Ege Journal of Medicine / *Ege Tıp Dergisi* 2016;55(2):78-81

The prevalence and distribution of congenital heart disease in neonates with Down syndrome in Southeastern Anatolian Region of Turkey

Türkiye'nin Güneydoğu Anadolu Bölgesi'ndeki Down sendromlu yenidoğanlarda konjenital kalp hastalığı prevalansı ve dağılımı

Bedri Aldudak[2] Muhittin Çelik[1] Melek Akar[1] Osman Akdeniz[2] Sertaç Hanedan Onan[2]
[1]Diyarbakır Children's Hospital, Clinic of Neonatology, Diyarbakır, Turkey
[2]Diyarbakır Children's Hospital, Clinic of Pediatric Cardiology, Diyarbakır, Turkey

Abstract

Aim: The prevalence of congenital heart disease (CHD) was reported as 40-60% in patients with Down syndrome (DS). As the prevalence and distribution of congenital heart defects in DS varies according to population and ethnicity, we aimed to investigate CHD in patients with DS in Southeastern Anatolian Region.

Materials and Methods: DS cases who were followed-up in neonatal intensive care unit between 2011 and 2013 were included. An experienced pediatric cardiologist examined all cases by transthoracic echocardiography using GE Vivid 3 device. Hospital records of all patients were reviewed.

Results: A total of 87 neonates (53 males) were evaluated. The mean age of the presentation was 8.6±5.2 days (range 0-30 days). The number of patients with CHD was 57 (65.5%); one defect in 37 cases (64.9%), two defects in 16 cases (28%), and three defects together in 4 cases (7%). The distribution of CHD in patients revealed atrioventricular septal defect (AVSD) in 23 patients (29.8%), ventricular septal defect (VSD) in 22 patients (28.5%), secundum atrial septal defect in 18 patients (23.3%), patent ductus arteriosus in 11 patients (14.2%), and tetralogy of Fallot in 1, univentricular heart in 1, and intermittent aortic arc in 1 patient.

Conclusion: To the best of our knowledge, this is the first study performed only on neonates with DS. The most common defect was AVSD although incidence of VSD was higher than expected. Performing CHD screening during neonatal period is more reliable in patients with DS. The variation in the prevalence and distribution of CHD indicates regional and ethnic variability among patients with DS.

Keywords: Congenital heart disease, Down syndrome, neonate.

Öz

Amaç: *Down sendromlu (DS) hastalarda konjenital kalp hastalığı (KKH) sıklığı %40-60 arasında değişmektedir. Down sendromlu hastalarda KKH sıklığı ve dağılımı toplumlara ve etnik kökene göre farklılık gösterebildiğinden bu çalışmada, Güneydoğu Anadolu Bölgesi'nde DS olan yenidoğanlarda KKH sıklığını ve dağılımını incelemeyi amaçladık.*

Gereç ve Yöntem: *Çalışmaya 2011-2013 yılları arasında yenidoğan yoğun bakım ünitesine izlenen DS olgular alındı. Deneyimli pediyatrik kardiyolog, tüm olguları GE Vivid 3 cihazı ile transtorasik ekokardiyografi ile incelendi. Tüm hastaların hastane dosyaları değerlendirildi.*

Bulgular: *Çalışmaya 53'ü erkek toplam 87 yenidoğan alındı. Olguların yaş ortalaması 8.6±5.2 gün (0-30) idi. Elli yedi olguda (%65.5) KKH saptandı; 37 olguda (%64.9) tek defekt, 16 olguda (%28) iki defekt, 4 olguda (%7) ise üç defekt birlikte bulundu. Defekt sıklığı olarak 23 (%29.8) atrioventriküler septal defekt (AVSD), 22 (%28.5) ventriküler septal defekt (VSD),18 (%23.3) sekundum atriyal septal defekt, 11 (%14.2) patent duktus arteriosus, 1 Fallot tetralojisi, 1 tek ventrikül ve 1 kesintili aortik ark saptandı.*

Sonuç: *Bilgilerimize göre, yenidoğan döneminde DS hastalarda yapılan ilk çalışmadır. AVSD en sık görülen defekt olmakla beraber VSD beklenenden daha yüksek bulundu. DS hastalarda KKH taramasının yenidoğan döneminde gerçekleştirilmesi daha güvenilirdir, KKH sıklığı ve dağılımının varyasyonu bölgesel ve etnik farklılıklar göstermektedir.*

Anahtar Sözcükler: *Konjenital kalp hastalığı, Down sendromu, yenidoğan.*

Corresponding Author: Muhittin Çelik
Diyarbakır Children's Hospital, Clinic of Neonatology,
Diyarbakır, Turkey
Received: 19.06.2015 Accepted: 03.08.2015

Introduction

The prevalence of congenital heart defects in patients with Down syndrome (DS) has been reported as 40-60% (1,2). The most common pathology is atrioventricular septal defect (AVSD) (3). However, studies performed in different populations indicated a wide variability in the distribution of congenital heart defects. While the most prevalent pathology in the western countries is AVSD, ventricular septal defect (VSD) has been reported as the most common congenital heart defect in the Asian societies (3,4). In the present study, we aimed to investigate the prevalence and distribution of congenital heart defects in neonates with Down syndrome (DS) in Southeastern Anatolian Region of Turkey.

