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ORIGINAL ARTICLE

Microalbuminuria As an Indicator of Renal Impairment Among Children with Congenital Heart Diseases

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ABSTRACT

Background: Congenital heart disease (CHD) is a prevalent congenital disability, affecting approximately 1% of live births. Survival rates have increased due to improvements in medical and surgical care, yet patients with CHD remain at risk for multi-organ complications, including renal dysfunction. This study aimed to investigate microalbuminuria as an early sign of renal impairment in children with congenital heart disease by assessing both urinary microalbumin levels and albumin-to-creatinine ratios (ACR), and comparing these parameters among cyanotic CHD patients, acyanotic CHD patients, and healthy controls. **Methods:** This study was conducted as a case-control study to evaluate microalbuminuria as an indicator of renal impairment among children diagnosed with CHDs. Fifty-one participants were allocated equally into Group 1: Children with acyanotic CHD, Group 2: Children with cyanotic CHD, and Group 3: Healthy controls. All participants underwent detailed clinical evaluation and laboratory investigations, including complete urine analysis, urinary microalbumin, urinary creatinine, and the calculation of the urinary albumin-to-creatinine ratio (ACR).**Results:** A significant increase in urinary microalbumin (2.54 ± 2.04 mg/dL) and ACR (42.11 ± 27.86 mg/g) was found in the cyanotic CHD group compared to acyanotic CHD (0.62 ± 0.51 mg/dL and 11.24 ± 7.64 mg/g, respectively) and controls (0.61 ± 0.24 mg/dL and 8.25 ± 2.61 mg/g, respectively), with $P < 0.0001$. Additionally, both systolic and diastolic blood pressures were significantly lower in the cyanotic group ($P < 0.0001$), and urinary creatinine levels were higher in CHD groups versus controls ($P = 0.0349$).**Conclusions:** This study's findings highlight microalbuminuria and elevated ACR as valuable early indicators of renal impairment in children with CHD, particularly among cyanotic cases. The markedly higher levels observed in the cyanotic group may reflect the effects of chronic hypoxia and altered hemodynamics commonly associated with these conditions. Further studies are warranted to directly evaluate correlations with oxygen saturation and hemodynamic parameters.

Keywords: Congenital Heart Disease; Microalbuminuria; Renal; Cyanosis.

INTRODUCTION

Congenital heart disease (CHD) refers to structural abnormalities of the heart or the major intrathoracic vessels that are either currently or potentially functionally significant [1]. CHD is the most common congenital anomaly, affecting approximately 0.8% of live births. These defects are a

leading cause of morbidity and mortality in children, contributing significantly to chronic illness and early death. This is particularly important in light of advances in interventional cardiology, which have improved both the survival and long-term outcomes of affected infants, leading to a growing population of children living with CHD-related complications [2].

As a result, individuals with CHD are at increased risk of developing complications—not only from the underlying disease process itself but also from the medications used and the interventions performed. Increasingly, CHD is being recognized as a multisystem disorder, given that its complications often extend beyond the heart to affect multiple organ systems. Cardiac-related complications may include infective endocarditis, congestive heart failure, and arrhythmias. Non-cardiac complications can involve pulmonary hypertension, neurological impairments, and renal dysfunction [3]. Nephropathy is a common symptom and possible consequence of congenital cyanotic heart disorders, according to several investigations [4].In congenital heart disease, structural and circulatory abnormalities of the heart can lead to a cascade of systemic effects. These include cardiac volume overload, altered intraglomerular hemodynamics, dysregulation of neurohormonal pathways, and autonomic nervous system dysfunction. These disturbances collectively contribute to glomerulosclerosis's development, often characterized by increased mesangial cellularity [5].In cyanotic congenital heart disease (CHD), in addition to the previously mentioned changes, chronic hypoxia stimulates increased erythropoietin production. This, in turn, promotes erythropoiesis, resulting in blood hyperviscosity. The elevated blood viscosity alters renal hemodynamics by increasing glomerular arteriolar resistance and intraglomerular pressure. These changes contribute to glomerular hyperfiltration, which may ultimately lead to proteinuria [5].Nephrotic syndrome is a rare consequence, renal biopsy has been seldom done, and proteinuria is the primary urinary anomaly in individuals with cyanotic CHD. Chronic hypoxia's negative impacts on renal tubular function have not been as well studied. Patients with prolonged cyanosis appeared to develop secondary tubular renal acidosis as an acquired consequence [6].Microalbuminuria is a far early indication of renal impairment before proteinuria becomes apparent, and it predicts future cardiovascular conditions even in physically normal individuals [6].

