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NOVEL ASSOCIATION OF INFLAMMATORY MARKERS IN CHRONIC KIDNEY DISEASE

Eswara rao Potagani [1], Dr.D.Rajeshwari [2], Dr.Lakshmi Latha [3], Dr.R.Viswa Kumar [4] and Dr.M.Prasad Naidu [5]

Assistant Professor, Department of Biochemistry, Great Eastern Medical School & Hospital, Srikakulam, A.P.

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ABSTRACT

Introduction: The mortality rate in persistent kidney disease conditions is progressing gradually. The thirst for early disease identification is quite interesting in the research. Aim: The current learning is intended to explore the novel association of inflammatory markers with Chronic Kidney Disease (CKD). Procedures: We conducted this cross-sectional experimental education for three years. We enrolled 400 cases and 50 controls in the education. We obtained knowledgeable consent by grouping all the participants into 4 groups based on the stages of CKD. After completing the biochemical measurements, we used the Enzyme-Linked Immunosorbent Assay (ELISA) to determine the levels of highly sensitive C-reactive protein (hsCRP), Tumor Necrosis Factor Alpha (TNFA), and Interleukine (IL-6). The results were tabulated, statistical analysis was performed and $p<0.05$ was found to be substantial. Results: The participants were divided into 54 males and 52 females during the unkind phase. 235 were males, and 165 were females. We found that CKD patients had higher levels of urea and creatinine than the controls. We found TNFA and IL6 to be significant, with P = 0.0001.Conclusion: Our findings proved novel associations of hCRP, TNFA, and IL6 with Chronic kidney disease.

INTRODUCTION

Kidney disease is a serious health ailment that carries a significant financial burden worldwide. This burden includes the cost of medications, doctors, dialysis, and department visits. [1]. The progressive loss of kidney function is the defining characteristic CKD, which develops over an extended period [2]. The global incidence of diabetes and hypertension may rise in tandem with the prevalence of renal disease. [3]. Additionally, CKD is a risk factor that is independent of the advancement of heart illness and renal disease that has reached the end stage. [4]. The search for new methods allows for fast and effective disease detection, and CKD monitoring will be improved.

There is a significant correlation between inflammation and the progression of chronic kidney disease. New findings from the CANTOS trial indicate that anti-inflammatory medication in patients with CKD can lower the incidence of major adverse cardiovascular events. Hence, the study focused on the novel role of inflammatory markers in detecting the disease.

One example is that C-reactive protein is a factor in the transmission of heart disease in patients with end-stage renal disease [5]. Researchers have found that cytokines, such as tumor necrosis factor-alpha (TNF-A) and interleukin-6 (IL-6), cause severe and long-lasting pain in people with heart problems, whether they are healthy or on dialysis [6, 7]. The recruitment of inflammatory cells to the site of injury and the activation of inflammatory pathways within the kidneys are two of the early reactions that occur in response to kidney injury. The inflammatory markers TNF-A and IL-6 are examples of such indicators

Nevertheless, several epidemiologic studies [8, 9] showed findings that were contradictory to the association with chronic renal disease. Therefore, an understanding of the relationship between hCRP, TNFA, and IL6 and chronic kidney disease remains incomplete.

Hence, the study aims to explore the association of inflammatory markers (hCRP, TNFA, and IL6) with CKD.

*Corresponding author: **Eswara rao Potagani**

Department of Biochemistry, Great Eastern Medical School & Hospital, Srikakulam, A.P.

MATERIALS AND METHODS

This cross-section observational study was led from 2020 to 2024 in urban and rural health centers of Narayana Medical College and Hospital Nellore, Andhra Pradesh, India Informed consent was obtained from all the subjects and they were conducted after getting approval from the institutional ethical committee.

Inclusion criteria: Patients of the age group 18 to 55 years, having been diagnosed with chronic kidney disease were included.

Exclusion criteria: Patients with a history of epilepsy, hypertensive encephalopathy malignancies, and infections. And 5th-stage of CKD patients were excluded from the present study.

Selection of cases: We noted patients with CKD in the age group of 18 to 55 years who had a Glomerular Filtration Rate (GFR) of less than 60 (ml/min/1.73 m2) at least twice in 3 months. As per the International Classification of Diseases, patients were divided with GFR 30-59 and 15-29 ml/min/1.73m^2) respectively. A Nephrologist confirmed the cases of chronic kidney disease for the study.

