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VACTERL Association in Neonates Hospitalized with Esophageal Atresia and Imperforate Anus

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Abstract

Background: VACTERL association is a congenital abnormality involving several organs. The percentage of involvement of different organs in this illness varies and treatment success depends on the intensity of the accompanied anomalies. This study aimed to investigate the prevalence of VACTERL association in neonates Hospitalized in Be'sat Hospital in Hamadan, Iran.

Materials and Methods: This retrospective study was conducted using the descriptive-analytic method and all the neonates who were hospitalized with esophageal atresia and imperforate anus abnormalities in Be'sat Hospital, Hamadan, Iran, from April 2009 to April 2018 were included in the study. Information on the neonates were extracted from the medical records and after being recorded in the checklist, they were analyzed using SPSS v.16 at a 95% confidence level.

Results: 127 neonates were included in this study. 42 neonates (33.1%) had esophageal atresia, 78 (61.4%) had imperforate anus, and 7 neonates (5.5%) had both anomalies. 87 of these neonates (68.5%) suffered from congenital heart disease. Atrial septal defect (31%), simultaneous presence of atrial septal defect and patent ductus arteriosus (24%), and patent ductus arteriosus (23%) were the most common congenital heart diseases, respectively. 32 neonates (25.2%) had VACTERL association. Heart, genitourinary, and spinal anomalies were present in 93.2%, 84.3%, and 9.3% of the neonates, respectively. VACTERL association was significantly observed in neonates with imperforate anus (P = 0.001)

Conclusion: VACTERL association is common in neonates who suffer from esophageal atresia or imperforate anus. Considering the high prevalence of anomaly of other organs, in addition to complete physical examination, echocardiography, abdominal ultrasound, and radiography of the spine are recommended.

Key Words: Associated Anomalies, Esophageal Atresia, Imperforate Anus, VACTERL.

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1- INTRODUCTION

Quan and Smith (1972) were the first ones to describe a certain pattern of several congenital abnormalities including vertebral, anal, cardiovascular, esophageal, renal and other limb abnormalities as VATER association (1-4). Most cases, in their study, were sporadic, while chromosomal abnormalities were rarely seen and no history of teratogenic diseases was observed (5). In some of the studies, the prevalence of this disease is estimated to be 1 in 10000-40000 neonates and the precise cause of this illness has not yet been determined (3). Some studies have suggested that it is more prevalent among boys. No particular distribution or geographical dominance was seen between different ethnic groups (6, 7). Based on a study by La Placa et al. (8), the diagnosis criteria for VACTERL association included esophageal atresia with or without fistula and at least two of the following defects: vertebral abnormalities (V), anal atresia (A), cardiovascular (C), renal (R), and limb abnormalities (L). Since there are extensive criteria for diagnosis, it is necessary to fully examine all the patients who are suspected of having VACTERL association. The diagnostic process consists of abdominal ultrasound, cardiac echocardiography, as well as spinal and limb imaging. Since there are few national studies regarding this disease and due to the fact that delay in diagnosis of pneumonia and accompanied anomalies, especially VACTERL association increases the mortality rate of these neonates, this study was designed and conducted to investigate the prevalence of VACTERL association anomalies in neonates who are hospitalized in the neonatal intensive care unit of Be'sat Hospital in Hamedan (Iran) with esophageal atresia and imperforate anus.

2- MATERIALS AND METHODS

2-1. Setting and participants

This was a retrospective descriptive-analytical review study performed in Be'sat Hospital of Hamedan, Iran, from April 2009 to April 2018. The statistical population included all the neonates suffering from congenital imperforate anus or esophageal atresia who were admitted to the hospital during the mentioned period of time.

