Original Article

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Congenital Heart Defects in Paediatric Patients with Congenital Urogenital Abnormalities: A Cross-sectional Study

Anaesthesia Section

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ABSTRACT

Introduction: Congenital Heart Defects (CHD) are the most significant co-morbidity in children with congenital anomalies of the kidney and urinary tract, according to past research. The fundamental cause is a combination of certain genetic factors and environmental influences on foetal development.

Aim: To investigate the incidence of CHD in congenital urogenital abnormalities in paediatric patients.

Materials and Methods: A cross-sectional study was conducted at Dr. D.Y. Patil Medical College, Pune, Maharashtra, India, from June 2023 to December 2023 on 110 patients with congenital urogenital abnormalities undergoing elective surgical procedures to find the incidence of CHDs. All routine investigations, clinical history and examination, ultrasonography, and echocardiography were done. The association of the variables that were quantitative and not normally distributed in nature was analysed using the Mann-Whitney's Test, and variables that were quantitative and normally distributed in nature were analysed using an independent t-test. The association of variables which were qualitative in nature was analysed using the Fischer's-exact test.

Results: The maternal demographic characteristics that were included were maternal age, gestational age, parity, and consanguinity of marriage. The mean maternal age was 25.65±2.79 years. The mean gestational age was 38.55±1.27 weeks. Consanguinity of marriage was observed in four out of 110 cases. Out of 110 cases, the mean primigravida was 37.27%, gravida 2 was 46.36%, gravida 3 was 13.4%, and gravida 4 was 2.73%. The demographic characteristics of children with urogenital anomalies showed a female-to-male ratio of 50:60. Clinically, a murmur was observed in 15% of cases, and other anomalies were detected in two cases. Out of the total 110 patients with urogenital abnormalities, 15 patients had CHD. Among the 15 cases, four cases were Atrial Septal Defects (ASD), six cases were Patent Ductus Arteriosus (PDA), and five cases were Ventricular Septal Defects (VSD). The total incidence of CHDs was 13.6%.

Conclusion: Therefore, authors infered that the incidence of CHD was 13.6% in paediatric patients with congenital urogenital abnormalities. Children with congenital urogenital abnormalities need to be investigated with routine echocardiography. Thus, early diagnosis and therapeutic intervention of CHDs shall not only improve the surgical outcome of congenital urogenital anomalies but also improve the long-term outcome of this high-risk patient population.

Keywords: Atrial septal defects, Consanguinity, Examination, Murmur, Surgical

INTRODUCTION

Agenesis of the kidney, horseshoe-shaped kidney, cystic and duplex kidneys, kidney dysplasia/hypoplasia, and multiple collecting ducts or ureters fall under the category of Congenital Anomalies of the Kidney and Urinary Tract Defects (CAKUT). Hydroureter, hydronephrosis, vesicoureteral reflux, and obstruction of the ureteropelvic junction can be caused by these anatomical anomalies. Certain genetic disorders and monogenic mutations may be the reasons [1]. CHD is mostly caused by mutations associated with cilia, according to recent research. Considering that cilia is well known to be important for kidney development and illness, some research revealed that CHD mutant mice had a higher prevalence of renal abnormalities found in a huge-scale mouse forward genetic screen [2,3]. Pregnancy-related medications and certain genetic factors may be the root cause of CHD in CAKUT. Thus, it is essential to understand the types, prevalence, maternal risk factors, and history of CAKUT linked to CHD [4]. Although there are strong reasons to believe that CHD and CAKUT are related, there is insufficient data available to determine the incidence of CHD in patients with CAKUT who are of Indian ethnicity. This has given us the idea to investigate this further. In a condition called Vertebrae, Anus, Cardiac, Tracheoseophageal, Renal and Limbs (VACTERAL) syndrome, there are birth defects linked to a minimum of three phenotypes, which include anal atresia, heart abnormalities, tracheoesophageal fistula, renal abnormalities, and limb defects. Fraser syndrome is an uncommon genetic condition that manifests as cardiac problems, syndactyly, kidney agenesis, and eye defects [5]. DiGeorge syndrome, which is associated with 22q11.2 chromosome deletion, is linked to several organ problems, including nervous system, heart, kidney, and thymus defects [5]. In fact, renal abnormalities are linked to 23.1% of CHD cases [6]. In a study by Alp EK et al., the proportion of CHD in patients with urogenital abnormalities was 11.2% [7]. The goal of present research was to determine whether CHD is associated with CAKUT in paediatric patients undergoing surgical procedures.

