Original Article

Cardiac Function in Pediatric Nephrotic Syndrome: Tissue Doppler Echocardiography

Noor Mohammad Noori[1], Elham Zarifi[2], Alireza Teimouri[1*]

[1] Children and Adolescents Health Research Center, Research Institute of Cellular and Molecular Science in Infectious Diseases, Zahedan University of Medical Sciences, Zahedan, Iran.
[2] Ali Asghar Hospital, Zahedan University of Medical Sciences, Zahedan, Iran.

Citation: Noori NM, Zarifi E, Teimouri A. Cardiac Function in Pediatric Nephrotic Syndrome: Tissue Doppler Echocardiography. Res Heart Yield Transl Med 2025; 20(2): 116-125.

https://doi.org/10.18502/jthc.v20i2.19707

Highlights

- Children with idiopathic nephrotic syndrome show early heart dysfunction before symptoms appear.
- Tissue Doppler Echocardiography revealed reduced myocardial velocities, elevated MPI, and altered relaxation times.
- These cardiac changes strongly correlate with kidney function.

Article info:

Received: 30 Sep. 2024
Revised: 05 Feb. 2025
Accepted: 03 Mar. 2025

* **Corresponding Author:**
Alireza Teimouri
Children and Adolescents Health Research Center, Research Institute of Cellular and Molecular Sciences in Infectious Diseases, Ali Ebn-Abi Taleb Hospital, School of Medicine, Zahedan University of Medical Sciences, Khalij Fars BLVD, Zahedan, Iran.
E-mail: Alirezateimouri260@gmail.com.
Tel: +989370242695

ABSTRACT

Background: Nephrotic syndrome (NS) is a common pediatric glomerular disorder traditionally considered renal-limited. Nonetheless, growing evidence suggests systemic implications, including subclinical cardiovascular involvement. This study aimed to evaluate early myocardial dysfunction in children with idiopathic NS using Doppler tissue echocardiography (DTE).

Methods: In a case-control study, 87 children with idiopathic NS and 87 age- and sex-matched healthy controls were enrolled between 2021 and 2023 at Ali Asghar Pediatric Hospital in Zahedan, Iran. All participants underwent comprehensive DTE from apical four-chamber views to assess systolic and diastolic function. Key parameters included S′, E′, and A′ velocities; isovolumetric contraction time (ICT); isovolumetric relaxation time (IRT); ejection time (ET); myocardial performance index (MPI); and E/E′ and A/A′ ratios. Laboratory data and treatment response were also analyzed. Data were analyzed using SPSS version 26, with a significance level set at 0.05.

Results: Children with NS demonstrated significantly reduced S′, E′, and A′ velocities; prolonged left ventricular IRT; shortened ICT and ET; and elevated MPI values, indicating early biventricular dysfunction. The right ventricular E/E′ ratio was significantly lower in treatment responders, suggesting improved diastolic function. MPI and timing parameters showed strong correlations with renal and metabolic markers, including blood urea nitrogen, serum albumin, and lipid levels.

Conclusions: DTE-derived MPI serves as a valuable noninvasive marker for the early detection of subclinical cardiac dysfunction in pediatric NS. Incorporating MPI into routine cardiac assessments may improve risk stratification and guide therapeutic monitoring in this population.

Keywords: Nephrotic Syndrome; Doppler Tissue Echocardiography; Children

Introduction

Nephrotic syndrome (NS) is one of the most common kidney diseases affecting children, typically occurring between the ages of 2 and 5 years.

Its incidence ranges from about 2 to 7 cases per 100,000 children each year.[1] While most children with NS respond well to corticosteroid treatment initially, many experiences frequent relapses or develop forms of the disease that are either steroid-dependent or steroid-resistant. These challenging cases often lead to complications such as infections, blood clots, and chronic kidney disease.[1] The cause of NS is complex, with growing evidence pointing to immune system dysfunction. Immune-related processes, including complement activation, increased blood vessel permeability, and inflammation in kidney tissues, are believed to damage the glomeruli, resulting in the characteristic protein loss in urine. The effectiveness of immunosuppressive drugs further supports the view that the immune system plays a key role in the disease.[2] Although NS was once thought to affect only the kidneys, it is now clear that it impacts multiple organs, including the heart.[3]

