IJN
Iranian Journal of Neonatology
http://ijn.mums.ac.ir

Open Access
Original Article

Congenital Heart Defects in Children with Upper Gastrointestinal Anomalies

Hassan Mottaghi Moghaddam Shahri[1], Fatemeh Soltan Zegheibizadeh[2*], Sina Afzoon[2], Hamid Reza Kianifar[3], Zahra Abbasi[4]

1. Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Department of Pediatrics, Mashhad university of Medical Sciences, Mashhad, Iran
3. Mashhad Universi of Medical sciences, Mashhad, Iran
4. Akbar Clinical Research and Development Unit, Mashhad University of Medical Sciences, Mashhad, Iran

ABSTRACT

Background: Congenital heart defect (CHD) is one of the leading causes of neonatal death. Although the majority of CHDs are isolated, a significant number of them are associated with noncardiac anomalies. Esophageal Atresia (EA)/ Tracheoesophageal Fistula (TEF) is the most common congenital disorder of the upper GI tract. It is estimated that up to 70% of EA/TEF infants have other associated congenital anomalies such as CHD. This study determined the proportion of heart anomalies among the diseases of the upper GI tract in Imam Reza Hospital of Mashhad.

Methods: The records of 38 infants with upper GI obstruction who were referred to the Pediatric Cardiology Clinic of Imam Reza Hospital in Mashhad between 2001 and 2017 were evaluated in this retrospective study. Data were coded and entered into SPSS software (version 16) and analyzed using Chi-square and T-test.

Results: In this study, 38 babies with upper GI obstruction were evaluated (20 patients were female, 52.6%), and the average birth weight was 2.390 +-0.870 gr. Among the parents, 13 patients (34.2%) were relative (third-degree or more) and 25 patients (65.8%) were nonrelative. The initial and final diagnosis was different at 14 pt (36.8%) that was confirmed with echocardiographic findings. CHDs were divided into two groups in this study. Malformations such as PFO (patent foramen ovale) or FMV without MR (floppy mitral valve without mitral regurgitation) considered as non-important congenital heart diseases. Other malformations that require interventional or medical management such as VSD, ASD, TOF, or other CHDs are considered important CHDs. Nineteen pt (50%) had important CHD and 16 pt (42.1%) had non-important CHD and 3 pt (7.9%) had normal echocardiographic findings.

Conclusion: The heart defect is the most common associated anomaly in children with EA/TEF, which is divided into two subgroups. The first important one is CHD, which is effective in gastric surgery and management, and VSD is the most common type. The other group is non important CHD such as PFO or FMV without MR that are not effective in their management. The patients with EA/TEF are at risk for low birth weight and preterm delivery.

Keywords: Cardiac malformation, Congenital disorder, Esophageal atresia, Neonate, Tracheoesophageal fistula

Introduction

The prevalence of gastrointestinal system malformations (GISM) is 1.3 per 1000 live births (1). Although Thomas Gibson first described esophageal atresia/ tracheoesophageal fistula (EA/TEF) in 1697, its first initial repair was performed 244 years later, in 1941 (2). The prevalence of CHD is about 20% in non-syndromic children with major GI malformations. Its incidence might be higher than 60% in syndromic cases with GI malformations. Previous studies have shown that children with a defect in the upper GI tract are much more likely to have CHD (3-6). EA/TEF is an anatomical defect in the upper GI tract that occurs in one case from 2500–4500 live births and is slightly more common in men. This anomaly might be isolated or part of the VACTERL (Vertebral anomalies, Anal atresia, Cardiac malformations, Tracheoesophageal fistula,

* *Corresponding author*: Fatemeh Zegheibizadeh, Mashhad University of Medical Sciences, Mashhad, Iran. Tel: +989156596021; Email: Zegheibif1@mums.ac.ir

Please cite this paper as:
Mottaghi Moghadam Shahri H, Zegheibizadeh F, Afzoon S, Kianifar HR, Abbasi Z, Zegheibizadeh FS. Congenital Heart Defects in Children with Upper Gastrointestinal Anomalies. Iranian Journal of Neonatology. 2021 Oct: 12(4). DOI: 10.22038/IJN.2021.52137.1928

Renal anomalies, and Limb abnormalities) or CHARGE syndrome (Coloboma, Heart defects, Atresia choanae, Retardation of growth and/or development, Genital hypoplasia, and Ear anomalies).

Careful examination of children with a defect in the upper GI tract is crucial for other malformations because the treatment strategy is different and difficult in the presence of concomitant malformation (7,8,9,10). A developmental defect of the upper gastrointestinal tract is called esophageal atresia (EA). It can happen with or without a tracheoesophageal fistula, which means an abnormal passage between the esophagus and trachea.