MATERIALS AND METHODS

A cross-sectional study was conducted on 110 patients with CAKUT at Dr. D Y Patil Medical College in Pune, Maharashtra, India, from June 2023 to December 2023. Institutional Ethics Committee Clearance with ethical approval number IESC/FP/60/2023 was obtained before the start of the study, and informed written consent was obtained from parents.

Sample size calculation: According to the study by Alp EK et al., the minimum sample size obtained was 107, assuming a proportion of 0.112 and an acceptable difference of 0.06% with a confidence level of 95%, calculated using WinPepi software version 11.38 [7].

Inclusion and Exclusion criteria: Patients aged 0 to 8 years of either sex, 110 patients of American Soceity of Anaesthesiologists (ASA) grade I and II posted for elective surgeries were included and patients

with ASA grade III, emergency procedures, and patients without parental consent for the study were excluded from the study.

Study Procedure

Preanaesthesia check-up was conducted the day before surgery, and detailed history and complaints were noted. Information about antenatal check-ups, drug history during pregnancy (no drug history), and consanguinity of marriage were obtained. General examinations, including history of cyanosis, presence of clubbing and murmur, were recorded. Systemic examinations of cardiovascular, respiratory, and central nervous systems were performed. Routine laboratory investigations such as haemogram, serum electrolytes, renal function tests, Bleeding Time and Clotting Time (BT and CT), chest radiographs, Prothrombin time/International normalised ratio were conducted. Echocardiographic findings, Ultrasonographic parameters, and micturating cystourethrogram were also obtained. Patients were nil by mouth for six hours for solid food and four hours for breast milk before surgery. All details were recorded on the proforma sheet.

STATISTICAL ANALYSIS

The presentation of the categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data with a normal distribution were presented as the mean±Standard Deviation (SD), and the data with a non normal distribution were presented as the median with the 25th and 75th percentiles (interquartile range). The data normality was checked using the Shapiro-Wilk test. In cases where the data were not normal, non parametric tests were used. The following statistical tests were applied for the results: The association of variables that were quantitative and not normally distributed in nature was analysed using the Mann-Whitney's Test, and variables that were quantitative and normally distributed in nature were analysed using the Independent t-test. The association of variables that were qualitative in nature was analysed using Fisher's exact test, as atleast one cell had an expected value of less than 5. Fischer's exact test was used to analyse the association of variables such as gender, CHD, consanguinity of marriage, murmur, cyanosis, clubbing, parity, and other abnormalities. For variables such as maternal age in years and gestational age in weeks, the independent t-test was used, while for age in years, the Mann-Whitney's test was used. Data entry was performed in a Microsoft Excel spreadsheet, and the final analysis was conducted using the Statistical Package for Social Sciences (SPSS) software, manufactured by IBM® in Chicago, USA, version 25.0. For statistical significance, a p-value of less than 0.05 was considered statistically significant.

RESULTS

In present study, out of 110 patients, 54.55% were males, and 45.45% were females. Among the 15 cases of CHD, 40% had PDA, 33.33% had VSD, and 26.67% had ASD. The patients' age ranged from 0 to 8 years (mean age 3.57±2.4 years), maternal ages from 20 to 35 years (mean age 25.65±2.79 years), and gestational ages from 35 to 42 weeks (mean age 38.55±1.27 weeks). A heart murmur was detected in 13.64% of cases, while cyanosis and clubbing were absent [Table/Fig-1].