Cardiac complications in NS arise from a combination of factors, including chronic fluid buildup, low albumin levels, systemic inflammation, oxidative stress, abnormal lipid levels, anemia, and toxins that accumulate as a result of kidney dysfunction. These changes can lead to remodeling and impaired heart muscle function, often before any obvious symptoms or abnormalities appear on routine heart imaging tests, such as ejection fraction measurements. [4] Recent advances in cardiac imaging, particularly Doppler tissue echocardiography (DTE), have made it possible to detect subtle heart muscle dysfunction early in children with NS. DTE measures heart muscle motion during contraction and relaxation, providing crucial information through velocities such as S' (systolic), E' (early diastolic), and A' (late diastolic). One key measure from DTE is the myocardial performance index (MPI), which combines both systolic and diastolic function into a single marker of overall heart performance. Studies have found that children with NS often have elevated MPI values even when conventional heart function tests appear normal, underscoring the sensitivity of DTE in detecting early heart impairment.[5–7]

Encouragingly, research shows that successful treatment and remission of NS can improve these DTE measures, including lowering the MPI and normalizing S' and E', suggesting that cardiac changes can be at least partially reversed.[6,7] This evidence underscores the importance of incorporating advanced echocardiographic techniques, such as DTE, into the routine monitoring of children with NS.

The current study aimed to explore how NS affects the heart, focusing on the use of DTE and MPI as sensitive tools for early detection, ongoing monitoring, and assessment of treatment response in affected children.

Methods

Study design and setting

This case-control study was conducted between 2023 and 2024 at the Pediatric Nephrology and Cardiology Clinics of Ali Asghar Pediatric Hospital, affiliated with Zahedan University of Medical Sciences. The study aimed to compare cardiac function in children with idiopathic NS against age- and sex-matched healthy controls with the aid of DTE.

Participants, group allocation, and diagnostic criteria

Children <18 years of age with confirmed idiopathic NS and no congenital renal anomalies were enrolled after informed parental consent was obtained. The diagnosis of NS was based on standard clinical and biochemical criteria, including proteinuria >40 mg/m²/hour, serum albumin <3 g/dL, total serum protein <5.5 g/dL, serum cholesterol >250 mg/dL, and the presence of clinical edema. Only cases of idiopathic NS were included, while secondary causes such as systemic diseases, infections, or structural kidney abnormalities were excluded.

Children with NS were assessed during the remission phase, defined as proteinuria reduced to trace or negative levels on dipstick for three

consecutive days (or <4 mg/m²/hour). Based on their response to corticosteroid therapy during the first month, patients were categorized as either steroid-sensitive or steroid-resistant. Exclusion criteria for both NS and control groups included severe cardiac dysfunction (left ventricular ejection fraction <50% or moderate/severe valvular regurgitation), hepatic or renal disease, secondary NS, and incomplete clinical or echocardiographic data. The control group consisted of healthy children matched for age and sex, presenting for routine checkups with no history of NS or chronic illness. All participants underwent standardized echocardiographic evaluation.

Data collection

Laboratory parameters

Venous blood samples (5 mL) were obtained from all participants. Following clotting and centrifugation, serum was isolated for analysis. Laboratory assessments included measurements of serum albumin, total cholesterol, urea, and creatinine, performed using the Abbott Architect C-8000 system (Abbott Laboratories, USA). These analyses employed advanced spectrophotometric techniques to ensure accuracy and reproducibility.

Echocardiography measurements

The major proceedings for patients included a review of their medical history, a physical examination, a chest X-ray, and an echocardiogram, all performed by a single pediatric cardiologist. Echocardiography was conducted on participants by the same pediatric cardiologist using the MyLab 60 with a 3–8 transducer (made in Italy). Measurements were repeated for three cycles, and the average was considered to achieve high precision in the echocardiographic findings. Echocardiography was performed on participants during normal respiration.

