

## Prevalence and Predictor of Cardio Renal Syndrome in Dilated Cardiomyopathy

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**Abstract:** Around 50 % of deaths in patients with renal failure is heart failure caused by Cardiovascular Disease. Epidemiology of the diseases affecting the heart and kidney is necessary for understanding various types of cardio renal syndrome. It is useful to calculate the burden of the disease in the community, natural history, morbidity, risk factors and mortality of Cardiorenal syndrome. We aimed to study the clinical profile of dilated cardiomyopathy patients in heart failure presenting as cardio renal syndrome and to assess the predictors of mortality in dilated cardiomyopathy heart failure patients with cardio renal syndrome. 54 known dilated cardiomyopathy patients admitted for heart failure who show elevated renal parameters without prior renal dysfunction were enrolled in the study.

**Results:** Mean Hb at admission for pts with readmissions was 10.23 grams /dl .Mean level. of e GFR associated with increased mortality was 23.55 ml/min. Patients with Oliguria at admission had 42.1 % mortality .Patients with oliguria had 68.42 % readmissions . Mean level of e GFR associated with increased mortality was 23.55 ml/min, Mortality was 20 %. Mortality was more in patients above 60Years, who presented with NYHA class IV symptoms on admission, oliguria at Presentation and left ventricular ejection fraction less than 30 %.

**Conclusion:** Cardiomyopathy patients with SHT and CAD have GFR less than 30ml/minute. patients GFR less than 30 ml/minute presented with NYHA class IV symptoms. Readmissions was more when e GFR less than 30 ml/minute, known hypertensive, previous myocardial infarction and cardiomyopathy, anemic patients and age above 50. There was no correlation between LV systolic function and readmissions. The predictors of mortality in cardiomyopathy developing cardio renal syndrome were age above 60 years, cardiomyopathy with previous history of MI, NYHA class IV symptoms on admission, oliguria and LVEF less than 30 % at the time of admission.

**Keywords:** CRS, cardiomyopathy, mortality predictors, LVEF

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### I. Introduction

The common condition seen in daily life is Heart failure. The society suffers from the economic burden caused by the morbidity and mortality of the cardiac failure. The cardio renal syndrome (CRS) is a disorder in which kidney as well as heart are affected at the same time and the disease process of one organ will have influence on the disease progression in the other organ. Acute or chronic dysfunction of heart or kidney induce acute or chronic dysfunction in the other organ. Around 50 % of deaths in patients with renal failure is caused by Cardiovascular disease .Progression of heart failure and atherosclerosis was increased in patients with chronic kidney disease. Epidemiology of the diseases affecting the heart and kidney is necessary for understanding various types of cardio renal syndrome. It is useful to calculate the burden of the disease in the community, natural history, morbidity, risk factors and mortality of cardio renal syndrome.[1]

Very few trials and registries have prospectively monitored renal parameters and its function during hospitalization or after the patients got discharged. 3 Patients admitted for heart failure (HF) and decreased left ventricular ejection fraction (LVEF) who shows evidence of worsening renal function (WRF), after the discharge of the patient, have not been studied well. The available data indicating the renal function in Heart failure patients is based mainly on retrospective analyses, [3,4,5] cohort and case-control studies or, [6,7,8] post hoc reviews of the data base of the clinical trials, 10,11 and meta-analyses of various studies. 2. Most studies assessed renal dysfunction during hospitalization [5,6,7,8]

The trial of Efficacy of Vasopressin Antagonism in Heart Failure. Outcome study with Tolvaptan (EVEREST) gives a detailed description of the patients admitted for Heart failure in relation to the emergence of renal Dysfunction at the time of hospitalization or after the patient was discharged and its impact on the outcomes. In the studies of left ventricular dysfunction (SOLVD) study, early development of renal failure was correlated with elevated mortality. Patients who took Enalapril had significant survival benefit in spite of the

early renal dysfunction.<sup>[9]</sup>Diuretics which are used in the treatment of heart failure with decompensation were associated with improved survival in spite of the worsening renal function.

