IJPSR (2022), Volume 13, Issue 3 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 25 January 2022; received in revised form, 27 February 2022; accepted, 28 February 2022; published 01 March 2022

OBSERVATIONS ON CARDIAC ABNORMALITIES IN PATIENTS WITH DEXTROCARDIA AND SITUS AMBIGUUS: A RETROSPECTIVE STUDY

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Keywords:

Dextrocardia, Patients, Tertiary, Retrospective study, Atrial isomerism

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ABSTRACT: Studies on dextrocardia have been limited by low numbers. Hence, finding the most common diagnosis in patients with dextrocardia and situs ambiguus is challenging among patients seeking medical attention in a tertiary care center. **Aims and objectives:** To identify the most common diagnostic pattern in dextrocardia (DC) patients with situs ambiguous (SA). **Methods:** It is a retrospective study with records dating backto the last 21yrs from a major tertiary care center in South India. In this study, researchers will include all the patients diagnosed with dextrocardia (defined as the right-sided baso-apical axis of the heart). The segmental analysis will be done as described previously. **Results:** There was a total of n=378 patients with dextrocardia, of which 71 had situs ambiguus with dextrocardia. The mean age was 2.3yrs, 36.6% were females 32 patients had right atrial isomerism (RAI), 18 patients had left atrial isomerism (LAI), and 21 patients had unidentified atrial isomerism (UAI). In the RAI group Double outlet right ventricle (DORV) was present in n=13 (40.6%), Single ventricle (SV) was present in n = 14 (43.8%). In the LAI group, DORV was present in n=5 (27.8%), SV was present in n = 4 (22.2%), and atrioventricular cushion defect (with normally related great arteries) was present in n=4 (22.2%). More patients with LAI had normally related great arteriesthan RAI (50% vs. 15.6%, $p<0.05$). **Conclusion:** RAI is the most common type of atrial isomerism in situs ambiguus and dextrocardia patients. The most common diagnoses in situs ambiguus and dextrocardia patients are double outlet right ventricle and single ventricle with pulmonary/sub-pulmonary obstruction. LAI had relatively simpler lesions as compared to RAI. Around one-third of the patients, atrial isomerism could not be identified.

INTRODUCTION: Dextrocardia is a rare condition with an estimated incidence of around 8.3 per 1000 fetal echoes Walmsley, Hishitani [1]. Another study by Bohun Potts, 2007 [2] has estimated the incidence of dextrocardia to be 1 in 12,019 pregnancies.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.13(3).1401-10

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.13(3).1401-10

Most of the studies conducted previously have been limited by their low numbers. Heterotaxy syndrome is a complex set of abnormal left-right axis patterning abnormalities.

Although rare (occurring in just over 1 in 10 000 live births Lin, Krikov, 2014 [3]), congenital heart defects associated with heterotaxy syndrome carry a disproportionate burden of morbidity and mortality Escobar-Diaz, Friedman, 2014 [4], Foerster, Gauvreau, 2008 [5]. Therefore, this study aims to identify the most common diagnostic pattern in patients with dextrocardia with situs ambiguus.

METHOD: This is a cross-sectional retrospective study spanned over the period of 21 years (1996-2017) with n=378 with post-natally diagnosed patients with dextrocardia from a major tertiary care center in South India. Authors have recruited patients from a computerized hospital database using the search term Dextrocardia, DC, DX, or ICD-10 diagnosis code of 759.3, 746.87. A total of 1322 patients came from records, of which 378 patients satisfied the inclusion criterion. The inclusion criterion for this study is that the long axis (Baso-apical axis) of the heart is directed towards the right side, with data sufficient to determine the situs. Situs will be defined mainly using atrial appendage morphology and relationship of IVC and aorta as identified by echocardiography; in case of ambiguity in identifying atrial morphology, splenic status and lung lobes will be used for identification. CT/MR Imaging, angiography, and surgical findings were available in 58% of the patients. Dextroposition of the heart towards the right due to non-cardiac (or lung) pathology, with the cardiac apex to the left, was excluded. Detailed segmental analysis for cardiac anatomy and associated malformations was done using previously suggested and well-accepted terms and definitions Calcaterra, Anderson, 1979 [6]. Cardiac situs will be confirmed by chest X-ray, Ultrasonography/echocardiography, catheter-rization, CMRI/CT, and during surgery.