DTE was performed from the apical four-chamber view, and a 3-mm pulsed Doppler sample volume was placed at the level of the lateral mitral annulus. Myocardial velocity profiles of the lateral tricuspid annulus and lateral mitral annulus were obtained by placing the sample volume at the junction of the tricuspid annulus and the right ventricular free wall and at the junction of the mitral annulus and the left ventricular posterior wall, respectively. With this modality, the recorded values were the early (E′) and late (A′) diastolic mitral and tricuspid annular velocities, and the E′/A′ ratio. Left and right S′ represented the systolic myocardial velocity above the baseline in the mitral and tricuspid valves. Left and right E′ indicated the early diastolic myocardial relaxation velocity below the baseline in the mitral and tricuspid valves. Left and right A′ denoted the myocardial velocity associated with atrial contraction in the mitral and tricuspid valves. Additional time intervals, such as isovolumetric relaxation time (IRT), isovolumetric contraction time (ICT), and ejection time (ET), were recorded to provide detailed insights into cardiac timing. MPI, which integrates both systolic and diastolic function, was calculated using the formula (ICT + IRT) / ET. Right and left ventricular filling pressures were estimated using the E/E′ ratio, while the A/A′ ratio assessed the atrial contribution to ventricular filling. All echocardiographic assessments were performed by the same experienced pediatric cardiologist to ensure reliability and reduce variability.

Ethical considerations

The study protocol was approved by the Ethics Committee of Zahedan University of Medical Sciences and the Children and Adolescent Health Research Center (approval code: IR.ZAUMS.REC.1402.007). Written informed consent was obtained from all participants' parents or legal guardians.

Statistical Analysis

Statistical analyses were performed using SPSS version 26 (IBM Corp., Armonk, NY). Continuous variables are presented as mean ± standard deviation (SD), while categorical variables are reported as frequencies and percentages. Normality was assessed using the Shapiro-Wilk test. Group comparisons between NS patients and controls were conducted using independent samples t-tests for normally distributed variables and the Mann-Whitney U test for non-normally distributed data. Correlation analyses examined relationships between echocardiographic parameters and laboratory findings. A P-value <0.05 was considered statistically significant.

RHYTHM
Research in Heart Yield and Translational Medicine

Results

The present study examined differences in clinical, laboratory, and cardiac function parameters between children with NS and healthy controls, as well as between treatment responders and non-responders. Age and sex were well matched between the case and control groups, with no significant difference in age (P=0.208) and only a borderline difference in sex distribution (Fisher's exact P=0.05) (Table 1). After the application of normality tests to the quantitative variables, the left E/E′ ratio was found to follow a normal distribution across all participants. Within the NS groups, ICT, ET, MPI, and E/E′ ratio also demonstrated normal distribution patterns.

(Table 2) presents significant differences in DTE parameters between the NS and control groups. Children with NS demonstrated higher systolic blood pressure, lower E′, A′, and S′ velocities in the right ventricle, along with prolonged IRT, shortened ICT and ET in the left ventricle, and elevated MPI bilaterally. The NS group also showed significantly higher E/E′ and A/A′ ratios (all Ps<0.001 except left ventricular E′ [P=0.001]), suggesting impaired diastolic function.

As depicted in (Table 3), comparisons between treatment responders and non-responders revealed significantly lower serum creatinine (P=0.002) and sodium levels (P=0.027) in responders. Urine protein-to-creatinine ratios were also lower, approaching borderline significance (P=0.050). Among echocardiographic parameters, only the right ventricular E/E′ ratio showed a significant difference (P=0.031), indicating improved diastolic function in responders.

(Table 4) demonstrates significant correlations between various DTE parameters and MPI. IRT exhibited the strongest positive correlations with MPI bilaterally (P<0.001), while ET showed negative correlations (P=0.001). Both A′ and S′ velocities were significantly associated with MPI (P-values ranging from 0.017 to 0.025). Among noncardiac parameters, only blood urea nitrogen and A/A′ ratios correlated significantly with MPI (P=0.044 and P=0.006/0.050, respectively), suggesting an association between renal and cardiac function in children with NS.

Table 1. Age and sex distribution in groups of participants

Variables	Groups	N	Mean	SD	Test Value	P
Age (year)	NS	87	9.22	3.681	1.264	0.208
	Control	87	9.86	3.001		
Sex	Girls	NS	n	36	3.875	0.05
			%	41.40%		
		Control	n	49		
			%	56.30%		
	Boys	NS	n	51		
			%	58.60%		
		Control	n	38		
			%	43.70%		

NS: nephrotic syndrome

Table 2. Comparison of Doppler tissue imaging parameters between children with nephrotic syndrome and healthy controls

