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Epidemology of down's syndrome among congential heart disease children in Faisalabad

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Abstract: Patients with Down's syndrome are prone to have congenital heart defects. This study was conducted to evaluate the frequency of various congenital heart defects in children with Down's syndrome. The data was collected from the Department of Cardiology in FIC (Faisalabad Institute of Cardiology) Hospital. Fifty-eight phenotypically Down syndrome children coming to the cardiology department for echocardiography, from birth to 13 years were included in this study. After detailed history and physical examination, all these patients were subjected to 2-dimentional echocardiography in addition to routine laboratory investigations. Congenital heart defects were found in 29 out of 58 patients (50%). Amongthe affected patients, 16 (55.2%) were males and 13 (44.8%) females with male to female ratio of 1.2:1. Acynotic lesions were more common (79.31%) than cyanotic lesion (20.69%). Among the isolated lesions ventricular septal defect, patent ductus arteriosus and complete atrioventricular defects were the commonest defects (20.69%) each, followed by pulmonary atresia (6.89%), atrial septal defect, tetralogy of Fallot, transposition of great arteries and double

outlet right ventricle with ventricular septal defect (3.45%) each. Among the mixed lesions ventricular septal defect with atrial septal defect (VSD+ASD) was most common (6.89%), followed by patent ductus arteriosus with coarctation of aorta (PDA+CoA), univentricle with atrial septal defect (univentricle+ASD), and double outlet right ventricle with ventricular septal defect, patent ductus arteriosus and pulmonary atresia (DORV+VSD+PDA+pulmonary atresia) (3.45%) each. Congenital heart defects are found in 50% children with Down syndrome. The commonest are ventricular septal defect, patent ductus arteriosus and complete atrioventricular septal defect in our set-up. All children with Down syndrome should have a cardiac evaluation at birth. Down syndrome, Congenital heart disease, Transposition of great arteries, Pulmonary atresia, Tetralogy of Fallot, Ventricular septal defect.

Key words: Down syndrome, congenital heart disease, epidemiology, prevalence, echocardiography

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1.Introduction

Down syndrome or trisomy 21 is a congenital chromosomal disorder. It is most common genetic disorder caused by the addition of partial or extra copy of chromosome 21. This syndrome is a cause of retardation of mental and physical development of children associated with several physical dysmorphic features (Ahmed, Ghafoor, Samore, & Chattha, 2005). The common features are decreased muscle tone (hypotonia), short stature, delayed development, flat nasal bridge, flat occipital, microcephaly, short neck with excess skin on the back, low set ears with particular folded appearance, open mouth with protruding tongue, broad and short hands often with a single deep crease across the palm of the hand (simian crease), clinodactyly, upward slanting eyes with epicanthal folds, strabismus, nystagmus, white spots on the colored part of the eye (Brush field spots), congenital heart diseases, wide gap between first and second toe. All these anomalies can be detected at birth (Nussbaum, 2010).

In developed countries the incidence of Down syndrome varies from 1 in 732 live births (Sherman, Allen, Bean, & Freeman, 2007). Studies conducted in Australia by Collins and

associates have shown the prevalence of Down syndrome as 10 per 10,000 live births (Collins, Muggli, Riley, Palma, & Halliday, 2008). In countries where abortion is illegal, the prevalence is higher such as United Arab Emirates and Ireland. Conversely in countries where pregnancy termination occurs in Down syndrome babies, the prevalence is low (Weijerman, 2011). The risk of Down syndrome with regular trisomy 21 increases with increasing maternal age however Robertsonian Translocation is not related to maternal age. There is a high recurrence risk in the carriers of Translocation (Nussbaum, 2010). A study conducted by a group of researchers in Korea showed that women older than 35 years old has increased risk of chromosomal aberrations in child (Kim, Lee, Kim, Shim, & Cha, 2013).

