

Presence of Fragmented QRS and its Correlation with Myocardial Performance Index in Patients with Primary Nephrotic Syndrome

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Abstract

Background: Nephrotic syndrome (NS) is a condition characterized by severe proteinuria, hypoalbuminemia as well as dyslipidemia. The QRS complex represents the electrical depolarization of the ventricular myocardium. The aim was to assess the presence of fQRS in children with primary NS. The study also evaluated the relationship between fQRS and myocardial functions.

Methods: This study was a control-sectional case-cross study carried out in the Nephrology clinic and Cardiology Unit, the period from 2020 to 2022, pediatric department at Benha University Hospital. It was conducted on fifty children suffering from primary nephrotic syndrome and thirty children apparently healthy of the same age and sex from the general clinic.

Results: The difference between both groups in conventional echo was not significant except for LVEDD and ESPAP which were significantly higher in Nephrotic. However, tissue doppler shows that the left ventricle was more affected on systolic and diastolic functions as (IVR, IVCT, MPI, DT) were significantly affected in the cases group. While values in the right ventricle were not significantly affected. Fragmented FQRS was present in (10%) of patients with tissue doppler values more significantly affected.

Conclusion: Nephrotic syndrome children generally have a high risk of cardiovascular complications. FQRS can be used as a marker of myocardial function impairment in this patient group.

Keywords: Fragmented QRS -Myocardial Performance Index – Primary Nephrotic Syndrome

I- Introduction:

Nephrotic syndrome (NS) is a condition characterized by severe proteinuria, hypoalbuminemia as well as dyslipidemia ⁽¹⁾. It is caused by impaired glomerular function, characterized by protein leakage from the blood to the urine through the glomeruli, resulting in proteinuria, hypoalbuminemia, hypercholesterolemia, and generalized edema ⁽²⁾.

The QRS complex represents the electrical depolarization of the ventricular myocardium. If the QRS complex has normal duration and contains notched R or S wave, various RsR' patterns in at least 2 contiguous ECG leads, this is called a fragmented QRS (fQRS) which includes an additional R wave (R') or notching in the nadir of the S wave, or the presence of >1 R' (fragmentation) in 2 contiguous leads, corresponding to a major coronary artery territory ⁽³⁾

fQRS is a novel ECG marker with more sensitivity and less specificity than the Q wave. A combination of fQRS with Q wave in a 12-lead ECG results in up to 74% sensitivity and 92% specificity ^(4;5).

The aim of this study was to assess the presence of fragmented QRS in primary nephrotic syndrome and to study its correlation with myocardial functions with echo and tissue Doppler.

II- Patients and Methods

This study was a case-control study carried out in the Pediatric Nephrology clinic and Cardiology Unit, pediatric department at Benha University Hospital. Informed written consent was taken from parents of children. This study was conducted on fifty children suffering from primary nephrotic syndrome and thirty children apparently healthy of the same age and sex from a general clinic.

- **Inclusion criteria:**

1. Primary nephrotic syndrome
2. Both sexes were involved
3. Age: from 1 _ to 16 years

- **Exclusion criteria**

1. 2ry nephrotic syndrome
2. Patients with a history of any cardiac abnormalities such as (Rheumatic diseases, Cardiomyopathy, congenital heart disease, and coronary artery disease)
3. Any arrhythmia as Bundle-branch block (left bundle-branch block, incomplete or complete right bundle-branch block)

All patients were subjected to:

1. **Complete history taking:** Including name, age, sex, and medicine used, (manifestation of systemic congestion as a history of edema, ascites) (manifestations of pulmonary congestion as hemoptysis and recurrent chest infections), symptoms of low cardiac output, cyanosis, chest pain, palpitation, symptoms of Hypertension, etiology, and duration of NS, a drug used and a number of recurrences of the disease.

2. **Thorough physical examination:**

a.General examination: vital signs, anthropometric measurements, skin, Head, Neck, UL, L L. with special emphasis on pulse rhythm to exclude arrhythmia, blood pressure (systolic & diastolic), and body mass index (BMI)

b.Local examination: Heart, chest, and abdomen.

