ECHOCARDIOGRAPHIC FINDINGS IN CHILDREN WITH CHRONIC RENAL DISEASE: LEFT VENTRICULAR STRUCTURE, SYSTOLIC AND DIASTOLIC FUNCTIONS

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SUMMARY: The purpose of this study was to evaluate the left ventricular structure, systolic and diastolic functions and to investigate the factors that may be contributing to the development of cardiac involvement in children with chronic renal failure. The study group consisted of 26 children (age 5 to 17 years) with chronic renal disease (creatinin clearance < 50 ml/min/1.73 m²), ten of them on hemodialysis. The control group consisted of 26 age - and sex - matched healthy subjects without clinical evidence of cardiac or renal disease. Interventricular septum and left ventricular posterior wall thickness were significantly increased in the study group (p<0.01). Left ventricular ejection fraction and fractional shortening were similar in both groups (p>0.05). Left ventricular mass index was significantly greater in the study group (p<0.01).

Key Words: Chronic Renal Failure, Cardiac Involvement.

INTRODUCTION

Cardiovascular complications contribute significantly to the morbidity and mortality of patients with chronic renal failure. Innumerable studies in adult populations have revealed that one consistent factor in uremic patients is left ventricular hypertrophy which can partially regress after renal transplantation (6, 8, 9). It has not been clarified to what extent the myocardial hypertrophy can be explained by uremic toxins, hypertension, anemia, fluid overload or hyperparathyroidism (1). It has been suggested that the most significant factors predictive of left ventricular hypertrophy include age and hyperparathyroidism (6). As opposed to the number of studies in adult populations, there have been very few studies in the pediatric age group about cardiac involvement of chronic renal disease (1).

The purpose of this study was to evaluate the left

ventricular structure, systolic and diastolic functions and to investigate the factors that contribute to the development of cardiac involvement in children with chronic renal failure.

MATERIALS AND METHODS

The study group consisted of 26 children and adolescents (17 males, 9 females) with chronic renal disease (creatinin clearence < 50 ml/min), ten of them were on hemodialysis. Their age ranged from 5 to 17 years. The control group consisted of 26 age - and sex - matched healthy subjects without clinical evidence of cardiac or renal disease.

The presence of primary renal diseases, followup duration, all measurements of arterial blood pressures in the last year and medications were data obtained from hospital records. Hematocrite, blood urea nitrogen, creatinin, calcium, phosphorus and alkaline phosphatase levels were measured by autoanalyser. Electrocardiographies and telecardiographies were obtained.

Each patient underwent M-mode, two dimensional and pulsed Doppler examination of the left ventricular inflow using a Toshiba SSH-160A Echocardiography and 3.75-5 mHz transducers. Two echocardiographic examinations were performed on hemodialysis patients, one before and one two hours after dialysis.

M-mode echocardiographic studies: Left ventricle chamber dimensions and wall thicknesses were measured according to the standart methods of the American Society of Echocardiography (5), over three cardiac cycles. Left ventricular myocardial mass was calculated using the corrected formula described by Devereux et al (6).

LV mass = $0.80 \{1.04[IVS+EDD+PW]_3-(EDD)_3\} + 0.6$, where IVS: thickness of intervent-ricular septum at end diastole (cm), EDD: end diastolic left ventricular dimension (cm) and PW: diastolic posterior wall thickness (cm).

Left ventricular mass index (gr/m²) was calculated from left ventricular mass divided by body surface area.

Doppler Echocardiographic Studies: All recordings were obtained from apical four chamber views. The Doppler cursor was placed in the mitral valve inlets at the level of the valve ring, as parallel as possible to the assumed diastolic inflow. No angle correction was made. The following Doppler indices were measured: 1) Peak early diastolic velocity (E), 2) Peak late diastolic (atrial) velocity (A), 3) Early to atrial peak velocity ratio (E/A), 4) The rate of decrease of flow velocity in early diastole (EF slope), 5) Deceleration time of flow velocity in early diastole (DT)

Statistical analysis: Data are reported as mean ± standart deviation. Studient's t test and Pearson's correlation analysis were used. P values less than 0.05 were considered to be statistically significant.

