Section: Biochemistry

Original Research Article

CHRONIC KIDNEY DISEASE: PROLONGED INFLAMMATORY MARKER ILLNESS

Eswara Rao. Potagani[1], Rajeshwari.D[2], Lakshmi Lalitha. D[3], Viswa Kumar[4], Prasad Naidu. M[5], Kusuma Papa. B[6]

[1]*Assistant Professor, Department of Biochemistry, Great Eastern Medical School & Hospital, Srikakulam, A.P, India.*
[2]*Professor, Department of Biochemistry, Narayana Medical College, Nellore, India.*
[3]*Professor, Department of Biochemistry, Great Eastern Medical School & Hospital, Srikakulam, A.P, India.*
[4]*Professor, Department of Biochemistry, Narayana Medical College, Nellore, India.*
[5]*Assistant Professor, Narayana Medical College, Nellore, India.*
[6]*Research Associate, Department of Research and Development, Great Eastern Medical School & Hospital, Srikakulam, A.P, India.*

Received *: 07/01/2025*
Received in revised form *: 10/01/2025*
Accepted *: 17/01/2025*

Corresponding Author:
Dr. Kusuma Papa.B,
Research Associate, Department of Research and Development, Great Eastern Medical School & Hospital, Srikakulam, A.P, India.
Email: drkusumagenetics777@gmail.com

DOI: 10.70034/ijmedph.2025.1.37

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (1); 212-216

ABSTRACT

Background: The death rate from chronic renal disease is steadily increasing due to various reasons. The research's emphasis in early disease detection is fascinating. The goal of the current course is to investigate the long-term effects of inflammatory indicators in patients with chronic kidney disease (CKD).

Material and Methods: This study measures the plasma levels of high sensitive C-reactive protein (hsCRP), Tumour Necrosis Factor alpha (TNFα), Interleukin-6(IL6) in 400 participants diagnosed with chronic kidney disease. Estimated Glomerular Filtration Rate (eGFR), glucose, urea and creatinine were quantitated for measuring the kidney function.

Results: Inflammatory markers frequencies revealed a statistically significance difference (p- value <0.05 between CKD and study population. Chi square p- values of detrimental habits and family history of diabetes and hypertension were statically significant with CKD in males than females. And elevated levels of urea, creatinine and eGFR were associated with increasing the inflammation in function. Mean P- values of hsCRP, TNFα and IL 6 were also strongly associated with CKD.

Conclusion: This study provides inflammation in kidney due to the abnormal plasma levels of CRP, TNFα and IL6. Detrimental habits and family history of diabetes and hypertension were also majorly associated with development of CKD in males than females. Additionally, we are determined males were excess amount salt intake in daily life and particularly in females, stress and hypertension were associated with development CKD.

Categories: Biochemical Genetics, Allergy/ Immunology
Keywords: Enduring offal illness, inflammation, c-reactive protein, TNF Alpha, Interleukin 6.

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 tumour 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 hsCRP, TNFA, and IL6 and chronic kidney disease remains incomplete.

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

MATERIALS AND METHODS

This cross-section observational study was led from 2020 to 2024 in urban and rural health centres 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. Males and females diagnosed patients were include in study population.

Exclusion Criteria

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

Procedure for sample collection

We are taking the samples after Nephrologist was confirmed the cases of chronic kidney disease for the study. 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 4 stages with GFR 30-59 and 15-29 ml/min/1.73m^2) respectively.

Measurement of Inflammatory Markers

In this study, high sensitivity ELISA Assay was used to measured plasma levels of hsCRP, TNFα, and IL-6. The samples were stored at -80^0C to performed at the time of initial thawing and calculated mean values were used in the statistical analysis.

Statistical Analysis

The chi-square (Hardy-Weinberg Equilibrium chi-square test) and mean ± SD (standard deviation) statistical tools were using for determine the frequencies and elevated plasma levels hsCRP, TNFα, and IL-6 with the help of Open Epi online application. A p-value of less than 0.05 was considered as statistically significant. The baseline data, including age group (18-55 years), prior history of diabetes, and history of hypertension, were calculated using the student T-test.

RESULTS

Table 1 represents demographic data of CKD patients. Mean average p values of weight (p-0.000), systolic (p-0.000) and diastolic blood pressure (p-0.000) were significantly associated with CKD in males and female patients. The mean average p values of age (p-0.455) and height (p-0.659) were does not show any association with CKD. [Table 1]

Table 2 shows association of detrimental habits and family history of CKD in males and females. The frequencies of smoking and alcohol consumption are shown to be higher in males (14.893%) (52.34a0%) than in females (0%) (3.636%). Also, the frequency of stress was higher in females than in males (31.063%). As well as if it comes to frequency of hypertension was higher in females (64.242%) than in males (62.127%) and frequency of diabetes was more in males (42.127%) than in females (27.272%). As well as frequencies of family history diabetes and family history of hypertension were higher in males (34.235%), (28.936%) than in females (17.575%), (15.151%) and the higher frequency of excess amount of salt intake in food among males (23.404%) than in females (16.969%). Chi-square p- values of smoking, alcohol consumption, stress, diabetes, family history of diabetes and family history of hypertension were significantly associated with CKD. [Table 2]

