, seemed to be the ultimate method in detecting CHD. Although the progress that has been achieved from a technical stand of point [22], the use of standard guidelines introduced in 2006, by the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) that address the "basic" and "extended basic" cardiac ultrasound examinations [23] and the Fellowships offered to pediatric cardiologist to subspecialize in fetal cardiology, rates of prenatal CHD detection remain low even in patients suffering from c-CHD [24]. Comparative study has shown that detecting rates can range from 42-83% [23,25]. These rates can improve up to 96% in centers dedicated to Fetal Medicine, equipped with specialists and up to date technology [19]. Taking in consideration the availability and cost of these methods, they are far from to be the ideal screening test for CHD.

Even more expensive, limited to the more privilege part of the world is the 1st TST combined to optional fetal echo-2D, which can deliver high rates in detecting CHD when indicated [17-22]. On the other hand, the only means of early universally offered postnatal detection, for CHD has been a physical examination that is delivered by a pediatrician in best cases, just before discharge from a maternity facility.

Current methods of Prevention/Early detection of CHD in a sequential time frame		
Prior to Pregnancy	**Immediate Prenatal**	**Immediate Postnatal**
Maternal risk factors: Age of potential mother -Suffering from CHD, or HOCM can increase risk up to 15-50% of reappearance in next generation - Diabetes Mellitus I or II - Maternal lupus erythematosus / Connective Tissue Diseases – Obesity - Rubella virus, HIV, Coxasackie virus, CMV, Parvovirus - Medicines (e.g. amphetamines, warfarin, retinoic acid, valproic acid, etc.) - Alcohol abuse - Poor OB/G F/U		
Family History: Previous sibling with CHD - Paternal suffering from CHD - Certain hereditary syndromes linked with CHD (e.g. T-21, CHARGE Association, VATER/VACTERL Association, Di George, Turner, Marfan, Williams, Noonan, Holt-Oram, Ellis van Greveld, Familial CMP, others)		
Avoidance of teratogenic agents: Medications - Viral infections – Radiation - Poor diet in folic acid		
Diet during Pregnancy: Rich with folic acid, minerals, Iron and Vitamins. - Balanced caloric intake		
	20-weeks anomaly Scan: Not adequate 4 chamber view and/or outflow tracts - Presence of extracardiac malformations that increase rate of CHD (e. g. Hydrocephalus, Esophageal atresia with TE fistula, imperforated anus, Renal dysgenesis, omphalocele, others)	
	Fetal Echocardiography-Cardiology Consultation When Indicated	
		Physician postnatal Assessment Using pulse oximetry and ECG in assessment of Apgar Score
		Pulse Oximetry Screening Test for c-CHD Simultaneous measurement of Pre- and Post DA after the 72h postnatally in term neonates with SatO2 > 95% and Pre/Post DA difference < 3%, with Pre- DA SatO2 >95%
		Hyperoxia Test When Indicated to differentiate Respiration/Cardiac cyanosis

Table 1: Prevention/Early detection of CHD

This can be done as early as in six hours after an uneventful vaginal delivery and not later than three days. Apgar score, "color" of baby skin index has nowadays been replaced with a pulse oximetry measurement of the oxygen saturation. This has established pulse oximetry (a low cost test) in every day practice [26]. It will detect mostly after the Ductus Arteriosus (DA) has physiologically closed (day 2 of life in term babies) all the cyanotic babies. Those that fail a hyperoxia test and proved not to have early sepsis onset will be babies suffering from c-CHD. This has been proven by Zhao et.al. Study of significance importance recently showing the addition of pulse oximetry to clinical assessment improves sensitivity for detection of c-CHD from 77·4% to 93·2%, when used in simultaneous pre and post DA measurements, after 72 hours of birth [27]. With the technological advances in pulse oximetry devises and improving the perfusion index we will be probable able to detect and noncyanotic c-CHD as critical Left Heart Obstructive diseases, e.g. Coarctation of Aorta, Interrupted Aortic Arch and severe Aortic valve stenosis, during the first week of life of the term neonate [28].

Conclusion

Till nowadays, the Holy Grail of CHD prevention/early detection has not been found. Taking in to consideration the vast patient's numbers in the less privilege parts of the world, our opinion is a combine strategy. Additional to avoiding the teratogenic elements or conditions, promoting a healthy pregnancy for the future mother and her fetus and selecting patients with risk factors for CHD, pulse oximetry combined with clinical assessment is a feasible and reliable postnatal early detection screening test. This simple, low cost, noninvasive and accurate method must be used in maternity hospitals to screen for c-CHD.

Financial source: Did not use financial resources.
Conflict of interest: None.