Variables	Groups	Mean	SD	Mean Rank	Test Value	P
Systolic Blood Pressure (mmHg)	Case	111.13	13.466	102.97	2439	<0.001
	Control	102.59	11.43	72.03		
Diastolic Blood Pressure (mmHg)	Case	69.79	12.92	94.32	3191	0.07
	Control	66.38	9.17	80.68		
E' Right (cm/s)	Case	11.47	1.82	61.37	1511.5	<0.001
	Control	14.3	2.97	113.63		
A' Right (cm/s)	Case	6.23	1.72	59.25	1327	<0.001
	Control	8.67	1.99	115.75		
A' Left (cm/s)	Case	6.9	1.39	69.25	2196.5	<0.001
	Control	8.06	1.48	105.75		
E' Left (cm/s)	Case	13.84	2.63	75.1	2706	0.001
	Control	15.19	2.48	99.9		

S' Left (cm/s)	Case	0.08	0.07	68.98	2173	<0.001
	Control	0.09	0.02	106.02		
IRT Left (ms)	Case	89.66	20.91	102.88	2446.5	<0.001
	Control	78.87	19.18	72.12		
ICT Left (ms)	Case	70.26	11.34	63.43	1690	<0.001
	Control	88.19	18.8	111.57		
ET Left (ms)	Case	226.37	23.63	52.07	702	<0.001
	Control	337.03	84.01	122.93		
MPI Left	Case	0.71	0.12	118.08	1124	<0.001
	Control	0.52	0.14	56.92		
S' Right (cm/s)	Case	0.08	0.01	75.01	2698	0.001
	Control	0.09	0.02	99.99		
IRT Right (ms)	Case	90.41	19.78	74.2	2627.5	<0.001
	Control	99.43	20.1	100.8		
ICT Right (ms)	Case	64.27	10.11	66.93	1995	<0.001
	Control	74.33	12.55	108.07		
ET Right (ms)	Case	223.34	27.16	55.22	976	<0.001
	Control	282.85	61.58	119.78		
MPI Right	Case	0.7	0.09	101.57	2560	<0.001
	Control	0.63	0.12	73.43		
E/E' Left	Case	7.72	1.64		4.775	<0.001
	Control	6.69	1.15			
E/E' Right	Case	6.93	1.29	124	609	<0.001
	Control	4.87	0.94	51		
A/A' Right	Case	8.04	2.36	120.21	939	<0.001
	Control	5.49	0.87	54.79		
A/A' Left	Case	8.38	2.34	112.53	1607	<0.001
	Control	6.5	1.4	62.47		

IRT: isovolumetric relaxation time, ICT: isovolumetric contraction time, ET: ejection time, MPI: myocardial performance index

Table 3. Comparison of laboratory and echocardiographic parameters between responders and non-responders to treatment in children with nephrotic syndrome

Variables	Response to Treatment	N	Mean	SD	Mean Rank	Test Value	P
White blood cell count (×10³/µL)	Yes	54	11974.07	10439.04	46.49	756.50	0.239
	No	33	10196.97	5316.39	39.92		
Hemoglobin (g/dL)	Yes	54	12.08	1.37	42.35	802.00	0.434
	No	33	12.17	1.96	46.70		
Platelet count (×10³/µL)	Yes	54	407.65	138.19	47.20	718.00	0.130
	No	33	367.97	135.37	38.76		
Mean platelet volume (fl)	Yes	54	7.49	1.03	41.43	752.00	0.223
	No	33	9.70	10.39	48.21		
Blood urea nitrogen (mg/dL)	Yes	54	15.92	9.55	40.42	697.50	0.090
	No	33	19.18	11.44	49.86		
Creatinine (in serum) (mg/dL)	Yes	54	0.61	0.20	37.51	540.50	0.002
	No	33	1.05	1.34	54.62		
Sodium (mEq/L)	Yes	54	137.02	4.21	39.34	639.50	0.027
	No	33	138.52	5.82	51.62		
Potassium (mEq/L)	Yes	54	4.29	0.47	43.03	838.50	0.638
	No	33	4.33	0.39	45.59		
Calcium (mg/dL)	Yes	54	8.02	0.77	43.66	872.50	0.869
	No	33	8.05	0.70	44.56		
Triglycerides (mg/dL)	Yes	54	229.70	112.53	43.33	855.00	0.753
	No	33	245.70	129.92	45.09		
Total cholesterol (mg/dL)	Yes	54	333.67	114.85	46.01	782.50	0.343
	No	33	308.52	89.50	40.71		
Albumin (g/dL)	Yes	54	2.19	0.49	44.74	851.00	0.726
	NO	33	2.20	0.65	42.79		
Protein in urine (random sample) (mg/dL)	Yes	54	429.93	349.73	39.84	666.50	0.050
	No	33	603.61	486.95	50.80		
Creatinine in urine (mg/dL)	Yes	54	115.44	102.84	39.85	667.00	0.050
	No	33	143.00	92.22	50.79		
Protein-to-creatinine ratio	Yes	54	4.64	3.88	42.53	811.50	0.487
	No	33	5.82	5.08	46.41		
E' Right (cm/s)	Yes	54	11.69	1.97	46.50	756.00	0.231
	No	33	11.12	1.49	39.91		
	Yes	54	6.37	1.76	46.32	765.50	0.263

