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RENAL FUNCTION AND CLINICAL PROFILE IN CHILDREN WITH CONGENITAL HEART DISEASE – AN OBSERVATIONAL STUDY FROM TERTIARY CARE HOSPITAL IN CENTRAL INDIA.

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ABSTRACT ***Purpose: To evaluate*** the renal function and clinical profile in children with congenital heart disease.

Method: After taking informed consent from the parents of 118 children aged 1 month to 14 years were recruited in study. Anthropometry and vitals were noted. Complete physical examination and USG abdomen done to identify any other associated congenital anomaly. Laboratory evaluation of serum creatinine was done on day 1 and day 5. 24 hours urine output was strictly measured till day 5 of admission.

Result: The maximum number of cases belonged to age group 1-6 month. Male children were affected more than females (1.5:1) and majority of the children belong to family of lower middle and lower socioeconomic status. Most of the children belong to rural area. Among syndromic features, microcephaly and cleft lip and cleft palate were most frequently observed. Most of the cases had weight /height <-3SD. There was no major significant difference in mean value of urine output and serum creatinine level in different age groups and in between cyanotic and acyanotic group.

Conclusion: Congenital heart disease forms a significant diagnosis in hospitalized children. Larger studies are needed to evaluate newer associations (like male gender and low socioeconomic status). Microcephaly and cleft lip/palate were most observed associated syndromic features. No significant effect was observed on the mean urine output and serum creatinine level in children with congenital heart disease.

KEYWORDS : Congenital heart disease, serum creatinine, urine output

INTRODUCTION

Acute kidney injury is associated with significant morbidity and mortality in patients with congenital heart diseases [1]. The current diagnosis of acute kidney injury largely depends on the functional biomarkers serum creatinine and oliguria [2].

There is clear association between renal and heart failure that can affect the patient survival [2]. Nephropathy is a well-known complication of congenital heart disease and the risk of developing renal impairment is particularly high in patient with cyanotic congenital heart disease. Although this complication was due to long duration of disease however tubular injury may occur even in first decade[3].

The evaluation of serum creatinine is mainstay for diagnosis of AKI serum creatinine is a byproduct of muscle metabolism and is affected by gender, muscle mass, hydration status and critical illness[2,3]. It is freely filtered and secreted by the intact nephron and therefore creatinine clearance overestimates the actual glomerular filtration rate[3].

The cardio-renal syndrome (CRS) is co-existence of cardiac and renal dysfunction [4]. Poor renal function due to poor perfusion. Poor cardiac output and a decrease in arterial flow led to hypovolemia and starting a neurohormonal cascade that result in increased sodium and water reabsorption in kidney and activate mechanoreceptors, increased central nervous system sympathetic outflow, renin-angiotensin system activation, non-osmotic arginine vasopressin release, and thirst stimulation [3,4]. Increase in sodium and water reabsorption leads to systemic venous congestion, which may impede forward flow through the renal vasculature leading to decreased glomerular filtration and increased protein excretion[5] Decreased glomerular filtration leads to oliguria, increased fluid overload, and leading to worsening heart failure. Slight changes in serum creatinine even as little as 0.3 mg/dL, has shown to predict morbidity and mortality in adult patients with heart failure[6]. The impaired renal perfusion and venous congestion results in AKI. Slight changes in serum creatinine affect patient morbidity and mortality and have been associated with an increased risk of hospitalization and death[5,6].

This study was done to know the effect on renal function in children with congenital heart disease and evaluate the clinical profile of these children.

MATERIALS AND METHODS.

Study Design - It was an observational study carried out from January 2019 to June 2020. A convenience sample of patients meeting the inclusion criteria within the time frame of 18 months was included in the study.

Study Location - The study was carried out in the Pediatric Ward and Pediatric ICU of Kamla Raja Hospital, Gwalior which is tertiary care center affiliated with Gajra Raja Medical College, Gwalior, Madhya Pradesh. It is the only medical college in the vicinity with a well-established pediatrics department which serves as a referral center for the district.