2-2. Measuring tools

The inclusion criteria of the study consisted of all patients with congenital imperforate anus or esophageal atresia or both with their echocardiography results reported in their files. In this study, the initial diagnosis of imperforate anus or esophageal atresia or both in the neonates was confirmed by the neonatologist. The data were collected in a researcher-made checklist including the following information: sex, gestational age, birth, cardiac diseases, and the type of associated abnormalities in other organs. Based on a study by La Placa et al. (8), the diagnosis criteria for VACTERL association included esophageal atresia with or without fistula and at least two of the following defects: vertebral (V), anal atresia (A), cardiovascular (C), renal (R), and limb abnormalities (L). The diagnostic process consists of abdominal ultrasound, cardiac echocardiography, and spinal and limb imaging.

3-5. Ethical considerations

Before being conducted, this study was presented to the University Research Ethic Committee on July 14th, 2018 and was approved by the special ID of IR.UMSHA.REC.1397.275. All the information was confidential and all the questionnaires were filled out with the consent of the parents.

2-4. Data Analyses

In this study, SPSS v.16 was used for data analysis. Tables, graphs, ratios and percentages were used to describe the data. Chi-squared test was used to analyze the nominal and ordinal qualitative data. The significance level was considered less than 0.5 in all the statistical analyses.

3- RESULTS

A total of 127 neonates were enrolled in this study, 85 (66.9%) of whom were males, 50(39.4%) weighed less than 2500 g, and 48(37.8%) were preterm. 42 neonates (33.1%) had esophageal atresia, 78 (61.4%) had imperforate anus and 7 neonates (5.5%) had both anomalies. 87 of these neonates (68.5%) suffered from congenital heart disease and 40 of them (31.5%) had no congenital heart disease. None of the neonates had any family history of heart disease. 85 out of 87 neonates (97.7%) had simple heart disease; and only two (2.3%) had complex heart diseases, one of whom was Tetralogy of Fallot (FOT) and one was Dextro-transposition of the great arteries. Atrial septal defect (31%), simultaneous presence of atrial septal defect and patent ductus arteriosus (24%), and patent ductus arteriosus (23%) were the most common congenital heart diseases, respectively (**Table 1**).

Table-1: Baseline characteristics of the neonates under study, n=127

Variable	Type of Anomaly			Number (Percentage**)** 127 (100.0)
	Imperforate anus 78 (61.4)	Esophageal atresia 42 (33.1)	Both 7 (5.5)	
Gender				
Female	24(30.8)	18(42.9)	0(0.0)	42(33.1)
Male	54(69.2)	24(57.1)	7(100.0)	85(66.9)
Gestational age				
Preterm	23(29.5)	23(54.8)	2(28.6)	48(37.8)
Term	55(70.5)	19(45.2)	5(71.4)	79(66.2)
Birth weight				
≤2500 gram	21(26.9)	25(59.5)	4(57.1)	50(39.4)
2501-4000	57(73.1)	17(40.5)	3(42.9)	77(60.6)
Congenital heart disease				
Yes	53(67.9)	30(71.4)	4(57.1)	87(68.5)
No	25(32.1)	12(28.6)	3(42.9)	40(31.5)
Anomaly of other organs				
Yes	36(46.5)	5(11.9)	3(42.8)	44(34.6)
No	42(53.5)	37(88.1)	4(57.2)	83(65.4)

Out of 127 neonates under study, 32 (25.2%) had VACTERL association and there was no difference between the two groups in terms of gender, pregnancy age, and weight at birth. Congenital heart disease was more observed in the group without VACTERL association (P=0.001). Although the group with VACTERL association had more anomalies in other organs, the difference was not significant (P=0.283). VACTERL association was observed significantly in neonates with imperforate anus (P=0.001) (**Table 2**).