REFERENCES

1. Schiefsk M (2005) Hippocrates on Ancient Medicine. Brill Academic Publishers
2. Rudolf AM (2009) Congenital Diseases of the Heart-Clinical & Physiological Considerations 3rd (Edn.), Wiley- Blackwell.
3. Boyd PA, Devigan C, Garne E, Khoshnood B, Loane M, et al. (2005) Prenatal Screening Policies in Europe. EUROCAT Special Report, Ulster.
4. Knowles R, Griebsch I, Dezateux C, Brown J, Bull C, et al. (2005) Newborn screening for congenital heart defects: a systematic review and cost effectiveness analysis. Health Technol. Assess 9(44): 1-152.
5. (2013) Jekel's Epidemiology, Biostatistics, Preventive Medicine, and Public Health Publisher 4th (Edn.), Saunders.
6. Mitchell SC, Korones SB, Berendes HW (1971) Congenital heart disease in 56,109 births. Incidence and natural history. Circulation 43(3): 323-332.
7. Wren C (2012) The epidemiology of cardiovascular malformations. In: Moller JH, Hoffman JIE, Benson DW, van Hare GF, Wren C (Eds.), Pediatric Cardiovascular Medicine. Wiley-Blackwell, Oxford, England, pp: 268-275.
8. Hoffman JIE (2013) The global burden of congenital heart disease Cardiovasc. Cardiovasc J Afr 24(4): 141-145.
9. Petropoulos AC, Moschovi M, Xudiyeva A, Qarayev F, Isayev I (2017) Late Coarctation Presenters Suffer Chronic Hypertension Resisting to Medicine Treatment. Peertechz J Pediatr Ther 3(1): 001-008.
10. (2012) Ministry of Health of the People's Republic of China. National birth defects control and prevention report.
11. List_of_sovereign_states_and_dependent_territories _b y_fertility_rate
12. Marino BS, Lipkin PH, Newburger JW, Peacock G, Gerdes M, et al. (2012) Neurodevelopmental outcomes in children with congenital heart disease: evaluation and management: a scientific statement from the American Heart Association. Circulation 126(9): 1143-1172.
13. Bernier PL, Stefanescu A, Samoukovic G, Tchervenkov CI (2010) The challenge of congenital heart disease worldwide: epidemiologic and demographic facts. Sem thorac cardiovasc surg. Pediatr Card Surg A 13: 26-34.
14. Brent RL (2004) Environmental causes of human congenital malformations: the pediatrician's role in dealing with these complex clinical problems caused by a multiplicity of environmental and genetic factors. Pediatrics 113(4S): 957-968.
15. Petropoulos AC, Xudiyeva A, Ismaylova M (2016) Congenital Heart Disease and Maternal Diabetes Mellitus. International Journal of Diabetes & Clinical Diagnosis 3: 118.
16. Bader RS, Hornberger LK, Huhta JC (2008) The Perinatal cardiology 1st (Edn.), Handbook, Elsevier

Inc, Mosby.
17. Midan MF, Alsheemy RI, Eid SM, Salam MEA (2016) Efficacy of fetal echocardiography in prenatal diagnosis of congenital heart diseases. Int J Reprod Contracept Obstet Gynecol 5(5): 1553-1557.
18. Kleiman CS, Hoddins JC, Jaffee CC, Lynch DC, Talner NS (1980) Echocardiography studies of the human fetus: prenatal diagnosis of congenital heart disease and cardiac dysrhythmias. Pediatrics 65(6): 1059-1067.
19. Simpson JM (2009) Impact of fetal echocardiography. Ann Pediatr Cardiol 2(1): 41-50.
20. Carvalho JS, Moscoso G, Tekay A, Campbell S, Thilaganathan B, et al. (2004) Clinical impact of first and early second trimester fetal echocardiography on high risk pregnancies, Heart 90(8): 921-926.
21. Maiz N, Nicolaides KH (2010) Ductus Venosus in the First Trimester: Contribution to Screening of Chromosomal, Cardiac Defects and Monochorionic Twin Complications, Fetal Diagn Ther 28(2): 65-71.
22. Wapner R, Thom E, Simpson JL, Pergament E, Silver R, et al. (2003) First-Trimester Screening for Trisomy's 21 and 18, N Engl. J Med 349(15): 1405-1413.
23. Rocha LA, Araujo Júnior E, Machado Nardozz LM, Moron AF (2013) Screening of fetal congenital heart disease: the challenge continues, Rev Bras Cir Cardiovasc 28(3): 5-7.
24. (2006) International Society of Ultrasound in Obstetrics & Gynecology. Cardiac screening
25. examination of the fetus: guidelines for performing the 'basic' and 'extended basic' cardiac scan. Ultrasound Obstet Gynecol 27(1): 107-113.
26. Quartermain MD, Pasquali SK, Hill KD, Goldberg DJ, Huhta JC, et al. (2015) Variation in Prenatal Diagnosis of Congenital Heart Disease in Infants, Pediatrics 136(2): e378-385.
27. (2016) Textbook of Neonatal Resuscitation Program (7th edition) Update; AAP.
28. Qu-ming Zhao, Xiao-jing Ma, Xiao-ling Ge, Fang Liu, Wei-li Yan, et al. (2014) Pulse oximetry with clinical assessment to screen for congenital heart disease in neonates in China:a prospective study, The Lancet 384(9945): 747-754.
29. de Wahl Granelli A, Wennergren M, Sandberg K, Mellander M, Bejlum C, et al. (2009) Impact of pulse oximetry screening on the detection of duct dependent congenital heart disease: a Swedish prospective screening study in 39,821 newborns. BMJ 338: a3037.