

# Myocardial Function in Egyptian Pediatric Patients With Acute Nephritic Syndrome

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## Keywords.

electrocardiography,  
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**Introduction.** Acute nephritic syndrome (ANS) is the most common cause of hypertensive heart failure in pediatric population. There are few publications on myocardial evaluation using electrocardiographic and echocardiographic data in pediatric patients with ANS. This study aimed to evaluate myocardial function by electrocardiography and 2-dimensional echocardiography in Egyptian pediatric patients with ANS.

**Materials and Methods.** Sixty children with ANS were included and subjected to clinical, laboratory, electrocardiography for corrected QT interval, and 2-dimensional echocardiographic study on admission, and repeated at 6 and 12 weeks to measure left ventricular ejection fraction, left atrium-aorta ratio, and the ratio of peak early filling (E wave) to late diastolic filling (A wave) velocities (E/A ratio).

**Results.** Prolonged corrected QT interval was reported in 22 patients (36.7%), of whom 18 had hypertension. Fourteen patients (23.3%) had left ventricular ejection fraction below 60%. The same children also had left atrium-aorta ratios more than 2 and E/A ratios more than 2. Left ventricular ejection fraction became within normal values by 6 weeks in 12 patients, and 2 become normal by 3 months of follow-up. 4 of 14 children with low left ventricular ejection fraction (28.6%) had normal arterial blood pressure. All of the 14 children completely recovered within 3 months.

**Conclusions.** Myocardial dysfunction in the acute phase of ANS was alleviated in almost all children within 12 weeks. Although elevated blood pressure was the commonest etiology of congestive heart failure in children with ANS, the impact of primary myocardial functional disturbance could also be put into consideration.

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## INTRODUCTION

Acute nephritic syndrome (ANS) is defined as a syndrome of acute onset of gross or microscopic hematuria, proteinuria, oliguria, hypertension, generalized edema, and azotemia.<sup>1</sup> In Pediatric age, the most common type is postinfectious by group A of beta-hemolytic streptococcal infection of the throat or skin.<sup>2</sup> Acute poststreptococcal glomerulonephritis (APSGN) remains a frequent

and urgent health hazard in developing Arab countries like Egypt.<sup>3</sup> Although the long-term prognosis of ANS in pediatric age is favorable, it may be associated with dangerous complications which may result in fatal sequelae in the early phases of the disease. Congestive heart failure (CHF) is one of these horrible complications that may complicate up to one-eighth to half of patients with ANS, resulting in unfavorable even

fatal sequelae.<sup>4,5</sup>

The heart-related complications may be presented in early phases of illness. Congestive heart failure in acute kidney injury may be attributed to salt and water retention, which results from acute kidney injury, hypertensive pressure overload on the left ventricle, or hyperkalemia.<sup>4</sup> Recent publications have reported that some patients with ANS may be complicated by CHF in absence of hypertension and or hyperkalemia or other electrolytes abnormalities.<sup>4,5</sup> In these patients, it was supposed that primary or idiopathic disturbances in cardiac muscles function was the underlying etiology precipitating CHF. In spite of the commonality of association between ANS and CHF, there was not enough previous research to discuss different clinical, electrocardiographic, and echocardiographic data in pediatric patients with ANS.<sup>4,5</sup> This study aimed to evaluate the myocardial function by electrocardiography and 2-dimensional (2-D) echocardiography data in Egyptian pediatric patients with acute nephritic syndrome and to evaluate their relationship with clinical and laboratory findings of these patients.

## MATERIALS AND METHODS

### Study Design and Setting

This randomized controlled trial was carried out during the period from February 2017 till February 2018 on 60 children with a diagnosis of APSGN which was the commonest form of ANS. Patients were under follow-up at the Pediatric Nephrology and Cardiology units of Pediatric Department of Tanta University Hospital. The study protocol was approved by the research ethical committee in accordance to declaration of Helsinki and informed written or oral consents obtained from all participants' parents.

The inclusion criteria were children with APSGN as the commonest form of ANS with ages ranged between 1 year and 12 years. The exclusion criteria were patients with preexisting cardiac diseases including cardiomyopathy, congenital or rheumatic heart disease, or chronic renal problems.<sup>6</sup>

Acute glomerulonephritis was defined as acute onset of edema, oliguria, and hematuria (gross or microscopic) with antecedent streptococcal infection as indicated by either a history of sore throat or pyoderma and raised antistreptolysin O titer over 200 Todd units or antideoxyribonuclease B greater

than 170 U. Patients were diagnosed to have hypertension if their blood pressure exceeded the 95th percentile for age, sex, and height, and severe hypertension if their blood pressure exceeded the 99th percentile.<sup>6</sup>

### Study Protocol

All of the patients received salt- and potassium-restricted diet and fluid restriction. Patients with hypertension received a loop diuretic (furosemide). An antihypertensive (nifedipine) was added if arterial blood pressure was not controlled despite these measures. All of the patients received a single dose of benzathine penicillin. The patients were monitored daily for weight, fluid intake and output, blood pressure, and signs of heart failure.