Congenital heart disease, in a definition proposed is “a gross structural abnormality of the heart or intra thoracic great vessels that is actually or potentially of functional significance” (Khajali et al., 2019). Congenital heart disease (CHD) includes major structural malformations of the heart and major vessels present at birth, or persisting abnormalities after birth. CHDs are a major cause of mortality and morbidity, especially in individuals where the heart defect is associated with additional organ malformations. Chromosomal aberrations are a frequent cause of CHDs, especially when they are associated with growth or developmental delay (Khajali et al., 2019; Thienpont et al., 2007).

Congenital malformation (CM) is emerging as one of the major childhood health disorder. CM can be divided into two main categories those with a single primary defect, and those with multiple malformation syndrome. Most of the single primary defects are of unknown etiology, and are based on multi-factorial inheritance. The etiology of disorders is divided into genetic, environmental factors and teratogenic agents, maternal condition, infections, mechanical problems, chemicals agents, drugs, radiation, hyperthermia, etc. and unknown. There are regional variations in the pattern of CM. Considerable variations in the frequency of CM in different populations have been reported, 4.3% in Taiwan, 7.92% in the UAE, 2.46% in Oman, 3.5% in Tehran (Iran), 1.04% in Arak (Iran) and 1.01% in Gorgan (Iran) (Gul, Nazir, Saidal, & Bahadur, 2020).

Echocardiography is the first line and indispensable investigation for the diagnosis of congenital heart defects. In fact, echocardiography has obviated the need of cardiac catheterization. Although most CHDs are diagnosed and dealt with during childhood, some of them are discovered for the first time on echo during adulthood in asymptomatic subjects (Sharma).

Congenital heart diseases are the main factor contributing in the course of downs syndrome. 4%-10% of all congenital heart diseases have association with down's syndrome and 40%-60% patients of down's syndrome have cardiac anomalies (Doná, Lawin, Maturana, & Felcar, 2015). Cardiac anomalies associated with down's syndrome include mainly patent ductus arteriosus (PDA), atrioventricular septal defect (AVSD), ventricular septal Defect (VSD), atrial septal defect (ASD), tetralogy of fallot (TOF), coarctation of aorta (CoA), transposition of great arteries (TGA), double outlet right ventricle (DORV), pulmonary valve atresia/stenosis and univentricle (Diogenes, Mourato, de Lima Filho, & da Silva Mattos, 2017).

Research has shown that neonatal mortality in DS is less dependent on CHDs and is caused by neonatal pathology such as asphyxia, low birth weight and prematurity, as in the general population (Weijerman, 2011). In these studies, we have shown the prevalence of congenital heart defect in patients of Down's syndrome 56.36% in Pakistan. It was 81% in Brazil, 45% in Libya, 43% in Netherlands ,58% in Mexico, 56% in Denmark, 56.9% in Korea, 41% in Bahrain, 56% in Italy, 38.7% in Spain, 44% in Atlanta, USA, 48% in Birmingham, UK (Al-Arrayed & Rajab, 1995; Diogenes et al., 2017; Doná et al., 2015; Elmagrpy, Rayani, Shah, Habas, & Aburawi, 2011; Freeman et al., 2008; JM, 1997; Khan & Muhammad, 2012; Paladini et al., 2000; Salih, 2011; Santoro & Steffensen, 2021; Weijerman, 2011).

2.Material method

2.1 Data collection procedure

A structured Performa was developed including all the variables of interest for use during the study. The Performa was pretested by before adopting a final version. All the data was collected by the investigator herself. After the investigator introduced herself, the echocardiography of phenotypically confirmed Down's syndrome patients was performed and findings of congenital heart defects were recorded on the Performa.

