Truncus arteriosus: A major cause of proteinuria in children

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ABSTRACT

Background: There are many studies about the association of nephropathy with congenital heart diseases (CHD), and the risk factors such as cyanosis and pulmonary hypertension have been evaluated. In our study, we have considered the relation of CHD associated nephropathy with other newer factors and the type of the structural heart defect. **Materials and Methods:** A prospective cross sectional study was carried out. 48 children were selected on the basis of specific inclusion criteria, and reviewed over a period of 9 months. Nine different simple and complex structural heart defects were evaluated and compared after obtaining the imaging, blood and urine test results. **Results:** Significant proteinuria occurred in 8 patients included in the study. More severe forms of pulmonary hypertension were observed in patients suffering from truncus arteriosus (TA); while the least values were detected in cases of pulmonary stenosis (PS) and tetralogy of fallot (TOF). The highest values of protein excretion were seen in patients of TA; and, the lowest values were observed in patients of PS and aortic stenosis (AS). Renal insufficiency was uncommon in infants and children with CHD. **Conclusion:** TA is an important cause of proteinuria among the infants and children suffering from CHD, probably because of the associated severe pulmonary hypertension (PH) and cyanosis. Also, proteinuria occurred at an earlier age in patients of TA as compared to other conditions, and was also found to be more severe if the TA was associated with moderate to severe tricuspid regurgitation.

Key words: Congenital heart disease, proteinuria, truncous arteriosus

INTRODUCTION

Nephropathy has long been recognized as a potential complication of cyanotic congenital heart disease (CCHD).[1,2] Many pathological changes can be seen in the renal system due to CHD, and are found to be linked to factors like age, blood viscosity or cyanosis; however, the number of studies studying these factors in children are scarce.[3] Truncus arteriosus (TA) is a rare congenital cardiac malformation in which a single common artery arises from the heart by means of a single semilunar truncal valve, and supplies the systemic, pulmonary, and coronary circulations.Pulmonary arteries originate from the common arterial trunk distal to the coronary arteries and proximal to the first brachiocephalic branch of the aortic arch.[4] Truncus arteriosus may be associated with syndromes which also have of renal components, such as, the Digeorge or the Goltz syndrome.[1,5,6] In this study, we have tried to study the renal protein excretion in different types of CHDs. This article also shows that some CHDs are associated with severe pulmonary hypertension and cyanosis, and can lead to severe proteinuria in an early age.

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MATERIALS AND METHODS

Fourty eight children were selected for the study. The inclusion criteria were as follows:

- filling out of consent forms by parents
- Children over one month of age;
- No preexisting renal diseases;
- Diagnosed with CHDs and some degrees of pulmonary hypertension;
- Normal ejection fraction ratio (shortening fraction: 0.28-0.4; ejection fraction; 54-75%) with or without cyanosis.

The children were diagnosed with CHD by angiography and echocardiography techniques. Patients taking drugs which can affect urine protein output or cause renal structural problems were excluded from the study. The urine samples of the participants were measured for protein to creatinine concentration in urine (Pr/Cr) two weeks after angiography and before the correcting operation, and their serum creatinine was measured and compared with normal values by using the following formula:

$$Cr\ (mg/dL) = 0.18 + age\ (year) \times 0.032.$$

The demographics (age and sex) of the patient, mean pulmonary artery pressure values, results of serum creatinine, hemoglobin levels and hematocrit tests were recorded and have been shown in Table 1. Echocardiography was performed to verify the type of structural defects and parameters about shunt characters, regurgitation and their gradients. Angiography was used to assess the the left and right ventricle and valvular structures in detail by using a standard left lateral decubitus position by a Vingemed system with a 2.5 MHz probe (GE Holten, Norway) in the apical four chambers image. Pulmonary hypertension was considered as a disorder characterized by progressive elevation of pulmonary artery pressure (PAP) and vascular resistance in the absence of left sided cardiac disease, pulmonary vein compression respiratory disorders or thrombo embolic disease. It was defined by a mean PAP over 25 mmHg at rest, or over 30 mmHg in exercise, and a pulmonary occlusion pressure (PAOP) of less than 15 mmHg.

RESULTS

Fourty eight patients affected with congenital heart disease and investigated from 2008 to 2009 were included in the study. The 9 different kinds of congenital heart defects and number of patients in each group in the study can be given as follows:

1. Large ventricular septal defect (VSD) 11;
2. Atrial septal defect (ASD) 5;
3. Aortic stenosis (AS) 4;
4. Truncous arteriosus (TA) 4;
5. Patent ductous arteriosus (PDA) 5;
6. Transposition of great arteries (TGA) 4; with or without other anomalies like as pulmonic stenosis(PS); VSD and single ventricle;
7. Pulmonary stenosis (PS) 4;
8. Tetralogy of fallot (TOF) 8
9. And, combination of VSD and ASD 3.