Inclusion Criteria – All patients admitted in the Pediatric Ward or Pediatric ICU of Kamla Raja Hospital fulfilling the following criteria -

- Age group – 1 month to 14 years.
- Diagnosis - Congenital heart disease

Sample Size – Total sample size was calculated to be of 117 children with congenital heart disease because prevalence of CHD in children of North India is 1 to 8%. This sample size was calculated after placing stated P and margin of errors 5% in following formula -

$4pq \quad L2\ 4\times8\times9225 = 117$

Subject Recruitment and evaluation – Patient suffering from congenital heart disease were identified by their clinical presentation and 2D echocardiography was done for confirmation. Children with confirmed congenital heart diseases were further classified into Cyanotic and Acyanotic Congenital Heart diseases.

Data Collection –

- Socio – demographic details were collected.
- Anthropometry (Height, Weight HC, MUAC) and vitals (Heart Rate, Respiratory Rate, Oxygen Saturation, Blood Pressure) were noted.
- Complete physical examination, USG abdomen and Renal Colour doppler were done to identify any other associated congenital anomaly.
- Laboratory evaluation of Serum creatinine was done on Day 1 and Day 5 in the Central Pathology Laboratory, Gajra Raja Medical College, Gwalior.

- 24 hours Urine output was strictly monitored till day 5 of admission using Foley's bag and Uro-bag.

Informed Consent and Ethical Issues – Institutional Ethical Committee approval was taken prior to the initiation of this study. Written Parental consent was taken before enrolling admitted children in this study.

Statistical analysis:

Data was entered in Microsoft Excel and analysed using SPSS version 20.0 and EPI INFO version 7.0. Pearson's Chi Square Test for association and trend (for categorical variables) for inferential statistics was used wherever applicable. A p value of <0.05 was considered to be statistically significant at 5% level of significance.

RESULTS

This study included 118 children having Congenital Heart Disease (CHD). Most of the cases were of acyanotic congenital heart diseases (n=105; 89%). Only 13 cases (11.02 %) were found to be of cyanotic congenital heart diseases. The most common congenital heart disease was found to be ventricular septal defect (n =55). Other common CHDs observed were ASD (n=24) and PDA (n=11).

Maximum number of cases of CHD were in the age group of 1-6 months (n=70; 59.32%). In this study most of the parents were farmers or unskilled worker belonging to rural areas (n=105; 88.98%). Most of the cases were found residing in rural areas 69.49%(n=82). The socioeconomic status was assessed by in accordance to the Modified Kuppuswamy scale. Most of the cases belonged to lower class (69.49%, n=82). **(Table. 1)**

Table 1. Socio-demographic characteristics of the study sample

S. No.	Characteristic	Number of cases	Percentage
1	Age Group (in months)		
	1-6 m	70	59.32 %
	6-12 m	25	21.18 %
	12-24 m	08	6.77 %
	24-60 m	09	7.65 %
	>60 m	06	5.08 %
2	Gender		
	Male	71	60.16 %
	Female	47	39.84 %
3	Parent's occupation		
	Farmer / Unskilled laborer	105	88.98%
	Government job	09	7.64 %
	Private Job	04	3.38%
4	Residence		
	Rural	82	69.49%
	Urban	36	30.50 %
5	Socioeconomic status		
	Lower	82	69.49%
	Middle – lower	25	21.18%
	Upper – middle	08	6.79%
	Upper	03	2.54%

Weight/height ratio was calculated and plotted on standard growth charts. WHO growth charts were used up to 5 years and IAP growth charts were used above 5 year. In the age group of 1-6 months most of the cases were of <-3SD(n=34). There were 55 cases of <-3SD followed by 21 cases <-2-3SD and remaining was normal for age. There was no statistically significant difference observed between different age groups (p value – 0.518).

In this study sample the urine output was measured between days 1 to 5 of admission. There was no statistical difference in the mean urine output in different age groups (p value – 0.999). **(Table 2)** The overall mean urine output (of all days) was calculated to be 2.00 ml/kg/hour in the acyanotic group and 2.03ml/kg/hour in the cyanotic group.