A' Right (cm/s)	No	33	6.00	1.64	40.20		
A' Left (cm/s)	Yes	54	6.98	1.35	45.90	788.50	0.359
	NO	33	6.76	1.46	40.89		
E' Left (cm/s)	Yes	54	14.22	2.77	47.20	718.00	0.126
	No	33	13.21	2.29	38.76		
S' Left (cm/s)	Yes	54	0.09	0.09	45.70	799.00	0.408
	No	33	0.08	0.01	41.21		
IRT Left (ms)	Yes	54	91.31	19.77	45.39	816.00	0.511
	NO	33	86.97	22.71	41.73		
ICT Left (ms)	Yes	54	70.11	11.80		-0.15	0.881
	No	33	70.49	10.73			
ET Left (ms)	Yes	54	227.12	22.69		0.37	0.709
	No	33	225.15	25.41			
MPI Left	Yes	54	0.72	0.12		0.47	0.638
	NO	33	0.70	0.12			
S' Right (cm/s)	Yes	54	0.08	0.01	45.74	797.00	0.398
	No	33	0.08	0.01	41.15		
IRT Right (ms)	Yes	54	91.61	19.36	46.32	765.50	0.272
	No	33	88.45	20.59	40.20		
ICT Right (ms)	Yes	54	64.47	10.42		0.23	0.818
	No	33	63.95	9.75			
ET Right (ms)	Yes	54	223.01	29.94		-0.14	0.886
	No	33	223.88	22.32			
MPI Right	Yes	54	0.71	0.10		1.20	0.232
	No	33	0.68	0.08			
E/E' Left	Yes	54	7.69	1.58		-0.22	0.830
	No	33	7.76	1.77			
E/E' Right	Yes	54	6.65	1.06	39.43	644.00	0.031
	No	33	7.40	1.50	51.48		
A/A' Right	Yes	54	8.08	2.53	43.81	880.50	0.927
	No	33	7.98	2.08	44.32		
A/A' Left	Yes	54	8.28	2.17	43.20	848.00	0.707
	No	33	8.55	2.64	45.30		

IRT: isovolumetric relaxation time, ICT: isovolumetric contraction time, ET: ejection time, MPI: myocardial performance index

Table 4. Correlations between Doppler tissue echocardiographic parameters, hematological, urinary markers, and left and right MPI in children with nephrotic syndrome