The highest pulmonary pressure reading in each group was recorded. The highest levels of pulmonary pressures were seen in the TA group, and the least were seen in TOF and PS groups (30 mmHg) [Figure 1].The highest Glomerular filtration rate (GFR) was observed in TOF and the least in TA (140 vs 87 ml/min /1.73m^2) [Figure 2]. In a case affected by TGA and PS, there was a high protein excretion and low GFR, and such abnormalities were not seen in other varieties of TGA associated with both PS and VSD

Table 1: Demographics (age and sex), mean pulmonary artery pressure, results of serum creatinine, hemoglobin and hematocrit tests of the patients included in the study

Type (case no)	Age (month) Mean(Minimum, Maximum)	Cr (mg/dl) Mean(Minimum, Maximum)	GFR:ml/ min/1.73m^2 Mean (Minimum, Maximum)	Pr/cr in urine Mean (Minimum, Maximu)	cyanosis	Significant proteinuria	MPA pressure (mm/hg) Mean (Minimum, Maximum)
VSD (11)	37 (7,108)	0.42 (0.3,0.65)	112 (65,180)	0.34, (0.1,1)	2/11	1/11	73 (25,100)
ASD (5)	66 (8,168)	0.45 (0.34,0.53)	116 (82,150)	0.2 (0.24,0.1)	0/5	0/5	40 (26,60)
AS (4)	59 (20,96)	0.48 (0.41,0.57)	102 (90,125)	0.1 (0.1,0.2)	0/4	0/4	32 (30,35)
TA (4)	6 (2,9)	0.37 (0.3,0.45)	87 (47,120)	4 (0.45,10)	3/4	3/4	85 (70,95)
PDA (5)	74 (5,96)	0.5 (0.38,0.89)	95 (60,132)	0.42 (0.1,0.66)	0/5	1/5	70 (37,120)
PS (4)	30 (12,72)	0.43 (0.35,0.54)	94 (70,115)	0.1 (0.05,0.1)	0/4	0/4	30 (25,50)
TOF (8)	64 (3,168)	0.4 (0.3,0.7)	140 (49,223)	0.5 (0.1,1.8)	7/8	1/8	30 (25,92)
ASD + VSD (3)	11 (3,24)	0.52 (0.51,0.53)	70 (42,94)	0.9 (0.15,1.92)	1/3	1/3	70 (65,75)
TGA(4)	20 (2,70)	0.35 (0.3,0.4)	90(60,150)	0.7(0.3,0.9)	4/4	1/4	80 (60-100)

Where, Cr = Creatinine; GFR = Glomerular Filtration Rate; Pr/Cr = protein to creatinine concentration; MPA = Main pulmonary artery; VSD = Large Ventricular Septal Defect; ASD = Atrial septal defect; AS = Aortic stenosis; TA = Truncous Arteriosus; PDA = Patent ductous arteriosus; PS = pulmonary stenosis; TOF = Tetralogy of Fallot. ; TGA: Transposition of great arteries

Table 2: Different types of truncous arteriosus and severity of proteinuria in the children included in the study

TA type 2, Large subtruncal VSD, small ASD, right aortic arch, AI^{2+}	1
TA type 1, Situs salitus, D loop, large subtruncal VSD, truncal valve regurgitation, PDA, left aortic arch	0.45
TA type 1, Mild truncal regurgitation, VSD (8 mm), TR (Pressure gradient 75 mmHg), left aortic arch	11
TA type 1, Large subtruncal VSD, small ASD2, moderate truncal insufficiency, moderate TR (Pressure gradient 27 mmHg), AI^{2+}, Left aortic arch	5

AI = aortic insufficiency; VSD = Ventricular Septal Defect; PDA = Patent ductous arteriosus; ASD = Atrial septal defect. TR=Tricuspid regurgitation

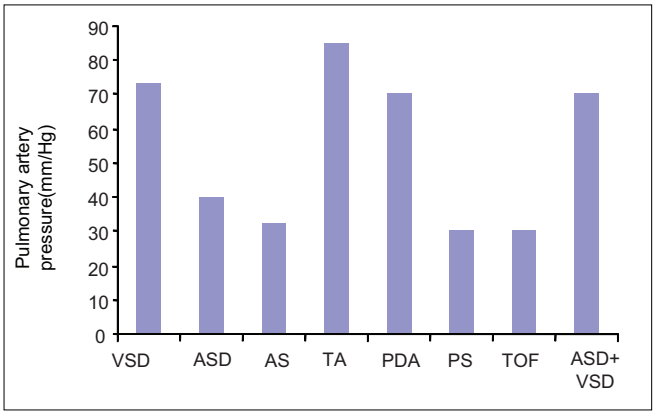

Figure 1: Pulmonary artery pressure showing a high pressure condition in truncous arteriosus type of cardiac malformation