2.2 Trans thoracic Echocardiography

Trans thoracic 2D echo studies were done by a standard technique. Situs was analyzed in sub costal view. Pulmonary venous connections to LA were assessed in apical and suprasternal window and flow was assessed on color Doppler echo. Ventricular morphology was checked on apical four chamber and two chamber views. Accurate identification of great arteries was done in short axis views at the base of the heart. Pulmonary artery was further assed on para sternal long axis and short axis views while aortic arch on suprasternal short axis views. Right ventricle and its inflow tracts were visualized on apical and sub costal four chamber views para

sternal long axis views and short axis views at the base. CoA was checked on supra sternal window. Doppler and short axis views were done for the detection of AS. 2D sub costal and apical dour chamber views were done to see ASD and VSD. Further analysis was done on M-mode and color Doppler imaging. Follow up was arranged according to the primary cardiac diagnosis.

2.3 Data analysis procedure

The data was managed and analyzed by using SPSS version 17. Data was described in terms of frequencies and percentages for categorical variables. Quantitative variables were expressed in the form of mean and standard deviation.

3. Results

Fifty-eight consecutive patients of Down's syndrome were studied. Echocardiography data was collected prospectively on a pre-designed Performa. All patients after clinical assessment were subjected to transthoracic echocardiography. Variables like patent ductus arteriosus (PDA), atrioventricular septal defect (AVSD), ventricular septal defect (VSD), atrial septal defect (ASD) tetralogy of Fallot's (TOF), coarctation of aorta (CoA), transposition of great arteries (TGA), double outlet right ventricle (DORV), pulmonary atresia/stenosis and univentricle were noted on the performa for each patient.

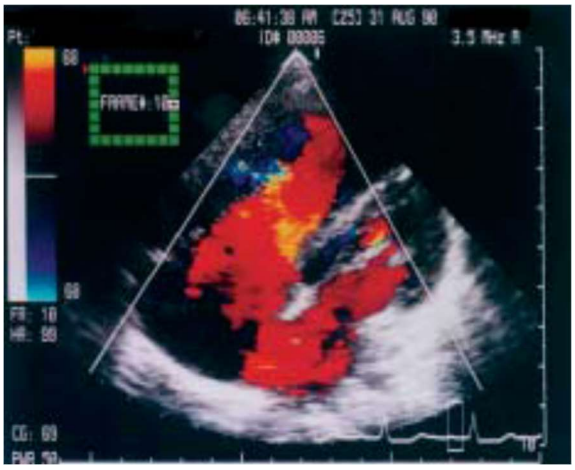

Fig 3.1: Four-chamber view is showing a large secundum type defect in the atrial septum. Blood flow crossing the ASD is apparent on **Doppler echocardiography.**

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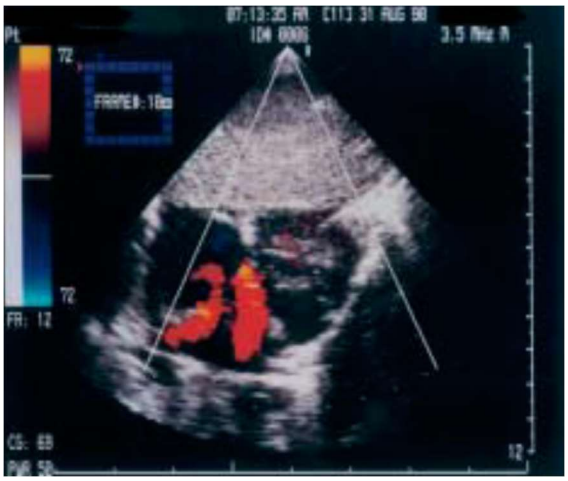

Fig 3.2: Sub costal four-chamber view with Doppler echocardiograph demonstrates blood flow crossing two defects, a primum ASD and a VSD of the inflow tract in a patient with an AVSD.

In 58 patients of Down syndrome, 63.793% (n=37) were males and 36.206% (n=21) females with male to female ratio of 1.7:1 and of these patients in which congenital heart defects were diagnosed were 55.171% (n=16) males and 44.827% (n=13) females with male to female ratio of 1.2:1 (Fig 4.1).

