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CT ANGIOGRAPHIC UTILIZATION IN PATIENTS WITH DEXTRO-TRANSPOSITION OF GREAT ARTERIES : A CROSS COUNTRY COMPARATIVE CROSS SECTIONAL ANALYSIS OF PAKISTAN AND IRAN

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Abstract

Introduction: Transposition of the Great Arteries (TGA) is one of the most common types of congenital heart disease (CHD). Recent advances in computed tomography angiography (CTA) have helped in the detection of this condition. The data regarding the prevalence of the

Material and Methods: A cross-sectional study was conducted comparing patient cohorts from Pakistan and Iran. Patients diagnosed with CHD as confirmed by CTA, aged less than 18-year-old were included in this study. Data regarding demographics, nationality, and any CHDs was extracted via patient interviews which were further supplemented by screening of the hospital records. Our data analysis was conducted using SPSS version 21 (Chicago, IL: IBM SPSS Statistics) where a *p*-value less than 0.05 was statistically significant.

Results: A total of 170 patients from Pakistan and 31 patients from Iran were included in this study. A total of 101 (59.4%) males were present in the Pakistani cohort. Levocardia was the most common cardiac axis in both of our populations (n=119, 70.0% for Pakistan and n=31, 100.0% for Iran). Ventricular septal defect (VSD) was noted in 154 (90.6%) and 15 (48.4%) of the patients from the Pakistani and Iranian cohort. The prevalence of patent ductus arteriosus (PDA) differed significantly between the Iranian population (n=27, 87.1%) and the Pakistani population (n=92, 54.1%) p<0.001.

Conclusion: Our study highlights an important association of PDA that warrants further investigation while considering the limitations of this study so that a more robust investigation can be performed in the future.

Keywords: Transposition of the Great Arteries, Congenital heart disease, Pakistan, Iran.

INTRODUCTION

Congenital Heart Defects (CHD) are among the most common birth defects and are one of the leading factors accountable for infant mortality (1-3). Transposition of great arteries (TGA) is one of the most

common type of CHD, accounting for about 1 in 3500-5000 live births. D-TGA is the type of TGA in which the switching between the aorta and the pulmonary artery, with the aorta arising from the right ventricle, and the pulmonary artery coming off from the left ventricle.

D-TGA is accountable for multiple organ damage in infants due to decreased oxygen levels in the brain, hence deferred diagnosis and intervention can lead to an increase in the risk of organ damage (6). The prognosis of the disease is related in accordance with the spatial relationship between the great arteries and the abnormalities of the coronary arteries, and mostly patients must undergo Arterial Switch Operation (ASO) in neonatal life to correct the disorder. Hence a comprehensive and precise evaluation of TGA and its associated abnormalities is important before surgical intervention can take place.

Conventional Angiography and Transthoracic echocardiography have been the main imaging techniques used to identify TGA in the past, but both have their limitations. Conventional Angiography, which was the "gold- standard" for CHDs detection, only provides a two-dimensional view, has a much higher radiation dose as compared to CTA, which is performed invasively, and needs frequent general anesthesia during the procedure (8,9). Transthoracic echocardiography is non-invasive; however, it provides only a minimal acoustic window and has a much-reduced spatial window as compared to CTA (10). To overcome these restrictions, advancements in CT has now led to the use of Computed Tomography Angiography (CTA) to identify TGA. CTA is an imaging technique that uses a combination of CT scan along with injecting of a contrast material to enable visualization of defects. It provides a non-invasive approach of detecting CHDs, by performing image reconstruction in 3-dimensional form by post-processing approach (11).

Our study will aim to assess the frequency and pattern of d-TGA in patients undergoing CTA along with a side-by-side comparison between the patient populations from Pakistan and Iran. To the best of our knowledge, this is the first research to be published on CHDs diagnosis through CTA, and the results of this would form a path for future studies to be conducted in this regard.

METHODOLOGY:

A cross-sectional study was conducted using a non-random sampling technique at the Department of Computer Tomography (CT) Angiography of National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan as well as Department of Cardiology of Birjand University of Medical Sciences, Birjand, Iran with the data being collected retrospectively. Approval from the ethical review committee of NICVD as well as Birjand University of Medical Sciences was acquired. An informed written consent was obtained before inclusion into the patient pool from either the patient or the guardian/parents in cases of pediatric population. 170 patients from Pakistan and 31 patents from Iran, all of whom were suspected of Congenital Heart Disorders by their Cardiologists and underwent CTA between January 2014 until June 2021 were included in the study. Patients who either had an incomplete CTA report or were pre-diagnosed with d-TGA or any other CHD through any other imaging modality instead of CTA were excluded from inclusion in this study.

