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STUDY OF RENAL PROFILE IN CHILDREN WITH CONGENITAL HEART DISEASE IN WESTERN RURAL MAHARASHTRA.

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ABSTRACT

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Introduction: The incidence of congenital heart disease (CHD) is 8-10 per 1000 in India and worldwide and due to recent advancements in diagnostic modalities, early diagnosis and management are possible leading to an increase in long-term survival. Renal involvement is one of the known complications of CHD, especially in cyanotic CHD.
Materials & method: It was a prospective longitudinal study conducted at a tertiary care hospital, including 112 cases ranging from 1 month to 12 years of age with ECHO-proven CHD were studied for the renal profile. Investigations included urea, serum creatinine, serum electrolytes (Na, K, Ca), along with the Urine analysis for protein creatinine ratio. USG abdomen study for kidney size, bladder wall thickness, post-void residue, and pelvi-calceal dilatation was done.
Results: 83.9% of CHD were acyanotic and 16.1% were cyanotic CHD. The most common CHD was VSD (39.3%). Male predominance was noted with Male to Female ratio of 1.24:1.
The most common presenting symptom of CHD in our study was poor weight gain (71.4%). Anemia was found in 42 out of the total CHD cases (37.5%). Serum creatinine was raised in 5 patients (4.5%) of CHD. Incidence of elevated creatinine was more common in cyanotic CHD (16.7%) than cyanotic CHD (2.1%) Blood Urea was found to be abnormal in 9.8% of CHD.
Conclusion: Children with CHD are prone to develop renal problems and therefore need monitoring of renal parameters. Serum creatinine levels are most deranged and hence should be checked serially as it is one of the easily available laboratory parameters.

INTRODUCTION:

Congenital heart disease (CHD) with an incidence of 8% is associated with various complications involving cardiopulmonary, neurological, renal, and hematological dysfunction. Renal dysfunction is one of the major causes of morbidity and mortality in CHD cases [1]. The majority of CHD cases develop significant proteinuria and reduction in glomerular filtration rate as a sign of glomerulopathy during the second decade of life [2]. Renal injury is an age-dependent complication of CHD, with incidence increasing with age and resulting in chronic renal disease in poorly managed cases [3]. The pathophysiological changes which occur due to the abnormal structure of the heart include polycythemia, chronic hypoxia, and intraglomerular hemodynamics with derangement of neurohormonal pathways due to chronic cyanosis resulting in nephropathy [4]. The renal injury in CHD had been characterized by glomerulomegaly, thickening of the capillary walls, capillary dilatation, segmental or global glomerulosclerosis and focal or diffuse proliferation of mesangial cells which is been attributed to the presence of chronic hypoxia and cyanosis [2,5]. In CHD, secondary renal tubular acidosis occurs due to chronic hypoxia which is one of the least documented complications [6].

The risk of chronic kidney disease (CKD) is higher with cyanotic CHD, but it is also seen in acyanotic CHD [7]. The majority of studies have been conducted in the second decade of life showing the association of renal impairments in CHD cases, although significant knowledge gap exists during the first decade and especially the early infancy period [8- 10]. With increasing surgical intervention and expertise in the field of cardiology has resulted into higher survival rates among CHD patients leading to an increased burden of kidney diseases due to CHD. Hence, understanding the complexities of cardiorenal functioning in CHD patients can result in better management and outcomes [11]. Our study focuses on the effect of congenital heart disease on renal function and distribution in cyanotic and acyanotic CHD.

MATERIALS & METHODOLOGY:

A prospective longitudinal observational study was conducted at a rural tertiary healthcare setup from September 2018 to August 2020 after institutional ethical approval and informed consent. All pediatric age groups [2 months-12 years] with CHD who attended outpatient and inpatient departments in our hospital were included and a thorough history and physical exam were conducted followed by hemoglobin level with the serum ferritin, renal profile including serum urea, serum creatinine, serum electrolytes, and urine analysis was done. The imaging studies including Ultrasonography abdomen & pelvis for kidney size, bladder wall thickness, post-void residue, pelvic-calyceal dilatation, and echocardiography with doppler were done. The collected data were tabulated and analyzed using SPSS software and appropriate statistical tool. All patients with abnormal values were admitted and treated accordingly before discharge.

RESULTS & OBSERVATIONS:

Out of 112 cases included in this study, the majority i.e., 94 (83.9%) were acyanotic congenital heart disease whereas, 18 (16.1%) cases were cyanotic CHD. The majority of the cases i.e., 57 cases (50.9%) were less than 1 year, 39 cases (34.8%) were 1-5 years age range, whereas 16 cases (14.3%) were more than 5 years. A male preponderance was seen in this study with the sex ratio of 1.24:1 and 33% were the product of consanguinity with a positive co-relation of consanguinity and cyanotic CHD.