In HF patients, increase in blood urea was associated with increased death rates. This mortality effect was not dependent on the serum creatinine and glomerular filtration rate (GFR) values. This increase in blood urea nitrogen seen in patients with reduced renal perfusion was due to pre renal azotemia<sup>[10]</sup>

## **II. Aim Of The Study**

To study the clinical profile of dilated cardiomyopathy patients in heart failure presenting as cardio renal syndrome, to study the implications of cardiac and clinical variables in the outcome of cardiorenal syndrome and to assess the predictors of mortality in dilated cardiomyopathy heart failure patients with cardio renal syndrome.

## **III. Materials And Methods**

### **3.1 Study setting:**

Department of cardiology, Govt. Villupuram medical college, Villupuram.

### **3.2 Study design:**

Single centre, prospective observational study.

### **3.3 Period of study:**

Study was conducted between December 2015 to March 2016.

### **3.4 Sample size:**

54 known dilated cardiomyopathy patients admitted for heart failure who show elevated renal parameters without prior renal dysfunction.

### **3.5 Inclusion Criteria**

Patient admitted with symptoms of heart failure with dilated left ventricle (LVEDD more than 2 standard deviation of the prescribed value for age and sex) in coronary care unit showing more than 0.3 mg /dl raise in serum creatinine from the baseline value during the hospitalization period<sup>[11]</sup>

### **3.6 Exclusion Criteria**

Age less than 18 years. Known chronic kidney disease, Atrial fibrillation, Atrial flutter, Atrial tachycardia, Ventricular tachycardia and fibrillation, Cardiogenic shock. Patient were explained about the study and consent was obtained from each patient. All patients more than 18 years of age admitted with symptoms of heart failure in the coronary care unit in the department of cardiology in the government Villupuram medical college hospital were subjected to renal function test like blood urea, serum creatinine. Patients who show 0.3 mg / dl increase in the serum creatinine from the baseline were taken up for the study. Renal parameters were checked at the time of discharge or at the end of 7 days. Again renal parameters were checked at a interval of one month.<sup>[12]</sup> Patients were followed for recurrent admissions in the coronary care unit and also mortality during the index admission or in the follow up period. Patient were subjected to detailed cardiac examination including vital signs. Mean arterial pressure was calculated by adding 1/3 pulse pressure to the diastolic pressure. Heart failure was described according to NEWYORK HEART ASSOCIATION (NYHA) criteria. Patients admitted for heart failure showing elevated renal parameters were subjected to baseline hematology like total count, hemoglobin. Biochemical analysis for estimation of blood urea, serum potassium and serum creatinine were done. Estimated glomerular filtration rate (eGFR) was calculated by the Modification of Diet in Renal Disease( MDRD ) formula.<sup>[13]</sup> Chest X ray were taken. Patients showing gross cardiomegaly were excluded from the study. Echocardiography was done with the Esoate machine My Lab 30 GOLD model with 3-5 mega Hertz frequency adult probe. Two dimensional echo, Motion mode echo, colour Doppler, pulse wave 34 Doppler and continuous wave Doppler were used for detailed echocardiography. Regional wall motion abnormality was observed in Left parasternal long and short axis as well as apical four chamber views. Left ventricle dimensions were measured in end diastole and end systole and ejection fraction was calculated. Fractional shortening was noted.<sup>[14]</sup> Left ventricular diastolic function was measured in apical four chamber view using pulse wave Doppler. The cursor was placed over the medial annulus of the mitral valve and the pulse wave doppler was obtained. the height of the E wave and A wave was measured and compared.