Doppler Tissue Echocardiographic Parameters	Statistics	Left MPI	Right MPI	Blood and Urine Indices	Statistics	Left MPI	Right MPI
E' Right (cm/s)	.p.c	0.074	-0.079	White blood cell count (×10³/µL)	.p.c	0.104	-0.001
	P-value	0.496	0.465		P-value	0.340	0.991
A' Right (cm/s)	.p.c	-0.133	-0.240	Hemoglobin (g/dL)	.p.c	0.101	0.143
	P-value	0.220	0.025		P-value	0.352	0.187
A' Left (cm/s)	.p.c	-0.013	-0.256	Platelet count (×10³/µL)	.p.c	-0.067	0.041
	P-value	0.908	0.017		P-value	0.536	0.704
E' Left (cm/s)	.p.c	-0.025	-0.167	Mean platelet volume (fl)	.p.c	-0.021	-0.056
	P-value	0.815	0.123		P-value	0.844	0.609
S' Left (cm/s)	.p.c	-0.088	0.091	Blood urea nitrogen (mg/dL)	.p.c	-0.217	-0.150
	P-value	0.418	0.403		P-value	0.044	0.166
IRT Left (ms)	.p.c	0.745	0.284	Creatinine (mg/dL)	.p.c	0.008	-0.099
	P-value	0.000	0.008		P-value	0.939	0.361
ICT Left (ms)	.p.c	0.451	0.270	Sodium (mEq/L)	.p.c	0.027	-0.109
	P-value	0.000	0.011		P-value	0.802	0.317
ET Left (ms)	.p.c	-0.342	-0.167	Potassium (mEq/L)	.p.c	0.084	-0.089
	P-value	0.001	0.123		P-value	0.441	0.410
S' Right (cm/s)	.p.c	-0.033	-0.251	Calcium (mg/dL)	.p.c	0.026	-0.027
	P-value	0.763	0.019		P-value	0.813	0.805
IRT Right (ms)	.p.c	0.315	0.589	Triglycerides (mg/dL)	.p.c	-0.019	-0.036
	P-value	0.003	0.000		P-value	0.864	0.742
ICT Right (ms)	.p.c	0.196	0.263	Total cholesterol (mg/dL)	.p.c	0.031	-0.041
	P-value	0.069	0.014		P-value	0.778	0.707

ET Right (ms)	.p.c	-0.069	-0.344	Albumin (g/dL)	.p.c	0.051	-0.044
	P-value	0.528	0.001		P-value	0.641	0.686
E/E' Left	.p.c	-0.025	0.165	Protein in urine (random) (mg/dL)	.p.c	-0.126	-0.168
	P-value	0.820	0.128		P-value	0.243	0.119
E/E' Right	.p.c	-0.001	-0.029	Creatinine in urine (mg/dL)	.p.c	0.007	-0.057
	P-value	0.991	0.789		P-value	0.945	0.597
A/A' Right	.p.c	0.152	0.210	Protein-to-creatinine ratio	.p.c	-0.179	-0.040
	P-value	0.159	0.050		P-value	0.097	0.710
A/A' Left	.p.c	0.114	0.291				
	P-value	0.293	0.006				

p.c: Pearson correlation

Discussion

The present study demonstrates that children with NS can exhibit early cardiac abnormalities before the manifestation of overt symptoms. Through the utilization of DTE, subtle changes in cardiac muscle motion and relaxation were identified, revealing that systolic and diastolic function of the heart is affected. Notably, the heart's capacity to relax and contract properly was diminished in both the left and right ventricles, and small yet significant reductions in the heart's pumping strength were also observed.

Temporal assessments revealed that the contraction phases (ICT and ET) were shorter bilaterally in NS patients than in normal subjects. Interestingly, relaxation timing exhibited discrepancies between the left and right ventricles, indicating distinct adaptive mechanisms for each side in response to the disease. MPI, a composite measure of cardiac function, was elevated in both ventricles, confirming the coexistence of systolic and diastolic dysfunction.

These observations correspond with previous research that recognized comparable early indications of cardiac involvement in children with NS.[5, 6] Notably, these cardiac alterations were present even in clinically stable children, underscoring the remarkable sensitivity of DTE in detecting early cardiac abnormalities.

In examining treatment responses, improved kidney function and decreased proteinuria were observed among children who showed positive responses. Conversely, children who responded poorly exhibited elevated right-sided cardiac filling pressures, as evidenced by an increased E/E′ ratio, a potential predictor of unfavorable treatment outcomes.[8] Other cardiac motion measurements did not vary substantially between responders and non-responders, suggesting that early, subtle alterations in right ventricular filling could precede the development of more pronounced cardiac issues.[6,9] These findings chime with previous research,[10] further emphasizing the potential of right-sided diastolic function in identifying patients who may experience difficulties with treatment.

Additional analysis revealed a close correlation between cardiac function and various hematological parameters. Reduced myocardial velocities and elevated MPI were associated with alterations in hemoglobin, platelets, electrolytes, and lipids, suggesting that the broader metabolic perturbations commonly observed in NS, such as protein loss, fluid imbalances, and dyslipidemia, may directly impact cardiac function. These findings are concordant with previous studies[5,11] and, thus, underscore the interplay between cardiac health and overall metabolic status in NS.