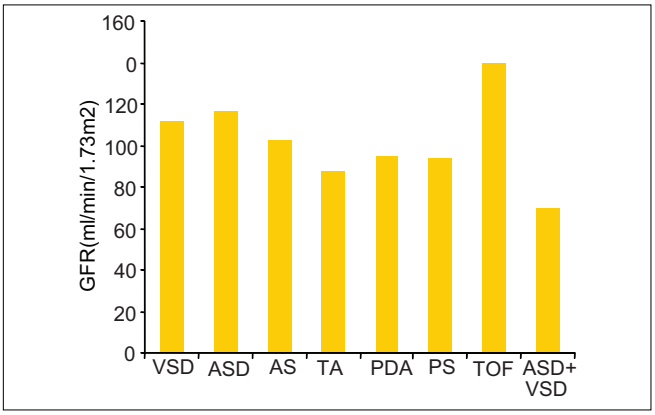

Figure 2: A higher glomerular filtration rate in tetralogy of fallot and in truncous arteriosus in comparison with mean age (6 months) of the patient. GFR is seen to be higher than normal (normal GFR in 6 – 12 months = 77 ± 14 ml/min/1.73m^2).

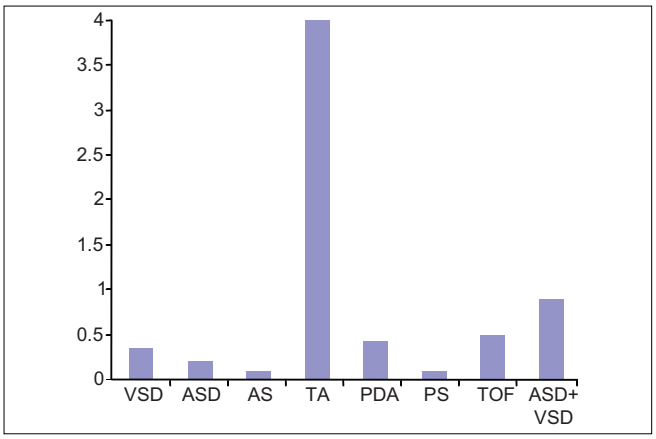

Figure 3: Urine protein to creatinine excretion is significantly higher in cases of truncous arteriosus, and in combination cases of Atrial septal defect and ventricular septal defect (VSD), compared to VSD alone cases

in one case, and single ventricle in another case. The highest Proteinuria measured as urine Pr/Cr index occurred in TA cases, and the least were observed in PS and AS groups (4 vs 0.1. urine Pr/Cr > 0.7 is abnormal at any age) [Figure 3]. The mean age of children in the TA group was 6 months and in the ASD group was 66 months. Cyanosis was seen frequently in the children of TA (3/4 of cases), TOF (7/8) and TGA (4/4) groups.

DISCUSSION

Krull *et al.* found that significant proteinuria develops in patients with CCHD, mainly of the glomerular origin in the second decade of life[7] Akita *et al.*[8] assessed 16 patients with CCHD (only 1 patient above 20 years of age) and found proteinuria and albuminuria in the 6 oldest patients. The relation of CCHD associated glomerular damage with elevated hematocrit and duration of cyanosis has been studied previously.[7,9,10] It seems that the duration of cyanosis and the extent of haematocrit elevation play a major role in the pathogenesis of CCHD-related kidney disease.[11] Although studies about the effects of CHD on the other organs are scarce, another study performed on adults affected by Eisenmenger syndrome shows a high rate of proteinuria, especially in cases of VSD, Truncus arteriosus and univentricular anomaly. Further, a higher incidence of proteinuria was seen in VSD, compared to truncus arteriosus or univentricular heart. Though in their study, 74% of VSD patients and 64% of truncus arteriosus patients excrete protein between +1 to +3, chronic renal failure was an uncommon finding.[3] Our study considered newer aspects besides to traditionally known factors for developing proteinuria, such as, severity of pulmonary hypertension, cyanosis and relation to hematocrit values. It seems that the types of cardiac anomalies have a major role in predicting the development of proteinuria in infants and children, as in our study higher proteinuria could be seen in 3 out of 4 cases of TA group. Also, the proteinuria was more severe when associated with tricuspid regurgitation [Table 2]. Further, cyanosis was common in cases of TA and TOF; however, in the latter, proteinuria

was an uncommon finding in spite of their higher mean age (duration of disease) which is necessary for formation of glomerolpathy. In simple structure heart diseases like VSD or ASD, proteinuria was uncommon; however, when these disorders were seen together, mean protein excretion increased dramatically [Table 1].

CONCLUSION

Thus, as per our study, the type of cardiac anomaly can be a predictive factor for protein excretion ratio, other than pulmonary hypertension and cyanosis in infants and children. TA anomaly is associated with high protein excretion rate in 3/4 of the affected infants, especially if it is associated with severe tricuspid regurgitation. Proteinuria was rare in PS and AS, and happened infrequently in TOF inspite of the fact that the affected children had a long duration of cyanosis, and long-term cyanosis is regarded as a principle cause of progressive nephropathy.

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