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Original Article

Evaluation of Left Ventricular Function in Patients with Acute and Chronic Renal Failure and Comparison of Results in Hemodialysis versus Peritoneal Dialysis

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Abstract:

Background: *Kidneys are the major excretory system in humans. The specific components of the kidney are the nephrons, the collecting ducts and a unique microvasculature.*

Objective: *To evaluate left ventricular function in patients with Acute and Chronic renal failure and to compare results in Hemodialysis versus Peritoneal dialysis groups of patients in Central Child Teaching Hospital.*

Patients and method: *A single center, case-control study was carried out in nephrological unit in Central Child Teaching Hospital. Over a period of 12 months from 1st of Mar. 2019 to the end of Feb. 2020, eighty child and adolescent aged between 2-15 years were included in the study.They were divided into three groups: Group A (HD group), Group B (PD group) and group C (control group).*

Results: *children with CKD had a significant higher serum creatinine and MAP levels than those with AKI (583.5 vs 355.4, P= 0.001) and (98.51 vs 82.88, P= 0.022). The patients with CKD had significantly higher LVEDD (P= 0.005), IVSD (P= 0.003), LVPWD (P= 0.005), and LV mass (P= 0.001), than those suffered from AKI. significant differences in terms of Hb (P= 0.001), and MAP levels (P= 0.043), while insignificant differences were seen in blood urea (P= 0.650), and serum creatinine (P= 0.807). LVEDD, EF%, and LV mas, were significantly different between children of this group (P= 0.048, 0.009, and 0.011, respectively).*

Conclusion: *more severe chronic kidney disease (higher stages),the more severe left ventricular hypertrophy, and Left ventricular hypertrophy occurs more in prolonged duration of chronic kidney disease.*

Keywords: *Renal Failure , Left Ventricular Function ,Hemodialysis ,Peritoneal Dialysis*

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1. INTRODUCTION

Kidneys are the major excretory system in humans. The specific components of the kidney are the nephrons, the collecting ducts and a unique microvasculature (1). The multipapillary kidney of humans contains approximately 1 million nephrons, although this number varies considerably. The number of nephrons is already established during prenatal development; after birth, new nephrons cannot be developed and a lost nephron cannot be replaced. Kidney have a lots of functions (2, 3, 4):

• Glomerular filtration of plasma and tubular reabsorbtion enabling them to regulate electrolyte, acid base balance and fluid balance

• Filtering waste material from food, medications and toxic substances

• Endocrine functions like productions of rennin, productions of erythropoietin and activation of vitamine D

• Autocrine function (Production of NO, endothelins, prostaglandins, natriuretic peptides)

There are many different kind of kidney disease. Some are inherited and others develop as growing older. It occurs in the context of a wide range of underlying conditions, and the patient can be anywhere on a clinical spectrum from asymptomatic to critically unwell. It is not well understood the exact cause of many kidney diseases (5). It can be divided into: acute kidney injury or chronic kidney disease.

2. PATIENTS AND METHODS

A single center, case-control study was carried out in nephrological unit in Central Child Teaching Hospital. Over a period of 12 months from 1st of Mar. 2019 to the end of Feb. 2020, eighty child and adolescent aged between 2-15 years were included in the study.. They were divided into three groups: Group A (HD group), Group B (PD group) and group C (control group)

Group A (HD group) included 20 patients (12 males and 8 females) with ESRD, attending AL-Zohor Dialysis Unit at Child's central teaching hospital.

Group B (PD group) {PD with a conventional glucose-based lactate-buffered PD solutions} included 15 patients (8 males and 7 females)

Group C (c group) includes 35 healthy individuals (20 males and 15 females) age and gender matched after taking consent from their families with the following inclusion criteria: normotensive children, normal renal function tests, GUE, and the abdominal US of the

genitourinary tract, with no clinical evidence of CV system abnormality and absence of congenital heart diseases. Those control individuals were attending the outpatient clinic of Child central teaching hospital for mild illnesses.

From them, 10 were lost during follow up (5 from group A and 5 from the control group).

Inclusion criteria:

1. Study population aged between 2 and 15 years old with eGFR < 60 ml/min/1.73m2 for more than 3 months (the criteria for duration longer than 3 months does not apply to infants younger than 3 months, and the GFR criteria of less than 60 mL/min/1.73 m2 cannot be used in children under 2 years of age since developmental immaturity in this age group is associated with mean GFR of less than this value (6).
2. Absence of congenital, structural, or primary myocardial disease and absence of other chronic disease like DM
3. No corticosteroid treatment during study period.