In our study, 18 cases (16.1%) were associated with extracardiac anomalies along with CHD, with the most common extra cardiac anomaly being cleft lip i.e., 2.7% closely followed by preauricular skin tag i.e.,1.8% with other anomalies being cleft

palate, polydactyly, trachea-esophageal defects, imperforated anus and trigonocephaly. Out of the total population, 27 cases (24.1%) were on medications for their CHD. The most common type of CHD in our study was ventricular septal defect (VSD) overall whereas tetralogy of Fallot (TOF) in cyanotic CHD as seen in Table 1.

Table 1: Distribution of congenital heart diseases as per echocardiography

	Cyanotic (N=18)		Acyanotic (N=94)		Total (N=112)	
2D Echo Finding	**n**	**%**	**n**	**%**	**n**	**%**
ASD	0	0.0%	26	27.7%	26	**23.2%**
ASD+Endocardial Cushion Defect	0	0.0%	1	1.1%	1	**0.9%**
ASD+PDA	0	0.0%	1	1.1%	1	**0.9%**
ASD+PDA+COA	0	0.0%	1	1.1%	1	**0.9%**
AVSD	0	0.0%	4	4.3%	4	**3.6%**
COA	0	0.0%	1	1.1%	1	**0.9%**
Complex Congenital Disease	1	5.6%	0	0.0%	1	**0.9%**
Ebstein Anomaly	1	5.6%	0	0.0%	1	**0.9%**
PDA	0	0.0%	14	14.9%	14	**12.5%**
TAPVC	4	22.2%	0	0.0%	4	**3.6%**
TGA	2	11.1%	0	0.0%	2	**1.8%**
Tricuspid Atresia	1	5.6%	0	0.0%	1	**0.9%**
VSD	0	0.0%	44	46.8%	44	**39.3%**
VSD+PDA	0	0.0%	2	2.1%	2	**1.8%**
TOF	9	50%	0	0%	9	**8%**

ASD- atrial septal defect; PDA-patent ductus arteriosus; COA-coarctation of aorta; AVSD-atrioventricular
septal defect; TAPVC-total anomalous pulmonary venous return; TGA-transposition of great arteries; VSD-
ventricular septal defect; TOF- tetralogy of Fallot; 2D Echo-2Dimensional echocardiography.

Table no 2: Laboratory parameters of the study population.								
		Cyanotic (N=18)		Acyanotic (N=94)		Total (N=112)		p value*
		n	%	n	%	n	%	
Hemoglobin (%)	Anemic	3	16.6%	41	43.6%	42	39.3%	*0.002*
Creatinine (mg/dl)	Abnormal	3	16.7%	2	2.1%	5	4.5%	*0.006*
Urine Protein/ Creatinine Ratio	Normal	18	100%	94	100%	112	100%	-
Sodium (meq/litre)	Abnormal	0	0.0%	5	5.3%	5	4.5%	0.317
Potassium (meq/litre)	Abnormal	2	11.1%	9	9.6%	11	9.8%	0.841
Calcium (mg/dl)	Abnormal	0	0.0%	2	2.1%	2	1.8%	0.532
Urea (mg/dl)	Abnormal	4	22.2%	7	7.4%	11	9.8%	0.054
mEq-miliequivalent; dl-decilitre; mg-milligram								

The difference in hemoglobin and serum creatinine among acyanotic and cyanotic CHD were found to be statistically significant as seen in above table 2 i.e., 16.7% cyanotic (CCHD) cases and 2.1% acyanotic (ACHD) cases had deranged serum creatinine levels whereas 16.6% cyanotic and 43.6% acyanotic CHD had anemia on their laboratory parameters. The mean serum ferritin level among the iron-deficient group was 8.6 ng/dl (±2.54) as compared to 38.2 ng/dl (±5.4) in a non-iron deficient group.