EA/TEF configurations are classified as EA with distal TEF (the most common type: 84%), Isolated EA (8%), H-type TEF without EA (4%), EA with proximal and distal TEF (3%), and EA with proximal TEF (1%).

The failure of midline mesodermal embryogenesis leads to the coexistence of defects in the upper GI tract and CHD. Although the association between CHD and mortality is not well understood, the relation between cardiac malformations such as ventricular septal defect (VSD), atrial septal defect (ASD), patent ductus arteriosus (PDA), and EA/TEF has already been established. These type of anomalies significantly affects anesthetic strategies and recovery time (11,12,13,14,15). This study determined the proportion of heart anomalies among upper gastrointestinal (GI) system malformations in Imam Reza Hospital in Mashhad.

Methods

A total of 38 patients with EA/TEF and CHD were referred to Imam Reza Hospital from 2001 to 2017. Children enrolled in the study if they needed surgical intervention and/or cardiac catheterization. Exclusion criteria were congenital diaphragmatic hernia, previous cardiac surgery, and illegible records. This study was approved by the Ethical Committee of Mashhad University of Medical Sciences, Mashhad, Iran (Code: IR.MUMS.MEDICAL.REC.1397.345).

The medical records of children were retrospectively reviewed for age, gender, type and interventions of CHD, gastrointestinal complications, and follow-up findings. Medical records, operative reports, procedure, discharge, and clinic notes were retrospectively evaluated for information on comorbidities, fundamental diagnosis, and the number of cardiothoracic and abdominal procedures. Follow-up records were also reviewed, structured telephone interviews were performed with patients, and referred cardiologists or primary care physicians if necessary.

A cardiologist or family physician made the first diagnosis. The final diagnosis was based on the echocardiographic findings of the pediatric cardiologist.

Descriptive statistics are shown as mean ± standard deviation for quantitative variables. Data were coded and entered into SPSS software (version 16) and analyzed using Chi-square and T-test based on their distribution. A P-value less than 0.05 was considered statistically significant.

Results

In this study, 38 patients were participated (18 males [47.4%] and 20 females [52.6%]). The average birth weight of children was 2.390+_0.87 gr. Of the total, 17 children had a low birth weight of less than 2500 gr. Parents of 13 patients (34.2%) and 25 patients (65.8) were relative and non-relative, respectively. The main reasons for the patient's referral were family physician referral (19 patients/ 50%), heart murmur (14 patients/ 36.4%), imperforate anus (2 patients/ 5.2%), abnormal fetal echocardiogram (one patient), and Marfan syndrome (one patient) and other cases of arthritis. Clinical manifestations were respiratory distress in three patients (7.8%), dyspnea in two patients (5.2%), and cyanosis in one. Tachycardia was not reported in any of the cases. The first and final diagnoses were the same in 24 children (63.1%) and the difference was observed in 14 ones (36.8%). Abnormal echocardiographic findings were reported in 35 cases (92.1%) and echocardiography was normal in three children (7.9%). Major cardiac malformations were reported in 19 patients (50%), which had a significant effect on the prognosis, anesthesia, and therapeutic management of the patient. Moreover, 16 patients (42.1%) had minor cardiac malformations such as PFO or FMV without MR. Septal defects were observed in 11 patients (28.9%) and right-sided obstructive lesions in four patients (10.5%). Additionally, left-sided obstructive lesions were reported in one patient (2.6%), great arterial abnormality in three patients (7.8%). Aortic Stenosis and Pulmonary Atresia and Truncus Arteriosus were not reported in any cases (Table 1).

Liver hemangioma was reported in one patient (2.6%). The imperforate anus in one patient (2.6%) and the lower gastrointestinal tract stenosis were observed in seven patients (18.4%).

Table 1. Patients Characteristics

gender		Male	18 (47.4)
		Female	20 (52.6)
Cause of referral		clinical suspicious	19 (50)
		Heart murmur	14 (36.4)
		Imperforate anus	2 (5.2)
		Echocardiographic findings	1 (2.6)
		Arthritis	1 (2.6)
Echocardiographic findings	Septal defects 11	VSD 10	10 (26.3%)
		ASD 1	1 (2.6)
		PDA 4	4 (10.5)
	Rt side obstractive lesions	PS 3	3 (7.9)
		TOF 1	1 (2.6)
	Lt side Lesions	COA 1	1 (2.6)
		Congenital mitral regurgitation 1	1 (2.6)
		FMV 6	6 (15.6)