Right ventricular systolic function was assessed by Trans annular planar systolic excursion of the Tricuspid valve. This is measured in M mode with cursor at the lateral annulus of the tricuspid valve. TAPSE value less than 16 mm was considered Right ventricular systolic dysfunction.<sup>[15]</sup> Mean pulmonary arterial pressure was calculated by adding Right atrial pressure to the peak tricuspid regurgitation velocity obtained in the apical four chamber view.<sup>[16]</sup>

### 3.7 Analysis

Descriptive statistics were expressed using mean and standard deviations for continuous variables and frequency and percentage for discrete variables. Means of continuous variables were compared by Independent sample t test. Discrete variables were compared by chi square test or Fisher Exact test whichever applicable. Repeated measure ANOVA is applied to compare three occasions. The level of statistical significance was 0.05. Statistical analyses were performed using SPSS statistical software version 19.0.39

### IV. Results

In the study maximum age of the patient was 75 and the minimum age was 21 years with mean age of 48.89 years. Minimum weight seen in study group was 47 kg and the maximum weight was 85 kg with mean body weight being 69.26 kg. Minimum mean arterial pressure was 68 mmHg and the maximum mean arterial pressure was 105 mmHg with mean value of 85.72 mmHg. The hemoglobin value was maximally 14 grams/dl and minimally 9grams/dl with mean value of 11.11 grams/dl. Minimum baseline blood urea value was 51 mg/dl and maximum value was 102 mg/dl with mean value of 72.13 mg/dl .Maximum baseline serum creatinine value was 3 mg/dl and the minimum value was 1.5 mg/dl with mean level of 2.14 mg/dl. Estimated glomerular filtration rate was minimally 17 ml/minute and maximally 58 ml/minute at the baseline with mean value of 33.43ml/minute. Mean serum potassium value at the time of admission was 4.77 mg/dl with maximum value being 5.5 mg/dl and the minimal value being 3.8 mg/dl.

**Table – 1:** Distribution of echo variables

Variables	Minimum	Maximum	Mean	Std. Deviation
Left Ventricle end diastolic diameter	4.5	6.4	50670	1.3204
Left Ventricle EJECTION FRACTION	22	35	30.00	3.359
Pulmonary artery systolic pressure	22	52	33.80	6.688
TAPSE	10	63	17.85	6.825

**Table - 2 :** Distribution Of Follow Up Variables

Variables	Minimum	Maximum	Mean	Std. Deviation
UREA 1	38	84	57.57	11.878
CREATININE1	1.0	2.6	1.691	0.3968
estimated GFR1	19	88	44.5	14.406
UREA 2	0	71	42.5	14.984
CREATININE2	0	2.1	1.241	0.4672
estimated GFR2	0	99	54.06	22.616

Maximum number of patients (33.33%) were in the 41 to 50 age group. Minimum patients (16.7 %) were between 51 to 60 years. 22.2% were above 61 years. Patients were in NYHA class III heart failure in 70.4 % of the patients. 29.6 % were in NYHA class IV. Patient had previous history of myocardial infarction in 63 % (34 out of 54)of cases. Dilated cardiomyopathy was the etiology for heart failure in 33 % (20 out of 54)of the cases. Diabetes mellitus was present in 46.3 % of the studied patients.

Systolic hypertension was seen in 31.5 % of the patients.47Regional wall motion abnormality was seen in 63 % of the cases. Readmission rate was 48.1 % among the study population. Death rate was 20.4 % among the study population. Readmission was seen in 26 out of the 54 patients (48.1 % ).20.4 % of the patient died during the study period (11 out of 54)patients. 3 patients died during the index hospitalisation. In our study 11 were above 61 years of age out of 27 patients (40.74 %)with eGFR less than 30 ml/minute. Among the patients with eGFR 30 to 60 ml/minute 13 were in the age group 41 to 50 years(48.18%).This was significant statistically ( p<0.01 )In the female group 14 patients (77.77 %) were having eGFR less than 30 and 4 patients had eGFR 30-60ml/minute. Among the male patients 13 were having eGFR less than 30 and 23(63.88 %) were in the eGFR 30 to 60 group (p <0.01).More patients were in NYHA class III in the eGFR 30 to 60 group (24 out of 27 patients) (p < 0.01). The distribution was equal between NYHA class III and IV in e GFR group less than 30 group. Oliguria was seen in 14 among 27 patients(51.85 %) in eGFR less than 30 group. Oliguria was not present in 22 out of 27 patients (81.48 %)in eGFR 30 to 60 group. This was significant statistically ( p<0.05 ).50