This study aimed to investigate microalbuminuria as an early sign of renal impairment in children with congenital heart disease by assessing both urinary microalbumin levels and albumin-to-creatinine ratios (ACR), and comparing these parameters among cyanotic CHD patients, acyanotic CHD patients, and healthy controls.

METHODS

This case-control study was conducted in the Pediatric Department of Zagazig University Hospitals after obtaining approval from the Institutional Review Board (IRB#549-6-Aug-2024) and written informed consent from all cases' legal guardians. The research was conducted under the World Medical Association’s Code of Ethics (Helsinki Declaration) for human research.

All children under 15 years of age with an echocardiographic diagnosis of congenital heart disease (CHD) were eligible for inclusion. Participants were recruited consecutively over a 6-month period from August 2024 to January 2025 at the Pediatric Cardiology Unit of Zagazig University Hospitals. Recruitment was conducted during outpatient clinic follow-up

visits, and only patients in a clinically stable condition were enrolled. Children who were hospitalized for acute illness or decompensated cardiac or renal conditions were excluded to avoid confounding factors that could affect renal parameters.

Any case with these criteria was excluded: renal or urinary tract malformations, acute or chronic urinary tract infections, endocarditis, diabetic cases, hypertension (HTN), or sickle cell disease. Patients with acute infections. Patients who had recently used nephrotoxic drugs or agents known to increase protein excretion in urine, such as nitrofurantoin or radio-opaque contrast agents, within the past two weeks, were also excluded from the study.

Sample Size:

The sample size was determined based on previously reported mean ± standard deviation (SD) values of microalbuminuria levels. The mean ± SD of microalbuminuria among children with acyanotic CHD was reported as 111.8 ± 61.5, while in the control group, it was 67.3 ± 31.66. Using OpenEpi software for sample size calculation, with a confidence interval (CI) of 95% and a power of 80%, the required sample size was estimated to be 51 participants, distributed equally among three groups: Group 1: Children diagnosed with acyanotic CHD. Group 2: Children diagnosed with cyanotic CHD. Group 3: Healthy children serve as the control group. Each group consisted of 17 participants, ensuring statistical validity and reliability for comparative analysis.

All participants underwent a structured evaluation process, which included obtaining a detailed medical history from each participant or their guardian, conducting a comprehensive general examination, and performing a detailed cardiovascular assessment to evaluate each participant's cardiac status.

Investigations

All study participants underwent a series of laboratory and imaging investigations to assess renal and cardiac function, identify potential risk factors, evaluate systemic health, complete urine analysis, and spot urine albumin/creatinine ratio (ACR).The albumin-to-creatinine ratio (ACR) was measured to assess microalbuminuria, a key indicator of early renal impairment. Urine samples were analyzed using immunoturbidimetric assays. Normal range: <20 mg/g creatinine. Microalbuminuria: 20–300 mg/g creatinine. Macroalbuminuria: >300 mg/g creatinine. Elevated ACR values suggested renal involvement and were analyzed in relation to congenital heart disease severity.

Echocardiography

A two-dimensional transthoracic echocardiogram (2D-TTE) was performed using Doppler imaging to assess cardiac structure and function.

Statistical Analysis:

Data was analyzed using IBM SPSS software version 20.0. (Armonk, NY: IBM Corporation) Qualitative data is defined as numbers and percentages. The normality of the distribution was verified using the Kolmogorov-Smirnov test. Quantitative data were presented as range, mean, standard deviation, and median. The chi-square test was used to compare categorical variables between groups. The Mann-Whitney test evaluated two study groups with improperly distributed quantitative data. The two-sample T-test was utilized to assess whether the means of the two independent groups differed significantly. A p-value < 0.05 indicates statistical significance.