All children participating in the study were subjected to careful history taking about demographic data, clinical course, and outcome from case record forms; full clinical examination, including full cardiac examination; and laboratory investigations: which were performed on admission. These included complete blood count, aspartate aminotransferase and antideoxyribonuclease B titre, serum electrolytes (sodium, potassium, calcium, and magnesium), serum complements levels (C3 and C4), complete urinalysis (proteinuria, hematuria, pyuria, casts, and urinary creatinine), blood urea nitrogen, and serum creatinine. Serum C3 was repeated at 8 weeks.

Electrocardiography and 2-D echocardiography were performed for all of the patients at admission and repeated after 6 weeks, and 12 weeks, if abnormal. Corrected QT interval in the electrocardiography was derived from the nomogram based on Bazett formula. Prolonged QT interval was defined by a value greater than 0.40 seconds. Parameters studied on 2-D-echocardiography were left ventricular ejection fraction (LVEF), left atrium-aortic root (LA/AO) ratio, and the ratio of peak early filling (E wave) to late diastolic filling (A wave) velocities (E/A ratio). Left ventricular systolic function was assessed using the LVEF; an LVEF greater than 60% was considered normal, 30% to 60% was considered mildly abnormal, and less than 30% was considered markedly abnormal. The LA/AO ratio was measured as an indication of left atrial enlargement; values greater than 2 were considered abnormal. The E/A ratio, ie, ratio of passive filling

of the ventricle, the early E wave and active filling due to atrial systole, the atrial A wave, was also determined, normal ratio ranging from 1 and 2. Diastolic dysfunction was diagnosed in patients presenting with heart failure and having a reversal of the E/A ratio.<sup>7</sup>

Echocardiography was performed at Pediatric Cardiology Unit of Pediatric Department of Tanta University Hospital, using a GE vivid 7 (GE Medical System, Horten, Norway with a 3.5-MHz multifrequency transducer). The echocardiography imaging included the 2-D study, including E/A ratio, were based on the average of the 6 regional values. Echocardiographic imaging took place in the left lateral decubitus position. Besides the standard parasternal (long and short axis) and apical (2- and 4-chamber) images, additional apical (4-chamber) images were obtained that included the interventricular septum, the apex and the RV-free wall up to tricuspid annulus. Images were digitally stored in the cine-loop format for off-line analysis. Longitudinal strain was assessed offline, on the 4-chamber cine-loop that included the RV-free wall, using speckle-tracking analysis.<sup>8</sup>

### Statistical Analysis

Statistical analysis was performed using the SPSS software (Statistical Package for the Social Sciences, version 17.0, SPSS Inc, Chicago, IL, USA). The mean and standard deviation values of quantitative data of the studied groups were calculated and compared using the Student *t* test. Correlation between variables was evaluated using the Pearson correlation coefficient.<sup>9</sup> A *P* value less than .05 was considered significant.

### RESULTS

A total of 60 patients with confirmed diagnosis of ANS were enrolled in this study. The demographic, clinical, and laboratory parameters of the studied patients are summarized in Table 1. The male-female ratio was 3:2. Forty-two of 60 patients (70%) were older than 6 years old and 18 (30%) were from 1 to 5 years of age. Forty patients (66.7%) were presented with hypertension, 10 (22.2%) with CHF, and 4 (6.7%) with hypertensive emergency in the form of encephalopathy. Twenty-four patients (40%) had a preceding upper respiratory tract infection and 20 (33.4%) had a preceding skin infection. Four of the 10 children with CHF were with normal

**Table 1.** Demographic, Clinical, and Laboratory Data of the Studied Children With Acute Nephritic Syndrome

Parameter	Number (%)
Age, y	
1 to 5	18 (30.0)
6 to 12	42 (70.0)
Sex	
Male	36 (60.0)
Female	24 (40.0)
Clinical symptoms	
Swelling	56 (93.3)
Oliguria	40 (66.7)
Dark colored urine	16 (26.7)
Shortness of breath	6 (10.0)
Convulsions	4 (6.7)
Headache and or epistaxis	32 (53.3)
Clinical signs	
Generalized edema	60 (100.0)
Tachycardia	14 (23.3)
Hypertension	40 (66.7)
Raised jugular venous pressure	6 (10.0)
Pulmonary edema	10 (22.2)
Disturbed consciousness	4 (6.7)
Laboratory Investigations	
Hematuria	56 (93.3)
Proteinuria	40 (66.7)
Azotemia	2 (3.4)
Hyponatremia	6 (10.0)
Hyperkalemia	4 (6.7)
Hypocalcemia	0

arterial blood pressure. All of the children had a hypocomplementenemia C3, which returned to normal values in 2 months' follow-up duration. Six children (10%) had hyponatremia and 4 (6.7%) had hyperkalemia. All of the 60 patients received a protocol of treatment in the form of fluid and sodium restriction and furosemide as loop diuretic. The 40 patients (66.7%) with hypertension also received nifedipine as a direct arterial vasodilator.

