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ORIGINAL ARTICLE

Plasma Fibrinogen and Echocardiography as Diagnostic Tool for Left Ventricular Hypertrophy among CKD Patients

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ABSTRACT

Background: Left ventricular hypertrophy is the most common cardiac event associated with chronic kidney disease.
Aim: To detect LVH by echocardiography among CKD patients and co-relationship between plasma fibrinogen and left ventricular mass index.
Study Design: Observational study.
Methodology: It was an observational study with total of 62 CKD patients enrolled through convenience sampling. Patient's age ranged from 35-65 years. Almost 3ml of blood was taken for measuring serum creatinine and fibrinogen. Blood was centrifuged for plasma separation than stored at -20°C. ECG findings were confirmed by echo in all enrolled patients. Data was evaluated by SPSS v.24. The results were presented as counts (percentage), means and standard deviation as appropriate. Spearman correlation was applied to check the correlation of variables.
Results: Echo confirmed that LVH was found in 41 (66.1%) patients with systolic dysfunction. There was a high level of plasma fibrinogen in 73% of enrolled participants. No correlation between plasma fibrinogen and LVMI was found.
Practical Implication: Current project helped health providers to diagnose cardiac event at an early stage among patients of kidney failure on echo findings along-with plasma fibrinogen levels thus the adverse outcomes could be prevented or delayed.
Conclusion: It was concluded that echocardiography is a helpful diagnostic tool as it confirms ECG abnormalities seen in hospitalized CKD patients. All CKD patients should have their echocardiography done. Plasma fibrinogen levels were raised with declining renal function. Thus combination of both echo and fibrinogen levels among CKD are handful investigations for LVH.
Keywords: Echocardiography, Chronic Kidney Disease, Left Ventricular Hypertrophy and Plasma Fibrinogen.

INTRODUCTION

Literature review revealed that when abnormality of kidney structure and function (GFR<60ml/min/1.73m^2) is present for more than 3 months than Chronic kidney disease (CKD) is labeled[1]. Classically, albuminuria precedes deterioration in renal functional as shown by decrease in GFR[2]. Chronic kidney disease (CKD) is a common health issue in developing countries according to many epidemiological surveys. Unfortunately, according to one estimate, incidence of CKD is 14% among Pakistani population, being highest in Punjab province followed by sindh[3,4]. Literature review revealed that incidence of end stage renal disease according to age is 229 per million population while more than one lac patients/year receive renal replacement therapy in India.[5,6] Diabetes and hypertension are the silent killers of humans. They both affect kidneys and result in CKD later in life.[5] Obesity is a mother cause of many diseases like diabetes and hypertension thus increases CKD chances among patients and ultimately cause glomerulosclerosis. Factors that cause renal injury include nephrotoxic drugs, alcohol, male gender and high protein diet[7].

CKD is a progressive and irreversible disease that result in loss of nephron function due to renal vasculature alterations and cell fibrosis. Previous study revealed that uremic signs and symptoms appear when at least two third of kidney function is lost[8]. Literature has shown that patients having End-Stage Renal Disease die early and have short life span. One study estimated that 221/1000 patients on dialysis die annually with 20% deaths contributed by cardiac issues among renal patients[8,9].

Left ventricular hypertrophy (25-70%) is the most common cardiac event associated with chronic kidney disease[8]. An association between cardiac and kidney functions exit. Any pathology involving heart or kidney usually results in cardio-renal Syndrome (CRS)[10]. Pathological factors like inflammation along-with increased fibrinogen levels due to decreased renal functions raises the risk for cardio-vascular disease[9].

Previous studies revealed that Sokolow Lyon index has a high (90%) specificity with low (40%) sensitivity for detecting cardiac pathology like LHV that is confirmed by echo later[11]. Unfortunately, being an over-burdened country for CRS, we need correct and early diagnosis of cardiac origin among CKD patients. Echo is a common investigation for cardiac issues nowadays. Due to lack of local data on the significance of Echo and plasma fibrinogen levels as diagnostic tool for LVH, we planned current study. Thus this project helped health providers to diagnose cardiac event at an early stage among patients of kidney failure on through echocardiography thus the adverse outcomes could be prevented.

The objective of the study was to detect LVH by echocardiography among CKD patients and co-relationship between plasma fibrinogen and left ventricular mass index.

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METHODOLOGY

It was an observational study with sample size of 62 patients enrolled through convenience sampling. Population studied was chronic kidney disease patients with age ranged from 35-65 years. Almost 3ml of blood was taken for measuring serum creatinine and fibrinogen. Blood was centrifuged for plasma separation than stored at -20°C. ECG findings were confirmed by echo in all enrolled patients. Plasma fibrinogen levels were measured by using Human fibrinogen ELISA kit. Five serum storage tubes were taken. These were labelled as 1,2,3,4,5. Standard was labelled as 0.50µl standard dilution was taken in tubes labelled as 1,2,3,4,5. 100µl standard was added to first tube, then 100 µl was taken out from the first tube into the second. 50 µl was transferred from the second tube to the third tube. Now same amount was transferred from third to fourth and then from fourth to fifth tube. So there were five calibrators.