Table-2: Comparing the variables in patients with or without VACTERL association, n=32

Variables	VACTERL ASSOCIATION		Significance level
	No =95 (74.8)	Yes =32 (25.2)	
Gender			
Female	33(34.7)	9(28.1)	0.323
Male	62(65.3)	23(71.9)	
Gestational age			
Preterm	38(40.0)	10(31.2)	0.253
Term	57(60.0)	22(68.8)	
Weight birth			
≤2500 gram	37(38.9)	13(40.6)	0.513
2501-4000	58(61.1)	19(59.4)	
Congenital heart disease			
Yes	57(60.0)	30(93.8)	0.001
No	38(40.0)	2(6.2)	
Type of the congenital heart disease			
Atrial septal defect (ASD)	19(20.0)	8(25.0)	0.005
PDA & ASD	12(12.6)	9(28.1)	
Patent ductus arteriosus	16(16.8)	4(12.5)	
ASD & VSD	3(3.2)	4(12.5)	
ventricular septal defect (VSD)	1(1.1)	3(9.4)	
PDA & VSD	1(1.1)	1(3.1)	
PDA and VSD & ASD	2(2.1)	0(0.0)	
Transposition of the great arteries (TGA)	1(1.1)	0(0.0)	
Tricuspid valve insufficiency	1(1.1)	0(0.0)	
Tetralogy of Fallot (FOT)	0(0.0)	1(3.1)	
TR & PDA & VSD & ASD	1(1.1)	0(0.0)	
Anomaly of other organs			0.283
A) Anomalies of the genitourinary system			
Hydronephrosis	5(35.7)	11(36.7)	
Ectopic Kidney	0(0.0)	2(6.7)	
Kidney agenesis	2(14.3)	5(16.7)	
Vesicoureteral reflux	1(7.1)	5(16.7)	
Hypospadias and genitalia anomaly	1(7.1)	4(13.4)	
B) Vertebral anomaly			
Myelomeningocele	0(0.0)	1(3.3)	
Hemivertebrae	2(14.3)	2(6.7)	
C) Limb anomalies			
Absent Radius	1(7.1)	0(0.0)	
Anomaly of fingers	2(14.3)	0(0.0)	
Anomaly type			0.001
Esophageal atresia	40(42.1)	2(6.2)	
Imperforate anus	52(54.7)	26(81.2)	
Both	3(3.2)	4(12.5)	

4- DISCUSSION

This study aimed to investigate the prevalence of VACTERL association in neonates Hospitalized in Be'sat Hospital in Hamadan, Iran. VACTERL association was seen in 25.2% of the neonates in our study. VACTERL association has been reported in 10000 childbirths and is a congenital abnormality involving several systems. Potential findings include vertebral, anorectal, cardiovascular, tracheoesophageal fistula/esophageal atresia, renal and limb abnormalities. The involvement percentage of different organs in this illness varies and treatment success depends on the intensity of the accompanied abnormalities (6). The prevalence of imperforate anus is 1 in every 1500-5000 neonates. In our study, VACTERL association was observed in 33.3% of the neonates with imperforate anus. Byun et al (9) also showed that 28.6% of the neonates with imperforate anus had VACTERL association, which is similar to our results. Involvement percentage of other organs in patients with imperforate anus is seen in 40%-70% of the cases. In our study, congenital heart diseases and renal and urinary tract diseases are seen in 78% and 36% of the cases, respectively. Also in the study conducted by Byun et al (9), 85.7% had congenital heart diseases and 57.5% were going through renal and urinary tract diseases.

Association of esophageal atresia was observed in 7.1% of the neonates in Byon's study (9) and in 8% of the neonates in the study by Casaccia et al (10), which is 5.5% more than our study. The most common associating abnormalities in our study were cardiovascular and urinary system problems; and they were not considerably different from the reported cases in previous studies (11, 12).