Table 2 summarizes the results of electrocardiography and 2-D echocardiographic findings. There were tachycardia relative to age in 14 patients (23.3%) and prolonged QT interval in 22 (36.7%), which returned to normal values by 1.5-month follow-up duration. Fourteen patients (23.3%) had an LVEF ranged from 30% to 60% on echocardiography at presentation, which returned to normal values after 6 weeks' follow-up duration in 12 (20%). The remaining 2 patients had normal ejection fraction by 3 months' duration of follow-up. Four of 14 patients (28.6%) with low LVEF were with normal blood pressure. The LA/AO

**Table 2.** Electrocardiographic and Echocardiographic Parameters of the Studied Children

Parameter	Children (%)		
	At Admission	At 6 Weeks	At 12 Weeks
Electrocardiographic findings			
Normal corrected QT	38 (63.3)	58 (96.7)	60 (100)
Prolonged corrected QT (> 0.4 s)	22 (36.7)	2 (3.3)	0
Two-dimensional echocardiography			
Left ventricular ejection fraction			
> 60 %	46 (76.7)	58 (96.7)	60 (100)
30% to 60%	14 (23.3)	2 (3.3)	0
< 30%	0	0	0
E/A ratio*			
< 2	46 (76.7)	60 (100)	60 (100)
≥ 2	14 (23.3)	0	0
Left atrial-aortic ratio			
< 2	46 (76.7)	60 (100)	60 (100)
≥ 2	14 (23.3)	0	0

\*E indicates early filling of ventricle-passive phase and A, active filling phase of ventricle due to atrial systole.

ratio was abnormal (> 2) in 14 children (23.3%), suggestive of left atrial enlargement. The E/A ratio was abnormal (> 2) in 14 (23.3%), suggestive of diastolic dysfunction. None of the patients with low LVEF had abnormal serum electrolytes.

Table 3 summarizes the relationship of the electrocardiography and echocardiographic parameters with the studied clinical and laboratory data. Prolonged corrected QT interval was reported in 22 patients (36.7%). All the children with prolonged corrected QT had normal serum total and ionized calcium levels. Twelve of these patients (54.5%) had hypertension and 2 (9.1%) had elevated serum potassium levels.

## DISCUSSION

In this study, 10 of the 60 children with ANS were presented with heart failure, of whom 14 had a reduced LVEF at time of clinical presentation, suggestive for reduction in left ventricular function (LVF). These results became within normal values in 12 children at 6 weeks. In the remaining children,

LVF returned to normal values at 3 months. Ten out of the 14 pediatric patients had elevated arterial blood pressure as the most possible etiology for disturbed LVF. The remaining 4 children were normotensive, indicating the possibility of primary myocardial disturbed function in ANS.

A previous research was conducted by Singh and colleagues on 34 children with APSGN.<sup>5</sup> In their study, CHF was present in 9 patients and 3 patients had decreased LVEF on echocardiography, out of which 2 were with normal blood pressure. In a previously published article conducted by Banapurmath and colleagues, 13 out of 50 patients had CHF.<sup>4</sup> Twelve of these patients had hypertension. One child was with normal blood pressure and was presumed to be having noninfective myocarditis as proven by auscultation of muffled cardiac sounds and low-voltage complexes on electrocardiography. The most common cause of CHF in patients with ANS was hypertension. However, some previously published articles have concluded a weak correlation between hypertension and signs of CHF.<sup>4,5</sup>

**Table 3.** Relationship Between Electrocardiography and Echocardiographic Findings and Demographic, Clinical, and Laboratory Data of the Studied Children With Acute Nephritic Syndrome\*

Parameter	Prolonged Corrected QT	LVEF < 60%	LA/AO ratio > 2	E/A ratio > 2
Hypertension without heart failure	12 (20)	4 (6.7)	4 (6.7)	4 (6.7)
Normotensive with heart failure	4 (6.7)	4 (6.7)	4 (6.7)	4 (6.7)
Hypertension and heart failure	4 (6.7)	4 (6.7)	4 (6.7)	4 (6.7)
Hyperkalemia with hypertension and heart failure	2 (3.4)	2 (3.4)	2 (3.4)	2 (3.4)
Hypocalcemia	0	0	0	0

\*LVEF indicates left ventricular ejection fraction; E, early filling of ventricle-passive phase; and A, active filling phase of ventricle due to atrial systole.