3. **Biochemical analysis**

- CBC
- BUN
- Albumin
- Creatinine, calcium (Ca), phosphorus (P)
- HDL, LDL and triglyceride
- Protein excretion was measured from 24h urine collection

4. **Cardiac Investigation:**

- a. Electrocardiography**

All ECGs were evaluated by two cardiologists blinded to the patient data. fQRS were defined by the presence of various RSR' patterns (QRS duration <120 ms) with or without Q wave, which includes an additional R wave (R prime) or notching of the R wave or S wave, or the presence of more than one R prime (fragmentation) without typical bundle-branch block in two contiguous leads corresponding to a major lead set for major coronary artery territory ⁽⁶⁾. Analysis of the standard 12-lead ECG was performed, and fragmentations were considered to be present if a visually identifiable signal is demonstrated in all complexes of a particular lead. QRS duration was determined by the longest QRS in any lead.

- b. Echocardiography**

Each patient undergone a complete baseline echocardiographic examination and the following values were recorded:

- LV end-diastolic and end-systolic dimensions, posterior wall thickness, interventricular septal thickness, and LV ejection fraction were evaluated by M-mode echocardiography in parasternal long axis.

- The mitral and tricuspid Doppler signals were evaluated in the apical four chamber view, The variables obtained included: early diastolic peak velocity (peak E, cm/s), mitral deceleration time of early filling (E-DT, millisecond), late diastolic peak velocity (peak A, cm/s) and early to late diastolic peak velocity ratio (E/A).
- Tricuspid annular plane systolic excursion (TAPSE) was assessed with M-mode in apical four-chamber view, placing the examination beam on the lateral mitral annulus.

c. Tissue Doppler imaging

Tissue Doppler imaging was obtained from an apical 4-chamber view to obtain longitudinal annular velocities (VEL) at the lateral mitral wall, septum, and lateral tricuspid wall adjacent to the atrioventricular valve hinge points Systolic (Sa), early diastolic (Ea), and late diastolic (Aa) tissue Doppler velocities, isovolumetric contraction and relaxation times were measured at the lateral mitral, septal, and lateral tricuspid walls

Transmitral and transtricuspid E/Ea ratios were calculated for each patient.

Myocardial Performance index (Tei index) is an index of combined systolic and diastolic Myocardial function and was calculated as the sum of isovolumetric contraction time (ICT) and isovolumetric relaxation time (IRT) divided by ejection time (ET) For each ventricle Separately .

• Statistical Analysis:

The collected data was tabulated and statistically analyzed using statistical package for social sciences (SPSS) software statistically computer package version 20. For quantitative data, the mean and standard deviation was calculated, the difference between two means was statistically analyzed using the student (t) test.

For qualitative data the number and percent distribution were calculated. Chi square was used as a test of significance and when found inappropriate fisher exact test was used significance was adopted to P<0.05 for interpretation of results of tests significance.

III- Results:

Mean value of 24-hour protein in urine was significantly higher among cases than control, Sodium and Calcium levels were significantly lower among cases. While there was no statistically significant difference between cases and control regarding Urea and Potassium level **Table (1)**.

Table (2) shows that Mean value of E' wave, and Ejection time were statistically significant lower among cases than control and ICT, IRT and MPI was statistically significant higher among cases.

There were no statistically significant difference between cases and control regarding Tissue doppler of right ventricle. **Table (3)**.

Table (4) show that fragmented QRS was present in (10%) and absent in (90%) among cases group.

Figure (1) shows that there was statistically significant positive correlation between disease duration and MPI of Lt ventricle.