Ischemic cardiomyopathy was seen in 24 out of 27 patients in eGFR less than 30 group (88.89 %). Dilated cardiomyopathy was present in 17among the 27 patients (62.96 %) in the eGFR 30 to 60 group. This

was statistically significant ( $p < 0.01$ ). Estimated Gfr & Nyha Class Correlation 13 out of 16 patients (81.25%) with NYHA functional class IV symptoms at the time of admission were with eGFR less than 30 ml/minute. 24 out of the 38 patients in with NYHA functional class IV (63.15 %) were having e GFR between 30 to 60 ml/min. This was statistically significant ( $p < 0.05$ ).

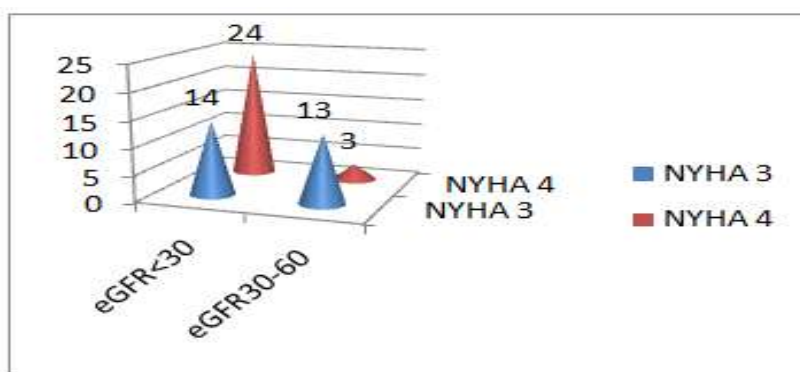


Figure-1: Estimated GFR & NYHA class correlation

Ischemic cardiomyopathy (88.88 %  $p < 0.01$ ) was more associated with patients reduced GFR (24 out of 27) than dilated cardiomyopathy. Systemic hypertension was seen in 14 out of 27 patients 51.8 % of the patients in eGFR less than 30 group ( $p < 0.01$ ). Diabetes mellitus was seen in 59.25 % of patients with eGFR less than 30 ml/minute. The correlation between diabetes and eGFR was not significant.

Comparison between GFR groups Readmissions was more in the eGFR less than 30 group 19 out of 27 (70.37 %) whereas it was seen only in 7 patient out of 27 (25.92 %) in eGFR 30 to 60 group ( $p < 0.01$ ).

Table - 3 : Primary end points according to e GFR

		Estimated GFR		P Value
		<= 30	31 - 60	
REGIONAL WALL MOTION ABNORMALITY	NO	3	17	$P < 0.01^*$
	YES	24	10	
READMISSION	NO	8	20	$P < 0.01^*$
	YES	19	7	
DEATH	NO	16	27	$P < 0.01^*$
	YES	11	7	