Moreover, cases of ANS with cardiomegaly but without hypertension have also been reported.<sup>10</sup> Apart from hypertension, other possible etiologies of CHF in ANS included circulatory congestion, hyperkalemia, administration of excessive amounts of intravenous fluids, especially if patients were presented with oligoanuria leading to cardiac muscle injury.<sup>4</sup> Gore and Saphir have observed significant patchy areas of myocardial damage in autopsies examination in 16 out of 160 studied children who died after AGN.<sup>11</sup> With regard to therapy of ANS, they recommended cautious administration of intravenous fluids. In studies performed by Manhas and colleagues and Puri and colleagues, 83% and 50% of patients, respectively, with CHF were normotensive, and they lacked evidence of myocarditis.<sup>12,13</sup>

Kaplan and coworkers have reported temporary vasculitic phenomena, which affect multiple organs, including that of the central nervous system in ANS.<sup>14</sup> It was likely that vasculitic phenomena involving the myocardial tissue might explain the decreased LVF in some patients of ANS who were normotensives.

In the present study, 36 children (60%) had evidence of electrocardiography abnormalities, which was within the range of 5% to 75% reported in various previous publications.<sup>4,12,13,15</sup> The electrocardiography changes seen in our work were tachycardia in 14 (23.3%) and prolonged corrected QT interval in 22 (36.7%), 18 (30%) of whom had hypertension. Eight patients (13.3%) with prolonged QT were normotensive and had decreased LVEF and tachycardia, suggesting myocardial dysfunction. Two patients (3.3%) with prolonged QT had hyperkalemia. A previous study performed by Banapurmath and coworkers found tachycardia in 11 cases, of whom 8 had hypertension.<sup>4</sup> In their study, prolonged QT interval was seen in 11 children, 9 of whom had hypertension.

The other electrocardiography abnormalities observed in the study were bradycardia, prolonged PR interval, ST segment elevation and depression, tall T wave, inverted T wave, U wave, low-voltage complexes, right axis deviation, and left axis deviation. Another study performed by Singh and colleagues reported 19 patients out of 34 (55.9%) with prolonged QT. Five out of these patients were normotensive with decreased LVF, suggesting myocardial dysfunction.<sup>5</sup>

There were many previous studies about cardiac dysfunction and its significance in chronic kidney diseases, but only seldom data exist regarding involvement of heart in acute glomerular diseases.<sup>4,5</sup> Kamisago and Hirayama studied left ventricular hemodynamics using M-mode and pulsed Doppler echocardiography in 18 patients with APSGN during the acute phase.<sup>16</sup> The results reported that in the acute phase of APSG, left ventricular preload, contractility, and after load were increased mainly due to circulatory congestion. In the present work, 14 patients (23.3%) had evidence of increased LA/AO ratio, thereby suggesting left atrial enlargement due to circulatory congestion. Sieck and coworkers described a 16-year-old adolescent male with APSGN whose echocardiography showed marked impairment of LV systolic and diastolic function with apical thrombus. Serial echocardiographic examinations showed improvement over 3 weeks with treatment.<sup>17</sup> In our work, 14 children had reversal of the E/A ratio and decreased LVEF on echocardiography, indicating the presence of systolic and diastolic dysfunction. Ten out of these 14 patients had hypertension. The remaining 4 children were within normal blood pressure suggesting primary myocardial involvement. The systolic and diastolic function in our patients became within normal values by 12 weeks of follow-up period.

One of the limitations of this study was small-sized sample of children, and therefore, further studies on a wider scale of children will be hoped to clarify the possibility of effects of primary myocardial dysfunction in the pathophysiology and etiology of heart failure in pediatric patients with ANS.

## CONCLUSIONS

This work has reported that myocardial functional abnormalities in electrocardiography and echocardiography were frequent in the acute phase of acute nephritic syndrome. These abnormalities were reported in some children even in the presence of normal arterial blood pressure and normal serum sodium and potassium levels.

Elevated arterial blood pressure was the commonest predisposing agent in etiology of hypervolemia of circulatory system in acute nephritic syndrome. However, fewer children presented by CHF without elevated blood

pressure, thus primary or idiopathic disturbed myocardial function might be the underlying etiology of CHF in these patients. Children with ANS might be presented by systolic and diastolic myocardial dysfunction, which was proven by echocardiographic data. The abnormalities in electrocardiography and echocardiographic data were temporary, meaning that they returned to normal values in majority of children by 12 weeks' duration of follow-up.

### CONFLICT OF INTEREST

None declared.

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