RESULT: There were total of n=378 patients with dextrocardia, of these 43.1% (n=163) had situs solitus, 38.1% (n=144) had situs inversus and 18.8% (n=71) had situs ambiguus. Overall, among n=378 patients, there were 43.6% females, and the median age was 0.98years. Among n=71 patients with situs ambiguus, 37% (26/71) were females with a mean age of 2.3 years. Among patients with right atrial isomerism, the male: female ratio was 1.7:1, while this ratio was 1:1 among patients with left atrial isomerism. Tripathi and Ajit Kumar, 2019 [7] have already compared morphologic findings in patients with dextrocardia with situs solitus versus situs inversus. This article will mainly focus on patients with dextrocardia and situs ambiguus. Patients are divided based on atrial isomerism, namely Right atrial isomerism (n=32), left atrial isomerism (n=18), and unidentified atrial isomerism (n=21).

TABLE 1: SUMMARIZES BASELINE CHARACTERISTICS OF THE POPULATION SUB-GROUPED ACCORDING TO THE TYPE OF ATRIAL ISOMERISM. ALL THE PERCENTAGES ARE COLUMN PERCENT IN EACH VARIABLE. AV-ATRIOVENTRICULAR, C-TGA- COMPLETE TRANSPOSITION OF GREAT ARTERIES, CC-TGA- CONGENITALLY CORRECTED TRANSPOSITION OF GREAT ARTERIES, DORV- DOUBLE OUTLET RIGHT VENTRICLE, DOLV- DOUBLE OUTLET LEFT VENTRICLE, NRGA- NORMALLY RELATED GREAT ARTERIES, LV-LEFT VENTRICLE, PA- PULMONARY ATRESIA, RV- RIGHT VENTRICLE

	Atrial Isomerism							
	Right Atrial Isomerism N=32		Left Atrial Isomerism N=18		Unidentified Atrial Isomerism N=21		Total N=71	
Age (years)	**1.77**		**1.44**		**3.85**		**2.30**	
Sex								
Female	12	37.5%	9	50.0%	5	23.8%	26	36.6%
Male	20	62.5%	9	50.0%	16	76.2%	45	63.4%
Pulmonary Venous Drainage								
Normal	10	31.3%	14	77.8%	16	76.2%	40	56.3%
Abnormal	22	68.8%	4	22.2%	5	23.8%	31	43.7%
Systemic Venous Drainage								
Normal	21	65.6%	3	16.7%	13	61.9%	37	52.1%
Abnormal	11	34.4%	15	83.3%	8	38.1%	34	47.9%
Mode of Atrio-Ventricular connection								
Two AV Valves	5	15.6%	9	50.0%	5	23.8%	19	26.8%
Common AV Valve	27	84.4%	8	44.4%	12	57.1%	47	66.2%
Single AV Valve	0	0.0%	1	5.6%	4	19.0%	5	7.0%
Atrioventricular Concordance								
Concordant	7	21.9%	11	61.1%	5	23.8%	23	32.4%
Discordant	2	6.3%	0	0.0%	1	4.8%	3	4.2%
Univentricular Double Inlet	23	71.9%	7	38.9%	11	52.4%	41	57.7%
Univentricular Single Valve Atresia	0	0.0%	0	0.0%	4	19.0%	4	5.6%
Ventriculoarterial Concordance								