Although NS is primarily recognized as a renal disorder, its wide-ranging cardiac implications are evident. DTE emerges as an instrumental tool for detecting early, subclinical cardiac alterations preceding symptom manifestation. The consistent decrease in E′ velocity, reflecting impaired ventricular relaxation, highlights a prevalent pattern observed across multiple investigations.[5,6]

The pathophysiology of cardiac dysfunction in NS involves multiple interrelated mechanisms. Hypoalbuminemia reduces plasma oncotic pressure, resulting in intravascular volume depletion and compromised coronary perfusion, particularly during diastole. Concurrent hyperlipidemia and systemic inflammation[12,13] may promote vascular endothelial injury and direct myocardial damage. Elevated ventricular filling pressures, exacerbated by potential complications such as pulmonary hypertension or fluid overload,[14]

further impair cardiac function in pediatric NS patients.

Conventional echocardiography often fails to detect these early functional changes, whereas DTE identifies subclinical impairments in myocardial contractility and global cardiac performance that standard assessments miss.[5,10] Chronic corticosteroid therapy, a mainstay of NS treatment, may induce structural and functional myocardial alterations. [15] Furthermore, uremic toxins and oxidative stress associated with renal impairment can disrupt myocardial energy metabolism and calcium homeostasis, progressively diminishing contractile efficiency.[16]

Intriguingly, the right ventricle appears to be affected earlier or more markedly than the left, potentially due to disparities in anatomy and hemodynamic conditions.[5,6,17] This underscores the importance of meticulously assessing both ventricles in children with NS, particularly in those with suboptimal treatment responses or atypical clinical courses.

The robust associations between cardiac measurements and blood chemistry emphasize the systemic impact of NS. Electrolyte disturbances not only serve as indicators of disease severity but also influence cardiac workload and oxygen supply. Hypoalbuminemia contributes to fluid leakage from blood vessels and altered drug pharmacokinetics, potentially impacting both treatment efficacy and cardiac function.[18] Moreover, hypertriglyceridemia and hypercholesterolemia may disrupt cardiac cell membranes and signaling, creating a cycle in which cardiac dysfunction and metabolic derangements exacerbate one another.[12]

Consequently, DTE findings should be interpreted in conjunction with clinical and laboratory data to facilitate individualized patient care. Regular cardiac monitoring with DTE is warranted even in the absence of overt cardiac symptoms, as it aids in identifying high-risk patients who may benefit from more intensive surveillance or targeted therapies.[2]

Early detection of right ventricular diastolic dysfunction or increasing MPI values could enable timely interventions, such as optimizing fluid management, to safeguard cardiac function and potentially avert lasting injury. Further, DTE-detected alterations appear connected not only to cardiac health but also to treatment responsiveness in children with NS, indicating that DTE may serve as a valuable prognostic indicator of overall disease activity and outcome.[19]

Study Limitations

This study has several important limitations. First, while our sample size provided adequate power for nonparametric analyses, the single-center design may limit the generalizability of findings to broader pediatric populations with nephrotic syndrome. Second, although DTE offers superior sensitivity for detecting subclinical dysfunction, its operator dependence and angle sensitivity may affect measurement reproducibility.

Conclusion

This study's findings indicate that alterations in DTE-derived parameters signify early impairment of both systolic and diastolic function in children with NS, with distinct ventricular involvement. These alterations included reduced E′, A′, and S′ velocities; elevated E/E′ and A/A′ ratios; prolonged IRT; and increased MPI. Furthermore, elevated right ventricular E/E′ ratios correlated with a poor treatment response, suggesting a prognostic role for right-sided diastolic assessment. The observed correlations between echocardiographic and biochemical parameters highlight the systemic impact of NS on myocardial performance.

Declarations:
Ethical Approval

The study protocol was approved by the Ethics Committee of Zahedan University of Medical Sciences and the Children and Adolescent Health Research Center (approval code: IR.ZAUMS.REC.1402.007).

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The authors declare no conflicts of interest regarding the publication of this study.

Acknowledgment

The authors gratefully acknowledge the staff of the Pediatric Nephrology Department at Ali Asghar Hospital in Zahedan for their valuable support and collaboration throughout this study. We also sincerely thank the participating children and their families for their contribution to this research.