RESULTS

Clinical and laboratory findings of the study group are shown on table 1. Twelve patients (46 %) were hypertensive. Nine of all patients (34 %) have exhibited electrocardiographic abnormalities such as the evidence of left ventricular hypertrophy (in four patients) or depression of ST segment and inversion of T wave. Pericardial effusion was obser-

ved in six hemodialysis patients on echocardiogram (Fig 1). M- mode echocardiographic findings of study and control groups are shown on table 2.

| | | |
|-------------------------|---------------------|-------------|
| | Mean | Min-Max |
| Cardiothoracic ratio | 0.53 ± 0.08 | 0.42 - 0.73 |
| Hematocrite (%) | 26.42 ± 7.18 | 14 - 36 |
| Ccr (ml/min) | 20.28 ± 15.38 | 5.2 - 38 |
| CaxP | 55.59 ± 16.46 | 31 - 111 |
| AP | 621.92 ± 362.78 | 209 - 1800 |
| Follow-up period (year) | 2.86 ± 2.25 | 0.5 - 8 |

Ccr : Creatinin clearance, CaxP : Calcium x Phosphorus,

AP: Alkaline Phosphatase.

Table 1: Clinical and laboratory findings of the cases.

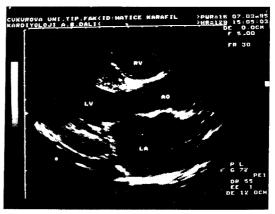


Fig - 1: 2-D Echocardiogram of patient shows the existence of pericardial effussion and left atrial enlargement.

Ao: Aorta, LA: Left Atrium, LV: Left Ventricle, RV: Right Ventricle

Interventricular septum and left ventricular posterior wall thickness were significantly increased in the study group (p<0.01) (Fig 2). Left ventricular ejection fraction and fractional shortening were similar in both groups (p>0.05). Left ventricular mass index (LVMI) was significantly greater in the study group (p<0.01). Measurements of LVMI exceeded 125 gr/m² in 16 (62 %) patients. Of the 16 patients with an increase in LVMI; ten were hypertensive. All of the hemodialysis patients have hypertrophic left ventricles with LVMI over 125 gr/m².

Mean values of the Doppler indices of left ventricular filling in the study and control group are shown in table 3.

| | Study group | Control group | P |
|---------------------------|--------------------|------------------|--------|
| LVEDD (mm) | 43.23 ± 8.49 | 38.88 ± 2.74 | < 0.05 |
| LVESD (mm) | 28.53 ± 7.64 | 25.72 ± 2.18 | > 0.05 |
| IVS (mm) | 10.61 ± 2.56 | 7.52 ± 0.49 | < 0.01 |
| LVPWT (mm) | 10.31 ± 2.64 | 7.64 ± 0.48 | > 0.01 |
| EF (%) | 65.00 ± 8.12 | 68.24 ± 5.12 | > 0.05 |
| FS (%) | 35.53 ± 5.80 | 38.15 ± 3.56 | > 0.05 |
| LVMI (gr/m ²) | 163.26 ± 79.00 | 85.52 ± 8.78 | < 0.01 |

LVEDD: Left Ventricular End - Diastolic Diameter

IVS: Interventricular Septal Thickness

EF: Ejection Fraction,

LVMI: Left Ventricular Mass Index

Table 2: M mode echocardiographic measurements in the study and control groups.

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FS: Fractional Shortening

LVESV: Left Ventricular End - Systolic Diameter

LVPWT: Left Ventricular Posterior Wall Thickness

cardiac relaxation in the study group.

Mean values of LVMI and E/A and without hypertension are given in table 4.

LVMI was significantly higher in hypertensive patients than normotensive patients. The reduction in E/A ratio was more significant in patients with hypertension.

In statistical analysis, there was no significant correlation between LVMI and CaxP, LVMI and CaxP, LVMI and E/A, LVMI and alkaline phosphatase values.