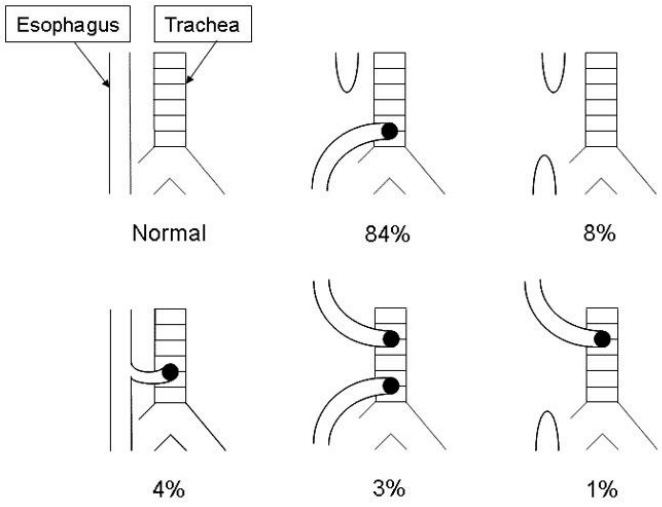

Figure 1. Types of Esophageal atresia

Rectovaginal fistula was observed in one patient (2.6%). Other anomalies were genitourinary anomalies in 9 patients (23.7%) , hearing loss in 2 patients (5.2%) and Tethered Cord in one patient (2.6%). Five patients (13.2%) were cases of down syndrome. Hypothyroidism was seen in two cases (5.2 %). Two patients had a family history of cardiac malformations. None of the patients had Biliary Atresia, Cirrhosis, Meckel's diverticulum, Omphalomesenteric Duct Cyst, Umbilical Hernia, Omphalocele, Midgut volvulus, Hirschsprung's disease, and Rectal prolapse. Cardiac treatment divided the three groups, one was medical management that included follow up with or without medication in 26 patients (67.6%), the second was cardiac intervention in five patients (13%), and third was cardiac surgery in four patients (10.5%). Gastrointestinal surgery was performed in one stage and four stages in 34 patients (88%) and one patient (2.6%), respectively. Two cases underwent colostomy and one need several Gastrointestinal surgeries. Two died at follow-up, one with tracheoesophageal fistula, another with the annular pancreas.

Only five children underwent Cardiac Catheterization of which one had Cardiac Catheterization and four had pulmonary artery abnormalities.

Discussion

The present study has revealed the high frequency of CHD in children with a defect in the upper GI tract. The incidence of a defect in the upper GI tract in the normal population is about 1.3 per 1000 live births (16,17,18,19,20). Although the prevalence of CHD is lower than 1% in the general population, it is 16.5%-28.5% in children with GISM (21,22,23,24,25). This frequency reaches 65% in syndromic cases (26-29). CHD is one of the most common birth defects with a higher prevalence among dead cases. These

types of malformations are frequently associated with chromosomal and extracardiac pathologies. These abnormalities negatively affect the prognosis and overall monitoring of the life quality of children (30,31,32).

In this study, 38 patients with EA/TEF, Duodenal atresia, Hypertrophic pyloric stenosis, and annular pancreas were followed over 16 years. The most common associated abnormalities were heart defects, major anomalies such as VSD, PDA, and minor defects such as PFO or FMV without MR. Leonard et al. in 2001 showed that the main common anomaly associated with EA/TEF in babies was CHD and he declared that the survival of children with EA/TEF and CHD significantly decreased without therapeutic interventions. Therefore, children should be examined for additional associated anomalies in the early stages of life. Careful physical examination and electrocardiography might be insufficient for discovering CHD in the neonatal period (33-34). Khalesi in 2009 revealed that EA/TEF is associated with cardiac, urinary, vertebral, anorectal malformations which confirmed our results (35).

Olgun and Thompson reported the incidence of CHD in patients with EA/TEF was 23% and 12%, respectively. It has been suggested that children with EA/TEF are at the risk of low birth weight and preterm labor. Of all patients, 44.7% had low birth weight and their mean weight was 2390±870 grams and their mean gestational age was 35.2±2.3 weeks. These findings confirmed the results of this study (36,37).

Mery and León showed that patients with thoracic GI have worse preoperative outcomes in comparison with controls; however, it has no significant effect on their long-term survival.

Ventricular septal defect was the most common CHD in patients with EA/TEF in the present study. A majority of the patients with CHD were candidates for medical follow-up. Although all patients underwent surgical treatment for EA/TEF, two of them died a year later (38).