Before the formal start of our data collection, a proforma was developed which underwent pilot testing using 20 patients. The feedback by subject experts was studied and the proforma was edited accordingly. These responses were discarded and were not used in the final analysis. The following data was collected using the proforma: patient age, sex, nationality, cardiac axis, position of thoracic organs, transposition type (if any), presence of patent ductus arteriosus, presence of ventral septal defect, presence of atrial septal defect, presence of ipsilateral juxtaposition of atrial appendages, presence of complete atrio-ventricular canal defect, presence of mitral atresia, type of pulmonary vale abnormality, type of coarctation of aorta, type of pulmonary venous return, type of systemic venous system anomaly, position of aortic arch, and any associated rare anomalies.

Data extraction was performed by authorized study authors who were given access to institutional patient records. They compiled this data on a spreadsheet using Microsoft Excel (Microsoft, Redmond, Wash, USA). Data entry and management was conducted using SPSS version 21 (Chicago, IL: IBM SPSS Statistics) and the data was saved in hard copy as well as soft copies. Continuous data

was presented as mean ± standard deviation while categorical data was reported as frequency and percentages. The Chi-square test was used to investigate any statistically significant associations between the two countries with a *p*-value<0.05 being considered significant.
Anonymity of the included patients was ensured by avoiding the use of potential identifiers, hence minimizing any bias. Rechecking of data was performed to avoid any human errors subsequently helping in avoiding the risk of misclassification bias.
CT technique, Image processing and Radiation dose calculation left. To be done when Dr Parveen sends.

RESULTS:

Our patient population constituted of 170 patients from Pakistan and 31 patients from Iran. A predominance of males (n=101, 59.4%) was observed for the Pakistani cohort with a male to female ratio of 1.5:1. The patient's age ranged from 3 days to 52-year-old.
In the study population, Levotransposition of the Great Arteries was observed in 68 (40%) and 1 (3.2%) patient for Pakistan and Iran respectively. Moreover, 96 (56.5%) and 30 (96.8%) patients had Dextrotransposition for the Pakistani and Iranian population respectively (Table 1). The cardiac axis of the patients constituted of 119 (70%) of them having Levocardia, 39 (22.9%) patients had Dextrocardia while 12 (7.1%) patients had Mesocardium in the Pakistani patient population while all patients from Iran reported with Levocardia (n=31, 100%) only. Analysis of positioning of aortic arch showed that 29 (17.06%) and 1 (3.2%) patient had a right sided positioning of the aortic arch in the Pakistani and Iranian cohort respectively. Double Aortic Arch and Hyperplastic Aortic Arch was each seen in 1 person in Pakistan cohort respectively (Table 1).

Table – 1: The frequency of various congenital cardiovascular anomalies among the population included in the study cohort.

Parameter		**Frequency (%)**		
		Pakistan (n=170)	**Iran (n=31)**	***p*-value**
Gender	Female	69 (40.6)	-	-
	Male	101 (59.4)	-	-
Cardiac Axis	Levocardia	119 (70.0)	31 (100.0)	N/A
	Dextrocardia	39 (22.9)	0 (0.0)	
	Mesocardia	12 (7.1)	0 (0.0)	
Position of thoracic organs	Solitus	119 (70.0)	-	-
	Inversus	24 (14.1)	-	-
	Ambiguous	27 (15.9)	-	-
Transposition	None	6 (3.5)	0 (0.0)	N/A
	Levotransposition	68 (40.0)	1 (3.2)	
	Dextrotransposition	96 (56.5)	30 (96.8)	
Patent Ductus Arteriosus	None	78 (45.9)	4 (12.9)	<0.001*
	Yes	92 (54.1)	27 (87.1)	
Ventricular Septal Defect	None	16 (9.4)	16 (51.6)	N/A
	Yes	154 (90.6)	15 (48.4)	
Atrial Septal Defect	None	106 (62.4)	-	-
	Yes	64 (37.7)	-	-
Ipsilateral juxtaposition of atrial appendages	None	161 (94.7)	-	-
	Yes	9 (5.3)	-	-
Complete AV canal defect	None	164 (96.5)	-	-

