Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jgjytm70

CORRELATION OF THE SEVERITY OF CHRONIC KIDNEY DISEASE WITH CRP

Sandeep Singh[1*], Dr. Rajinderjit Singh Ahi[2], Varun Khanna[3]

[2]Department of biochemistry, Adesh Institute of Medical Sciences & Research, Bathinda
[3]Tutor Biochemistry, CMC Ludhiana, Punjab

***Corresponding author:** Sandeep Singh
*Department of biochemistry, Adesh Institute of Medical Sciences & Research, Bathinda

Abstract

Background: Chronic kidney disease (CKD) is marked by kidney damage or a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m2 for at least three months, regardless of the underlying etiology. When a variety of renal problems are present, albuminuria defined as an albumin-to-creatinine ratio >30 mg/g in two out of three spot urine samples can serve to determine kidney failure. The three most typical CKD causes are glomerulonephritis, diabetes mellitus and hypertension. One in three persons with diabetes and one in five adults with hypertension both have CKD.[6] The etiology of chronic kidney disease also known as chronic kidney disease of undetermined etiology (CKDu), is uncertain in some cases. C-polymer, a polysaccharide present on the cell walls of pneumococcus was initially found to interact with a component in the serum of individuals undergoing acute inflammation, hence the name CRP. CRP is mostly utilized as an indicator of inflammation. There are only a few known conditions that prevent the formation of CRP, other from liver failure. The interferon alpha-induced suppression of CRP generation from liver cells may account for the relatively low levels of CRP observed during viral infections compared to bacterial infections.

Objective: The aim of the study was to assess the CRP in CKD and study the correlation between eGFR (which is a marker of severity of CKD) and CRP in CKD.

Materials and Methods: The present study was observational study. The study was conducted over a period of six months on 180 patients. Blood samples were obtained in Becton Dickinson's commercially available red capped tubes vacutainers (BD). After that, blood samples were left undisturbed at room temperature for 15-30 minutes to coagulate. For 5 minutes, the tubes were centrifuged at 3000 rpm. After centrifugation, the sample solution (serum) was transferred to a fresh polypropylene tube with a Pasteur pipette. Serum creatinine was done on fully automated SYSMEX BX-3010 and CRP were done on fully auto-analyzer NANOLAB 200.

Results: Our results show that mean and standard deviation of CRP with p value between males and females in the different stages of chronic kidney disease which shows a statistically significant difference in stage II (p=0.0286).

Conclusion: The present study highlights the progressive increase in CRP levels as CKD advances through its stages. This finding shows the increase in CRP levels as CKD progresses through its stages, particularly evident in Stage II in the present study underscores the importance of addressing inflammation in CKD management.

1.Intoduction

An international public health issue, kidney failure has a rising frequency and incidence, significant expenditures and unfavourable consequences. Even more people have chronic kidney disease (CKD), which has side effects such renal function loss, cardiovascular disease (CVD) and early death.[1] This global initiative's justification for tackling the issue is straightforward and obvious. Throughout in the world, CKD is common. The harmful effects of CKD are well known, as are the underlying scientific and evidence-based methods for prevention, detection, evaluation, and therapy. Utilizing current knowledge and resources is crucial for improving chronic disease care and outcomes internationally, even though risk factors and care resources differ locally.[2]

Chronic kidney disease (CKD) is marked by kidney damage or a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m2 for at least three months, regardless of the underlying etiology. When a variety of renal problems are present, albuminuria defined as an albumin-to-creatinine ratio >30 mg/g in two out of three spot urine samples can serve to determine kidney failure.[3]

The estimated global rate of CKD is 13.4%.[4] In India, one of the most widespread illnesses that is not transmissible. CKD has a significant morbidity, mortality rate, and financial impact. Around 5.2 million people in India died from CKD-related causes in 2008 and that number could rise to 7.63 million by 2023. Some Indian states including Puducherry, Andhra Pradesh, Maharashtra and Odisha have been identified as CKD hotspots.[5]

The three most typical CKD causes are glomerulonephritis, diabetes mellitus and hypertension. One in three persons with diabetes and one in five adults with hypertension both have CKD.[6] The etiology of chronic kidney disease also known as chronic kidney disease of undetermined etiology (CKDu), is uncertain in some cases.[7] Initially, there are usually no symptoms apparent but later signs and symptoms could include confusion, exhaustion, nausea and leg edema.[8] Initial signs of CKD are the absence of symptoms and regular blood tests performed for screening often reveal it by either rising levels in serum creatinine or a protein in the urine.[9] There may be an increase in unpleasant symptoms when kidney function declines.[10] By releasing vasoactive hormones through the renin-angiotensin system, the kidneys and fluid excess increase the risk of developing hypertension and heart failure. In CKD patients compared to the general population, atherosclerosis and cardiovascular disease are more common, and uremic toxins may contribute to at least some of this elevated risk. One of the risk factors is a family history of chronic renal illness.[11] Despite the fact that there are various contributing factors, some of them include elevated inflammation, a drop in erythropoietin, and hyperuricemia, which suppresses the bone marrow because the kidneys are unable to produce enough erythropoietin.[12] Cachexia may progress and cause inadvertent weight loss, loss of muscle weakness, and anorexia in its final stages. Another new sign of CKD in patients is cognitive loss. Cognitive impairment and/or dementia are 35–40% more likely to occur in CKD patients.[13]