Exclusion criteria:

1. Inborn error of metabolism (like cystinosis).
2. History of passive or active smoking.
3. Congenital heart diseases discovered incidentally by echocardiography.
4. Individuals lost during follow up.

Data collection and distribution of patients:

A pre-constructed data collection sheet used to collect the data through full history taking and thorough clinical examination , demographic and clinical data included patients' age, gender, duration on dialysis for CKD (for cases' group only) (<6 or ≥ 6 months.

The medical records were reviewed for cause of CKD, and patients were further divided according to their diagnoses: group I – congenital renal abnormalities, group II – acquired renal diseases, and group III_ hereditary nephropathies, and group IV_ CKD of unknown cause. The causes of AKI (pre renal, renal, post renal, acute on chronic). Mode of treatment (HD, PD) were recorded. Symptoms related to the cardiovascular system were reported. History of other chronic diseases , smoking, medications use that may affect the cardiac function.

Thorough Clinical examination, included complete cardiovascular examination, Hypertension was defined as average SBP and/or DBP >95th percentile for gender, age, and height (7).

Weight (Wt), Height (Ht), Body Surface Area (BSA) and Body Mass Index (BMI) were measured and reported. The following formulae were applied to calculate BSA, BMI and estimated GFR (eGFR) :

BSA (m^2) = [Wt (kg) X Ht (cm)] / 3600

BMI (kg/m^2) = Wt (kg) / [Ht (in meters)] ^{2}

Estimation of GFR using Schwartz formula (6):

GFR (ml/min/1.73m2) = Height in centimeters/ Serum creatinine (mg/dl) * K

k = constant based on age: 0.70 in adolescent boys

0.55 In adolescent girls and children

0.45 In full-term newborns

0.33 In preterm infants

The eGFR divided into two groups: first are those eGFR<15 ml/min/1.73m^2, second are those eGFR > 15 ml/min/1.73m^2.

Electrocardiogram (ECG) was performed in all patients to exclude arrhythmia.

Laboratory investigations were performed for all patients and blood samples obtained in the day of echocardiographic study. All routine laboratory investigations were tested for including hemoglobin levels, blood urea and serum creatinine. Anemia in children with CKD is defined when hemoglobin level was less than 11 g/dl (8).

Echocardiographic studies: one board-certified, pediatric cardiologists had done the echocardiography using Philips CX50 Ultrasound Machine (Philips Healthcare, USA, and Model 2012) with the S5-1 transducer. All cases were examined in supine and left lateral recumbent position; and the examination was done at the echo clinic in central child's teaching hospital.

Two dimensional (2-D) and M- mode echocardiography; cases were examined using the parasternal long axis, apical and 4-chamber views which provide measurements of:

1. Left ventricular end diastolic diameter (LVEDD).
2. Left ventricular end systolic diameter (LVESD).
3. Interventricular septum diameter (IVSD).
4. Left ventricular posterior wall diameter (LVPWD).
5. Left ventricular outflow tract diameter (LVOT).

6. Ejection fraction (EF %): It is the percentage of blood that is pumped out of a filled ventricle as a result of a heartbeat. Normal mean ejection fraction is 66% with ranges of 56% to 78% (9).

7. Fractional shortening (FS): It is a reliable and reproducible index of LV function, it simply looks at the degree of shortening of the left ventricular diameter between end-diastole and end-systole. Mean normal value is 36%, with 95% prediction limits of 28% to 44 % (9)

The following formulae were used to obtain:

1. LV mass (gm): is the total weight of the myocardium, derived by multiplying the volume of myocardium by the specific density of cardiac muscle, it is an indication of LVH.

LV mass = 0.8{1.04 [(LVEDD+ IVSD+ LVPWD) 3 LVEDD3]} + 0.6 (10).

2. A mean arterial pressure index was computed in a similar fashion as

MAP= {SBP+2(DBP)}/3 (11).

Statistical Analysis

The data analysed using Statistical Package for Social Sciences (SPSS) version 25. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Independent t-test (two-tailed) was used to compare the continuous variables among study groups accordingly. A level of P.value less than 0.05 was considered significant.

