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Original research article

EVALUATION OF LEVELS OF GFR AND PROINFLAMMATORY MARKER IN CARDIORENAL SUBJECTS

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Abstract

Background: Patients with cardiovascular disease have an increased risk of developing chronic kidney disease (CKD). However, there is insufficient data on CKD incidence in patients with multiple vascular comorbidities. This study examined predictors of CKD stages 3-5 in patients at risk of cardiovascular disease and used estimated glomerular filtration rate (GFR) to create a nomogram to predict the 5-year risk of incident CKD.

Methodology: Out of 100 subjects, 50 were diagnosed with chronic kidney disease and 50 had chronic kidney disease with a cardiovascular complication of either sex and an age range of 18-65 years. Blood urea, Creatinine and CK-MB levels were estimated by EM-200 fully automated machine. IL-6 by ELISA Method.

Results: There were 58 males and 42 females among the 100 patients, with an average age of 53.37±24.43 years. The mean levels GFR and IL-6 in CKD 78.39±11.58 and 86.4±21.3 ng/L and in CKD with CVD 98.99±19.36 and 101±10.3 ng/L respectively.

Conclusion: Observed value of study parameters highlight the risk prediction with better prognosis for cardiovascular complication in CKD patients.

Introduction

Chronic renal failure is one of the slowest progressive and irreversible diseases of kidney function which is characterized by low glomerular filtration (GRF), which results end stage renal disorder. Chronic kidney diseases (CKD) are the 17th cause of disability and 12th major cause of death. Cardiovascular disease (CVD) is closely associated with chronic kidney diseases and end stage renal disorder; and have concomitant leading cause of morbidity and mortality. An estimated 18.5 million

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people died from CVDs in 2019, representing 32% of all global deaths [1]. Urea is a product of protein metabolism that is often used as a proxy for CKD severity. Elevated serum urea levels are common in moderate-to-advanced chronic kidney disease (CKD). Studies have shown that urea is a direct and indirect uremic toxin, especially with regard to cardiovascular disease. Researchers have found that higher serum urea levels are associated with a higher incidence of adverse CV outcomes and a higher all-cause mortality rate [2]. Creatinine is an amino acid derivative with a molecular mass of 113 Da. It is a waste product of creatine and phosphocreatine and is found almost exclusively (90%) in skeletal muscle tissues. The normal muscle concentration of total creatine is about 125 mmol/kg dry mass. About 2% of the body's creatine is converted to creatinine every day, resulting in the daily generation of creatinine at a fairly constant rate (male: 0.18 to 0.22 mmol/kg/day [20 to 25 mg/kg/day], female: 0.13 to 0.18 mmol/kg/day [15 to 20 mg/kg/day]). It is freely filtered through the glomerulus and is also secreted by the proximal tubules (5% to 10% of the excreted creatinine) [3]. Typically, serum creatinine rises 1 to 2 mg/day in acute kidney injury, but it can exceed 5 mg/day in patients with severe rhabdomyolysis, due to massive breakdown of skeletal muscle. In patients with acute and rapidly progressive glomerulonephritis, 90% of renal function can be lost within weeks to months owing to glomerular destruction and this manifests as a 'galloping' rise in serum creatinine [4, 5].

It is well established that chronic kidney disease (CKD), diagnosed by an estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m^2 is an important risk factor for CVD and cardiovascular mortality. (6) CKD is a long-term condition characterized by a gradual and progressive loss of kidney function over time and can lead to end-stage renal disease (ESRD). A diminished estimated glomerular filtration rate (eGFR) has been shown to increase the risk of CVD morbidity and mortality [7].

Systemic inflammation plays an important role in the development and progression of cardiovascular (CV) disease and chronic kidney disease (CKD). One of the proinflammatory cytokines that play an essential role in the pathogenesis of CKD is interleukin-6 (IL-6) [8]. IL-6 release is stimulated by acute infection, chronic inflammatory conditions, obesity, and physiological stress. IL-6 is also associated with atherosclerosis and cardiovascular disease, which may also be a vital mediator of the inflammatory response in ischemic stroke [9, 10]. Blood vessels are responsive to IL-6 generated from vascular and non-vascular sources. IL-6 signalling mediates various effects on blood vessel walls, including endothelial activation, vascular permeability, immune cell recruitment, endothelial dysfunction, and vascular hypertrophy and fibrosis [10]. Therefore, the present study has planned to evaluate levels of GFR and proinflammatory marker to making decisions about diagnosis and prognosis of Cardiorenal diseases.