	Yes	6 (3.5)	-	-
Mitral atresia	None	164 (96.5)	-	-
	Yes	6 (3.5)	-	-
Pulmonary Valve Abnormality	None	41 (24.1)	-	-
	Pulmonary Stenosis	82 (48.2)	2 (6.5)	-
	Pulmonary Atresia	46 (27.1)	-	-
	Pulmonary Stenosis and Atresia	1 (0.6)	-	-
Coarctation of Aorta	None	166 (97.7)	29 (93.5)	N/A
	Coarctation of Aorta	1 (0.6)	2 (6.5)	
	Bovine aortic branching	3 (1.8)	0 (0.0)	
Pulmonary Venous Return	None	155 (91.2)	-	-
	TAPVR	3 (1.8)	-	-
	PAPVR	12 (7.1)	-	-
Systemic Venous System Anomaly	None	133 (78.2)	-	-
	PLSVC	24 (14.1)	-	-
	Interrupted IVC	10 (5.9)	-	-
	PLSVC and IIVC	3 (1.8)	-	-
Aortic Arch	Left	141 (82.9)	30 (96.8)	N/A
	Right	29 (17.1)	1 (3.2)	
Associated rare anomalies	Tricuspid atresia	2 (1.2)	-	-
	Severe pulmonary valve stenosis	1 (0.6)	-	-
	Right pulmonary artery stenosis	1 (0.6)	-	-
	Right pulmonary artery atresia	1 (0.6)	-	-
	Left pulmonary artery stenosis	3 (1.8)	-	-
	Left pulmonary artery atresia	1 (0.6)	-	-
	Double aortic arch	1 (0.6)	-	-
	Hyperplastic aortic arch	1 (0.6)	-	-
	Single coronary artery from right coronary cusp	1 (0.6)	-	-
	Aberrant left subclavian artery	1 (0.6)	-	-
	ALCAPA anomaly	1 (0.6)	-	-
	Multiple ventricular septal defects	2 (1.2)	-	-
	Hypoplastic right ventricle	1 (0.6)	-	-

AV: Atrio-ventricular, TAPVR: Total Anomalous Pulmonary Venous Return, PAPVR: Partial Anomalous Pulmonary Venous Return, PLSVC: Persistent Left Superior Vena Cava, IVC: Inferior Vena Cava, IIVC: Interrupted Inferior Vena Cava, ALCAPA: Anomalous Left Coronary Artery from the Pulmonary Artery, N/A: Not Applicable
**p-value<0.05. Statistically significant*

Intracardiac defects were also assessed in the study, in which Ventral Septal Defect (VSD) was the most common in the Pakistani population, being present in 154 (90.59%) of the population with the Iranian population showing no significant difference between presence (n=15, 48.4%) and absence (n=16, 51.6%) of VSD (Table 1). Atrial Septal defect (ASD) was found in 64 (37.65%) of the population, while 4 (3.35%) had Coarctation of Aorta, of whom 3 had a Bovine aortic branching for the Pakistani patients. Patent Ductus Arteriosus was also found in 92 (54.12%) and 27 (87.1%) patients from Pakistan and Iran (Table 1). The odds of encountering cases of PDA in the Pakistani

population were decreased compared to the Iranian population (χ^2: 16.883, OR: 0.132, p<0.001) signaling towards the higher risk of PDA in the Iranian cohort (Table 1).
Assessment of Pulmonary valve abnormalities showed that Pulmonary Stenosis (PS) was associated with 82 (48.24%) patients while Pulmonary Atresia (PA) was present in 46 (27.06%) patients. Only 1 (0.6%) patient had both PS and PA present (Table 1). Regarding the Iranian cohort, only 2 (6.5%) patients reported with PS. Analysis of the anomalies of Systemic Veins showed the presence of Persistent Left Superior Vena Cava (PLSVC) in 24 (14.12%) patients, while Interrupted IVC was found in 10 (5.88%) patients. Presence of both IIVC and PLSVC together was found in 3 patients of Pakistani origin (Table 1).