3. RESULTS

A total of 70 children were the subjects of this study. They were divided into three groups, case group; included 35 children with KD, group A included 20 children diagnosed with CKD, group B included 15 patients diagnosed with AKI, and group C included 35 healthy children enrolled as control group. The distribution of study groups by age, gender is shown in (**Figure 1**). The age of patienrs was ranging from 2 to 15 years with a mean of 8.42 and standard deviation (SD) of ± 3.34 years. The highest proportion of patients in group A and group B, were aged 5-9 years (50% in group A and 53% in group B), while 57.1% of those in control group were aged ≥ 10 years. Regarding gender, proportion of males was higher than females in group A (60% versus 40%) and in group B (53.3% versus 46.7%). In control group, 57.1% of subjects were females and 42.9% were males. The highest mean of BMI level (15.78) was found in control group. The comparison in mean age, BMI, and gender between study groups is shown in (**Table 1**). There were no statistically significant differences

between the groups in terms of age (P = 0.120), BMI (P = 0.093) and gender (P = 0.452). Regarding the causes of renal failure, in group A, the most frequent cause was dysplastic kidney in 5 (25%), followed by reflux nephropathy, HUS, and unknown causes which was reported in 4 (20%) of CKD patients, separately. In group B, HUS was recorded as the cause of AKI in 6 (40%) of children, while dehydration was recorded among 5 (33.3%) of patients in this group. Peritoneal dialysis was done for all patients with AKI. All of the 20 children who had CKD had undergone hemodialysis, and the duration of hemodialysis was < 6 months for 16 (80%) of them, and ≥ 6 months for the other 4 (20%) as shown in (**Table 2**). The comparison between case group (CKD and AKI) and control group by certain laboratory parameters and echocardiographic parameters is shown in (**Table 3**). In this study, the patients in case group had a significant lower mean Hb level and higher blood urea, serum creatinine, and MAP levels compared with children in control group (10.01 vs 12.18, P= 0.001; 29.46 vs 10.13, P= 0.001; 485.7 vs 96.42, P= 0.001; and 89.81 vs 74.42, respectively. Regarding echocardiographic findings, there were significant differences between case and control groups in regards to LVEDD (3.62 vs 3.32, P= 0.001), IVSD (0.75 vs 0.64, P= 0.012), LVPWD (0.72 vs 0.66, P= 0.003), and LV mass (61.16 vs 54.32, P= 0.011). There were differences in means of LVESD, LVOT, EF%, and FS% between case and control groups, but these differences were not significant (P= 0.065, 0.967, 0.431, and 0.121, respectively. It was clear that children with CKD had a significant higher serum creatinine and MAP levels than those with AKI (583.5 vs 355.4, P= 0.001) and (98.51 vs 82.88, P= 0.022), while there were no significant differences between group A and group B in regards to Hb (P= 352) and blood urea (P= 0.603). The patients with CKD had significantly higher LVEDD (P= 0.005), IVSD (P= 0.003), LVPWD (P= 0.005), and LV mass (P= 0.001), than those suffered from AKI. Insignificant differences (P > 0.05) were seen between group A and B regarding IVSED, LVOT, EF%, and FS%. This comparison is shown in (**Table 4**). The comparison in group A regarding the duration of hemodialysis (< or ≥ 6 months), is shown in (**Table 5**). Concerning the difference in laboratory & clinical parameters between the patients with CKD, there were significant differences in terms of Hb (P= 0.001), and MAP levels (P= 0.043), while insignificant differences were seen in blood urea (P= 0.650), and serum creatinine (P= 0.807). LVEDD, EF%, and LV mas, were significantly different between children of this group (P= 0.048, 0.009, and 0.011, respectively). Insignificant differences (P > 0.05) were seen in other echo findings between the patients of this group.

Table 1 Demographic characteristics of the studied groups

Variable	Group A (n=20)		Group B (n=15)		Group C (n=35)		P. value
	No.	%	No.	%	No.	%	
Age							
< 5	2	10	6	40	2	5.7	0.002
5--9	10	50	8	53.3	13	37.1	
≥ 10	8	40	1	6.7	20	57.2	
Mean ± SD	9.12 ± 3.17		8.97 ± 2.44		9.42 ± 2.78		0.12
Gender							
Male	12	60	8	22.9	15	42.9	0.452
Female	8	40	7	20	20	57.1	
BMI kg/m2							
Mean ± SD	16.08 ± 1.90		14.56 ± 1.52		15.12 ± 3.10		0.093