Table 2. Age wise distribution of mean urine output (ml/kg/hour)

S. N.	Age (months)	Urine Output (ml/kg/hour)						P value
		Day 1	Day 2	Day 3	Day 4	Day 5	Mean	
1	1 - 6	1.79	1.88	1.91	1.93	2.01	1.90	0.999
2	6 – 12	1.87	2.11	1.95	2.06	1.97	1.99	
3	12 – 24	2.07	2.45	2.37	2.02	2.3	2.18	
4	24 – 60	2.11	3.16	2.51	2.64	2.47	2.52	
5	>60	1.88	2.41	2.11	2.4	2.37	2.23	

The serum creatinine values on Day 1 and day 5 of admission of all patients in different age groups were estimated. The results were statistically insignificant (p value – 0.801). **(Table 3)**

Table 3. Age wise distribution of mean Serum creatinine (mg/dl) values

S.N.	Age (months)	S. Creatinine (mg/dl)		P value
		Day 1 Mean	Day 5 Mean	
1	1 – 6	0.64	0.67	.800799
2	6 – 12	0.64	0.57	
3	12 – 24	0.51	0.61	
4	24 – 60	0.53	0.61	
5	>60	0.48	0.47	

Various syndromic features were most common in the age group of 1–6 months (11%). **(Table. 4)** The abdominal ultrasonography was found to be normal in 78.9% (n =93) of the cases. Amongst the abnormal findings, the most commonly observed were hepatomegaly in 5.08% (n=6) and hepatosplenomegaly in 5.08% (n=6) of the cases. Other abnormal findings included - right ectopic kidney (3.38%), hepatomegaly and contracted gall bladder (1.69%), subsequently hepatomegaly with edematous gall bladder (0.84%), hepatomegaly with massive ascites (0.84%), polycystic kidney (0.84%), renal calculi and cystitis (0.84%), contracted gallbladder plus small urinary bladder (0.84%) and right absent kidney (0.84%).

Table 4. Syndromic features in different age groups

Age in months	Number of cases	Percentage	Syndromic features
1-6	14	11%	3 microcephaly, 3 cleft palate, 1 cleft lip, palate, ankyloglossia hydrocele and short philtrum, 1 ranula and parrot beak nose, 1 CTEV, 1 prominent occiput, micrognathia, low set ears and small left eye, 1 Apert syndrome, 1 undescended testes, 1 cleft palate, micrognathia, short philtrum, ear tag and webbing of neck, 1 Down phenotype, cleft palate, micrognathia, anal atresia, depressed nasal bridge and low set ears
6-12	2	1.7%	1 microcephaly 1 frontal bossing 1 telecanthus and short lower limbs
12-24	4	3.4%	1 depressed nasal bridge and frontal bossing 1 left leg hypoplasia, 1 frontal bossing 1 case of GM1 gangliosidosis
24-60	1	0.8%	1 right CTEV
>60	1	0.8%	1 ear tag and depressed nasal bridge

DISCUSSION

In this study, it was observed that Congenital heart disease (CHD) is a common developmental defect among pediatric population, that contributes significantly to childhood morbidity and mortality. There are various genetic, environmental and socioeconomic factors attributed to poor outcome in children with congenital heart disease[7].

USG whole abdomen was done in this study in all children having CHD to find out of other associated congenital anomaly. No significant finding was observed (table 2) in most of the cases (78.9%). The most common abnormality that was found in this study were hepatosplen omegaly(n=6) and hepatomegaly(n=6). Other findings such as right ectopic kidney(n=4),right absent kidney (n=1), contracted gall bladder plus small urinary bladder (CGB UB small)(n=1), hepatomegaly plus contracted gall bladder (HM,CGB)(n=2), hepatomegaly plus edematous gall bladder(HM,EGB)(n=1), hepatomegaly with massive ascites (HM,M)(n=1), polycystic kidney (POC)(n=1), renal calculi (n=1) were also infrequently observed. In a recent study by Hussam K et al[8] conducted on 100 children with congenital heart defect, they similarly observed normal renal ultrasound in most of the cases. The renal abnormalities included ectopic kidney in 3 patients, single