Concordance	7	21.9%	9	50.0%	9	42.9%	25	35.2%
Discordance	6	18.8%	3	16.7%	1	4.8%	10	14.1%
DORV	12	37.5%	5	27.8%	4	19.0%	21	29.6%
DOLV	3	9.4%	0	0.0%	1	4.8%	4	5.6%
Single Outlet PA	3	9.4%	1	5.6%	5	23.8%	9	12.7%
Missing	1	3.1%	0	0.0%	1	4.8%	2	2.8%
Great artery relation to Ventricles								
Normal	5	15.6%	9	50.0%	7	33.3%	21	29.6%
C-TGA	4	12.5%	3	16.7%	0	0.0%	7	9.9%
CC-TGA	4	12.5%	1	5.6%	2	9.5%	7	9.9%
DORV	17	53.1%	5	27.8%	9	42.9%	31	43.7%
Missing	2	6.3%	0	0.0%	3	14.3%	5	7.0%
Aortic valve Position in relation to pulmonary valve								
Aorta Anterior	3	9.4%	2	11.1%	4	19.0%	9	12.7%
Aorta Right Anterior	11	34.4%	3	16.7%	2	9.5%	16	22.5%
Aorta Left Anterior	13	40.6%	2	11.1%	6	28.6%	21	29.6%
Aorta to Right	0	0.0%	0	0.0%	1	4.8%	1	1.4%
Aorta to Left	2	6.3%	1	5.6%	2	9.5%	5	7.0%
Aorta Right Posterior	0	0.0%	0	0.0%	1	4.8%	1	1.4%
Aorta Left Posterior	0	0.0%	5	27.8%	3	14.3%	8	11.3%
Missing	3	9.4%	5	27.8%	2	9.5%	10	14.1%
Pulmonary Outflow Tract Obstruction								
Yes	28	87.5%	10	55.6%	15	71.4%	53	74.6%
No	4	12.5%	8	44.4%	6	28.6%	18	25.4%
Systemic Outflow Tract Obstruction								
Yes	1	3.1%	1	5.6%	0	0.0%	2	2.8%
No	31	96.9%	17	94.4%	21	100.0%	69	97.2%
Aortic Arch sidedness								
Left	12	37.5%	8	44.4%	10	47.6%	30	42.3%
Right	12	37.5%	9	50.0%	8	38.1%	29	40.8%
Missing	8	25.0%	1	5.6%	3	14.3%	12	16.9%
Superior Vena Cava								
Right	3	9.4%	1	5.6%	5	23.8%	9	12.7%
Left	6	18.8%	7	38.9%	5	23.8%	18	25.4%
Bilateral	22	68.8%	9	50.0%	9	42.9%	40	56.3%
Missing	1	3.1%	1	5.6%	2	9.5%	4	5.6%
Atrial Septal Defect								
Yes	30	93.8%	17	94.4%	19	90.5%	66	93.0%
No	2	6.3%	1	5.6%	2	9.5%	5	7.0%
Ventricular Septal Defect								
Yes	32	100.0%	12	66.7%	18	85.7%	62	87.3%
No	0	0.0%	6	33.3%	3	14.3%	9	12.7%
Patent DuctusArteriosus								
Yes	12	37.5%	4	22.2%	6	28.6%	22	31.0%
No	20	62.5%	14	77.8%	15	71.4%	49	69.0%
Pulmonary Blood Flow								
Normal/Increased	4	12.5%	9	50.0%	6	28.6%	19	26.8%
Decreased	28	87.5%	9	50.0%	15	71.4%	52	73.2%

Table 1 summarizes baseline characteristics of the entire study population with situs ambiguus and dextrocardia sub-grouped according to the type of atrial isomerism.

More patients with LAI had normal pulmonary venous drainage as compared to RAI (77.8% *vs.* 31.3%, p<0.05). More patients with LAI had a concordant atrioventricular connection as compared to RAI (61.1% *vs*.21.9%, p<0.05). More patients with LAI had two separate atrioventricular valves as compared to RAI (50% *vs*. 15.6%, p<0.05). More patients with LAI had a concordant ventriculoatrial connection as compared to RAI (50.0% *vs*. 21.9%, p<0.05). More patients with LAI had normally related great arteries as compared to RAI (50.0% *vs*. 15.6%, p<0.05).

TABLE 2: SHOWS THE PATIENT'S DIAGNOSIS WITH SITUS AMBIGUUS AND DEXTROCARDIA, GROUPED ACCORDING TO PULMONARY BLOOD FLOW. NOTE THAT ALL THE PERCENTAGES ARE COLUMN PERCENT. ASD-ATRIAL SEPTAL DEFECT, AVCD- ATRIOVENTRICULAR CUSHION DEFECT, C-TGA- COMPLETE TRANSPOSITION OF GREAT ARTERIES, CC-TGA- CONGENITALLY CORRECTED TRANSPOSITION OF GREAT ARTERIES, DORV- DOUBLE OUTLET RIGHT VENTRICLE, NRGA- NORMALLY RELATED GREAT ARTERIES, PDA-PATENT DUCTUS ARTERIOSUS, VSD-VENTRICULAR SEPTAL DEFECT

Diagnosis of patients with Situs Ambiguus and dextrocardia	RV outflow tract obstruction		
	RV outflow tract obstruction present N=53	RV outflow tract obstruction absent N=18	Total
Double Outlet Right Ventricle	21 (39.62%)	4 (22.22%)	25 (35.21%)
Complete transposition of great arteries	4 (7.55%)	0 (0.00%)	4 (5.63%)
Congenitally corrected transposition of great arteries	2 (3.77%)	0 (0.00%)	2 (2.81%)
SV-RV Morphology	10 (18.87%)	2 (11.11%)	12 (16.9%)
SV- Undetermined Morphology	3 (5.66%)	2 (11.11%)	5 (7.04%)
SV-LV Morphology	7 (13.21%)	1 (5.56%)	8 (11.27%)
Atrioventricular cushion defect with Normally related great arteries	2 (3.77%)	3 (16.67%)	5 (7.04%)
Left to Right shunt	0 (0.00%)	5 (27.78%)	5 (7.04%)
Tetralogy of Fallot physiology with normally related great arteries	3 (5.66%)	0 (0.00%)	3 (4.23%)
Cris Cross Heart	1 (1.89%)	1 (5.56%)	2 (2.82%)