RESULTS

The demographic analysis of the study group revealed a broad age distribution, with a mean age of 53.09±44.93 months, indicating a considerable variation in the age of the participants. Regarding the sex

distribution, the study population comprised 31 male children, representing 60.78% of the total sample, while females accounted for 39.22%. The body mass index (BMI), an important indicator of overall nutritional status, had a mean value of 15.93±4.54. The mean systolic blood pressure was recorded at 104.67±12.22 mmHg. Similarly, the diastolic blood pressure values showed a mean of 64.08±13.4 mmHg. (Table 1)

Among the 34 children diagnosed with congenital heart disease, the most frequently observed defect was Fallot's tetralogy, found in 12 cases (35.29%), followed by ventricular septal defect (VSD), present in 6 cases (17.65%). Other less common defects included atrial septal defect (ASD), patent ductus arteriosus (PDA), double outlet right ventricle (DORV), and transposition of the great arteries (TGA). Pulmonary hypertension was identified in 12 out of 34 CHD patients (35.29%). Chamber enlargement was noted in 17 children (50%) within the CHD group, suggesting structural cardiac strain associated with their underlying lesions. (Table 2)

The laboratory data revealed significant differences in renal function markers between the study groups. Urinary microalbumin and albumin-to-creatinine ratio (ACR) were significantly higher in children with cyanotic CHD (2.54 ± 2.04 mg/dL and 42.11 ± 27.86 mg/g, respectively) compared to both acyanotic CHD patients (0.62 ± 0.51 mg/dL and 11.24 ± 7.64 mg/g) and healthy controls (0.61 ± 0.24 mg/dL and 8.25 ± 2.61 mg/g), with $P < 0.0001$. Additionally, urinary creatinine levels were slightly elevated in both CHD groups compared to controls ($P = 0.0349$), suggesting subtle renal involvement even in the absence of overt kidney disease (Tables 3, and 4).

In this study, significant differences were observed between the three groups in age, weight, height, systolic and diastolic blood pressures, urinary microalbumin, and ACR ($P < 0.0001$) (Table 4). Notably, the control group had a significantly higher mean age compared to the cyanotic and acyanotic CHD groups, Urinary creatinine levels were slightly higher in both acyanotic and cyanotic CHD groups compared to controls, with a statistically significant difference ($P = 0.0349$) (Table 4).

The analysis of cardiac conditions among children with congenital heart disease (acyanotic and cyanotic groups) revealed significant differences in the type of congenital heart defects, presence of pulmonary hypertension, and cardiac chamber enlargement (Table 5). Fallot's tetralogy was the most frequent lesion in the cyanotic group, while ventricular septal defect and atrial septal defect were more common in acyanotic cases. Pulmonary hypertension and chamber enlargement were significantly more prevalent in acyanotic CHD patients (Table 5)

Table 1: Demographic, anthropometric and blood pressure data distribution in all study population

Demographic Data n=(51)	
• **Age in months**	
Mean± SD	53.09±44.93
Range **(Min-Max)**	1-144
• **Sex**	
-Male	31**(60.78%)**
-Female	20**(39.22%)**
• ***Anthropometric Data n=(51)***	
-Weight	
Mean± SD	15.44±9.08
Range **(Min-Max)**	12114

Demographic Data n=(51)	
-Height	
Mean± SD	94.31±29
Range **(Min-Max)**	50-145
-BMI	
Mean± SD	15.93±4.54
Range **(Min-Max)**	9.72-36
• ***Blood Pressure Measurements Data n=(51)***	
-Systolic Blood Pressure	
Mean± SD	104.67±12.22
Range **(Min-Max)**	85-125
-Diastolic Blood Pressure	
Mean± SD	64.08±13.4
Range **(Min-Max)**	40-80

Table 2: Cardiac Conditions Data distribution in all study population

Cardiac Conditions Data n=(51)	
Congenital Heart Defects	
Normal	17**(33.33%)**
A.S.D	3**(5.88%)**
Common A-V canal + V.S.D + mild LPA narrowing	1**(1.96%)**
Fallot tetralogy	12**(23.53%)**
D. TGA	1**(1.96%)**
DORV + mild P.S Fallot type	1**(1.96%)**
DORV + TGA + P.S	1**(1.96%)**
mild MVP Tiny PDA	1**(1.96%)**
mild P.S - mild A.S - mild R - P.A stasis	1**(1.96%)**
P.D.A	2**(3.92%)**
PFO + V.S.D	3**(5.88%)**
TGA + DORV + P.S	1**(1.96%)**
tricuspid atresia hypoplastic RV	1**(1.96%)**
V.S.D	6**(11.76%)**
Pulmonary Hypertension	
No Pulmonary Hypertension	17**(33.33%)**
Pulmonary Hypertension	34**(66.67%)**
Chamber enlargement	
Negative Chamber enlargement	34**(66.67%)**
Positive Chamber enlargement	17**(33.33%)**