Table 2. Causes of renal failure in CKD and AKI groups

Variable		No.	%
CKD (n = 20)	SSK	5	25.0
	Reflux N.	4	20.0
	HUS	4	20.0
	Nephrotic Syndrome	2	10.0
	Medullary N.	1	5.0
	Unknown	4	20.0
AKI (n=15)	HUS	6	40.0
	Dehydration	5	33.3
	Sepsis	3	20.0
	GN	1	6.7

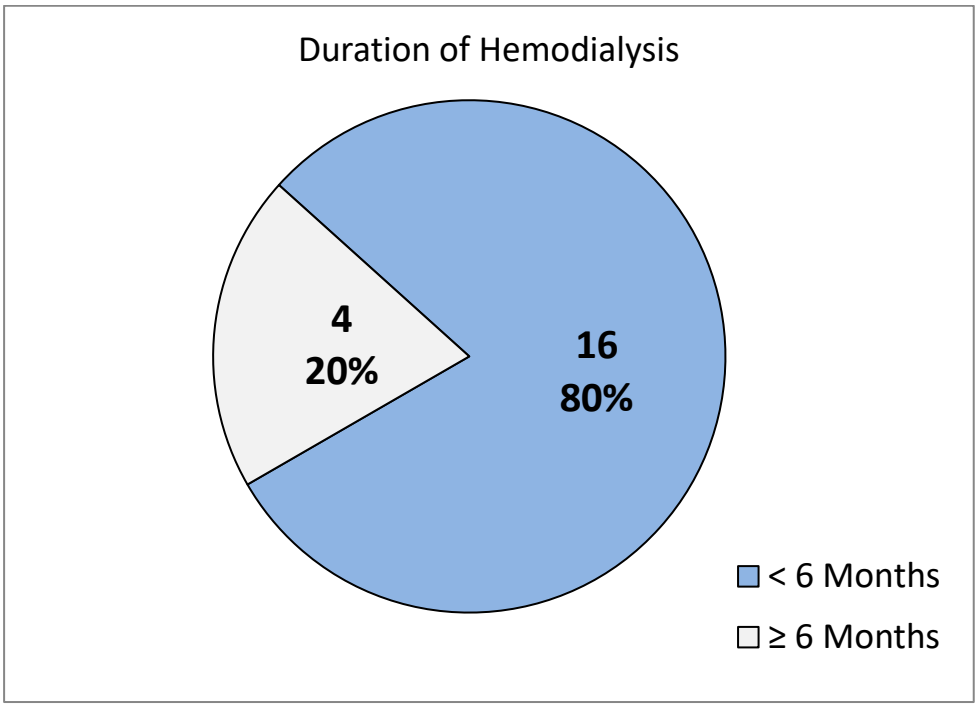

Figure 1. Distribution of CKD patients by duration of hemodialysis

Table 3. Comparison of Laboratory and echocardiographic parameters of cases and controls groups

Parameter	Cases (n=35)	Control (n=35)	P. Value
	mean ± SD	mean ± SD	
Hemoglobin	10.01 ± 1.79	12.18 ± 0.70	0.001 sig
Blood Urea	29.46 ± 9.43	10.13 ± 1.94	0.001 sig
S. Creatinine	485.7 ± 175.9	96.42 ± 22.12	0.001 sig
MAP	89.81 ± 21.30	74.42 ± 5.11	0.001 sig
LVEDD	3.62 ± 0.29	3.32 ± 0.41	0.001 sig
LVESD	2.03 ± 0.30	2.08 ± 0.34	0.065 ns
IVSD	0.75 ± 0.10	0.64 ± 0.13	0.012 sig
LVPWD	0.72 ± 0.14	0.66 ± 0.13	0.003 sig
LVOT	1.39 ± 0.21	1.37 ± 0.24	0.967 ns
EF%	68.58 ± 9.45	70.68 ± 4.80	0.431 ns
FS%	38.84 ± 2.55	39.20 ± 3.99	0.121 ns
LV Mass	61.16 ± 19.95	54.32 ± 18.03	0.011 sig

SD: standard deviation. sig: significant. ns not significant

Table 4. Comparison of Laboratory and echocardiographic parameters of cases and controls' groups