Study limitations: this was a retrospective study conducted at a single referral center, so some of the patients were not followed up. On the other hand, the files of children with GI problems were reviewed and those with CHD were selected. Therefore, some cases with EA/TEF were missed which have not been referred.

Conclusion

The results in this study indicated that heart defect is the most common associated anomaly in children with EA/TEF. In addition, septal defects are the main type of heart defect in these children and the most common cardiac treatment is medical treatment. These patients are at risk for low birth weight and preterm delivery.

Acknowledgments

The present article is the research project of a medical student approved by the Ethical Committee of Mashhad University of Medical Sciences, Mashhad, Iran (Code: IR.MUMS. MEDICAL.REC.1397.345). This study was financially supported by the Research Deputy of the Mashhad University of Medical Sciences, Mashhad, Iran. The authors would like to express their sincere gratitude to the Clinical Research Development Center of Imam Reza and Akbar Hospitals, Mashhad, Iran for their contributions.

Conflicts of Interest

The authors declare that there is no conflict of interest.

References

1. Gilboa SM, Salemi JL, Nembhard WN, Fixler DE, Correa A. Mortality resulting from congenital heart disease among children and adults in the United States, 1999 to 2006. Circulation. 2010; 122(22): 2254-63.
2. Kliegman RM, Stanton BM, Geme JS, Schor NF. Nelson textbook of pediatrics. 21st ed. New York: Elsevier Health Sciences; 2020.
3. Hoffman JI, Michell SC. The incidence of congenital heart disease. J Am Coll Cardiol. 2002; 39(12): 1890-900.
4. German JC, Mahour GH, Woolley MM. Esophageal atresia and associated anomalies. J Pediatr Surg. 1976; 11(3):299-306.
5. Mohsenzadeh A, Saket S, Ahmadipour S, Baharvand B. Prevalence and types of congenital heart disease in babies born in the city of Khorramabad (2007-2011). Yafteh. 2014; 15(5):23-9.
6. Mohsenzadeh A, Saket S, Ahmadipour S, Baharvand B. Prevalence and types of congenital heart disease in babies born in the city of Khorramabad (2007-2011). Yafteh. 2014; 15(5):23-9.
7. Jenkins KJ, Correa A, Feinstein JA, Botto L, Britt AE, Daniels SR, et al. Noninherited risk factors and congenital cardiovascular defects: current knowledge: a scientific statement from the American Heart Association Council on Cardiovascular Disease in the Young: endorsed by the American Academy of Pediatrics. Circulation. 2007; 115(23):2995-3014.
8. Strauss A, Toth B, Schwab B, Fuchshuber S, Schulze A, Netz H, et al. Prenatal diagnosis of congenital heart disease and neonatal outcome--a six years experience. Eur J Med Res. 2001; 6(2):66-70.
9. Verheugt CL, Uiterwaal CS, Grobbee DE, Mulder BJ.