ASD: Atrial Septal Defect, AV: Atrioventricular, CHD: Congenital Heart Disease, DORV: Double Outlet Right Ventricle, DTGA: Dextro-Transposition of the Great Arteries, LPA: Left Pulmonary Artery, MVP: Mitral Valve Prolapse, PA: Pulmonary Artery, PDA: Patent Ductus Arteriosus, PFO: Patent Foramen Oval, PS: Pulmonary Stenosis, RV: Right Ventricle, TGA: Transposition of the Great Arteries, TOF (Fallot tetralogy): Tetralogy of Fallot, VSD: Ventricular Septal Defect, R: Regurgitation, AS: Aortic Stenosis.

Table 3: Laboratory Data distribution in all study populations

Laboratory Data n=(51)	
Urinary Creatinine (39-259)	
Mean± SD	58.78±29.29
Range **(Min-Max)**	25.5-166.9
Urinary Microalbumin	
Mean± SD	1.26±1.51

Laboratory Data n=(51)	
Range **(Min-Max)**	0.2-7.5
Albumin-to-Creatinine Ratio (up to 20)	
Mean± SD	20.53±22.54
Range **(Min-Max)**	3.47-103.2

Table 4: Relations between Demographic, anthropometric, blood pressure, and laboratory data and different groups.

	Control N=17	*A cyanotic CHD N=17*	*Cyanotic CHD N=17*	*P value*
• **Age**	100.24±29.68	45.84±33.11	13.2±14.9	<0.0001
• **Sex**				
Male	10**(19.61%)**	8**(15.69%)**	13**(25.49%)**	0.2095
Female	7**(13.73%)**	9**(17.65%)**	4**(7.84%)**	
• **Weight**	25.18±5.57	14.21±5.98	6.94±3.43	<0.0001
• **Height**	122±12.58	93.41±25.46	67.53±15.65	<0.0001
• **BMI**	16.69±1.1	16.78±7.42	14.31±2.01	0.1999
• **Systolic Blood Pressure**	115.06±6.95	103.82±10.83	95.12±9.4	<0.0001
• **Diastolic Blood Pressure**	75.35±3.82	63.65±13.55	53.24±10.15	<0.0001
• **Urinary Creatinine**	58.78±29.29	64.79±40.83	67.5±25.28	0.0349
• **Urinary Microalbumin**	0.61±0.24	0.62±0.51	2.54±2.04	<0.0001
• **Albumin-to-Creatinine Ratio**	8.25±2.61	11.24±7.64	42.11±27.86	<0.0001

Statistical test used: One Way ANOVA, *p-value≤0.05 considered significant*

Table 5: Relations between Cardiac Conditions and different groups.

	A cyanotic CHD N=17	*Cyanotic CHD N=17*	*P value*
• **Congenital Heart Defects**			
Normal	0**(0%)**	0**(0%)**	<0.0001
A.S.D	3**(5.88%)**	0**(0%)**	
Common A-V canal + V.S.D + mild LPA narrowing	1**(1.96%)**	0**(0%)**	
Fallot tetralogy	0**(0%)**	12**(23.53%)**	
D. TGA	0**(0%)**	1**(1.96%)**	
DORV + mild P.S Fallot type	0**(0%)**	1**(1.96%)**	
DORV + TGA + P.S	0**(0%)**	1**(1.96%)**	
TGA + DORV + P.S	0**(0%)**	1**(1.96%)**	
tricuspid atresia hypoplastic RV	0**(0%)**	1**(1.96%)**	
mild MVP Tiny PDA	1**(1.96%)**	0**(0%)**	
mild P.S - mild A.S - mild R - P.A stasis	1**(1.96%)**	0**(0%)**	
P.D.A	2**(3.92%)**	0**(0%)**	
PFO + V.S.D	3**(5.88%)**	0**(0%)**	
V.S.D	6**(11.76%)**	0**(0%)**	
• **Pulmonary Hypertension**			
No Pulmonary Hypertension	11**(21.57%)**	11**(21.57%)**	0.0198
Pulmonary Hypertension	6**(11.76%)**	6**(11.76%)**	
• **Chamber enlargement**			
Negative Chamber enlargement	0**(0%)**	17**(33.33%)**	<0.0001
Positive Chamber enlargement	17**(33.33%)**	0**(0%)**	