Table 3 represents association of biochemical parameters and inflammatory markers with CKD in males and females. The p- values of eGFR(p-0.046), urea (p-0.001) and creatinine (p-0.017) were significantly difference with CKD in males and females. Also, if it comes to be inflammatory markers like hsCRP, TNFα and IL-6 were significantly associated with CKD (p-0.000). [Table 3]

Table 4 represents association between inflammatory markers and stages of CKD in males and females. The highest frequencies of hsCRP [males stage 2- (39.574%), stage 3(35.319%); females stage 2-(29.696%), stage 3- (31.489%)], TNF-α[males stage 2-(41.702%) stage 3-(37.872%); females stage 2-(33.939%), stage 3 - (45.454%)] and IL-6 [males stage 2- (31.063%), stage 3-(45.106%); females stage 2- (32.121%); stage 3 -(47.878%)] were present in stage-2 and stage -3 among males and females. Chi-square p- values of

CRP, TNF-α, IL-6 was insignificant with stages of CKD in males and females. [Table 4]

Table 1: Demographic Data of CKD in Males and Females

Basic Parameters	Males (N=235)	Females (N=165)	P-Value
Age	49.70638 ± 13.71856	47.14705882 ± 14.20673484	0.455
Height	159.8112 ± 27.21632	160.7561± 4.953592	0.659
Weight	60.73932 ± 7.806172	65.4939± 15.87163	0.000
Systolic	139.0598 ± 23.51515	125.6707 ± 21.36018	0.000
Diastolic	87.26496 ± 11.33212	82.07317 ± 9.138208	0.000

Table 2: Association of detrimental Habits and family history of CKD in Males and Females

Detrimental Habits In CKD	Males N=235 (%)	Females N=165(%)	Chi- Square	P-Value
Smoking habits				
Yes	35 (14.893%)	0 (0%)	26.93	0.000
No	200 (85.106%)	165 (100%)		
Alcohol Consumption				
Yes	123 (52.340%)	6 (3.636%)	66.63	0.000
No	112 (47.659%)	159 (96.363%)		
Stress				
Yes	73 (31.063%)	110 (66.666%)	49.51	0.000
No	162 (68.936%)	55 (33.333%)		
Hypertension				
Yes	146 (62.127%)	106 (64.242%)	0.186	0.666
No	89 (37.872%)	59 (35.757%)		
Diabetes				
Yes	99 (42.127%)	45 (27.272%)	9.284	0.002
No	136 (57.872%)	120 (72.727%)		
Family history of diabetes				
Yes	82 (34.235%)	29 (17.575%)	14.5	0.000
No	153 (65.106%)	136 (82.424%)		
Family history of hypertension				
Yes	68 (28.936%)	25 (15.151%)	10.32	0.001
No	167 (71.063%)	140 (84.848%)		
Excess amount of salt intake in food				
Yes	55 (23.404%)	28 (16.969%)	2.441	0.118
No	180 (76.595%)	137 (83.030%)		

Table 3: Association of Biochemical Parameters and inflammatory markers with CKD in males and Females

Biochemical Parameters	Males (N=235)	Females (N=165)	P-Value
e GFR	41.95319 ± 27.65305	47.37195122 ± 26.0780151	0.046
Glucose	154.0603 ± 18.87883	154.9411765 ± 13.67251682	0.588
Urea	116.8879 ± 40.42954	131.1470588 ± 44.08690105	0.001
Creatinine	9.127536 ± 10.31231	7.5 ± 1.401784577	0.017
Inflammatory Markers			
CRP	3.53293 ± 3.392563	2.594117647 ± 1.307656453	0.000
TNFα	12.11905 ± 23.68596	9.067058824± 9.301823834	0.000
IL6	26.42026 ± 21.59306	24.82647059 ± 3.6347432	0.000

Table 4: Association between inflammatory markers and stages of CKD in males and females

Inflammatory Markers	Gender	Stage-1	Stage-2	Stage- 3	Stage- 4	Chi Square	P-Value
CRP	Males (%)	30 (12.76%)	93 (39.574%)	83 (35.319%)	29 (12.340%)	5.658	0.129
	Females (%)	25 (15.151%)	49 (29.696%)	74 (31.489%)	17 (10.303%)		
TNF-α	Males (%)	26 (11.063%)	98 (41.702%)	89 (37.872%)	22 (9.361%)	3.79	0.285
	Females (%)	22 (13.333%)	56 (33.939%)	75 (45.454%)	12 (7.272%)		
IL-6	Males (%)	39 (16.595%)	73 (31.063%)	106 (45.106%)	17 (7.234%)	5.736	0.125
	Females (%)	15 (9.090%)	53 (32.121%)	79 (47.878%)	18 (10.909%)		