TABLE 3: DIAGNOSIS OF PATIENTS WITH THE TYPE OF SITUS AMBIGUUS AND DEXTROCARDIA. ALL THE PERCENTAGES ARE COLUMN PERCENTAGES. DORV- DOUBLE OUTLET RIGHT VENTRICLE, TGA- TRANSPOSITION OF GREAT ARTERIES, C-TGA- COMPLETE TGA, CC-TGA- CONGENITALLY CORRECTED TGA, SV- SINGLE VENTRICLE, SV-LV SV OF LEFT VENTRICULAR MORPHOLOGY, SV-RV- SV OF RIGHT VENTRICULAR MORPHOLOGY, NRGA-NORMALLY RELATED GREAT ARTERIES, VSD-VENTRICULAR SEPTAL DEFECT, ASD-ATRIAL SEPTAL DEFECT, AVCD-ATRIOVENTRICULAR CANAL DEFECT, AVCD-COMP-COMPLETE AVCD, PS- PULMONARY STENOSIS, PA- PULMONARY ATRESIA, POTO-PULMONARY OUTFLOW TRACT OBSTRUCTION, RAI-RIGHT ATRIAL ISOMERISM, LAI-LEFT ATRIAL ISOMERISM, UAI-UNIDENTIFIED ATRIAL ISOMERISM

		Atrial Isomerism			
Diagnosis		Right Atrial Isomerism N=32	Left Atrial Isomerism N=18	Unidentified Atrial Isomerism N=21	Total N=71
DORV	POTO+	12 (37.5%)	4 (22.2%)	5 (23.8%)	21(29.6%)
	POTO-	1 (3.1%)	1 (5.6%)	2 (9.5%)	4 (5.6%)
C-TGA	POTO+	3 (9.4%)	1 (5.6%)		4 (5.6%)
CCTGA	POTO+	1 (3.1%)		1 (4.8%)	2 (2.8%)
SV-RV Morphology	POTO+	5 (15.6%)	2 (11.1%)	3 (14.3%)	10(14.1%)
	POTO-	1 (3.1%)	1 (5.6%)	0	2 (2.8%)
SV- Undetermined	POTO+	2 (6.2%)		1 (4.8%)	3 (4.2%)
Morphology	POTO-	1 (3.1%)		1 (4.8%)	2 (2.8%)
SV-LV Morphology		4 (12.5%)	1 (5.6%)	2 (9.6%)	7 (9.9%)
		1 (3.1%)	0	0	1 (1.4%)
AVCD WITH NRGA	POTO+		1 (5.6%)	1 (4.8%)	2 (2.8%)
	POTO-		3 (16.7%)	0	3 (4.2%)
Left to Right shunt			3 (16.7%)	2 (9.5%)	5(7.04%)
TOF physiology with NRGA			1 (5.6%)	2 (9.5%)	3 (4.2%)
Cris Cross Heart	POTO+	1 (3.1%)			1 (1.4%)
	POTO-			1 (4.8%)	1 (1.4%)
Total	POTO+	28 (87.5%)	10 (55.6%)	15(71.4%)	53(74.6%)
	POTO-	4 (12.5%)	8 (44.4%)	6 (28.6%)	18(25.4%)

Table 2 shows the diagnosis of the patients with situs ambiguus and dextrocardia. There is a total of n=71 patients in this group, of which 74.6% had lesions with reduced pulmonary blood flow. The most common diagnosis in patients with situs ambiguus was Single ventricle (35.2%); double outlet right ventricle (35.2%). Complete transposition of great arteries was seen in 5.6% and

congenitally corrected transposition in 2.8% of patients. Left to right shunt lesions and atrioventricular cushion defect was seen in 7% each. **Table 3** shows the diagnosis of patients based onthe type of situs ambiguus. There is a total of n=71 patients with situs ambiguus, of which right atrial isomerism was more common than left atrial isomerism (43.7% *vs.* 26.8%, p<0.01). Single ventricle and double outlet right ventricle were the most common diagnosis in patients with right atrial isomerism. While in left atrial isomerism, double outlet right ventricle, single ventricle, and atrioventricular cushion defect (with normally related great arteries) were the most common diagnosis see **Fig. 1**. It is to be noted that overall common atrioventricular valve was present in 84% of patients with right atrial isomerism. Still, it was associated with more complicated lesions like transposition of great arteries, double outlet right ventricle, and single ventricle.