Statistical test used: One Way ANOVA, *p-value≤0.05 considered statistically significant.* ASD: Atrial Septal Defect, AV: Atrioventricular, CHD: Congenital Heart Disease, DORV: Double Outlet Right Ventricle, DTGA: Dextro-Transposition of the Great Arteries, LPA: Left Pulmonary Artery, MVP: Mitral Valve Prolapse, PA: Pulmonary Artery, PDA: Patent Ductus Arteriosus, PFO: Patent Foramen Oval, PS: Pulmonary Stenosis, RV: Right Ventricle, TGA: Transposition of the Great Arteries, TOF (Fallot tetralogy): Tetralogy of Fallot, VSD: Ventricular Septal Defect, R: Regurgitation, AS: Aortic Stenosis, ANOVA: Analysis of Variance.

DISCUSSION

Advances in medical and surgical care have considerably enhanced the survival of children with CHD; however, these patients remain at risk for multi-organ complications, including renal dysfunction. Renal impairment in CHD patients is increasingly recognized as a critical concern, particularly in cyanotic CHD cases, where chronic hypoxia and hemodynamic alterations may contribute to glomerular damage and proteinuria [7].

This study aimed to investigate microalbuminuria as an early sign of renal impairment in children with congenital heart disease by assessing both urinary microalbumin levels and albumin-to-creatinine ratios (ACR), and comparing these parameters among cyanotic CHD patients, acyanotic CHD patients, and healthy controls. By investigating the extent of microalbuminuria in these groups, we seek to better understand CHD's impact on renal function and highlight the need for routine renal monitoring in affected children. Identifying early markers of renal dysfunction in CHD patients may facilitate timely interventions and improve long-term outcomes in this vulnerable population.

Our study findings regarding age differences in CHD subtypes, where cyanotic CHD patients had a lower mean age at diagnosis compared to acyanotic CHD patients and controls, align with existing literature while also presenting points of divergence.

Talolena et al. [6] reported remarkable variations in mean age (p=0.004) between patients with double outlet right ventricle (DORV) and tetralogy of Fallot (TOF), which is consistent with our findings on cyanotic CHD being diagnosed at an earlier stage.

Overall, our study findings are supported mainly by existing research, which indicates that cyanotic CHD cases are diagnosed earlier due to more severe and immediately recognizable symptoms.

Our study found no remarkable variation in sex distribution between the control and the acyanotic CHD groups, which aligns with several existing studies, while some literature presents contrasting results.

Similarly, Chang et al. [8] investigated demographic differences in CHD subtypes and found no remarkable variation in sex distribution between acyanotic CHD and control groups. Their findings suggest that acyanotic CHD occurs at approximately the same rate in both males and females, which aligns with our study's results.

Overall, while our study is supported by research indicating no significant sex-based disparity in acyanotic CHD, conflicting evidence highlights the need for further investigations into potential sex-related variations within specific CHD subtypes.

Our study's finding of a highly significant difference in systolic blood pressure (SBP) among the control, acyanotic CHD, and cyanotic CHD groups ($P < 0.0001$) is well-aligned with existing literature.

Overall, our study contributes to the growing body of evidence indicating that cyanotic CHD patients exhibit significantly lower SBP due to the hemodynamic consequences of chronic hypoxia. While variations exist depending on the CHD subtype and associated conditions such as pulmonary hypertension, the overarching trend remains consistent with prior research, underscoring the importance of early intervention to mitigate the cardiovascular impact of hypoxia in cyanotic CHD patients.

Our study's finding that DBP was substantially reduced in the acyanotic CHD group compared to the control group ($P < 0.0001$) suggests potential implications for vascular tone, systemic circulation, and renal function. This finding is supported by several studies examining the impact of CHD on hemodynamics and perfusion dynamics.