Consanguinity of marriage was observed in 3.64% of cases (p-value=0.449), and 1.82% had other abnormalities (p-value=0.255) such as cleft lip or limb anomaly. CHD was significantly more common in males (20%) compared to females (6%) (p-value=0.049). No significant associations were found between CHD and consanguinity of marriage (p-value=0.449), parity (p-value=0.805), other abnormalities (p-value=0.255), age (p-value=0.948), maternal age (p-value=0.116), or gestational age (p-value=0.774) [Table/Fig-2,3] showed different types and numbers of each type of CAKUT included in the study.

Demographic and clinical characteristics	n (%)
Gender	
Female	50 (45.45%)
Male	60 (54.55%)
ˣCHD	
Atrial Septal Defect (ASD)	4 (26.67%)
Patent Ductus Arteriosus (PDA)	6 (40.00%)
Ventricular Septal Defect (VSD)	5 (33.33%)
ˣConsanguinity of marriage	
No	106 (96.36%)
Yes	4 (3.64%)
Murmur	
Yes	15 (13.64%)
Cyanosis	
Yes	0
Clubbing	
Yes	0
Parity	
1	41 (37.27%)
2	51 (46.36%)
3	15 (13.64%)
4	3 (2.73%)
Other abnormality absent/present	
Absent	108 (98.18%)
Present	2 (1.82%)
Various other abnormalities	
Cleft lip	1 (50.00%)
Limb anomaly	1 (50.00%)

[Table/Fig-1]: Demographic and clinical characteristics distribution (N=110).

Demographic and clinical characteristics	CHD absent (n=95)	CHD present (n=15)	Total	p-value
Gender				
Female	47 (94%)	3 (6%)	50 (100%)	0.049*
Male	48 (80%)	12 (20%)	60 (100%)	
Consanguinity of marriage				
No	92 (86.79%)	14 (13.21%)	106 (100%)	0.449*
Yes	3 (75%)	1 (25%)	4 (100%)	
Parity				
1	34 (82.93%)	7 (17.07%)	41 (100%)	0.805*
2	44 (86.27%)	7 (13.73%)	51 (100%)	
3	14 (93.33%)	1 (6.67%)	15 (100%)	
4	3 (100%)	0 (0%)	3 (100%)	
Other abnormality absent/present				
Absent	94 (87.04%)	14 (12.96%)	108 (100%)	0.255*
Present	1 (50%)	1 (50%)	2 (100%)	
Age (years)	3 (1.75-5)	3 (2-5)	3 (2-5)	0.948‡
Maternal age (years)	25.82±2.86	24.6±2.1	25.65±2.79	0.116†
Gestational age (weeks)	38.57±1.34	38.47±0.64	38.55±1.27	0.774†

[Table/Fig-2]: Association of demographic and clinical characteristics with CHD (N=110).
†Independent t-test; ‡Mann-whitney's test; *Fisher's-exact test

DISCUSSION

The present study included 110 patients. There were 15 patients with CHD in total. The most common CHDs were ASD, VSD, and PDA. The total incidence of CHD was 13.6%. There was no statistically significant difference in maternal age, consanguinity of marriage, parity, or gestational age between the patients with CHD and without CHD (p-value >0.05).

Types of CAKUT	Number of cases
Pelvi-ureteric junction obstruction	54
Posterior urethral valve	40
Renal agenesis	2
Horse-shoe kidney	1
Ureteric reimplantation	10
CAPD catheterisation	3

[Table/Fig-3]: Distribution of types of CAKUT.
CAPD: Continuous ambulatory peritoneal dialysis

Authors did not find maternal age to be a significant factor, but in the study conducted by Jiang D et al., maternal age was a significant factor (p-value of 0.03) [4]. In the study by Tain YL et al., maternal risk factors such as age and parity (p-value of 0.80), as well as gestational age (p-value of 0.77), were not significant factors, which aligns with present study [8]. The p-value for consanguinity in marriage was 0.449 (non significant). Similar to present study, abnormalities were more frequently found in males than in females in the study by Jiang D et al., [4]. In present study, the p-value between female and male sexes was 0.049 (significant), while the p-value for other congenital anomalies was 0.255 (non significant). In 10% of the patients included in the study by Jiang D et al., other anomalies were identified [4].