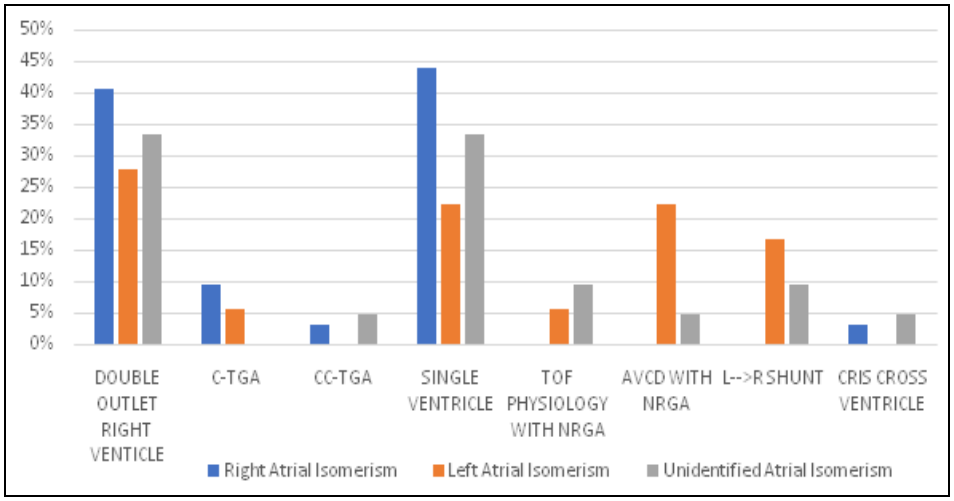

FIG. 1: DIAGNOSIS OF PATIENTS WITH SITUS AMBIGUUS GROUPED ACCORDING TO THE TYPE OF ISOMERISM. Note that Left-----Right shunt includes atrial septal defect (including primum atrioventricular defect), Ventricular septal defects, AVCD-atrioventricular canal defect, TGA- transposition of great arteries, C-TGA- complete TGA, CC-TGA- congenitally corrected TGA,NRGA-normally related great arteries.

Double Outlet Right Ventricle (n=26): Out of 26 patients with Double Outlet Right Ventricle, 13 had Right atrial isomerism, 5 had left atrial isomerism, and 7 had unidentified atrial isomerism. Among n=13 patients with right atrial isomerism, 12 patients had common atrioventricular valves, while one had two separate atrioventricular valves. Among the 12 patients with common atrioventricular valve, 2 had balanced atrioventricular cushion defect, while 10 had unbalanced atrioventricular cushion defect.

Among five patients with left atrial isomerism, one patient had two separate atrioventricular valves, while 4 had common atrioventricular valves (2 balanced and 2 unbalanced). Among seven patients with unidentified atrial isomerism, six patients had common atrioventricular valves. In contrast,one patient had a single atrioventricular valve (right-sided atrioventricular valve was atretic, most likely mitral valve atresia as the patient was in dextrocardia. He also had obstructed supra-cardiac total anomalous pulmonary venous connection draining to the right-sided superior vena cava; left-sided inferior vena cava was present).

Complete Transposition of Great Arteries (n=4): Out of n=4 patients with complete transposition of great arteries, 3 had right atrial isomerism, while one had left atrial isomerism. Among three patients with right atrial isomerism, two patients had complete balanced atrioventricular cushion defects. In contrast,one patient had two separate atrioventricular valves (although this patient had right atrial isomerism, he had abdominal situs inversus, pulmonary veins were draining to the right-sided atrium, IVC was draining to the left-sided atrium, the aorta was arising from the morphologic right ventricle (which itself was left and anterior in position compared to morphologic LV), and aortic root was arising left and anterior to pulmonary valve- so morphology of this patient was more like situs inversus with dextrocardia and transposition of great arteries except that he had

right atrial isomerism). One patient with left atrial isomerism had an unbalanced complete atrioventricular cushion defect with interrupted inferior vena cava, and the aortic root was arising anterior to the pulmonary valve.

Congenitally Corrected Transposition of Great Arteries (n=2): One patient with right atrial isomerism had CC-TGA with inflow VSD and severe pulmonary stenosis. Aorta was left and anterior to the pulmonary valve. Another patient with unidentified atrial isomerism had CC-TGA with large sub-pulmonary ventricular septal defect, moderate pulmonary stenosis, and moderate pulmonary arterial hypertension. He had bilateral trilobed lung, and abdominal situs was normal on computed tomography.

Single ventricle (n=25): Out of the total n=25, 11 patients had single ventricle of right ventricular morphology, 5 had undetermined morphology, and eight had left ventricular morphology. They are described as below-

Single Ventricle of Right Ventricular Morphology (n=12): Out of n=12 patients, six patients had right atrial isomerism, while both left atrial isomerism and unidentified atrial isomerism had three patients. Among the n=6 patients with right atrial isomerism, five patients had common atrioventricular valve out of which 3 (out of 5) had aortic position left and anterior in relation to pulmonary valve, other 2 (out of 5) had aortic root in right and anterior position.