Similarly, Romans et al. discussed the physiological implications of congenital heart defects, noting that cyanotic CHD patients, due to chronic hypoxemia, may experience systemic vasodilation and lower DBP. They also observed that acyanotic CHD patients with increased pulmonary blood flow often exhibit reduced diastolic pressure, which can lead to systemic congestion and an increased cardiac workload. These findings support our study's conclusion that reduced vascular tone in acyanotic CHD cases may contribute to lower DBP levels [9].

Our study contributes to the growing body of evidence indicating that reduced DBP in acyanotic CHD patients may have significant physiological consequences, particularly concerning systemic circulation and renal perfusion.

Our study's finding of a highly remarkable variation ($P < 0.0001$) in the distribution of CHD among the acyanotic CHD, and cyanotic CHD groups aligns well with established research in the field.

A study by Madsen et al. [10] reported a clear distinction between cyanotic and cyanotic CHD groups, with cyanotic CHD being more prevalent. Their study supports the classification approach used in our study, where cyanotic and cyanotic CHD cases were analyzed separately to assess structural differences.

A comparative study by Dey et al. [11] in a tertiary care hospital confirmed significant differences in CHD distribution, noting that acyanotic CHD is generally more prevalent than cyanotic CHD in pediatric populations. Additionally, their study highlighted anthropometric variations among CHD subtypes, suggesting that cyanotic CHD cases tend to be associated with more pronounced growth impairments compared to acyanotic CHD patients. This adds a new dimension to the discussion, as growth disparities may contribute to systemic differences beyond structural anomalies.

Overall, our study contributes to the broader understanding of CHD distribution by confirming established patterns in the prevalence of cyanotic and cyanotic CHD. Our findings align with prior research.

Our study found that 11.76% of acyanotic CHD patients and 11.76% of cyanotic CHD patients had pulmonary hypertension (PH), based on echocardiographic assessment. This relatively equal distribution between the two CHD subgroups ($P = 0.0198$) is consistent with previous literature reporting PH as a common complication in various types of CHD. It is important to note that healthy controls were preselected to have normal pulmonary pressures, and thus were not included in this analysis.

A study by Pascall and Tulloh [12] reviewed the association between pulmonary hypertension and CHD, highlighting that pulmonary hypertension (PH) is a relatively common complication of CHD, with a reported prevalence of 5–10% in adults. This aligns with our study's finding of 11.76% prevalence in pediatric CHD cases, suggesting that PH can develop early in life and may progress over time.

While our study provides valuable insights into PH prevalence in CHD cases, further investigation is needed to assess the long-term implications of PH development in pediatric CHD populations, particularly regarding disease progression, response to treatment, and potential genetic predispositions.

Our study's finding that a notable association ($P < 0.0001$) was observed between cardiac chamber dilation and cardiomegaly among the three groups aligns with existing research on CHD and its structural effects.

Similarly, Kannan [13] highlighted that cardiac chamber dilation is a hallmark of acyanotic CHD, particularly in conditions such as atrial septal defects (ASD) and PDA, where excessive pulmonary blood flow results in volume overload, leading to dilation of the left-sided cardiac chambers. This reinforces our study's findings that left atrial and left ventricular dilation were predominant in acyanotic CHD patients.

Our study contributes to the growing body of evidence highlighting the distinct structural changes observed in CHD patients, particularly regarding chamber dilation and its correlation with cardiomegaly. The findings emphasize the importance of early detection and monitoring of chamber size changes in acyanotic CHD patients, as progressive dilation can have significant long-term implications for cardiac function and hemodynamic stability.

Our study contributes to the growing body of evidence highlighting the distinct structural changes observed in children with CHD. Notably, all patients in the acyanotic CHD group (100%) exhibited chamber enlargement, whereas none of the cyanotic CHD patients or controls did. This significant association ($P < 0.0001$) suggests that chamber dilation is particularly prevalent in acyanotic CHD, likely due to volume overload in lesions such as atrial and ventricular septal defects. These findings underscore the importance of early detection and echocardiographic monitoring of chamber size in acyanotic CHD patients, as progressive dilation may compromise cardiac function and contribute to long-term hemodynamic instability.

Furthermore, Mohamed and Rabeea [14] assessed renal function in infants and children with CHD and found that albumin/creatinine ratios were higher in CHD patients compared to controls, suggesting early renal dysfunction in CHD patients even in the absence of overt kidney disease. Their study emphasized the need for longitudinal renal monitoring in CHD patients, which is particularly relevant to our study's conclusion that even small increases in urinary creatinine may indicate early renal dysfunction. This highlights the importance of routine renal function assessment in CHD populations to identify and manage potential kidney complications early.