Figure 4.2 is a bar chart showing the percentages of isolated congenital heart defects along with their gender distribution in 58 cases of Down syndrome in the present study. In males patent ductus arteriosus (PDA) was most common (13.793%) followed by venticular septal defect (VSD) and complete atrioventricularseptal defect (CAVSD) (10.171%) each, least common were transposition of great arteries (TGA), double outlet right ventricle (DORV) and pulmonary atresia (3.448%) each. In females most common were venticular septal defect (VSD) and complete atrioventricular septal defect (CAVSD) (10.171%) each followed by patent ductus arteriosus (PDA) (6.8896%), atrial septal defect (ASD), tetrology of Fallot's (TOF) and pulmonary atresia (3.448%) each. Figure 4.3 is also a bar chart showing the percentages of mixed congenital heart defects along with their gender distribution in 58 cases of Down syndrome in the present study. In males venticular septal defect with atrial septal defect (VSD+ASD), double outlet right ventricle+ ventricular septal defect+patent ductus arteriosus+pulmonary atresia (DORV+VSD+PDA+pulmonary atresia) and univentricle with atrial septal defect (ASD) were found (3.448%) each, while in females PDA+CoA and VSD+ASD were found (3.448%) each.

Patients were catagorized in four age groups; below 1 year , one to five years, six to ten years and more than ten years of age. Most of the congenital heart defects were found in 1-5 years

age group about 51.724% (n=15) patients followed by below one year age group 41.379% (n=12), six to ten years of age 6.896% (n=2) and all patients above ten years of age group were without any cardiac defect (Table 4.1). Congenital heart defects were found in 50% (n=29) patients on echocardiography out of 58 paitients of down syndrome. Congenital heart defects were catagorized into cynotic and acynotic, isolated and mixed lesions. Among the 29 patients of congental heart defects acynotic lesion were more common in 79.310% (n=23) than cynotic lesions in 20.689% (n=6) patients. Among the acynotic lesions most common were isolated venticular septal defect (VSD) patent ductus arteriosus (PDA) and complete atrio venticular defect (CAVSD) each in 20.689% (n=6) followed by atrial septal defect with venticular septal defect (ASD+VSD) (mixed lesion) in 6.896% (n=2) and isolated atrial septal defect (ASD), double outlet right ventricle (DORV) and patent ductus arteriosus with coarctation of aorta (PDA+CoA) (mixed lesion) each in 3.448% (n=1) (Table 4.2).

Among the Cynotic lesions 20.689% (n=6) out of 29 patients, isolated pulmonary atresia was more common in 6.896% (n=2) followed by tetrology of fallots (TOF), transposition of great arteries (TGA) each in 3.448% (n=1) and mixed lesions of univentricle with atrial septal defect (univentricle+ASD) and double outlet rihht ventricle with ventricular septal defect, patent ductus arteriosus and pulmonary atresia (DORV+VSD+PDA+Pulmonary atresia) also each in 3.448% (n=1) (Table 4.3).

4 Statistical analysis

Figure 4.1: Pie chart showing distribution of patients with congenital heart defects according to gender in 58 cases.