Materials and Methods

In the study, we included 87 cases at the age of 0-30 days with DS stigmata who admitted to Diyarbakır Children's Diseases Hospital between 2011 and 2013. Data were retrospectively collected from the hospital records. All patients were screened for congenital heart disease (CHD) in pediatric cardiology clinic. Down syndrome diagnosis was confirmed by karyotype analysis from peripheral blood samples. All cases were examined by transthoracic echocardiography using GE Vivid 3 device by an experienced pediatric cardiologist. AVSD was described as complete in the presence of inlet VSD and primum atrial septal defect (ASD) with a single atrioventricular (AV) valve, and incomplete in the presence of primum ASD with two valves without an interventricular shunt (4-5). The cases found to have patent ductus arteriosus (PDA) within the first three days of life, were re-examined two weeks later.

Statistical analyses were performed using SPSS 16.0 for Windows statistical software. Data was presented as mean±SD. Ratio were compared using chi-square test. A p value <0.05 was considered statistically significant.

Results

A total of 87 neonates (53 males) were enrolled in the study. The mean age of the presentation was 8.6±5.2 days (range 0-30). Echocardiographic evaluation showed CHD in 57 out of 87 cases (65.5%) from whom 37 cases (64.9%) had one, 16 cases (28%) had two, and 4 cases (7%) had three defects. There was no statistically significant difference between the frequency of CHD in females (73.5%) and males (60.4%) (p=0.208). In total, 77 congenital heart defects were detected in 57 cases. The most prevalent CHD was AVSD (n=23; 29.8%) followed by VSD (n=22; 28.5%), secundum ASD (n=18; 23.3%) and PDA (n=11; 14.3%) (Table-1).

Discussion

Down syndrome is the most common chromosomal abnormality occurring in neonates with an incidence of 1/660 (5). Congenital heart defects have been reported at a rate of 40-60% (3,6). Association of CHD is one of the most important predictive factor affecting morbidity and mortality in these patients (5). AVSD has been reported as the most common congenital heart defect in children with DS (3). On the other hand, studies reported that prevalence and distribution of CHD among children with DS varies by regions and ethnic groups (3-5). The studies from western countries reported AVSD as the frequent defect in DS (3). The studies performed in the US reported CHD prevalence as 44-48% in DS. In these studies, prevalences of four common congenital defects were informed as AVSD (38.8-60%), VSD (15.6-35%), secundum ASD (9.6-28.6%) and tetralogy of Fallot (TOF) (3-7.3%) (4,6,7). In the studies from Europe, the prevalence of CHD was 44.6%, and AVSD was the predominant defect with a prevalence of 41.9-59%.

Table-1. Distribution of congenital heart disease in patients with Down syndrome*.

Defect type	n	% of cases	% of defects
AVSD	23	40	29.8
VSD	22	38.5	28.5
ASD secundum	18	31.5	23.3
PDA	11	20	14.2
TOF	1		
UVH	1		
IAA	1		

* AVSD: Atrioventricular septal defect, VSD: Ventricular septal defect, ASD: Atrial septal defect, PDA: Patent ductus arteriosus, TOF: Tetralogy of Fallot, UVH: Univentricular heart, IAA: Intermittent aortic arc

The prevalence of CHD in Asian countries differed between 46.4 to 65.5% (Table-2). In contrast to the western countries, the most prevalent pathology is VSD in Asian countries with the rates of 39.2-52.9% (3). The prevalence of AVSD in Asian countries decreases to 11.8-22%, whereas secundum ASD and TOF were found as 11-23.4% and 3.5-13.4%, respectively (3,8,9). In a study reporting a large cohort of 385 patients from Singapore, PDA was reported as the second most common lesion preceded by VSD with a rate of 34.3% (3). However, secundum ASD was informed to be the most common defect with the prevalence of 40% in Latin America (10).

The only study conducted on the prevalence and distribution of CHD in Turkish patients with DS was reported by Nisli et al. (5). In this largest cohort assessing CHD in DS patients, Nisli et al. evaluated 1042 cases with DS and reported the prevalence of CHD as 39.5%. Single defect was detected in 77.6% of the cases, and the others were found to have multiple defects. Besides, AVSD was the most common pathology followed by secundum ASD and VSD, and there was a remarkable low rate of TOF

that was detected in only two cases (1/160) in this study (Table-2).

Table-2. A Summary of Studies Evaluating the Congenital Heart Defects in Down Syndrome*.

	Current study	Nisli et al. 2008 Turkey	Tan et al. 2013 Singapore	Hoe et al. 1990 Malaysia	Hijii et al. 1997 Japan	Freeman et al. 1998 USA	Stoll et al. 1990 France	Pradat 1992 Sweden
Study period	2011-2013	1994-2007	1996-2010	1986-1987	1971-1994	1989-1995	1979-1987	1981-1986
Number of cases (n)	87	1042	588	34	373	227	139	167
Cases with CHD (%)	65.5	39.5	65.5	50	46.4	44	44.6	-
Types of CHD (%)								
AVSD	29.8	34.2	15.6	11.8	22	45	41.9	59
VSD	28.5	16.5	39.2	52.9	45.1	35	29	31.7
Sec. ASD	23.3	16.7	23.4	0	11	26	N/A	N/A

* CHD: Congenital heart disease, AVSD: Atrioventricular septal defect, VSD: Ventricular septal defect, ASD: Atrial septal defect.