Table (1): Renal functions in study groups

Characteristics	Cases (n=50) (mean ± SD)	Control group(n=30) (mean ± SD)	Test of sig.	p-value
24-hour protein in urine (mg/day)	50.6±27.9	22.3±6.5	6.9	<0.001*
Urea (mg/dL)	22.7±6.4	22.2±4.5	0.4	0.4
Creatinine (mg/dL)	0.9±0.2	0.7±0.1	4.7	<0.001*

Sodium level (mmol/L)	138.3±1.8	139.6±1.9	3.01	0.002*
Potassium level (mmol/L)	4.17±0.5	4.18±0.45	0.1	0.4
Calcium level (mg/dL)	8.2±0.7	8.8±0.5	3.6	<0.001*

Table (2): Comparison between cases and control groups regarding Tissue doppler Parameter of Left Ventricle

Characteristics	Cases (n=50) (mean ± SD)	Control group(n=30) (mean ± SD)	Test of sig.	p-value
S' wave	7.6±0.8	8.4±1.3	2.9	0.03
E' wave	11.6±1.8	13.4±2.2	3.9	<0.001*
A' wave	6.2±1.2	6.7±1.7	1.4	0.9
ICT	42.3±10.2	37.6±9.7	2.03	0.04*
IRT	49.2±7.6	45.9±6.4	1.9	0.04*
Ejection time	252.2±26.1	271.4±28.7	3.1	0.003*
MPI /seconds	0.35±0.06	0.32±0.04	2.7	0.009*
E/EA	8.9±1.9	6.9±1.5	5.3	<0.001*

isovolumetric contraction time (ICT), isovolumetric relaxation time (IRT) Myocardial performance index (MPI)

Table (3): Comparison between cases and control groups regarding Tissue doppler Parameter of Right Ventricle

Characteristics	Cases (n=50) (mean ± SD)	Control group(n=30) (mean ± SD)	Test of sig.	p-value
s' wave	10.8±2.02	10.7±2.5	0.2	0.4
E' wave	14.5±2.4	14.8±3.1	0.4	0.3
A' wave	8.8±2.8	9.6±2.8	1.3	0.09
ICT	39.2±8.6	37.4±4.3	1.2	0.2
IRT	43.1±9.3	42.8±4.9	0.2	0.4
Ejection time	277.2±28.6	285.7±26.1	1.4	0.09
MPI /seconds	0.29±0.06	0.27±0.03	1.2	0.1

isovolumetric contraction time (ICT), isovolumetric relaxation time (IRT), Myocardial performance index (MPI)