Parameter	Group A (n=20)	Group B(n=15)	P. value
	mean ± SD	mean ± SD	
Hemoglobin	10.26 ± 1.79	9.68 ± 1.80	0.352 ns
Blood Urea	30.11 ± 12.24	28.60 ± 2.33	0.603 ns
S. Creatinine	583.5 ± 149.4	355.4 ± 114.04	0.001 sig
MAP	98.51 ± 24.10	82.88 ± 16.38	0.022 sig
LVEDD	3.99 ± 0.95	3.42 ± 0.15	0.005 sig
LVESD	2.29 ± 0.34	2.28 ± 0.15	0.784 ns
IVSD	0.74 ± 0.98	0.67 ± 0.06	0.003 sig
LVPWD	0.76 ± 0.15	0.69 ± 0.07	0.005 sig
LVOT	1.92 ± 0.22	1.89 ± 0.19	0.123 ns
EF%	59.37 ± 11.09	64.53 ± 5.79	0.085 ns
FS%	36.20 ± 2.74	35.36 ± 2.29	0.335 ns
LV Mass	74.79 ± 21.57	56.41 ± 8.74	0.001 sig

SD: standard deviation. sig: significant. ns not significant

Table 5. Comparison of Laboratory , echocardiographic and clinical parameters in group A according to duration of hemodialysis

Parameter	HD ≥ 6 Months (n=16)	HD < 6 Months (n=4)	P. value
	mean ± SD	mean ± SD	
Hemoglobin	7.20 ± 1.90	10.50 ± 1.47	0.001 sig
Blood Urea	29.46 ± 11.74	32.70 ± 15.78	0.650 ns
S. Creatinine	587.7 ± 151.2	566.5 ± 163.1	0.807 ns
MAP	101.22 ± 25.87	95.66 ± 16.99	0.043 sig
LVEDD	3.97 ± 0.15	3.10 ± 0.59	0.048 sig
LVESD	2.60 ± 0.32	2.34 ± 0.39	0.179 ns
IVSD	0.74 ± 0.12	0.71 ± 0.08	0.481 ns
LVPWD	0.74 ± 0.16	0.63 ± 0.09	0.115 ns
LVOT	1.79 ± 0.23	1.86 ± 0.24	0.656 ns
EF%	55.78 ± 11.66	62.75 ± 6.84	0.009 sig
FS%	36.65 ± 1.75	34.37 ± 5.15	0.140 ns
LV Mass	78.83 ± 16.28	59.51 ± 28.19	0.011 sig

SD: standard deviation. sig: significant. ns not significant

4. DISCUSSION

From the current study, we found that in case group: the number of males in group A (60%), and number of females are (40%), in group B males (53.3%), females are (46.7%), this is consistent with many studies including Harambat et al (5) as the incidence and prevalence of CKD is greater in males than females because of the higher frequency of CAKUT in males and with Joel Neugarten et al (12) as male gender is associated with an increased incidence of hospital-associated AKI. But in contrast to CKD where female gender is reno-protective, the direction of sexual dimorphism has been reported to be reversed in several specific forms of acute kidney injury in humans, including contrast-associated nephropathy, aminoglycoside nephrotoxicity and cardiac surgery-associated AKI (13). On the basis of these observations, the KDIGO AKI guideline concludes that female gender is a risk factor for AKI (13). This conclusion, however, was qualified by the observation that males predominate in reports of AKI complicating infections and other community acquired forms of AKI. In concern to BMI in study patients, there was no significant difference (P=0.093) between case group and control group, this was consistent with Gao et al (14) and Rodig et al (15). The BMI does not reflect real body composition and fat mass, and a patient who has an appropriate BMI for height or chronologic age may not have an ideal body composition. (16). Regarding the causes of renal failure in our study, the highest proportion of patients among case group had CKD due to congenital renal abnormalities; dysplastic kidney is found in 25% of them. This is nearly consistent with Dogan et al (17) and Ataei et al (18). In AKI, HUS was recorded as the most frequent cause (40%) while dehydration was recorded among 33.3% of patients. This consistent with Rabson et al (19). The incidence of HUS is high proportional to dehydration in school age children, a possible contributing factor might be that the prevalence of STEC is high, a known source of infection. In regard to MAP in study group; in control group, all children were normotensive, with MAP was 89.81 vs 74.42 with a significant association with increase blood pressure (P=0.001) in CKD. This is consistent with many studies including Dillon et al (20) and Iman et al (21) In contrast to AKI, initiation of peritoneal dialysis (PD) often results in blood pressure (BP) control, this consistent with Saldhana et al (22) in which they conclude that blood pressure was controlled better in PD than in HD patients. Better fluid volume control and greater clearance of vasoconstrictor factors compared with HD have been considered responsible for the initial improvement.