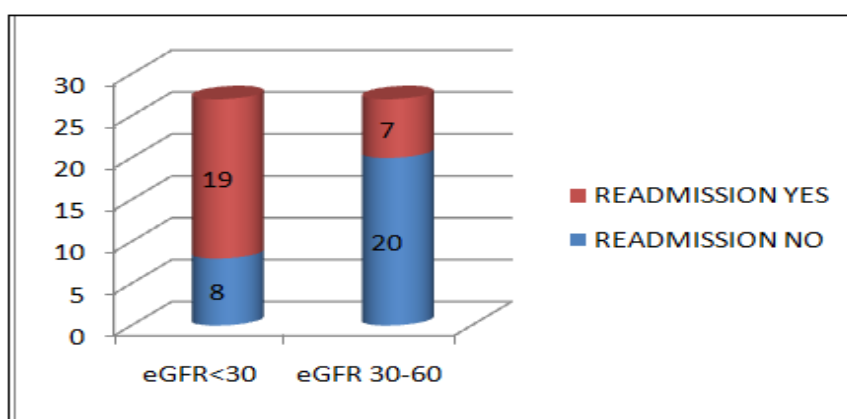


Figure -2 : Readmission Rates According to e GFR

Readmissions were seen significantly in 70.37 % (19 out of 27 patients ) ( $p < 0.01$ ) of the patients with e GFR less than 30 ml/min. Death was present in 11 out of 27 patients (40.74 % ) in eGFR less than 30 group and no death was seen in eGFR 30-60 group ( $p < 0.01$ ) 12 out of the 16 patients (75 % ) who were in the NYHA class IV functional class had readmissions [ $p < 0.05$ ]. Readmission was present in 14 out of the 38 (36.84%) patients who were in NYHA class III functional class. This was statistically significant ( $p < 0.05$ ). 13 patients out of 19 patient who had oliguria at admission (68.42%) got readmission during the follow up period In the non-oliguric group, 13 out of 35 patients (52%) had readmissions. This was statistically significant. [ $p < 0.05$ ]

Readmission was significantly seen in 23 out of 34 (67.64 %) ischemic cardiomyopathy patients. Readmissions were seen in 3 out of 20 (15 %) idiopathic dilated cardiomyopathy patients. [p < 0.01] Patients with diabetes mellitus had readmissions in 16 out of 25 patients in the study group (64 %). Readmission was seen in 10 out of 29 non diabetic patients (34.48 %). This result was statistically significant. [p < 0.05] In the study group with systemic hypertension readmission was present in 13 out of 17 patients (76.47 %). Readmission in non hypertensive group was seen in 13 out of 37 patients (35.13 %). This was statistically significant. [p < 0.01] Death was common in the readmission group 34.61 % which is statistically significant p < 0.05. Death was seen in 7.14 % of the not readmitted group. The primary end point death was significantly more in 7 out of 12 (58.33 %) patients above 60 years of age and death was not seen in patients less than 40 years of age presenting with heart failure and elevated renal parameters. This was statistically significant [p < 0.01]. Death was seen in 11 out of 34 patients in ischemic cardiomyopathy patients (32.35 %) which is statistically significant [p < 0.01]. Death was not seen in dilated cardiomyopathy patients. Death was significantly more in patients with diabetes mellitus and systemic hypertension. It was seen in 8 out of 25 diabetic patients (32 %) and in 7 among 17 patients with systemic hypertension [p < 0.05]. The mean Left Ventricle end diastolic diameter was 5.22 cm in patients with e GFR less than 30 ml/min and the mean Left Ventricle end diastolic diameter was 4.92 cm in patients with e GFR more than 30 ml/min. This was statistically significant. [p < 0.32]

The mean left ventricular ejection fraction in patients with e GFR less than 30 ml/min was 28.81 % and the mean left ventricular ejection fraction in patients with e GFR more than 30 ml/min was 31.19 %. This was statistically significant. [p < 0.008]. The mean Pulmonary artery systolic pressure was 32.78 mmHg in patients with e GFR less than 30 ml/min. In patients with e GFR more than 30 ml/min the mean Pulmonary artery systolic pressure was 34.81 mmHg. The mean value of TAPSE in patients with e GFR less than 30 ml/min was 16.89 mm and the mean TAPSE value in patients with e GFR more than 30 ml/min was 18.81 mm. The mean value for blood urea nitrogen at discharge or at 7 day of hospitalization was 71.45 mg/dl in the death group. The mean value for survivors is 54 mg/dl. This was statistically significant. [p < 0.001]. The mean value for serum creatinine at discharge or at 7 days of hospitalization was 2.164 mg/dl in the death group. This value was 1.57 mg/dl in the survived group. This was statistically significant. [p < 0.001] The mean value for estimated GFR at discharge or at the end of 7 days was 29 ml/min in the patients who died in the study period. This was 48.47 ml/min in the survived group. This was statistically significant. [p < 0.001]