Table (4): Prevalence of fragmented QRS among cases group

		No.	%
Prevalence of fragmented QRS	Present	5	10%
	Absent	45	90%

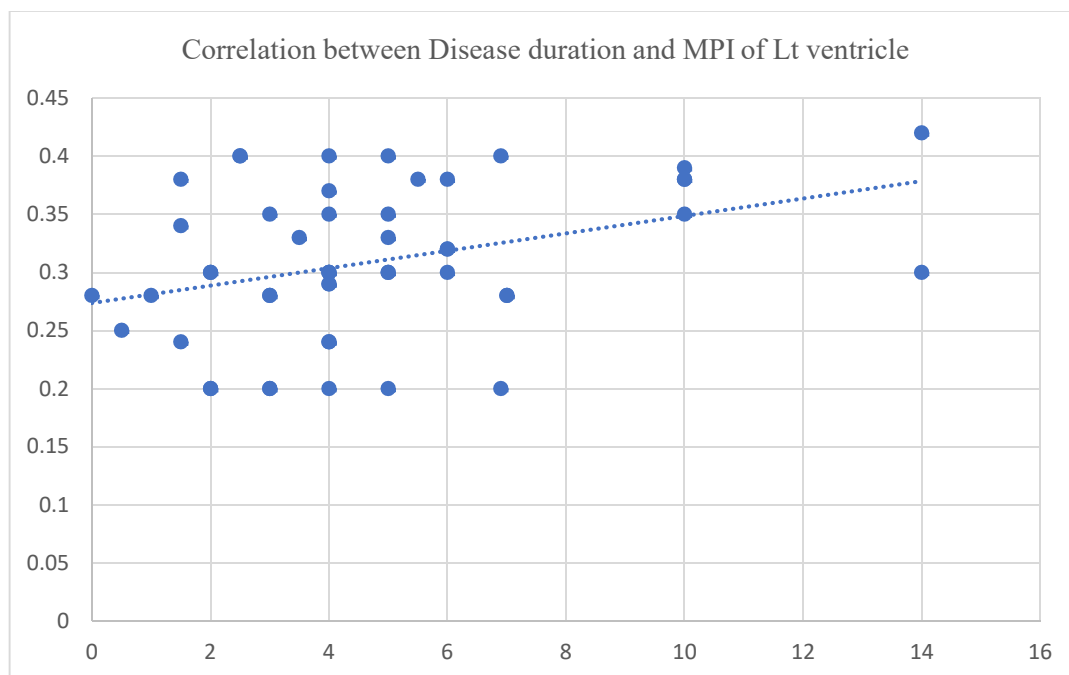


Figure (1): Correlation between disease duration and MPI of Lt ventricle.

IV- Discussion

In current study the mean \pm SD of age of studied children of NS was 9.3 ± 3.9 years. With no statistically significant difference between cases and control.

This is in agreement with Moon et al.,⁽⁷⁾ who investigated the effects of glucocorticoids on BMD and bone geometry in children with NS and they found the mean of age was 10.7 ± 3.1 years.

During study sex distribution in our cases, we found the male predominance (58%). With no statistically significant difference between cases and control.

Our results were supported by Rhuma et al.,⁽⁸⁾ and Ephraim et al.,⁽⁹⁾ as they reported that INS were affected males more than females.

In our study according to response to steroids, dependent was present in 39 (78%) then Resistance was present in 6 (12%), response was 4 (8%) and Relapse was 1 (2%).

In contrast to our study, Sahana,⁽¹⁰⁾ found 63% of cases were on relapse.

In our results, Mean value of LVEDD was statistically higher among cases than control (3.8, 3.3) $p = 0.004$ There were no statistically significant difference between cases and control regarding LVEDS, IVSd, LVPWd, LVPWs, EF% and ESPAP. Mean value of IVSs was statistically higher among cases than control (1.2, 1.1) $p = 0.04$ Mean value of ESPAP was statistically higher among cases than control (30.02, 25.2) $p < 0.001$

There was no statistically significant difference between cases and control regarding s' wave, A' wave and Ejection time. Mean value of E' wave was statistically lower among cases than control. Mean value of ICT was statistically higher among cases than control. Mean value of MPI was statistically higher among cases than control. While Mean value of E' wave was statistically higher among cases than control (14.5, 13.2) $p = 0.006$. There was no statistically significant difference between cases and control regarding Tissue doppler (Ant. Wall).

Kamel et al.⁽¹¹⁾ reported that tissue Doppler imaging of the right and left ventricles yielded significant differences between PNS patients and the healthy controls. As regards the right ventricle, tissue Doppler echocardiography showed that isovolumetric contraction time (IVCT) was significantly prolonged in the patient group compared to the control group ($p < 0.001$).

Saleh et al.⁽¹²⁾ who found that IVCT was significantly increased in NS patients ($p = 0.02$). Prolonged IVCT indicates systolic dysfunction and occurs in cases of increased afterload as ventricular contraction is slower than in control subjects⁽¹³⁾.

Our results revealed that QRS positive was present in 5 (10%) of our cases and absent in the other 45 (90%).

According to **Liu et al.** ⁽¹⁴⁾ who aimed to investigate the prevalence of fragmented QRS (fQRS) on electrocardiograms (ECG) in patients with different stages of chronic kidney disease (CKD) and to examine the association between fQRS and left ventricular systolic function. They found that the prevalence of fQRS in patients with CKD was 30.32% and there were no significant differences in prevalence among the three different CKD stages.

Abd Elaziz et al. ⁽¹⁵⁾ reported that, fQRS was present in 56.7% of patient group, and absent in the other 43.3% with a statistically significant increase in presence in case than control. (p value= 0.003).

V- Conclusion:

The determination of fQRS in patients with primary NS in surface ECG, an easily accessible technique, can be used as a parameter in the prediction of myocardial functions.

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