References

1. Mishra OP, Sidar M, Batra VV, Gulati A, Pohl M, Agarwal I. Outcomes of children with idiopathic steroid-resistant nephrotic syndrome: a single-centre observational study. Braz J Nephrol. 2022;45(5):199-209.
2. Sadeghi-Bojd S, Noori NM, Teimouri A, Khaleghi A. Echocardiographic findings in children with nephrotic syndrome compared with healthy children. J Compr Ped. 2025;16(2):e161047.
3. Wendt R, Sobhani A, Diefenhardt P, Trappe M, Völker LA. An updated comprehensive review on diseases associated with nephrotic syndromes. Biomedicines. 2024;12(10):2259.
4. Echefu G, Stowe I, Burka S, Basu-Ray I, Kumbala D. Pathophysiological concepts and screening of cardiovascular disease in dialysis patients. Front Nephrol. 2023;3:1198560.
5. Kamel A, Abo Elnour S, Ragaey M. Cardiac performance evaluation in children with nephrotic syndrome. Fayoum Univ Med J. 2020;6(1):18-27.
6. Saleh SM, Elmaghraby KS, Abdelfadil AM, Mohamed HS. Myocardial performance index in nephrotic syndrome. J Clin Exp Cardiol. 2018;9(4):1000583.
7. Al Mamun A, Rahman MH, Jesmin T, Sultana S, Nahar N, Sarker SK. Echocardiographic assessment of systolic myocardial dysfunction in children with chronic kidney disease. J Pediatr Nephrol. 2020;8(3):1-6.
8. Santens B, Van De Bruaene A, De Meester P, D'Alto M, Reddy S, Bernstein D, et al. Diagnosis and treatment of right ventricular dysfunction in congenital heart disease. Cardiovasc Diagn Ther. 2020;10(5):1625-45.
9. Lammers AE, Apitz C, Michel-Behnke I, Koestenberger M. A guide to echocardiographic assessment in children and adolescents with pulmonary hypertension. Cardiovasc Diagn Ther. 2021;11(4):1160-79.
10. Vaziri ND. Disorders of lipid metabolism in nephrotic syndrome: mechanisms and consequences. Kidney Int. 2016;90(1):41-52.
11. Abd Elaziz L, Abouzeid H, Abu Fares K. Myocardial dysfunction in children with nephrotic syndrome: a tissue Doppler study. Zagazig Univ Med J. 2019;25(5):708-17.
12. Tao M, Wang HP, Sun J, Tian J. Progress of research on dyslipidemia accompanied by nephrotic syndrome. Chronic Dis Transl Med. 2020;6(3):182-7.
13. Evers PD, Scottoline B, Armsby LB. Acute right ventricular failure associated with pulmonary hypertension in pediatrics: understanding the hemodynamic profiles. J Perinatol. 2022;42(1):139-42.
14. Mahgoob MH, Setouhi AM. Subclinical systolic dysfunction in children with steroid-resistant nephrotic syndrome identified by speckle tracking echocardiography. BMC Pediatr. 2025;25(1):91.
15. Nalcacioglu H, Ozkaya O, Kafali HC, Tekcan D, Baysal K. Cardiac functions in children with steroid-sensitive nephrotic syndrome. Pediatr Int. 2020;62(12):1364-8.
16. van Ham WB, Cornelissen CM, van Veen TA. Uremic toxins in chronic kidney disease highlight a fundamental gap in understanding their detrimental effects on cardiac electrophysiology and arrhythmogenesis. Acta Physiol (Oxf). 2022;236(3):e13888.
17. La Via L, Merola F, Schembari G, Dezio V, Astuto M, Sanfilippo F. The interplay between left ventricular diastolic and right ventricular dysfunction: challenges in the interpretation of critical care echocardiography. J Anesth Analg Crit Care. 2023;3(1):47.
18. Idasiak-Piechocka I, Lewandowski D, Świgut W, Kalinowski J, Mikosza K, Suchowiejski P, et al. Effect of hypoalbuminemia on drug pharmacokinetics. Front Pharmacol. 2025;16:1546465.

19. Tavazzi G, Bergsland N, Alcada J, Price S. Early signs of right ventricular systolic and diastolic dysfunction in acute severe respiratory failure: the importance of diastolic restrictive pattern. Eur Heart J Acute Cardiovasc Care. 2020;9(6):649-56.