DISCUSSION

This study revealed significant increase in the thickness of the interventricular septum of the left ventricular posterior wall and in the left ventricular mass index (LVMI) in children with chronic renal failure. LVMI was found to be over 125 gr/m² in all

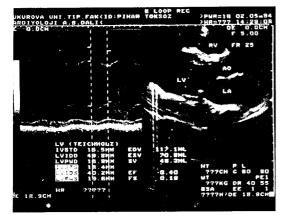


Fig - 2: Thickened left ventricular anterior and posterior walls are seen in M-Mode and 2-D Echocardiogram of a patient. Ao: Aorta, LA: Left Atrium, LV: Left Ventricle, RV: Right Ventricle.

| | Study group | Control group | P |
|-------------------------------|------------------|------------------|--------|
| E (cm / sn) | 41.9 ± 13.5 | 65.96 ± 6.45 | < 0.01 |
| A (cm/sn) | 35.19 ± 5.56 | 39.16 ± 4.19 | < 0.01 |
| E/A | 1.3 ± 0.2 | 1.7 ± 0.1 | < 0.01 |
| DT (msn) | 102.6 ± 13.7 | 99.8 ± 8.6 | > 0.05 |
| EF slope (m/sn ²) | 0.8 ± 0.1 | 0.9 ± 0.2 | > 0.05 |

E: Peak Early Diastolic Velocity

E/A : Early to Late Peak Velocity Ratio

A : Peak Late (atrial) Diastolic Velocity

DT: Deceleration Time of Flow Velocity in Early Diastole

EF: Slope: The Rate of Decrease of Flow Velocity in Early Diastole.

Table 3: Pulsed doppler echocardiographic measurements of diastolic mitral inflow in study and control groups.

A significant decrease in the early (E) and late (A) peak transmitral velocities was found with a reduction in the E/A ratio, indicating abnormality of

dialysed patients and 60 % of the other patients. Experimental studies have clearly established an increase in heart weight and myocardial fiber mass in rats with renal insufficiency (9). Harnett et al found

| | HT (+) | HT (-) | P |
|---------------------------|-------------------|-------------------|--------|
| LVMI (gr/m ²) | 210.4 ± 86.1 | 123.5 ± 42.7 | < 0.01 |
| E/A | 1.109 ± 0.065 | 1.338 ± 0.172 | < 0.01 |

LVMI: Left Ventricular Mass Index

HT: Hypertension

E/A: Early to Late (atrial) Peak Velocity Ratio

Table 4: Comparison of the mean LVMI and E/A values in subjects with and without hypertension.

that 55 % of adult patients under treatment for an end-stage renal disease had left ventricular hypertrophy (6). In children with chronic renal disease, the prevalance of left ventricular hypertrophy (LVH) has not yet been determined. Hypertension, chronic anemia, fluid overload, hyperparathyroidism and uremic toxins may play a role in the occurence of LVH in varying degrees. The most important factors associated with LVH are not clearly identified (1, 5, 6, 8, 9). Experimental studies suggested that increased arterial blood pressure is the most logical explanation for the increased heart weight in renal insufficiency (9). However, the genesis of myocardial hypertrophy appears to be more complex than a direct response to mechanical loading and may involve circulating factors such as parathyroid hormone which is thought to be one of the important uremic toxins (7).

Although we found that LVMI was significantly higher in hypertensive patients, ten of the 16 patients with elevated LVMI values were hypertensive, 6 were normotensive. This finding supports the theory that there must be some other factors that play a role in the development of left ventricular hypertrophy besides hypertension.

We found that there was significant diastolic dysfunction showing an abnormality of cardiac relaxation in children with chronic renal failure, while systolic functions were not significantly affected. In many systemic diseases affecting cardiovascular system, systolic dysfunction is a relatively late occurence. Among the causes of disturbances in diastolic relaxation are increased ventricular pressure and systemic hypertension (2, 5, 11, 12). Furthermore, experimental studies have documented that cardiac compliance is commonly impaired by myocardial interstitial fibrosis. Mall et al have suggested that uremia causes activation of interstitial cells and interstitial fibrosis by mechanisms independent of hypertension (7). However, we observed diastolic dysfunction only in hypertensive uremic patients.

As a conclusion, in children with chronic renal disease, early findings of cardiac involvement are an increase in LVMI and abnormality of cardiac relaxation before the occurence of systolic dysfunction. Although hypertension may play a significant role, further investigations are needed to determine the contributions of other factors such as hyperparathyroidism, fluid overload, anemia or uremic toxins in the development of cardiac complications.

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