functional kidney in 2 patients and bilateral grade IV hydronephrosis in one patient. A comparative study was done by Rosana CM et[9] a between CHD group and control group abdominal ultrasonography they found abnormalities 15.9% of patients with CHD and in 7.3% of controls. Malformations were identified in 20% of patients with CHD and syndromic appearance and in 8.3% of patients with CHD but no syndromic appearance, However, the frequency of abdominal malformations with clinical significance in the group with CHD and syndromic appearance was significantly higher than in controls. They found 117 cases normal abdominal ultrasonography study out of 136 cases. 19 cases found abnormal finding, asymmetric kidney (2), accessory spleen (2), mild distension of the renal pelvis (4), moderate dilatation of the collecting system (2), multiple kidney (2), duplication of the renal pelvis (2), ectopic kidney (1), renal hypoplasia (1), situs inversus (1) and multiloculated gallbladder (2).These discrepancies observed can be multifactorial depending on difference in sample size, difference in the frequencies of different congenital heart diseases observed in the study sample, age of diagnosis, ongoing treatment and genetic variations in different study populations.

In this study, the urine output was monitored from day 1 to day 5 of admission in pediatric ward or pediatric ICU. There was no significant difference in the mean of urine output from day 1 to day 5 of hospitalization in different age group of study population. There was also no significant difference observed in the mean of urine output between acyanotic and Cyanotic group. No significant difference in mean of urine output can be explained because use of diuretics and fluid management based on critical situation of admitted child.

In this study, laboratory values of serum creatinine were estimated on day 1 and day 5 of admission. There were no significant difference in mean serum creatinine values between different age groups on day 1 and day 5 of admission, also no significant difference was observed in serum creatinine values between cyanotic (mean=0.575) and acyanotic group (mean=0.629mg/dl). Similar study was done by Pinar Isik et al[10,6]: they investigate renal tubule function in pediatric patient with CHD, compared cyanotic and acyanotic groups they find (FeNa) mean of and urinary NAG/creatinine were significantly higher in the cyanotic group than the control group but there is no significant difference among group with respect to urinary β2 microglobulin/ creatinine, urinary macroglobulin/creatinine or glomerular filtration rate because tubular injury can be detected before glomerular injury occurs even within the first decade of life in patient with cyanotic CHD. This difference in results can be explained because of smaller sample size and shorter duration of study.

On clinical examination of cases in the study sample (table 3), most commonly the syndromic features were observed in the age group of 1-6 months (11%). Probably this decrease in the prevalence of syndromic features in older age groups can be explained by the poor prognosis and survival rate of patients with congenital heart diseases associated with any syndrome. Most frequently observed defect was cleft palate either alone or associated with other malformations. Other features that were observed included- 3 cases of microcephaly, 3 cases of cleft palate, 1 case of cleft lip plus palate plus ankyloglossia plus hydrocele plus short philtrum, 1 case of ranula plus parrot beak nose,1 case of CTEV,1 case of prominent occiput plus micrognathia plus low set ears plus small left eye,1 case of Apert syndrome, 1 case of undescended testes,1 case of cleft palate plus micrognathia plus short philtrum plus ear tag plus webbing of neck,1 case of Down phenotype plus cleft palate plus micrognathia plus anal atresia plus depressed nasal bridge and low set ears, 1 case of microcephaly and 1 case of frontal bossing plus telecanthus plus short lower limbs. Similar study was done by Grech V et al[11] studied they found (9%) had chromosomal anomalies had CHD ,four (2%) had non-chromosomal syndromes and 14 (6%) had other, major non cardiac malformation, The commonest non-cardiac anomalies were musculoskeletal anomalies. Down syndrome accounted for 95% of all syndromic congenital heart disease. Gretch V et al[12] studied malformation associated with CHD orofacial clefts was most common finding , of 2180 cases reported as having orofacial clefts, 657 (30.1%) had other congenital abnormalities, significantly more common in cleft palate than that in cleft lip or cleft lip and palate. Disorders of the central nervous system skeletal anomalies were also frequently associated.

CONCLUSION

Congenital heart disease forms a significant diagnosis in hospitalized children. Larger studies are needed to evaluate newer associations (like male gender and low socioeconomic status). Early diagnosis and treatment along with proper growth monitoring are key determining factors of outcome. Complete physical examination (syndromic features) and USG whole abdomen should be done for prognosis and appropriate management. Microcephaly and cleft lip/palate were most observed associated syndromic features. No significant effect was observed on the mean urine output and serum creatinine level in children with congenital heart disease.

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Conflict of Interest: None

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