Methodology

An observation and analytical design of study was conducted on total 100 subjects in the department of Biochemistry in association with Medicine department at Nootan Medical college and research centre, visnagar, Gujarat in duration two years (December 2022- November 2023). Out of 100 subjects 50 were diagnosed with chronic kidney

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diseases and 50 were diagnosed chronic kidney with cardiovascular complication of either sex with age group of 30-65 years. Present study has been obtained ethical approval from institutional ethical committee from Nootan Medical college. Written and verbal consent were taken from all the subjects.

Inclusion Criteria

- Subject who are willing to participate.
- 18-65 years of age groups of either sex.
- Diagnosed patients of chronic kidney diseases
- Diagnosed patients of chronic kidney diseases with cardiovascular complication.

Exclusion criteria

- A non-cooperative and not willing subjects.
- Diagnosed cases of Diabetes, hypertensin, trauma, infusion, Liver diseases etc.
- Pregnant women.
- Any venerable disorders such as HIV and any STDs.
- Subjects, who have routine habits Smoking, Nicotine and alcohol consumption.

Sample collection ana analysis

Under aseptic precautions 5 ml of the patient's intra-venous blood was obtained and centrifuged at 4000rpm for 8-10 minutes to obtained serum sample. Two ml of Serum sample was preserved for the analysis Interleukin-6 by ELISA methods. Blood urea, Creatinine and CK-MB levels were estimated by EM-200 fully automated machine.
Glomerular filtration rate was calculated with the help MDRD equation by using a web calculator. The Modification of Diet in Renal Disease (MDRD) equation.

MDRD = 186 x (Serum Creatinine level - 1.154) x (Age - 0.203) x 1.212 (If black) x 0.742 (If female) in millilitres per minute per 1.73 m^2.

Study tools: Data were collected in case record form (CRF). The CRF comprise of details regarding diagnosis, cause of renal failure, serum biochemical marker values.

Statistical Analysis: The data were entered into Microsoft office excel and analyzed by Statistical Package for Social Sciences (SPSS) version 21 for windows software. Descriptive statistics were reported in the form of mean, standard deviation. Normal distribution of data was checked by Shapiro - Wilk test. Comparison between two groups of serum biochemical markers was done by paired t-test. P-value < 0.05 will be considered as statistically significant.

Results

A total of 100 patients, 50 were diagnosed for renal failure and 50 were renal failure with cardiovascular complication by the respective clinician and were retrospectively studied. Glomerular filtration rate was calculated. Biomarkers such as serum creatinine, serum urea and CK-MB levels were screened. Demographic data were also analyzed

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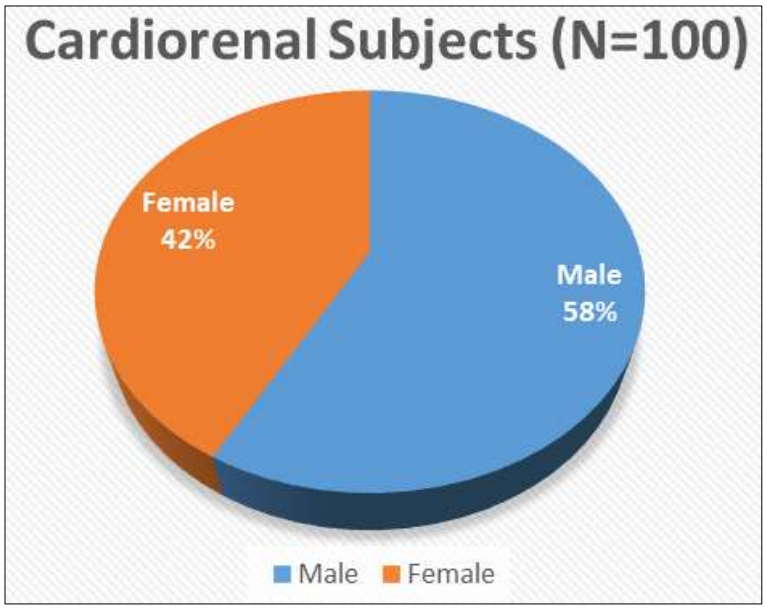
like on the basis of age and gender. Out of the100 patients, male 58 (58%) and females 42 (42%) and Mean age of the subjects were 53.37±24.43 years.