DISCUSSION

One of the most common diseases in the world is chronic kidney disease (CKD), which affects up to 50% of patients because of renal inflammation. Kidney function may be impacted by age and blood pressure levels, both diastolic and systolic. According to Yu Hao et al., the cross-sectional investigation demonstrated that systolic and diastolic blood pressure, as well as advanced age, were risk factors for the development of chronic kidney disease. According to his research, distinct biological processes that are closely linked to aging are reflected in the solitary elevation of systolic and diastolic blood pressure, which characterizes hypertension subtypes. Blood vessels undergo structural alterations as people age.[10]

The present investigation found a strong correlation between CKD and the mean p value of weight, systolic blood pressure, and diastolic blood pressure.

Both diastolic and systolic blood pressure were risk factors for the onset of chronic kidney disease and age was do not show significant with CKD in this study. Our analysis is consistent with Yu Hao et al.'s findings.

Kazancioglu was noticed that those who were older, female, smoked, drank alcohol, had diabetes, high blood pressure, and were underweight had a higher incidence of renal diseases. Furthermore, CKD is believed to be closely linked to genetic inheritance, family history of hypertension, and family history of diabetes.[11]

According to the current study, having a history of diabetes raises the risk of chronic kidney disease. This discovery aligns with the outcomes of Michael et al., Paul et al., and Li et al., on the same topic.[12,13,14] 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.[15]

A history of hypertension was the other factor linked to an elevated risk of chronic kidney disease (CKD). Our findings align with those of xu et al., and Sepanlou et al. investigations.[16,17] According to report of Mehaffey et al., hypertension both causes and worsens CKD, hastening the disease's progression to end-stage renal disease (ESRD).[18]

According to our research, men were more likely than women to smoke, drink alcohol, have diabetes, and have a family history of the disease, whereas women were more likely to experience stress and high blood pressure. Males were also consuming too much salt in their diet. Both men and women are at risk for developing CKD because of these. The risk of chronic kidney disease (CKD) was significantly correlated with smoking, alcohol use, diabetes, hypertension, and family histories of diabetes and hypertension. The Kazancioglu study was correlated with the current investigation.

Gupta et al., was reported on CKD patients with lower eGFR values had higher plasma levels of hsCRP, TNF-α, and IL-6. The results of his study, those with CKD had lower eGFR and urine albumin to creatinine ratios (UACR), and their inflammation scores were greater.[19]

The current study found that both males and females with CKD had substantial mean p values for eGFR, urea, and creatinine. As shown in this study, those with CKD have higher plasma levels of the inflammatory markers TNFα, IL-6, and CRP in males and females. Additionally, there is a favourable connection between these inflammatory markers and measures of disease severity such as eGFR, urea, and creatinine. This study supports the investigation of Gupta et al.

Ridker PM 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.[20] This aligns with our findings, which highlight the mean average P – value significant correlation between CRP and chronic kidney disease (CKD).

As per the study of Mehaffey et al., TNFα 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.[8]

The results of our investigation showed that the development of CKD was closely correlated with the mean p value of TNFα. The present work is consistent with research by Mehaffey et al., and Gupta et al.[18,8]

In the words of Tanaka et al. and Su et al., IL6 is a proinflammatory marker that can act as an early warning sign of systemic inflammation and kidney injury. In order to reduce the risk of renal inflammation, prompt actions are made possible by this marker, which can offer a crucial tool into the course of kidney disease.[22,23] Increased IL6 levels control the inflammatory response by binding to the IL6 receptor, which causes systemic circulation and membrane-bound forms on certain cells, such as leukocytes and kidney podocytes, which results in the development of CKD.[24]

The present study showed a significant difference between CKD and IL6. The findings of the present investigation aligned with those of Tanaka et al., and Su et al., and Bhatra et al. studies. Both males and females in the current study had greater levels of CRP, TNFα, and IL6 in stages two and three. Based on these findings, the phases of CKD were also associated with increased levels of hsCRP, TNFα, and IL6 inflammation. With regard to CKD stages, the chi-square p-values for hsCRP, TNFα, and IL6 were not significant.

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

In our study, we are concluded the weight, systolic and diastolic blood pressure were significant with CKD in males and females. As well as detrimental habits like smoking, alcohol consumption and other diseases like diabetes, stress, hypertension, family history of diabetes and hypertension were acts as risk factors and associated with CKD males and females. Elevated levels of Urea, creatinine, e GFR were also associated with CKD. Finally, hsCRP, TNFα and IL-6 were playing an important role to causing the inflammation in kidney among development of CKD. Particularly in our study,

stages of CKD do not show any association with development of CKD.

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