The mean value for blood urea nitrogen at the end of one month follow up was 43.56 mg/dl for patients survived in the study period. The mean value for serum creatinine at the end of one month was 1.258 mg/dl in the survived group in the study population. The mean value for estimated GFR at the end of one month in survived population was 62.3 ml/minute. This was statistically significant. [p < 0.001]

## **V. Discussion**

In the PRIME II -Prospective randomized study of Ibopamine on mortality and efficacy HF patients who were in NYHA III or IV, 80% of the study population were men with mean age 70.  $64 \pm 9.5$  years. In our study majority of the patients were males comprising 66.7 % of the study population. Patients presenting with functional class NYHA class IV at admission had 50 % mortality and 75 % readmissions during the study period. The mortality in patients with NYHA functional class III at admission was 7.89. Baseline GFR calculated by Cockcroft Gault equation predicted the mortality better than left ventricular ejection fraction. Estimated GFR less than 44 ml/minute was associated with three times more mortality than estimated GFR more than 76 ml/minute. In our study the mean level of estimated GFR associated with increased mortality was 23.55 ml/minute. Patients with oliguria at the time of index admission had increased mortality (42.1 %) Patients who had oliguria during index hospitalization had more readmissions. This was observed during the follow up period to be 68.42 % in the oliguric group. This was statistically significant. [p < 0.05]. In the CHARM Study in chronic Heart failure due to reduced Ejection fraction as well as preserved Ejection fraction estimated GFR is significant predictor of worse outcome during 3 month follow up. After adjusting baseline characteristics Cardiovascular death risk or recurrent hospitalization and risk for all cause mortality increased when estimated GFR was less than 60 ml/min. [17] SOLVD - Studies of left ventricular dysfunction. Moderate impairment in renal function causes relative risk of 1.41 when creatinine clearance < 60 ml/min. In our study oliguria at the time of admission and estimated GFR less than 30 ml/minute was associated with more readmissions and death.

In our study the mortality was 20 %. Mortality was more in patients above 60 years of age, ischemic cardiomyopathy as the cause of heart failure, who presented with NYHA class IV symptoms on admission, oliguria at presentation and left ventricular ejection fraction less than 30 %.

## **VI. Limitations Of The Study**

It was single centered study and the sample size was small. Period of follow up was one month. This time interval was too short to observe for long term adverse events. Glomerular filtration rate was not measured. It was estimated using the MDRD equation. Use of drugs during the hospitalisation period were not taken into

account. Use of high dose diuretics and angiotensin converting enzyme inhibitors can influence elevation of renal parameters which could confound the results.

## VII. Conclusion

The cardiomyopathy patients with previous history of myocardial infarction and known hypertensive patients were having estimated GFR less than 30 ml/minute. Patients with estimated GFR less than 30 ml/minute presented with NYHA functional class IV symptoms. Readmissions was more in patients with estimated GFR less than 30 ml/minute, known hypertensive, previous myocardial infarction and cardiomyopathy, anemic patients and age above 50 years. There was no correlation between left ventricular systolic function and readmissions. The predictors of mortality in cardiomyopathy patients admitted for heart failure developing cardiorenal syndrome were age above 60 years, cardiomyopathy with previous history of MI, presentation with NYHA class IV symptoms on admission, oliguria at presentation and left ventricular ejection fraction less than 30 % at the time of admission.

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