Graph 1: Gender Distribution among cardiorenal patients

Table 1: Descriptive analysis of Study variables

Study Groups	Study Variables					
	Age (Years) (Mean ± SD)	**GFR (mL/min/1.73 m2) (Mean ± SD)**	**Urea (mg/dl) (Mean ± SD)**	**Creatinine (mg/dl) (Mean ± SD)**	**CK-MB (IU/L) (Mean ± SD)**	**IL-6 (ng/L) (Mean ± SD)**
Only CKD	64.24±8.39	78.39± 11.58	112.66±43.52	10.19±4.66	20.43±12.65	86.4± 21.3
CKD with CVD	62.35±3.54	98.99±19.36	108.66±32.87	7.32±2.77	50.87±6.87	101±10.3
P-value	0.05	0.001	0.001	0.001	0.001	0.001

Discussion

It is well known that patients with chronic kidney disease (CKD) have a strong risk of cardiovascular disease (CVD).Multiple epidemiological studies have consistently demonstrated that individuals with chronic kidney disease (CKD) or those experiencing a decline in kidney function over time are at a higher risk of CVD events such as heart attacks, strokes, and heart failure, independent of traditional risk factors of CVD [11]. Several mechanisms have been identified to explain these associations. As kidney function declines, waste products and toxins accumulate, triggering a chronic inflammation that contributes to the development and progression of CVD [12].

The association between CKD and CVD was first reported by Dr. Bright in 1836 [13].

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Impairment in renal function can increase the risk of CVD two- to fourfold. CKD is considered present when impaired kidney function is confirmed in two or more occasions at least 3 months apart. The estimated glomerular filtration rate (eGFR) can be calculated using serum creatinine and the chronic kidney disease epidemiology collaboration (CKD-EPI) equation [14].

Additionally, declining kidney function compromises blood pressure regulation, leading to hypertension, a major CVD risk factor [6]. Imbalances in minerals such as calcium and phosphate, which can occur with declining kidney function, result in vascular calcification and increased CVD risk. Another mechanism is the activation of the Renin-Angiotensin-Aldosterone System (RAAS) in response to declining kidney function, promoting the production of angiotensin II and aldosterone, hormones that contribute to CVD [15, 16].

eGFR is an important predictor of the development of these disease stages in both the general and high-risk population. Unexpectedly, our study revealed that individuals without CVD experienced a slight decline in eGFR, compared to those having CVD. Only a few studies have investigated the relation between slopes of eGFR and the subsequent risk of CVD. Hyperfiltration could be the one of the potential explanations. Hyperfiltration refers to the kidneys filtering blood at a higher rate than normal. However, prolonged hyperfiltration can eventually lead to kidney damage and the progression of diabetic kidney disease. A decrease in GFR below a critical level result in a vicious cycle of worsening kidney function that contributes to CVD, which in turn perpetuates further nephron loss [17].

Serum biomarkers [such as serum creatinine or urea, or blood urea nitrogen (BUN), which reflects only the nitrogen content of urea], are routinely used in clinical settings to evaluate kidney function. Urea is the main metabolite derived from dietary proteins and tissue protein turnover. The compound is almost exclusively excreted by the kidneys in the urine, after filtration in the glomerulus and a certain degree of reabsorption from the filtrate. Although several nonrenal factors affect the serum urea concentration, reduced urinary elimination of urea (due to CKD) is the main factor that increases serum urea levels. Volume depletion by diuretics or a decrease in the effective circulating volume induced by heart failure might contribute to the elevation of urea levels in our CKD patients. Under normal conditions, the serum urea level ranges from 13-43 mg/dl [18, 19]. However the present study has observed that the levels of urea and creatinine is significantly increased in both the group; but have difference in their mean values.

Sensitivity of CKMB as a cardiac marker in general population is found to be inferior when compared to Troponin levels. But due to its short half-life, it shows good correlation with acute coronary syndrome in cases of re-infarction especially after revascularization, current recommendations suggest its use in such cases [20] In our present study we observed normal values of CKMB according to manufacturer's guidelines in the CKD patients than the CKD with CVD [21].

IL-6 are cytokines that play an important role in the inflammatory response seen during the process of atherosclerosis [1]. Based on these observations, we and others have shown that increasing levels of IL-6 are associated with cardiovascular events [22,

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[23]. Similarly, chronic kidney disease (CKD) is associated with cardiovascular disease (CVD). The underlying mechanism connecting CKD and CVD remains not fully understood, with inflammation proposed as a potential link. Still, it is unknown whether inflammatory activity as reflected by biomarkers are associated with cardiovascular outcomes across the range of kidney function [24].

Conclusion

- The present study highlighted the cardiovascular risk in patients with CKD by estimating GFR, proinflammatory marker and CK-MB with other routine biomarkers.
- The observed value of study parameters reflects that there is a predicting risk for the development of cardiovascular diseases those who have end stage of renal diseases.
- This can also highlight the risk prediction with better prognosis for cardiovascular complication in CKD patients.

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