Selection of controls: GFR was calculated and individuals with normal GFR and no history of CKD were taken as controls.

5 ml of Venus blood samples were withdrawn from each subject and transferred in Serum vacuums at the sample collection center. The serum was separated using centrifugation at 3000 rpm for 13 minutes at chamber temperature.

Separated serum trials were allocated and used for the estimation of basic biochemical parameters like glucose urea, creatinine, and lipid profile using a fully automated analyzer. Inflammatory markers h CRP, TNF alpha, and IL- 6 using high sensitivity latex enhanced immune nephelometric assay and ELISA.

Statistical Analysis

With an alpha value of 0.05 (2-sided) and a power of 80%, the sample size was estimated. The mean of all the study subjects was calculated for biochemical parameters and inflammatory markers. Pearson parallel analysis was performed to find the connotation of 1seditious markers with CKD and $p<0.05$ is measured as statistically substantial.

RESULTS

An overall of 400 samples were collected and grouped into 4 of 100 each based on the stages of CKD. 62 control samples were also collected. The basic features of the study subjects were tabularized in Table 1.

Table 1 Baseline and demographic characteristics of study subjects

Variable	Number of cases (N)
Mean Age (years) Males Females	 54 ± 2.3 52 ± 3.5
Males	235 (58.75%)
Females	165 (41.25%)
Mean weight (Kg)	58
Mean Height (m)	1.64
Mean BMI (kg/m^2)	24
Systolic BP (mm Hg)	120
Diastolic BP (mm Hg)	80
Family history of CKD (number)	120 (30%)
Smoking (only males)	168(42%)
Chewing betel (both males and females)	98(24%)
Consumption of Alcohol (only males)	76(19%)
History of Hypertension	89(22%)
Diabetes mellitus	20(5%)
History of Malaria	55(13%)

The Baseline and demographic characteristics are represented in Table 1.A total of 400 participants, 235 were males and 165 were females. The mean weight of the applicants was 58 kg, height was 1.64 meters and BMI was 24 kg/m^2. Mean systolic blood pressure was 120 mm Hg and Systolic blood pressure remained 80 mm Hg. 120 participants had an early history of CKD, and 168 males had the habit of smoking. 98 males and females were chewing betel leaf, 76 were consuming alcohol, 89 had a history of hypertension, 20 were having diabetes mellitus and 55 had an antiquity of malaria.

Table 2 Unadjusted association between demographic variables and risk of CKD

Variables	Cases (N)	Controls (N)	P value
Sex			
Female	165(41%)	30(48%)	0.34
Male	235(59%)	32(52%)	
Age			
18-30	120(30%)	12(19%)	0.42
30-40	142(35.5%)	18(30%)	
41-55	138(34.5%)	32(51%)	

There was no association between demographic variables and CKD risk

Table 3 Adjusted association between variables and the risk of CKD

Variables	OR	95% CI	P value
History of diabetes			
Yes	3.24	2.21-5.23	0.001*
No	1	-	
History of Hypertension			
Yes	2.62	1.78-3.2	0.001*
No	1	-	

Table 3 shows the strong association between health care variables and CKD with $P<0.001$.

Table 4 shows the biochemical limitations in different stages of chronic kidney disease. Concerning urea, the stages are advanced in kidney disease of all stages associated to control. Creatinine levels are higher in diseased patients than in controls. eGFR levels were lower in the case cluster than in the control cluster. The glucose points are lower in stage 4 CKD patients than in the controls.