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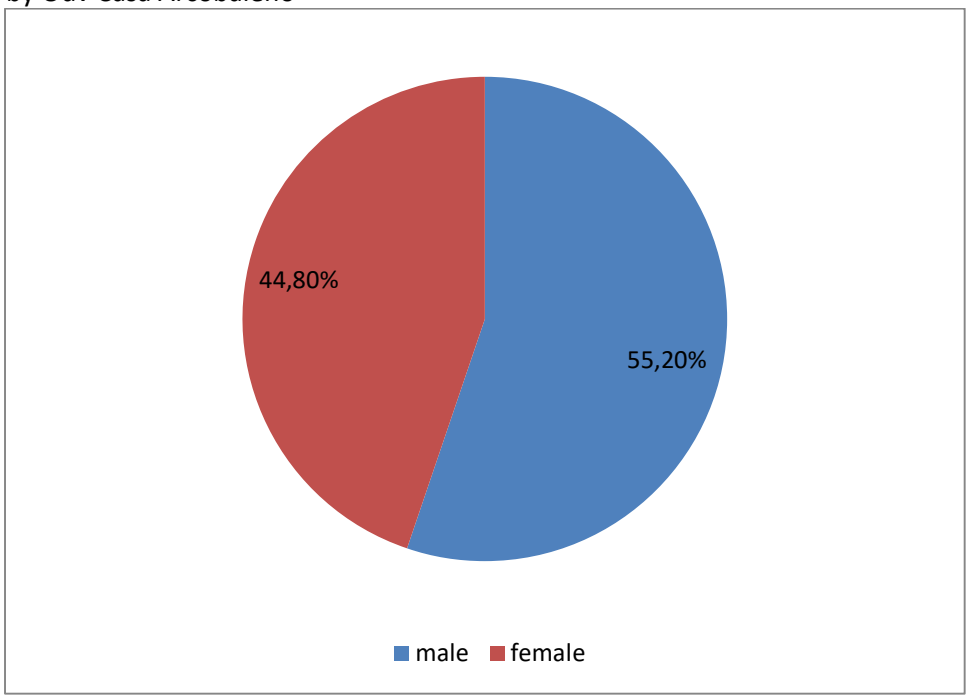

Figure 4.2: The percentages of isolated congenital heart defects along with their gender distribution in 58 cases.

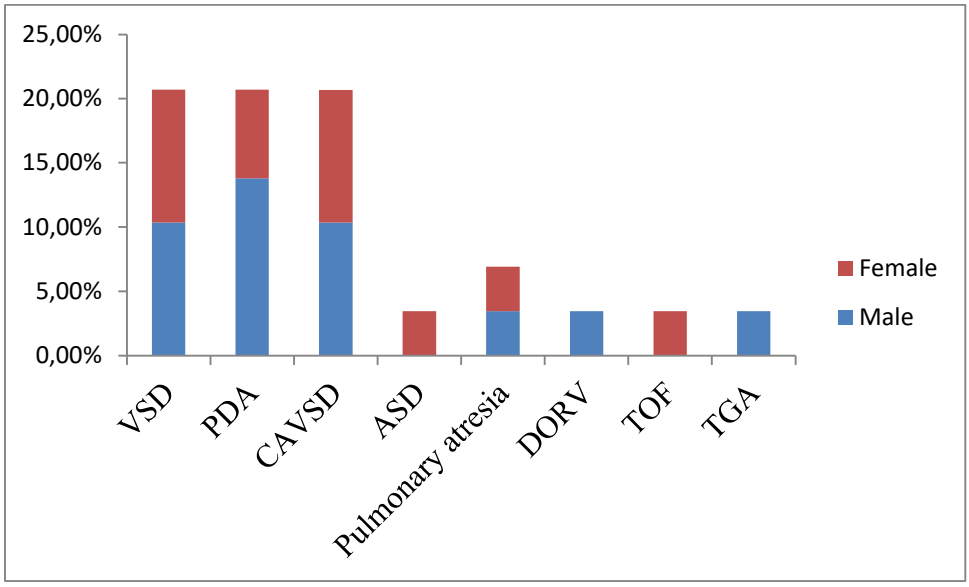

Figure 4.3: The percentages of mixed congenital heart defects along with their gender distribution in 58 cases.