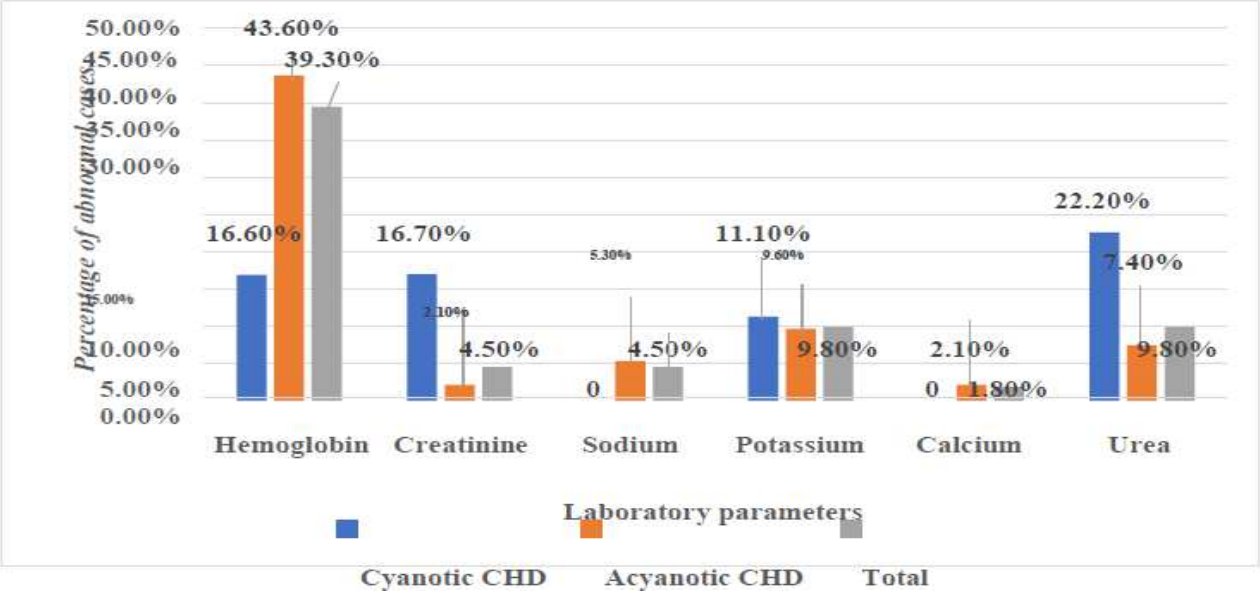

Figure 1: Laboratory parameters in CHD patients.
Hb-hemoglobin; mEq-milliequivalent; dl-decilitre.

In all CHD patient's urine protein/creatinine ratio was within the normal range. The Blood Urea was found to be abnormal in 9.8% of CHD. Among CCHD it accounts for about 22.2% and in ACHD it accounts for about 7.4%. The serum sodium was found to be abnormal in 4.5% of CHD. Out of these, 4.5% were ACHD and none of CCHD had abnormal serum sodium levels.

The serum calcium was found to be abnormal in 1.8% of CHD. Out of these, 1.8% were ACHD and none of CCHD had abnormal serum calcium levels. The serum potassium was found to be abnormal in 9.8% of CHD. Out of these, 2 were CCHD patients (1.78%) and about 9 were ACHD patients (8.03%).

The ultrasonography was found normal in the majority of the cases, but a few abnormalities were found as shown in table 3. The abnormalities were as follows nephrocalcinosis in 1 (0.9%) patient, ectopic kidney in 1 (0.9%) patient, hydronephrosis in 1 (0.9%) patient, multicystic dysplastic kidney in 1 (0.9%) patient, renal pylectasis in 1 (0.9%) patient as shown in table 3.

Table 3: Ultrasonography findings in the CHD patients.

USG Abdomen Findings	Cyanotic (N=18)		Acyanotic (N=94)		Total (N=112)	
	n	%	n	%	n	%
Bilateral Nephrocalcinosis	0	0.0%	1	1.1%	1	0.9%
Ectopic Kidneys	0	0.0%	1	1.1%	1	0.9%
Hydronephrosis of left kidney	1	5.6%	0	0.0%	1	0.9%
Left Multicystic Dysplastic Kidney	0	0.0%	1	1.1%	1	0.9%
Left Renal Pylectasis	0	0.0%	1	1.1%	1	0.9%
NAD	17	94.4%	90	95.7%	107	95.5%

CHD-congenital heart disease; USG-ultrasonography; NAD- no abnormality detected

DISCUSSION:

The occurrence of renal function failure is one of the most critical complications of CHD and this study focus on the aspect of renal function in CHD. The majority of the demographic data seen in our study was complying with other similar studies. We observed a higher prevalence of acyanotic CHD among the overall disease, which was the consistent majority of studies except with some showing equal distribution as shown in table 4. Whereas the gender distribution in our study showed a male predominance which was consistent with vakil et al [12] but female predominance was seen in Thakur et al [13].