Esophageal atresia is seen in 1 out of 2500 childbirths (13). In studies performed by Gupta et al (13), Chang et al (14), and Seo et al (15), VACTERL association was seen in 11.6%, 19.4%, and 40.1% of the neonates with esophageal atresia, respectively. Prevalence of congenital heart diseases in neonates who suffered from esophageal atresia, imperforate anus or both was 71.4%, 67.9%, and 57.2%, respectively and 68.5% in total. Heart abnormalities, ASD, PDA & ASD, and PDA were the most common heart diseases in neonates suffering from esophageal atresia or imperforate anus. In the study by Lautez et al (2015), (16) in the US on 2689 neonates undergoing esophageal atresia surgery, the prevalence of congenital heart diseases was 59.1%. In the research carried out by Gokhroo et al (17) in India on neonates dealing with anorectal abnormalities, the prevalence of congenital heart abnormalities was reported to be 60.46%. Based on the results of these two recent studies, the prevalence of congenital heart diseases in these anomalies was more than the normal population, but 10% less than our study. The difference is that in Lautez's study (16), the target group was only the neonates suffering from esophageal atresia, but Gokhroo et al (17) investigated the anorectal abnormalities. The sample size of the present study is bigger than that of Gokhroo et al (17) and smaller than that of Lautez et al (16). Given the big sample size and multi-centricity of Lautez's study (16), the mentioned findings are of higher validity. In the domestic studies, the prevalence of congenital heart diseases in patients with imperforate anus was about 30% (18 and 19), which is lower than that among the patients with esophageal atresia which is about 60% (20, 21). This difference is not that clear in our study with percentages of 67% and 71%, respectively. In the two studies conducted in our country on neonates with imperforate anus, although the total number of congenital heart diseases was lower than that in our study, the amount of complex congenital heart diseases was less

than 5%, which is similar to our study (20, 21). In the study performed by Samadi et al (21), the prevalence of congenital heart diseases was 56.8%, which is lower than that in our study. This difference between studies might be due to the fact that in many of them, some less significant disturbances such as small ASD and PDA are not considered as anomalies and that is why the reported heart diseases are lower.

Especially regarding the prevalence of congenital heart disease in VACTERL association, Khoury et al (22) showed that congenital heart disease is observed in 80% of the VACTERL patients; VSD, PDA, ASD, and TGA are seen in 30%, 26%, 20%, and 10% of these patients. Cunningham (23) showed that congenital heart diseases were seen in 67% of the VACTERL patients and VSD was the most common congenital heart disease with the prevalence of 58%. The percentage found in our study is 93.2%, which is similar to that of Khoury et al (22) and more than that reported in Cunningham et al (23).

In Ahn et al (24), almost 60% of the VACTERL patients had renal abnormalities, some of which accompanied with chronic kidney disease (CKD). With improved medical care, majority of these patients survive in adulthood and even kidney transplant has been reported in these patients. Our study shows genitourinary anomalies in 84.3% of VACTERL neonates and 28.3% of all neonates. This percentage really underlines the importance of evaluating the kidney and urinary tracts as the second most common abnormality in these patients.

Raam et al (25) show that significant abnormalities associated with VACTERL include 40% vertebral anomaly, 50% cardiac and 50% renal abnormalities. 3 (9.3%) of the VACTERL neonates were diagnosed with vertebral anomalies in our study. Chen et al (26) demonstrated that vertebral anomaly is one of the most important defects that has been reported in 60%-95% of all VACTERL patients. Recent advances manifest that genetic factors have an important role in VACTERL association, especially among people who have vertebral phenotypes. Typically, radial abnormalities (aplasia/hypoplasia) and other limb abnormalities such as distal tibial aplasia and polydactyly have been described in relation to VACTERL. In our study, like in Bghagat et al (27), absence of radius and finger anomalies were seen in 1 and 2 neonates, respectively.

4-1. Study Limitation

This study was conducted only in one institution, Hamedan province, Iran, which is different from the other provinces in terms of socio-economic and cultural conditions. Therefore, the results of this study may not represent the country's population.

5- CONCLUSION

Based on the results, VACTERL association is common in neonates who suffer from esophageal atresia or imperforate anus; and given the high prevalence of anomalies of other organs, in addition to complete physical examination, echocardiography, abdominal ultrasound, and radiography of the spine are recommended.

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7- CONFLICT OF INTEREST: None

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