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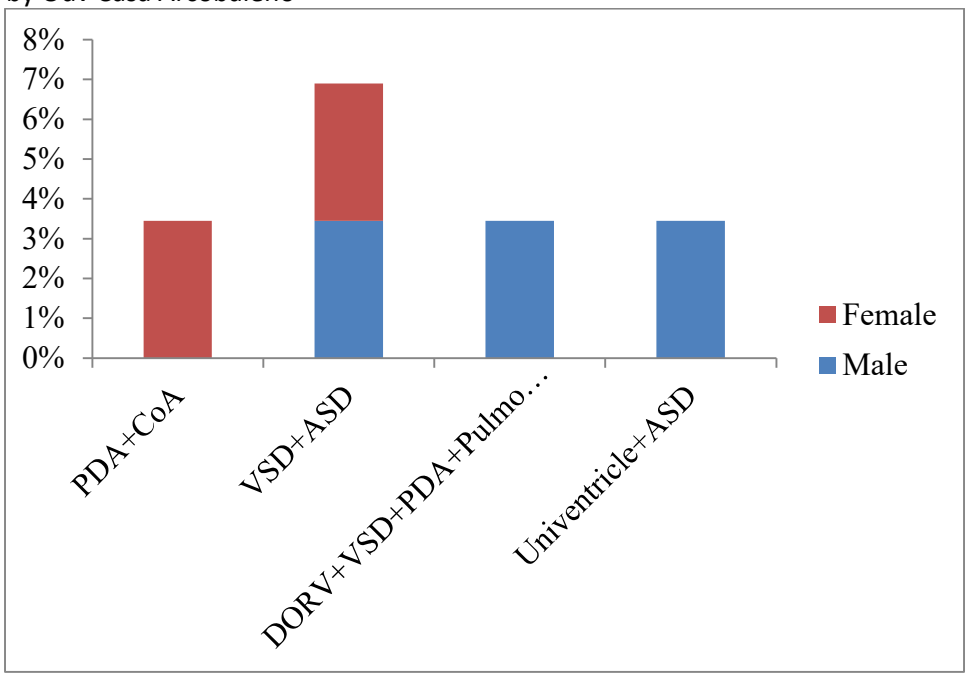

Table 4.1: Frequency distribution of different categories of age for 58 cases.

Age in years	**Acyanotic lesions** **Number (%age)**	**Cyanotic lesions** **Number (%age)**
Below 1 year	8 (27.586%)	4 (13.793%)
1 to 5 years	13 (44.827%)	2 (6.896%)
6 to 10 years	2 (6.896%)	0 (0%)
>10 years	0 (0%)	0 (0%)
Total	23 (79.310%)	6 (20.689%)

Table 4.2: Frequency distribution of different isolated cardiac lesions with major categories of acynotic and cyanotic lesions for 58 cases.

Isolated cardiac lesions (n=24)

Acyanotic lesions (n=20)	Percentage	Cyanotic lesions (n=4)	Percentage
VSD	20.989%	Pulmonary atresia	6.896%
PDA	20.989%	TGA	3.448%
CAVSD	20.989%	TOF	3.448%
ASD	3.448%		
DORV+ VSD	3.448%		

Table 4.3: Frequency distribution of different mixed cardiac lesions with major categories of acynotic and cyanotic lesions for 58 cases.

Mixed cardiac lesions (n=5)			
Acyanotic lesions (n=3)	**Percentage**	**Cyanotic lesions (n=2)**	**Percentage**
VSD+ ASD	6.896%	DORV+VSD+PDA+ Pulmonary atresia	3.448%
PDA+ CoA	3.448%	Univentricle +ASD	3.448%

5.Conclusion And Discussion

The high incidence of congenital heart disease in Down's syndrome is well known, and many authors have published figures on the frequency with which congenital heart defects are found. These figures vary from 35 to 65 percent (Khan & Muhammad, 2012). The frequency of CHD