While one patient (out of 6) had two separate atrioventricular valves, he also had infra-diaphragmatic TAPVC. Among n=3 patients with left atrial isomerism, all had common atrioventricular valves, out of which 1 had aorta in the right, and anterior position and 2 had aorta in the left and anterior position. Among n=3 patients with unidentified atrial isomerism (one patient had trilobed lung, while the other 2 had asplenia), all had common atrioventricular valves.

Single Ventricle of Undetermined Ventricular Morphology (n=5): Out of n=5, three patients had right atrial isomerism, and two had unidentified atrial isomerism. Among n=3 patients with right atrial isomerism, all had common atrioventricular valve, and two had pulmonary atresia. Among n=2 patients with unidentified atrial isomerism (both patients had IVC interruption), one patient had a common atrioventricular valve, while the other had an atretic right-sided atrioventricular valve.

Single Ventricle of Left Ventricular Morphology (n=8): Out of n=8 patients, 5 had right atrial isomerism, one had left atrial isomerism, and 2 had unidentified atrial isomerism. Among n=5 patients with right atrial isomerism, all patients had common atrioventricular valves, and 4 out of 5 had pulmonary outflow tract obstruction. 3 out of 5 had an anomalous pulmonary venous connection. One patient with left atrial isomerism had a common atrium. The right-sided atrioventricular valve was atretic, and the aorta was anterior to the pulmonary valve. Among two patients with unidentified atrial isomerism, one patient had a common atrioventricular valve and severe pulmonary stenosis. The aorta was arising to the left of the pulmonary valve. While other patients had atretic right-sided atrioventricular valve, pulmonary atresia, the aorta was left and anterior to the pulmonary outflow, interrupted IVC, the right pulmonary vein was draining to the right-sided atrium while left pulmonary vein was draining to left-sided atrium.

Atrioventricular Cushion Defect with Normally Related Great Arteries (n=5): Four patients had left atrial isomerism, while one had unidentified atrial isomerism. Among n=4 patients with left atrial isomerism, all had partial atrioventricular cushion defect with ostium primum atrial septal defect; three of these patients had interrupted inferior vena cava. One patient with unidentified atrial isomerism had completed an atrioventricular cushion defect with severe pulmonary stenosis; he also had asplenia.

Left → Right Shunt Lesions (n=5): Out of n=5 patients, three had left atrial isomerism, while 2 had unidentified atrial isomerism. Among the n=3 patients with left atrial isomerism, one had a ventricular septal defect with moderate pulmonary arterial hypertension. The second patient had a common atrium. Superior and inferior vena cava was draining into the left-sided atrium, and pulmonary veins were draining into the right-sided atrium. The third patient had a hemi-anomalous left

pulmonary venous connection draining to the right-sided atrium. In all these 3 cases aorta was arising left and posterior to the pulmonary valve. Among n=2 patients with unidentified atrial isomerism, one patient had sinus venosus atrial septal defect and interrupted inferior vena cava, while the second patient had 3 mm ostium secendum atrial septal defect and interrupted inferior vena cava.

Other Lesions: Three patients had tetralogy of Fallot and two patients had Cris cross heart.

DISCUSSION: In our study, 43.4% of patients had right atrial isomerism, 26.8% had left atrial isomerism, and 29.6% had unidentified atrial isomerism. 74.6% of patients had reduced pulmonary blood flow, majority of them had cyanosis. Single ventricle and DORV are the two most common diagnoses. 32.4% had concordant AV connection 63.3% had univentricular connection. Similar findings were also present in previous studies.

TABLE 4: SHOWS THE INCIDENCE OF SITUS IN STUDIES PERFORMED BY VARIOUS AUTHORS AND THE CURRENT STUDY

Situs	Current study	Arcilla and Gasul, 196 1 [8]	Van Praagh, Van Praagh, 1964 [9]	Ellis, Fleming, 1966 [10]	Lev, Liberthson, 1968 [11]	Squarcia, Ritter, 1973 [12]	Calcaterra, Anderson, 1979 [6]	Garg, Agarwal, 2003 [13]
Solitus	43.1%	56.7%	47.3%	61%	36.6%	73%	48%	34.4%
Inversus	38.1%	33.3%	25%	11.9%	12.2%	18.3%	33%	39.2%
Ambiguus	18.8%	10%	27.14%	10.2%	51.2%	8.4%	18%	26.4%
Total	378	30	48	59	41	60	33	125

Heterotaxy syndrome is a rare condition that lacks data in the medical literature. This study attempts to study the pattern of cardiac morphological abnormalities in patients with cardiac atrial isomerism and dextrocardia. Perhaps this is the most complicated set of patients in pediatric cardiology. Authors have tried to summarize these patients and classify them according to segmental diagnosis as broadly as possible; however, it may not be possible to do this many times. Sex distribution of patients among different atrial isomerism. In this study, patients with left atrial isomerism were 47% females, similarly to previously published studies that showed 50% female prevalence Eronen, Aittomäki, 2012 [14].