Table 4: Distribution of cyanotic and acyanotic CHD among similar studies						
CHD	**Our study**	**Deo et al 14**	**Vijayalakshmi et al[15]**	**Suguna et al[16]**	**Kasturi et al[17]**	**Agras et al[10]**
Cyanotic	16.07%	33.3%	22.1%	26%	18%	53.5%
Acyanotic	83.93%	66.7%	77.9%	74%	82%	46.5%

A positive association between consanguinity and familial occurrence was found in our study which is consistent with other studies [14, 18-21]. The laboratory parameters play a pivotal role along with clinical features in assessing renal function as our study included parameters like serum urea, creatinine, electrolytes, and urine protein: creatinine ratio for the assessment. There was a high prevalence of anemia i.e., 39.3% found in our study which can be attributed mostly to iron deficiency or other nutritional causes which is predominant in the rural population, and none of the cases had anemia due to chronic renal disease. It can be stated from our study that anemia is more common in acyanotic CHD i.e., 43.6% than cyanotic CHD i.e., 16.6% which was found statistically significant (p = 0.002) which can be attributed to the proneness to various infections, feeding difficulties and nutritional deficiencies. The mean serum ferritin level among the iron deficient group was 8.6 ng/dl (±2.54) as compared to 38.2 ng/dl (±5.4) in non-iron deficient group.

Table 5: Comparison of prevalence of anemia/ iron deficiency among similar studies.				
Prevalence of anemia	**Studies in comparison**			
	Our study	**Amoozgar et al 22**	**Lang et al[23]**	**Mukherjee et al[24]**
Cyanotic CHD	16.6%	75.9%	16.9%	47.06%
Acyanotic CHD	43.6%	50.7%	Not included	Not included

The prevalence of iron deficiency in congenital heart disease is common which is due to hypoxia-induced erythropoiesis as seen in our study the prevalence of anemia was quite significant in other studies as seen in table 5.

On comparing the renal parameters, only 5 cases i.e., 4.5% had abnormal serum creatinine levels, with predominance in the cyanotic CHD group (16.7%), which was statistically significant. Also, all these patients with raised serum creatinine were not diagnosed case of chronic kidney disease. The serum urea levels were found deranged in 11 cases i.e., 7 (9.8%) acyanotic CHD and 4 (22.2%) being cyanotic CHD, with predominance in cyanotic CHD as seen in table 2. Whereas the electrolyte levels were deranged in acyanotic cases more commonly than acyanotic cases. On admission deranged renal profile in all the cases can be attributed to the initial signs of failure which was reverted to normal limits by initial management by intravenous fluids, correction of iron deficiency, oxygen support and correction of metabolic acidosis supporting the fact of being pre-renal insult.

TABLE 6: Profile of patients with raised serum creatinine value and their outcome.

No.	Age	Diagnosis	CKD (YES/NO)	Sr. creatinine	
				At admission	at discharge
1	4 years	PDA	NO	1.1	0.3
2	6 years	AVSD	NO	1.9	0.6
3	1.5 months	TOF	NO	1.6	0.4
4	6 months	TOF	NO	1.5	0.5
5	31 days	TGA	NO	1.0	0.3

CKD-chronic kidney disease; PDA-patent ductus arteriosus; AVSD-atrioventricular septal disease; TOF- tetralogy of Fallot; TGA- transposition of great arteries.

In our study, all the cases had normal urine protein/ creatinine ratio, not in agreement to similar studies which can be attributed to the fact that the majority of the study population comprises of less than one-year age group whereas other studies had older populations [25,26]. As seen in a study conducted by Maleki et al [27], where they found that creatinine and glomerular filtration rate is lower in cyanotic CHD patients than in acyanotic CHD patients, whereas urine protein to creatinine ratio was found higher in cyanotic CHD group which was not seen in our study.

Due to financial constraints and unavailability of certain laboratory parameters such as NAG (N-acetyl-bet D-glucosaminidase)/ creatinine ratio, creatinine clearance, fractional excretion of sodium, and urinary levels of microalbumin which would have provided a better understanding of the illness. This can be considered as one of the major limitations of the study along with lacking a long-term follow-up.

CONCLUSION:

Our study is conducted in a resource-limited set-up still concludes that children with cyanotic CHD have a higher risk of developing renal dysfunction which can be attributed due to chronic hypoxia, polycythemia and hyperviscosity can be diagnosed in early infancy and childhood i.e., within 1 year of life and hence regular follow up in cases of CHD should be done. The use of more sensitive and specific predictors of renal dysfunction such as NAG, FeNa, and urinary levels of microalbumin should be used for early diagnosis and management of the dysfunction but serum creatinine and urea are easily available and cheaper choices for follow-up.

CONFLICT OF INTEREST: Nil

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