40 µl sample dilution was added to testing sample well, 10µl testing sample was added to the testing sample well. It was mixed gently without touching the well wall. 50µl calibrators from five calibrators were added to each well. Testing sample well was covered with adhesive strip and was incubated for 30 minutes at 37^{o}C.

Washing buffer was made by adding 5 ml wash solution to 100 ml distilled water. Testing sample well was uncovered, liquid was discarded, 300 µl washing buffer was added to every well for washing. Testing sample wells were dried. 50 µl HRP (horse Reddish Per Oxide) was added to each dried well. Incubation was done for 30 min at 37°C. Washing was repeated again, wells were dried.

50 µl chromagen solution A and 50 µl chromogen solution B was added to each well. It was incubated for 15 min at 37°C. Appearance of blue colour was seen in each well. 50 µl stop solution was added to each well, the colour change was from blue to yellow. Reading was taken from Stat Fax 303 strip reader. Patients with ECG abnormalities, receiving digitalis therapy, transplant patients were ruled out from study. Written informed consent with demographic data was taken.

Statistical analysis: Data was evaluated by using SPSS v.24. Qualitative parameters were presented as frequencies and percentages. Median and interquartile range (IQR) given for non-normally distributed variables (age). Quantitative variables were presented as Mean ± SD. Spearman correlation was applied to check the correlation of variables. P value of < 0.05 was considered significant. .

RESULTS

Age ranged from 35 to 65 years. Other parameters like gender, BMI and CTSI were shown as frequency and percentage in table-1. Males were 58% while rest (42%) were females in study.

Table-1: Demographic data (n=62)

Parameters	Groups	Frequency (%)
Age (years)	35-45	21(33.9%)
	46-55	17(27.4%)
	56-65	24(38.7%)
	Median IQR for Age	54.50 (41.75-60)
BMI (kg/m^2)	Normal Weight	7(11.3%)
	Over Weight	26(41.9%)
	Obese	29(46.8%)
	Mean ± SD	27.85±3.88

Different types of hypertrophies were demonstrated by echo. Our results showed concentric hypertrophy in 27(43.5%) patients as shown by Various echocardiographic parameters were presented as frequency in table-2.

Figure-1: Concentric Hypertrophy on Echocardiography

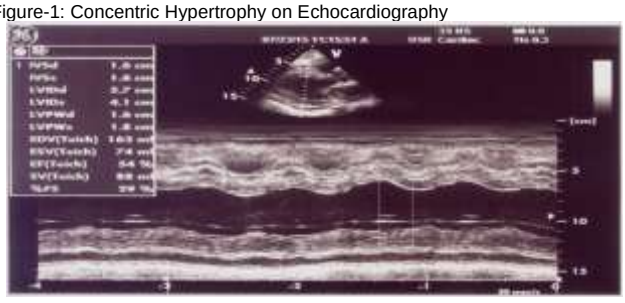

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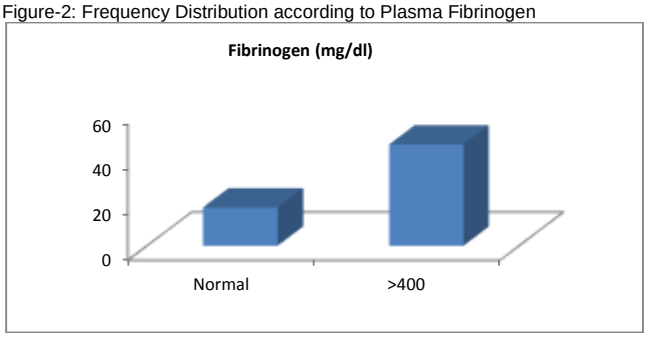
Table-2: Frequency distribution of echocardiographic parameters

Variable	Status	Frequency
LVH	Positive	41
	Negative	21
LVMI For Female (g/m^2)	43-95 (-)	9
	> 95 (+)	17
Mean ± SD	117.115±50.04	
LVMI For Male (g/m^2)	49-115 (-)	12
	> 115 (+)	24
Mean ± SD	132.25±47.05	
RWT (Hypertrophy)	< 0.42 (N)	14
	≤ 0.42 (E)	16
	≥ 0.42 (C)	27
	≥ 0.42(CR)	05
EF	Normal	28
	<45%	24
	>70%	10

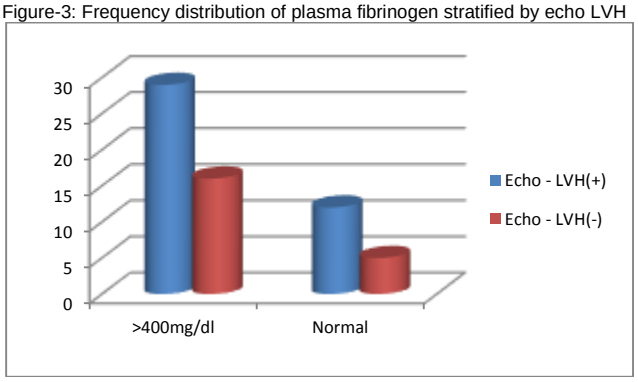
Distribution of participants on basis of plasma fibrinogen levels was presented as frequency as shown by Figure-2. Normal fibrinogen level ranges from 150-400mg/dl.