TABLE 5: SUMMARIZES THE FINDINGS OF VARIOUS SERIES ON RIGHT ATRIAL ISOMERISM. CAVV-COMMON ATRIOVENTRICULAR VALVE, APVD-ANOMALOUS PULMONARY VENOUS DRAINAGE

	Yan, Jianpeng, 2016 [16] (n = 33)	Cheung, Cheng, 2002 [17] (n = 116)	This study N=32	Eronen, Aittomäki, 2013[18] n=32	Sadiq, Stümper, 1996[19] n=20	Hashmi, Abu Sulaiman, 1998[15] N=91
Male	20 (61 %)	71 (61 %)	20 (63%)	20 (62%)	12 (60%)	54 (59%)
Levocardia	20 (61 %)	81 (70 %)	0	18 (56%)	NA	56 (%)
Dextrocardia/mesocardia	13 (39 %)	35 (30 %)	32 (100%)	14 (44%)	NA	33 (36%)
Single or functionally single atrium	20 (61 %)	69 (59 %)	20 (63%)	NA	7 (35%)	76 (84%)
Single or functionally single ventricle	19 (58 %)	96(83 %)	23 (72%)	21 (66%)	NA	66 (73%)
Pulmonary/sub-pulmonary obstruction	33(100 %)	96 (83 %)	28 (88%)	29 (91%)	20 (100%)	76 (84%)
CAVV	16 (51 %)	107 (92 %)	27 (84%)	32 (100%)	19 (95%)	74 (81%)
Pulmonary vein obstruction	0	15 (13 %)	3 (9%)	5 (16%)	9 (45%)	25 (27%)
APVD	21 (63 %)	60 (52 %)	22 (69%)	28 (88%)	14 (70%)	82 (90%)
Systemic outflow obstruction	0	4 (3 %)	11 (34%)	NA	NA	11 (12%)

Our study showed 39% female prevalence in patients with right atrial isomerism, similar to a previous study by Hashmi, Abu-Sulaiman, 1998 [15], having 40% female prevalence. It is to be noted that most studies on atrial isomerism had a combined set of patients with dextrocardia and levocardia, while our study exclusively had patients with dextrocardia; hence there could be some

difference in the numbers compared from other studies. **Table 5** summarizes various series published in the literature on right atrial isomerism and male predominance was present in all the studies ranging from 59-62%; our study had 63% males. 30-44% had either dextrocardia or mesocardiac, while our study was designed to select all the patients with dextrocardia. The single or functionally single atrium was present in the 35-84% range, while our study had 63%. The single or functionally single ventricle was present in the 58-83% range, while this study had 72%. Pulmonary / Sub-pulmonary obstruction was present in 83-100% of the patients, while this study had 88%. A common atrioventricular valve was present in 51-100% of the patients, while our study had 84.4%. Pulmonary vein obstruction was present in 9-45% of the patients, while this study had 9%. Anomalous pulmonary venous drainage was present in 52-90% of patients, while this study had 69%. Systemic outflow obstruction was present in 3-12%, while this study had 34%.

TABLE 6: SUMMARIZES THE FINDINGS OF VARIOUS SERIES ON LEFT ATRIAL ISOMERISM. CAVV-COMMON ATRIOVENTRICULAR VALVE, APVD-ANOMALOUS PULMONARY VENOUS DRAINAGE, LVOTO-LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION

	Eronen, Aittomäki, 2012 [14] N=38	This study N=18	Gilljam, McCrindle, 2000 [20] N=163	Yim, Nagata, 2018 [21] N=37
Male	19 (50%)	9 (50%)	61 (37%)	NA
Levocardia	28 (74%)	0	96 (62%)	26 (70%)
Dextrocardia/mesocardia	10 (26%)	18 (100%)	60 (38%)	11 (30%)
Single or functionally single atrium	19 (50%)	7 (39%)	82 (50%)	NA
Single or functionally single ventricle	15 (40%)	7 (39%)	70 (43%)	NA
Pulmonary/sub-pulmonary obstruction	23 (61%)	9 (50%)	45 (28%)	12 (32%)
CAVV	28 (73%)	8 (44.4%)	80 (49%)	25 (68%)
Pulmonary vein obstruction	1 (3%)		3 (2%)	
APVD	11 (29%)	4 (22%)	13(8%)	NA
Interrupted inferior vena cava	38 (100%)	15 (83%)	149 (92%)	29 (78%)
Bilateral Superior vena cava		9 (50%)	68 (42%)	17 (46%)
LVOTO ± Coarctation of aorta	9 (24%)	1 (6%)	43 (26%)	9 (24%)