Approximately 3-6 children out of 1000 live births worldwide are born with CAKUT [7]. In the study by Jiang D et al., the prevalence of children with CHD who had concurrent CAKUT was 7.4% [4].

Research indicates that the annual occurrence of CAKUT has increased, likely due to advancements in imaging technologies such as ultrasonography and 2D echocardiography, which have improved detection rates [9,10]. Moreover, more couples are undergoing routine pregnancy check-ups, providing a better opportunity for early detection and treatment of CHD and CAKUT [3]. Ultrasound screening is crucial for identifying the onset of CAKUT and for preventing impaired renal function and slowing down disease progression [11-14].

Recent research suggests that mutations in cilia are a major factor in the genetic aetiology of CHD [2]. It is well recognised that cilia play a crucial role in kidney development and function. Cilia are membrane-bound organelles that regulate protein trafficking. There are two main types of cilia: motile and non motile, also known as primary cilia. Primary cilia are present in all body cells, including developing heart and kidney cells. Motile cilia are responsible for functions such as sperm motility and mucociliary clearance. Mutations in cilia can lead to ciliopathies, a group of diseases affecting the heart, kidneys, and other organs. Several ciliopathies can manifest as renal anomalies, including polycystic kidney disease, nephronophthisis, Meckel-Gruber syndrome, and Joubert syndrome. Additionally, primary ciliary dyskinesia, skeletal malformations, and cardiomyopathy are other structural birth defects classified as ciliopathies [2]. Some studies have shown that a large-scale mouse forward genetic screen identified renal anomalies that were more common among CHD mutant mice [2,15]. Identifying CAKUT and CHD genes in these studies was challenging due to incomplete penetrance [2,16].

Other causes of CHD and CAKUT phenotypes include genetic syndromes such as Di George syndrome, which is associated with a 22q11.2 chromosome deletion and is linked to defects of the heart and kidney, as well as affecting the thymus and nervous system. A birth defect known as "VACTERAL association" is linked to limb abnormalities, renal abnormalities, cardiac problems, anal atresia, trachea-esophageal fistula, and vertebral defects. Fraser syndrome, a rare genetic disorder, causes genitourinary abnormalities in addition to congestive heart failure and presents with syndactyly and eye defects as well [2,17].

A clinical study involving 77 CHD patients selected from the Children's Hospital of Pittsburgh validated the significance of CAKUT abnormalities in CHD. Of the 77 patients whose medical records were retrospectively reviewed, 23 (30%) also had renal defects, including renal cysts, kidney agenesis, cystic dysplastic kidneys, and horseshoe kidneys [10]. According to a prior epidemiological study conducted in the Atlanta metro area, 23% of 8000 individuals with CHD also had renal abnormalities [18].

Parents frequently overlook or disregard anatomical malformations without evident clinical symptoms in the early stages of a newborn's development due to the hidden locations of the kidneys, ureters, and bladder. Furthermore, symptomatic manifestation of CAKUT occurs when renal reserves are significantly reduced due to renal injury or when compensated for due to increased pathological or physiological demands. An imaging examination is essential for the follow-up process. Studies have shown that even within the same group of newborns, postpartum ultrasonography has a higher diagnostic rate for CAKUT than prenatal ultrasonographic screening [19,20]. This confirms that a subset of patients with CAKUT is detected later in life in children who have normal prenatal ultrasonographic findings. Understanding the types of congenital cardiac defects can help with fluid control during surgery, particularly in cases like cystoscopies where a lot of irrigation fluid is required. Therefore, maintaining better haemodynamics throughout the surgery is crucial.

Limitation(s)

The major limitation of the study was that only the patients with CAKUT who were scheduled for surgery were included, while patients with CAKUT in the general population were missed out.

CONCLUSION(S)

The study concludes that there is a notable incidence (13.6%) of CHD in paediatric patients with congenital urogenital abnormalities. Gender appeared to be a significant factor, with CHD being more common in males. However, other demographic and clinical factors such as maternal age, consanguinity of marriage, parity, and gestational age did not show a significant association with CHD. This highlights the importance of considering cardiac evaluation in paediatric patients with congenital urogenital abnormalities.

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