Figure-2: Frequency Distribution according to Plasma Fibrinogen



Echo LVH and raised plasma fibrinogen was found in 29 (70.73%) CKD patients. Echo LVH was stratified for plasma fibrinogen as shown by figure-3.

Figure-3: Frequency distribution of plasma fibrinogen stratified by echo LVH



Among CKD patients, data was stratified for various types of hypertrophies among stage -3 and 4 CKD as shown by table-3. Correlation between plasma fibrinogen and other echo parameters was shown by table-4.

Table-3: Pattern of LVH stratified by CKD Stages

LVH	Stage-3	Stage-4
CH	27.77%	61.53%
EH	25%	26.92%
CR	13.85%	0
Normal	11(30.55%)	03(11.54%)

Table 4: Correlation between plasma fibrinogen and other echo parameters

Correlation of plasma fibrinogen	Rho	p value
Age	-0.039	0.76
BMI	0.316	<0.001 *
Serum creatinine	0.038	0.76
eGFR	-0.121	0.34
LVMI=Left ventricular mass index	-0.099	0.44
LVEF	0.104	0.42
RWT	0.193	0.13

*Statistically significant

DISCUSSION

According to literature review echo is an investigation of choice to get direct information concerning left ventricular wall thickness and chamber size[12]. In the present study, almost 66.1% CKD patients

had LVH on echo. Our results were similar to many other studies that showed more than 50% LVH were identified by echo[12,13].

Our results showed that 80.76% patients of CKD stage 4 while 55.55% stage 3 patients have LVH. Similar results have been reported by previous studies that documented higher prevalence of hypertrophy (34-80%) with declining renal function among CKD patients.[14] It has been reported that wide variation in its prevalence has been contributed by non-availability of medical record and use of different methodology for calculating LVM[15].

One previous study reported that plasma fibrinogen levels were raised in ESRD patients undergoing dialysis and increased fibrinogen levels were associated with decreased ejection fraction indicating that it was a better marker of myocardial involvement in these patients. This can be due to more pronounced inflammation in ESRD patients[16]. Whereas our study population comprises of stage 3 and stage 4 CKD patients. However another study, first time reported that significant positive correlation between LVMI and plasma fibrinogen in pre-dialysis CKD patients. This finding may be attributed to high prevalence (78%) of LVH and diabetes in the study population and higher prevalence of vascular disease among diabetics[17]. Their results were paradoxical to our results that showed negative relationship between LVMI and plasma fibrinogen.

Present study showed that mean LVMI was non-significantly greater in males than females. It has been documented that LVMI increases with age, male gender and body size.[16] Present results were in line with above mentioned study that showed higher percentage of LVMI (79.16%) among 56-65 years age group. However, LVMI was significantly higher in patients with LVH in our study. Similar results were documented in one study that showed patients having high LVMI with LVH[17,18].

Left ventricular relative wall thickness (RWT) was calculated. In present study, majority of CKD patients had concentric hypertrophy (41.93%). Similarly, it has been documented that this is a frequent abnormality with regard to cardiac geometry[18]. Presently, concentric hypertrophy` increased with declining renal function and increasing CKD stage (27.7% in CKD-3 and 61.53% in CKD-4). This finding was similar to the results of another study that reported increasing stage of CKD results in higher concentric hypertrophy[19,20].

Our results showed that plasma fibrinogen level was insignificantly greater in CKD stage 4 compared to stage 3 (p=0.13). Similar results have been demonstrated by previous studies thus in line with our results[20-22]. Many studies previously showed insignificant correlation between plasma fibrinogen and LVMI. Similarly our results showed insignificant relation between them as well thus in line with above mentioned study (r= -0.09, p= 0.44)[23].

Limitations: Single centre study with financial constrains and limited resources.

CONCLUSION

It was concluded that echocardiography is a helpful diagnostic tool as it confirms ECG abnormalities seen in hospitalized CKD patients. All CKD patients should have their echocardiography done. Plasma fibrinogen levels were raised with declining renal function. Thus combination of both echo and fibrinogen levels among CKD are handful diagnostic investigations for LVH.

Author's contribution: HH&MS: Overall supervision, write up and literature review, **HNL&SK:** Statistics application, analysis literature review, help in write up.

Conflict of interest: None

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Ethical permission: Approval was obtained from IRB.

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