To the best of our knowledge, the present study is the first study including only neonates with DS. The prevalence of CHD in our study (65.5%) was extremely higher than the rate in the study published by Nisli et al. from Turkey, and studies from western countries such as US and Europe (Table-2). However, it was similar to the prevalence reported in the study from Singapore (3). In addition, the distribution of CHD revealed a similar rate of AVSD (29.8%) and VSD (28.5%) in our study whereas ASVD was predominant in western countries and in the study of Nisli et al., and VSD was predominant in Asian countries (5). We detected TOF in one patient which was similar to Nisli et al. (5). These results suggested a marked variability in the prevalence and distribution of CHD in DS arising from ethnic and regional differences.

On the other hand, it is well known that patients with DS have higher rates of morbidity and mortality compared to the general population (11). In the presence of CHD, relative mortality risk depending on age differed from 1.5 to 5.8 in patients with DS (12). Therefore, we suggest that investigating the prevalence of CHD during the neonatal period could be more reliable and provide more accurate results in patients with DS. This could also explain the marked variations between the prevalence of CHD in the present study and the study of Nisli et al. that were performed in children with DS in Turkey. In addition, our study was performed in the part of Turkey where Kurdish population was the largest ethnic subgroup with a high rate of consanguineous marriage. Thus, apart from DS, other genetic causes influencing congenital heart defects may play a role in the high prevalence in our study. A disadvantage of performing CHD screening in neonatal period could be high rate of false positivity due to physiological PDA. Thus, we strongly recommend that cases diagnosed with PDA especially in the first three days of life should be re-examined later (13-14).

Conclusion

CHD prevalence among patients with DS varies by regions, ethnicity and time of evaluation. Our study is the first investigation performed in neonates with DS in the Southeastern Anatolia Region of Turkey. Further studies including larger number of patients are required to confirm the exact prevalence and distribution of CHD in DS in this region.

References

1. Rodriguez LH, Reyes JN. Cardiopatias congenitas en el syndrome de Down. Bol Med Hosp Infant Mex 1984;41(11):622-5.
2. Khoury MJ, Erickson J. Improved ascertainment of cardiovascular malformations in infants with Down's syndrome, Atlanta, 1968–1989. Am J Epidemiol 1992;136(12):1457-64.
3. Tan M, Xu C, Sim SKR, Seow ALH, Tan TH, Quek SC. Types and distribution of congenital heart defects associated with trisomy 21 in Singapore. J Paediatr Child Health 2013;49(3):223-7.
4. Freeman SB, Taft LF, Dooley KJ, Allran K, Sherman SL, Hassold TJ et al. Population-Based Study of Congenital Heart Defects in Down Syndrome. Am J Med Genet 1998;80(3):213-7.
5. Nisli K, Oner N, Candan S, et al. Congenital heart disease in children with Down's syndrome: Turkish experience of 13 years. Acta Cardiol 2008;63(5):585-9.
6. Ferencz C, Neill CA, Boughman JA, Rubin JD, Brenner JI, Perry LW. Congenital cardiovascular malformations associated with chromosome abnormalities: An epidemiologic study. J. Pediatr 1989;114(1):79-86.
7. Martin GR, Rosenbaum KN, Sardegna KM. Prevalence of heart disease in trisomy 21: An unbiased population. Pediatr Res 1989;25(1):77.
8. Lo NS, Leung PM, Lau KC, Yeung CY. Congenital cardiovascular malformations in Chinese children with Down's syndrome. Chin Med J 1989;102(5):382-6.

9. Hijii T, Fukushige J, Igarashi H, Takahashi N, Ueda K. Life expectancy and social adaptation in individuals with Down syndrome with and without surgery for congenital heart disease. Clin Pediatr 1997;36(6):327-32.
10. Vida VL, Barnoya J, Larrazabal LA, Gaitan G, De Maria GF, Castenada AR. Congenital cardiac disease in children with Down's syndrome in Guatemala. Cardiol Young 2005;15(3):286-90.
11. Epstein CJ. Trisomy 21: Down Syndrome in Rudolph Pediatrics. 20th ed. Appleton&Lange. USA 1996;298.
12. Day SM, Strauss DJ, Shavelle RM, Reynolds RJ. Mortality and causes of death in persons with Down syndrome in California. Developmental Medicine & Child Neurology 2005;47(3):171–6.
13. Çil E. Yenidoğan ve prematürelerde patent duktus arteriyozus. Güncel Pediatri 2006;3(1):69-71.
14. Aldudak B, Kervancioglu M. Effect of mode of delivery on postnatal decline in pulmonary artery pressure. Saudi Med J 2011;32(6):579-83.