Mean Hb in case group and control group were (10.01 vs 12.18) with a significant association between KD and hemoglobin level (P=0.001). This also consistent with many studies including Dry et al (23), Yilmaz et al, (24) and Iman et al (21) which showed that CKD patients presented with anemia (renal anemia) due to inappropriate levels of erythropoietin as the main cause. In contrast to AKI , anemia is multifactorial, since in one-quarter of the patients it precedes onset of renal failure (22). Concerning LV Doppler diastolic velocities, they were significantly impaired in case groups compared to healthy children, high LVM (61.16 vs 54.32) and the association was statistically significant (P=0.011). Our results agreed with Hyashi et al (25) and Sood et al (26) who reported that LV diastolic dysfunction was a prognostic factor for HD patients and added that 2D Echo underestimate LV function. Regarding LEVDD, it was significantly higher in HD patients compared to PD patients (p=0.005), this was consistent with Paneni et al (27) who reported that LV dysfunction was significantly higher in HD patients compared with PD patients, particularly in the presence of a brachial arteriovenous fistula. However, most of the available studies have focused on LV function in dialysis patients; data about right ventricular (RV) function are lacking. Due to some difficulties with echocardiographic evaluation of the RV owing to the complex anatomy and retrosternal localization, assessment of RV function with 2-dimensional and tissue Doppler imaging (TDI) is an accurate and reproducible method of detecting preclinical ventricular abnormalities (28). The global LV systolic function was normal in our patients group, there was no statistical significant association (P=0.065), Our results also agreed with Rathod et al who concluded that renal patients have a higher incidence of both systolic and diastolic dysfunctions, and added that diastolic dysfunction occurred earlier than the systolic dysfunction (29). It is also consistent with Huis, et al (p value = 0.12) (30), Iman et al (21) (p value = 0.189), and Dogan, et al (17) (P. value: non-significant) Left ventricular hypertrophy; as an adaptive response to chronic pressure or volume overload, is a beneficial response initially, because it maintains systolic function, allows an increase in working capacity, and reduces wall stress and energy consumption. Persistent LVH, however, may become detrimental, mainly because it reduces the coronary perfusion reserve and alters diastolic left ventricular function (22). In concern to the means of IVSD and LVPWD, they were significantly thicker in case group when compared to control group (P value = 0.003), this work was also in agreement with de Bie et al (31) who reported diastolic dysfunction as a prevalent event among their uremic patients

and also concluded that LV mass and PWV were the only markers of diastolic dysfunction in their CRF patients . And it is consistent with Vilija et al (p value < 0.0001) (19) and Iman et al (p value = 0.0001) (21). Also, it was found that PD patients demonstrated a statistically significant both IVSEDD (p<0.001) and PWEDD (p<0.001). This is consistent with Duygu Ersan Demirci et al (32), that is because high levels of inflammatory cytokines may influence LV diastolic dysfunction directly by altering calcium handling protein concentration and function. In regard to duration of CKD area, the prevalence of LVH and the higher LV dysfunction advances in patients undergoing maintenance dialysis for more than six months than that among patients who had CKD less than six months' period with a mean (78.83 versus 59.51) with a significant association (P=0.011) and LVEDD (P=0.048). This is consistent with Mitsnefes et al (33) who found that 19% of CKD children had LVH and LV dysfunction at baseline; the prevalence had increased to 39% at 2-year follow-up.

5. CONCLUSION

1. Left ventricular hypertrophy is a common cardiovascular complication of patient with acute kidney injury and chronic kidney disease, and the more severe chronic kidney disease (higher stages),the more severe left ventricular hypertrophy.

2. Left ventricular hypertrophy occurs more in prolonged duration of chronic kidney disease.

3. High risk of cardiovascular complication in individuals with PD is related to several factors. These comprise traditional and non-traditional risk factors; toxic, metabolic, and vascular factors; and considerations like hypervolemia, hypertension, and anemia. It has been demonstrated in this study and several other studies that LV hypertrophy, LV dilatation and diastolic dysfunction can develop as a result of these factors.

4. Early changes in diastolic dysfunction is LVPWD and IVSD in both acute and chronic renal failure

5. Systolic function is not impaired in both acute and chronic renal failure.

Ethical Issues: All ethical issues were approved by the authors from the Iraqi Ministry of Health. Verbal and signed informed consents were obtained from all patients who included in the study during their first visit.

Conflict of interest: None

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