in this study 50% is quite comparable to these studies. It is quite close to 56.9% in Korea and 56.36% in Khyber Pakhtunkhwa province in Pakistan (Khan & Muhammad, 2012). The frequency of congenital heart defects is quite higher 81% in Brazil and comparatively lower frequencies 45.10% in Libya and 43% in Netherlands (Elmagrpy et al., 2011; Mourato, Villachan, & Mattos, 2014; Weijerman, 2011). The various reasons for this difference may include the genetic make-up of each nation and the specific embryological mechanisms. In 58 patients with Down's syndrome, 37 (63.793%) were males and 21 (36.206%) females with male to female ratio of 1.7:1 and of these patients in which congenital heart defects were diagnosed were 16 (55.171%) males and 13 (44.827%) females with male to female ratio of 1.2:1. These results are very close to the study in which they found among the affected patients, 19 (61.3%) were males and 12 (38.7%) were females with male to female ratio of 1.5:1. These findings are quite different from study in Brazil, where females prevailed (56.1%) with male to female ratio of about 1:1.3 (Khan & Muhammad, 2012; Mourato et al., 2014). The most common type of congenital heart defects was isolated in 24 (82.758%) these values are very close to 90.3% in study (Khan & Muhammad, 2012). And are comparable to the Libyan population with 65% isolated lesion, 80% in Guatemala, 74% in Mexico and 78% in Turkey (Elmagrpy et al., 2011). This difference may be because of age at diagnosis where patients with more complex lesions die earlier before diagnosis. Among the acyanotic isolated and mixed lesions most common defects were ventricular Septal defect (VSD), patent Ductus Arteriosus (PDA) and complete atrioventricular septal defect (CAVSD) each in 6 (20.689%) followed by atrial septal defect with venticular septal defect (ASD+VSD) (mixed lesion) in 2 (6.896%) and isolated atrial septal defect (ASD), double outlet right ventricle (DORV) and patent ductus arteriosus with coarctationof aorta (PDA+CoA) (mixed lesion) each in 1 (3.448%). Among the Cynotic lesions isolated pulmonary atresia was more common in 2 (6.896%) followed by tetralogy of fallot (TOF), transposition of great arteries (TGA) each in 1 (3.448%) and mixed lesions of univenticle with atrial septal defect (univenticle+ASD) and double outlet right ventricle with ventricular septal defect,patent ductus artriosus and pulmonary atresia (VSD+DORV+PDA+Pulmonary atresia) also each in 1 (3.448%). These findings were quite different from the findings in Korean children in which atrial Septal defect (ASD) was most common about 30.5%. 2nd most common was ventricular Septal defect (VSD) with percentage of 19.3%, this was followed by patent Ductus Arteriosus (PDA) (17.5%) and AVSD (9.4%) (Diogenes et al., 2017). Also, in Brazil ASD secundum type was maximum (51.8%), followed by atrioventricular Septal defect (AVSD) (46.6%), ventricular Septal defect (VSD) (27.7%),

tetralogy of Fallot (TOF) (6.3%) and other cardiac anomalies (12.5%) (Mourato et al., 2014). Elmagrpy also analyzed the association of CHD and DS in Libya. Among the isolated most common was ASD (23%) followed by AVSD (19%) and VSD (14%) (Elmagrpy et al., 2011). ASD was most common in (54%), followed by VSD (33.3%) and PDA (5.8%). PPHN was (5.2%) and it was higher than normal public incidence in Netherlands. In Sudan AVSD was most common in about (48%) followed by ASD in 23% and TOF in (6%) at the time of presentation (10%) had Eisenminger syndrome (Ali, 2009).

This study shows quite similar to the study in Khyber Pakhtunkhwa province where ventricular septal defect was the commonest defect (22.6%), followed by patent ductus arteriosus (PDA) (19.4%), atrioventricular septal defect (VSD) (19.4%), atrial septal defect (ASD) (16.1%) and tetralogy of fallot (Khan & Muhammad, 2012). The results were quite comparable to study in India where Atrioventricular Septal defect (AVSD) was most common in about 13 (37.142%) among 35 down's syndrome patients, while ventricular Septal (VSD) in 26 (68.421%) was most common among the 38 non syndromic patients (Tanghöj, Liuba, Sjöberg, & Naumburg, 2020).

From this epidemiological study it can be concluded that the congenital heart defects are common in children with down's syndrome. The commonest congenital heart diseases in down's syndrome are isolated acynotic lesions including ventricular septal defect (VSD), patent ductus arteriosus (PDA) and complete atrioventricular septal defect (CAVSD) in our set-up.

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