Discussion

Our study demonstrates the presence of TGA and its associated anomalies among Pakistani pediatric population. In our study the patients having a concordance of atrioventricular and a discordance of ventriculoarterial constitute about 5–7% of all the cases of congenital heart diseases, which comes up to 20 to 30 new cases per 100 000 live births [12]. There is a male predominance with a male/female sex ratio that varies, in the literature, from 1.5:1 to 3.2:1; this same frequency was found in our study where 59.4% patients were males with a male to female ratio of 1.5:1 (Table 1) [12-14].
In 50% of the cases, the ventriculoarterial discordance is an isolated finding. This condition is designated as simple transposition. By contrast, complex transposition includes all the cases with coexisting malformations, such as ventricular septal defects, left ventricular outflow tract obstruction, aortic arch anomalies, and anomalous venous systemic return. The vast majority of patients included in our study had more than one congenital heart disease at the time of diagnosis. VSD was the most common entity with 154 (90.6%) patients in the Pakistani cohort (Table 1).Echocardiography has limited use in the visualization of aorta because of this limitation and a lack of availability of cardiac MRI across the centers .CTA is the imaging of choice for many patients with congenital heart disease. .In our study commonly presenting intracardiac lesion were less frequently detected. The reason behind this could be that ECG gated cardiac CT has a higher sensitivity in detection of intracardiac lesions compared to non-ECG gated CT therefore patients with isolated intracardiac defects without high suspicious for extracardiac defects should not routinely undergo CT [13]. The Cardiac CT can be useful in detecting the associated defects with primary congenital heart defect. The cardiac CT is the preferred modality of imaging in small critically ill patients owing to the minimal sedation and reduction of the total scan time required to complete the scan as compare to the cardiac MRI. The cardiac CT is also useful in patients with Right-sided aortic arch. In our study we reported 29 (14%) patients with right sided aortic arch this is in stark contrast to the reported overall prevalence in the population of <0.1% and in the similar vein Tetralogy of Fallot with an overall prevalence of 7-10% of all congenital heart diseases was not reported in any of our patients. One possible reason could be NICVD being the premier heart institute in the country was being referred complex and un common cases from around the country[13,14].
The anatomically normal cardiovascular blood flow doesn't allow for any direct communication to exist between the aorta and the pulmonary arteries. There are various congenital diseases in which an abnormal communication between the aorta and pulmonary arteries is created which includes Patent ductus arteriosus(PDA) and Major aortopulmonary collateral artery (MAPCAs). The PDA is an abnormal vascular connection between the aorta and pulmonary artery, its usually located from the proximal descending aorta and the main pulmonary artery [13]. It is considered essential during the fetal life but if it persists beyond the first few weeks of life it's considered an abnormality.[15]. Patent ductus arteriosus (PDA) can occur as an isolated cardiovascular defect or in association with other congenital heart diseases. In patients with transposition of the great arteries, the patency of the ductus arteriosus is critical for survival since parallel circuits without a PDA or ventricular septal defect are incompatible with life. Our study found a significantly higher prevalence of patent ductus arteriosus (PDA) in Iranian patients (n=27) compared to Pakistani patients (n=92), with 87.1% and 54.1% having PDA, respectively (p<0.001). This observation is consistent with the findings of Bagher

Nikyar et al. in their cohort study, but differs from the results reported by F. Rahim et al. in their study [16, 17]. Anomalous pulmonary venous return can cause an extra-cardiac left-to-right shunt which results in the pulmonary venous blood draining directly into the right side of the heart or into the systemic veins. The presence of TAPVR and TGA together is rare and in our study TAPVR was present in only 3 patients (1.8%) in Pakistani population and zero cases in Iranian population. TGA in combination with TAPVR can result in regression of the left ventricle mass and present as a big challenge to correct surgically.[18] The persistent left superior vena cava makes up about 8% of congenital heart diseases.The prevalence of TGA together with PLSVC is remains unknown. In our study 24 Pakistani patients had PLSVC while 3 had persistent left superior vena cava (PLSVC) with Inferior vena cava [19]. The exact factor for the population remains unknown, further studies are required in this regard.

This study is the first of its kind to compare data regarding CHDs between Pakistan and Iran, two low-and middle-income countries (LMICs).

Limitations

The small sample size especially of the Iranian population impairs the genralizability of the study findings. The selection bias regarding the patient cant be ruled out since the cases have been collected from tertiary care centers which perhaps resulted in higher number of various congenital heart diseases in Pakistani population.

Conclusion:

Our study found a significant difference in the study prevalence Persistent ductus arteriosus between Pakistani and Iranian population.The prevalence of d-TGA was in contrast significantly higher in Iranian population compared to Pakistani population.

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