Table 4 Biochemical parameters noted in different stages of CKD patients

Biochemical parameters (mean)	Stage 1 CKD	Stage 2 CKD	Stage 3 CKD	Stage 4 CKD	Control
Urea (mg/dL) Male Female	37 38	38 32	44 42	46 48	32 30
Creatinine (mg/dl) Male Female	1.4 1.32	1.5 1.46	2.1 2.5	2.8 2.7	1.0 1.1
eGFR (ml/min) Male Female	68 62	63 62	42 43	30 31	110 108

Glucose (mg/g) Male Female	79 77	200 201	76 74	15 12	70 43

Table 5 Impact of Inflammatory markers in different stages of CKD patients

Stages of CKD	h CRP (mg/L)	TNF A (pg/mL)	IL 6 (pg/mL)	P value
Stage 1 Male Female	2.3 2.2	110 112	23 22	0.04 0.03
Stage 2 Male Female	2.8 2.9	128 123	27 28	0.02 0.01
Stage 3 Male Female	3.4 3.5	143 144	31 32	0.001 0.001
Stage 4 Male Female	3.9 3.4	154 155	38 39	0.0001 0.0001
Control Male Female	0.8 0.4	24.43 28.5	1.0 1.2	0.07 0.06

There was a substantial increase in inflammatory markers in CKD patients in all stages than controls.

DISCUSSION

The study detects elevated values of inflammatory markers hCRP, TNFA, and IL-6 in individuals with CKD compared to those without CKD. Furthermore, eGFR, urea, and creatinine measurements of the disease severity show a positive correlation with these inflammatory markers.

Researchers have studied CRP as a risk factor in the progression of cardiovascular diseases, as it increases mortality, and it also has a similar effect on patients with end-stage renal disease [10]. This aligns with our findings, which highlight the significant correlation between CRP and chronic kidney disease (CKD). Various studies contradict the present study by showing no correlation between CRP and CKD in patients using antihypertensive, antidiabetic, and aspirin [11–13].

TNFA plays an important role in inducing an inflammatory response, activating vascular endothelial cell expression, and increasing the leukocyte adhesion molecules that trigger immune cell infiltration. Various studies in the literature [14-16] have supported the increased levels of TNFA in chronic kidney disease. The present study aligns with these results, demonstrating elevated TNFA levels across all stages of CKD patients.

We measure proinflammatory cytokines to determine whether they are encouraging or exacerbating. In many patients with diabetes and diabetic nephropathy, we observed advanced levels of IL-6. IL-6 was present. Il-6 [19]. There are problems in the endothelium, damage to podocytes, and an increase in fibronectin by the mesangium when IL-6 levels are high in people with CKD. Researchers have found a correlation between the growth and IL-6 mRNA levels. The current study observations coincided with an increase in IL-6 levels.

This observation relates to Shankar et al.'s study, which suggested a positive link between TNFA and IL-6 and the development of CKD.

According to the current study, having a history of diabetes raises the risk of chronic kidney disease. This discovery aligns with the outcomes of prior research on the same topic [20, 21, 24–27]. Given that over 40% of individuals with diabetes go on to acquire chronic kidney disease (CKD), it is not unexpected that those who have the disease have a higher chance of developing the disease [27].

A history of hypertension was the other factor linked to an elevated risk of chronic kidney disease (CKD). Our findings align with those of multiple previous investigations [20, 24, 25, 28]. According to reports, hypertension both causes and worsens CKD, hastening the disease's progression to end-stage renal disease (ESRD) [29].

The current study's methodology was able to establish a causal relationship between the associated variables and CKD, the results could be important and easily applied in the prevention of CKD due to the associated factors' potential importance and modifiability.

Limitation

The study limitation is that there was not enough number of controls included as compared with cases.

CONCLUSION

The present study findings quote that inflammatory markers like hCRP, TNFA, and Il6 are allied with the severity of the kidney illness i.e.; CKD independent of the hazard factors. Another crucial component in the prevention of CKD is the routine monitoring and care of diabetic individuals. Our recommendation is that endocrinologists and nephrologists work closely together to treat diabetes people who have kidney issues. Furthermore, for appropriate treatment regarding kidney function, surgeons performing large procedures should refer their patients—especially those with AKI—to a nephrologist. One of the most crucial therapies to slow down the course of CKD is the treatment of hypertension. Furthermore, CKD screening ought to be performed on all individuals with recently diagnosed hypertension. We recommend that the GFR and urine albumin-to-creatinine ratio (UACR) be measured yearly in all diabetic patients. Lastly, there is a notable increase in the absolute number of individuals with diabetes and kidney disorders due to aging populations and obesity. This will necessitate a better coordinated strategy between the primary care teams and dialectologists/nephrologists.

This is one of the first studies to communicate the result that, hCRP is associated with the development of disease.

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