Overall, our study contributes to the growing evidence that CHD, particularly in cyanotic cases, is associated with subtle but significant changes in renal function.

Our study's finding that urinary microalbumin levels were remarkably elevated ($P < 0.0001$) in the cyanotic CHD group (2.54 ± 2.04 mg/dL) compared to the acyanotic CHD (0.62 ± 0.51 mg/dL) and control (0.61 ± 0.24 mg/dL) groups aligns with existing research on renal dysfunction in CHD. The markedly elevated microalbumin levels in cyanotic CHD patients suggest a strong association between chronic hypoxia and early renal impairment.

Agras et al. [15] investigated renal function in children with CHD, measuring urinary microalbumin levels as a marker of glomerular dysfunction. Their results indicated that cyanotic CHD cases had substantially increased urinary microalbumin values than acyanotic CHD cases and controls ($P = 0.022$), reinforcing our study's finding that cyanotic CHD is associated with increased renal stress and glomerular injury. These findings highlight the potential role of chronic hypoxia in compromising renal function at an early stage.

Similarly, Amornchaicharoensuk and Werawatganon [16] found that both glomerular (microalbuminuria) and tubular (fractional excretion of magnesium) dysfunction were significantly more pronounced in cyanotic CHD patients compared to acyanotic CHD patients and controls. Their study concluded that hypoxia-induced endothelial damage in cyanotic CHD patients contributes to increased glomerular permeability, leading to higher microalbuminuria. This aligns with our study's observation that cyanotic CHD patients exhibited the highest urinary microalbumin levels, reflecting greater renal involvement and the potential for progressive renal dysfunction.

Our study's findings indicate that the cyanotic CHD group had a dramatically elevated mean ACR (42.11 ± 27.86) compared to the control (8.25 ± 2.61) and cyanotic CHD groups (11.24 ± 7.64) ($P < 0.0001$), align with established research on renal complications in CHD. The significantly higher ACR values in cyanotic CHD patients suggest a strong association between chronic hypoxia, glomerular stress, and early renal impairment.

A study by Opotowsky et al. [7] analyzed GFR estimation in adults with CHD and found that cyanotic CHD patients exhibited higher markers of renal dysfunction, including increased cystatin C levels, compared to acyanotic CHD patients. Although their study did not specifically report ACR values, their findings suggest that cyanotic CHD patients experience more significant renal impairment, supporting our study's observation of significantly elevated ACR in this group.

Hamed et al. [17] further supported these findings, noting that the significantly elevated ACR in cyanotic CHD patients compared to acyanotic and control groups suggests more significant glomerular stress and a higher risk of early renal dysfunction in cyanotic CHD patients. Their study emphasized that cyanotic CHD contributes to renal stress through chronic hypoxia, systemic vasodilation, and altered renal hemodynamics, all of which may exacerbate proteinuria and renal dysfunction over time.

One of the key limitations of this study is the lack of strict age- and sex-matching between the CHD cases and the control group. The control group had a significantly higher mean age, which may have introduced confounding, particularly in age-sensitive parameters such as blood pressure, urinary creatinine, and albumin-to-creatinine ratio. Additionally, while patients with overt renal impairment were excluded based on clinical history and standard criteria, a statistically significant increase in urinary creatinine was observed in CHD patients. This finding, although subtle, may reflect early or subclinical renal changes. However, interpretation of urinary creatinine levels in pediatric populations is complex, as it can vary with age, muscle mass, and hydration status. Future studies are recommended to include more precise age-matching and consider using serum creatinine, cystatin C, or estimated glomerular filtration rate (eGFR) to enhance renal function assessment.

Conclusions

The findings of this study highlight microalbuminuria as a valuable early marker of renal impairment in children with CHD, particularly in cyanotic CHD cases. The significant increase in urinary microalbumin and ACR in cyanotic CHD patients underscores the impact of chronic hypoxia and hemodynamic stress on renal function. Further research with larger cohorts and longitudinal follow-up is recommended to explore the progression of renal impairment in CHD patients and evaluate potential protective strategies.

Conflict of interest:

The authors declare no conflict of interest.

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