Long-term prognosis of congenital heart defects: a systematic review. Int J Cardiol. 2008; 131(1):25-32.
10. Ein SH, Shandling B, Wesson D, Filler RM. Esophageal atresia with distal tracheoesophageal fistula: associated anomalies and prognosis in the 1980s. J Pediatr Surg. 1989; 24(10):1055-9.
11. Hassink EA, Rieu PN, Hamel BC, Severijnen RS, Vd Staak FH, Festen C. Additional congenital defects in anorectal malformations. Eur J Pediatr. 1996; 155(6):477-82.
12. Olgun H, Karacan M, Caner I, Oral A, Ceviz N. Congenital cardiac malformations in neonates with apparently isolated gastrointestinal malformations. Pediatr Int. 2009; 51(2):260-2.
13. Wojtalik M, Mrówczyński W, Henschke J, Wronecki K, Siwińska A, Piaszczyński M, et al. Congenital heart defect with associated malformations in children. J Pediatr Surg. 2005; 40(11):1675-80.
14. Thompson AJ, Mulholland HC. The incidence of cardiac lesions in infants born with major gastrointestinal malformations in Northern Ireland. Ulster Med J. 2000; 69(1):23-6.
15. Tulloh RM, Tansey SP, Parashar K, De Giovanni JV, Wright JG, Silove ED. Echocardiographic screening in neonates undergoing surgery for selected gastrointestinal malformations. Arch Dis Child Fetal Neonatal Ed. 1994; 70(3): F206-8.
16. Fyler DC, Dc F, We H, He C. Report of the New England regional infant cardiac program. Pediatrics. 1980; 65(2):377-461.
17. Rosenthal A. Congenital cardiac anomalies and gastrointestinal malformations. The genetics of cardiovascular disease. Boston, MA: Springer; 1987. P. 113-26.
18. Kumar A, Singh K. Major congenital malformations of the gastrointestinal tract among the newborns in one of the English Caribbean Countries, 1993-2012. J Clin Neonatol. 2014; 3(4):205.
19. Lin AE, Pober BR, Adatia I. Congenital diaphragmatic hernia and associated cardiovascular malformations: type, frequency, and impact on management. Am J Med Genet Part C Semin Med Genet. 2007; 145C(2):201-16.
20. Hashemizadeh H, Boroumand H, Hirafard M. Investigating the prevalence of congenital heart disease in imperforate anus infants referred to pediatric surgery department of Dr. Sheikh hospital in Mashhad Iran. Iran J Obstet Gynecol Infertil. 2012; 15(27):21-7.
21. Kouwenberg M, Severijnen RS, Kapusta L. Congenital cardiovascular defects in children with intestinal malrotation. Pediatr Surg Int. 2008; 24(3):257-63.
22. Feenstra B, Gørtz S, Lund M, Ranthe MF, Geller F, Melbye M. Co-occurrence of infantile hypertrophic pyloric stenosis and congenital heart defects: a nationwide cohort study. Pediatr Res. 2019; 85(7):955-60.
23. Tuo G, Pini Prato A, Derchi M, Mosconi M, Mattioli G, Marasini M. Hirschsprung's disease and associated congenital heart defects: a prospective observational study from a single institution. Front Pediatr. 2014; 2:99.
24. Fattouh AM, Mogahed EA, Hamid NA, Sobhy R, Saber N, El-Karaksy H. The prevalence of congenital heart defects in infants with cholestatic disorders of infancy: a single-center study. Arch Dis Child. 2016; 101(9):803-7.
25. Uğuralp S, Paç FA, Gürbüz N, Demircan M. Congenital heart disease associated with gastrointestinal system malformations in the newborn: is it sufficiently evaluated? J Inonu Univ Med Facul. 2002; 9(4):229-32.
26. Gokhroo RK, Gupta S, Arora G, Bisht DS, Padmanabhan D, Soni V. Prevalence of congenital heart disease in patients undergoing surgery for major gastrointestinal malformations: an Indian study. Heart Asia. 2015; 7(1):29-31.
27. Chéhab G, Fakhoury H, Saliba Z, Issa Z, Faour Y, Hammoud D, et al. Congenital heart disease associated with gastrointestinal malformations. J Med Liban. 2007; 55(2):70-4.
28. Orun UA, Bilici M, Demirçeken FG, Tosun M, Ocal B, Cavusoglu YH, et al. Gastrointestinal system malformations in children are associated with congenital heart defects. Anadolu Kardiyol Derg. 2011; 11(2):146-9.
29. Abbag FI. Congenital heart diseases and other major anomalies in patients with Down syndrome. Saudi Med J. 2006; 27(2):219-22.
30. Colombo JN, McCulloch MA. Acyanotic congenital heart disease: left-to-right shunt lesions. Neo Reviews. 2018; 19(7):e375-83.
31. Marino B. Congenital heart disease in patients with Down's syndrome: anatomic and genetic aspects. Biomed Pharmacother. 1993; 47(5):197-200.
32. Prasad C, Chudley AE. Genetics and cardiac anomalies: the heart of the matter. Indian J Pediatr. 2002; 69(4):321-32.
33. Cho S, Moore SP, Fangman T. One hundred three consecutive patients with anorectal malformations and their associated anomalies. Arch Pediatr Adolesc Med. 2001; 155(5):587-91.
34. David TJ, O'Callaghan SE. Cardiovascular malformations and oesophageal atresia. Br Heart J. 1974; 36(6):559-65.
35. Yigiter M, Yildiz A, Firinci B, Yalcin O, Oral A, Salman AB. Annular pancreas in children: a decade of experience. Eurasian J Med. 2010; 42(3):116-9.
36. Khalesi N, Taghipour R, Aflatoonian M. A case report of cerebral nocardiosis in a patient with Crohn's disease. Razi J Med Sci. 2010; 16:40-63.
37. Leonard H, Barrett AM, Scott JE, Wren C. The influence of congenital heart disease on survival of infants with oesophageal atresia. Arch Dis Child Fetal Neonatal Ed. 2001; 85(3): F204-6.
38. Mery CM, De León LE, Rodriguez JR, Nieto RM, Zhang W, Adachi I, et al. Effect of gastrointestinal malformations on the outcomes of patients with congenital heart disease. Ann Thorac Surg. 2017; 104(5):1590-6.