Table 6 summarizes various series published in the literature on left atrial isomerism; male predominance was present in all the studies ranging from 37-50%, our study had 50% males. 26-38% of patients had either dextrocardia or mesocardiac, while this study had 100%. 50% had single atrium, while this study had 39%. The single ventricle was present in 40-43%, while this study had 39%. Pulmonary/sub-pulmonary obstruction was present in 28-61% of patients, while this study had 50% cases. The common atrioventricular valve was present in 49-73% of patients, while this study had 44.4%. Anomalous pulmonary venous drainage was present in 8-29% of the patients, while this study had 22%. Pulmonary venous obstruction was present in 2-3% of cases in other studies, while this study had none. Interrupted inferior vena cava was present in 78-100% of the cases, while this study had 83%. Bilateral superior vena cava was present in 42-46% of the patients, while this study had 50% cases. Left ventricular outflow tract obstruction/ coarctation of the aorta was present in 24-26% of the cases, while this study had only 6% cases. In our study, unidentified atrial isomerism was noted in every 2 out of 7 patients. In a retrospective analysis of non-invasive CT/MRI imaging data from 114 patients with heterotaxy (Yim, Nagata, 2018 [21]), they noted the breach in the classic pattern of isomerism in 1 out of every 5 patients. They could not identify atrial appendage morphology and splenic status in 15% and 3.5% of patients, respectively. Indeed, the challenge is not related to imaging technique, as illustrated by the study of Louise Calder, 2011 [22], who examined 56 autopsy cases of heterotaxy syndrome and 205 autopsy cases with atrial situs solitus. Similar to Yim, Nagata, 2018 [21], atrial appendage morphology and bronchial pattern were discordant in 16% of patients with heterotaxy. As with previous post-mortem studies, the author identified several other deviations from the expected visceral and cardiac anatomy pattern, irrespective of classifying patients based on the status of the spleen or atrial appendages. Recently good progress has been made regarding the lateralizing information in lateral plate mesoderm, the 2-cilia modelHirokawa, Tanaka, 2012 [23]. During the last gastrulation phase, the extracellular fluid flows from right to left in the

primitive pit at the rostral end of the lateral plate mesoderm. This stimulates receptors in cilia at the leftward edge of the pit, leading to the initiation of transcription cascade, hence the formation of left-sided structures in the left lateral plate mesoderm. The right-sided structures are formed by default on the right lateral plate mesoderm. For such a fundamental process, left-right axis establishment is remarkably complicated, with multielement effector and receptor cilia leading to the expression of distinct chains of essential gene products on either side of the embryo. Limitations of this study are the retrospective nature of the study, single-center experience. Given the study's retrospective nature, we did not have CT/MRI of all the patients; however, we did have CT or MRI findings for patients with atrial situs that could not be determined by echocardiography.

CONCLUSION: RAI is the most common type of atrial isomerism in situs ambiguus and dextrocardia patients. The most common diagnoses in situs ambiguus and dextrocardia patients are double outlet right ventricle and single ventricle with pulmonary/sub-pulmonary obstruction.

Patients with LAI had relatively simpler lesions as compared to RAI. The most common diagnosis in right atrial isomerism is double outlet right ventricle and single ventricle. At the same time, atrioventricular cushion defect (with normally related great arteries) has a higher frequency in left atrial isomerism in addition to the above two diagnoses. In one-third of the patients, the type of atrial morphology could not be identified

Compliance with Ethical Standards:

Funding: This study project has no funding.

Ethical Approval:"All procedures performed in studies involving human participants were as per the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

ACKNOWLEDGEMENT: The authors would like to acknowledge Dr. Arun Gopalakrishnan and Dr. Deepa for valuable insight and suggestions.

CONFLICTS OF INTEREST: The authors declare no conflict of interest.

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How to cite this article:
Tripathi S, Kumar VKA, Pandey UK and Jain D: Observations on cardiac abnormalities in patients with Dextrocardia and Situs ambiguus: a retrospective study. Int J Pharm Sci & Res 2022; 13(3): 1401-10. doi: 10.13040/IJPSR.0975-8232.13(3).1401-10.