This correlation depends on how severe each patient's CKD is, but patients with CKD at any stage are more likely to experience these cognitive problems. Regularly, both men and women with CKD experience sexual problems. Most men struggle to develop an erection and have decreased sex drive, and these issues worsen as they age. Menstruation pain and difficulties with sexual arousal are frequent in women.[14] High blood pressure, bone disease and anemia are a few complications that can be linked to hormonal malfunction of the kidneys.[15] Additionally, cardiovascular problems in CKD patients are substantially more common and carry higher mortality and hospitalization risks. People with CKD often have sleep disturbances, which makes it difficult for them to get adequate rest.[16] Compared to controls with a healthy weight, obesity may increase the probability that CKD may proceed to ESKD or renal failure. When the disease is advanced, obesity may also make it more difficult for persons to qualify for kidney transplantation.[17]

The primary elements of the diagnosis of CKD are the estimated glomerular filtration rate (eGFR), serum creatinine level and patient's medical history.[18] Distinguishing CKD from acute kidney injury (AKI) is important since AKI can be reverted. One diagnostic marker that aids in differentiating CKD from AKI is a gradual increase in serum creatinine over several months or years as opposed to a rapid surge over a few days to weeks. Numerous CKD patients have a history of renal disease or other underlying illnesses.[19]

The underlying cause may be discovered through ultrasound or a kidney biopsy. At risk individuals should be screened. Screening is not recommended for people without CKD symptoms or risk factors. People who have hypertension, a history of cardiovascular disease, diabetes or considerable obesity, who are older than 60 have a history of kidney disease or who have relatives with kidney disease who required dialysis should be checked out.[20] The serum creatinine serves as the foundation for the eGFR, which is proportional to 1/creatinine meaning that two are inversely correlated, with the eGFR decreasing as creatinine increases.[21] Serum creatinine is waste product of muscle metabolism that is easily measured and eliminated by the kidneys, it serves as an essential biomarker of renal function. In the body, creatine, phosphocreatine also referred to as creatine phosphate and adenosine triphosphate (ATP) work together to make creatinine.[22] The by-product of creatine phosphate in muscles, creatinine is created continuously by the body. The kidneys completely remove it from the blood. Raised serum creatinine levels are the result of decreased renal clearance. Depending on one's muscle mass, the body releases it at a steady pace.[23]

The majority of the methylation of glycocyamine, also known as guanidino acetate, which is produced in the kidney from the amino acids arginine and glycine, results in the production of creatine. S-Adenosyl methionine participates in the process by contributing a methyl group.[24] After being produced, creatine is then transported by the blood to various tissues, including the brain and muscles, where it is phosphorylated and changed into the high-energy molecule phosphocreatine. Creatine kinase is the enzyme that catalyses the transformation of creatine into phosphocreatine, and it also causes the creatine phosphate to spontaneously transform into creatinine. The daily production of creatinine is influenced by muscle mass. As a result, just as there are differences in the ranges of creatinine between males and women. There are also differences in the ranges of creatinine and lower creatinine values are seen in young people and those with less muscle mass. Diet can also affect creatinine levels. Creatinine levels are altered by 30% as a result of eating red meat. Additionally, a rise in serum creatinine only occurs after a 50% reduction in renal function.[25]

Both the CKD-EPI equation and the Modified Diet in Renal Disease (MDRD) equation incorporate serum creatinine to determine GFR.[26] These eGFR equations are preferred over serum creatinine alone because they take into consideration variables including race, age, and gender.[27]

Chronic kidney disease is classified into different stages based on the eGFR.

Table 1 chronic kidney disease stages based on eGFR [28]

Stages	GFR value ml/ min/1.73m^2	Classification
I	>90	Normal or High
II	60-89	Slightly decline
III A	45-59	Mild to moderately decline
III B	30-44	Moderately to severely decline
IV	15-29	Severely decline
V	<15	Renal failure

Stage I, kidney impairment or mildly reduced function is accompanied by persistent albuminuria and a normal or relatively high GFR (90 mL/min/1.73 m2). In stage II, there is a little decline in GFR (60-89 mL/min/1.73 m2) along with renal injury. GFR is reduced moderately (30-59 mL/min/1.73 m2) in stage III. For the purposes of screening and referral, British guidelines make a distinction between stage III A (GFR 45-59) and stage III B (GFR 30-44). GFR (15–29 mL/min/1.73 m2) is severely reduced in stage IV. Established renal failure (GFR 15 mL/min/1.73 m2) manifests in stage V.

C-reactive protein (CRP), an annular (ring-shaped) pentameric protein found in blood plasma rises in response to inflammation. It is a hepatic derived acute phase protein that increases when macrophages and T cells release interleukin-6. Its physiological purpose is to bind to the lysophosphatidylcholine expressed on the surfaces of dying or dead cells, as well as certain microorganisms. As a result, C1q can be used to activate the complement system.[29] The liver releases

CRP in response to chemicals released by adipocytes and macrophages. It is a member of the pentraxin family of proteins. C-reactive protein was the initially identified pattern recognition receptor (PRR).[30]

C-polymer, a polysaccharide present on the cell walls of pneumococcus was initially found to interact with a component in the serum of individuals undergoing acute inflammation, hence the name CRP.[31] Phosphocholine is expressed on the surface of several bacterial cells, including pneumococcus bacteria and CRP binds to it. By triggering the complement system, this encourages macrophage phagocytosis, gets rid of pathogens, apoptotic and necrotic cells. This so-called acute phase response is caused by an increase in IL-6, which is produced by macrophages and adipocytes in response to a number of acute and chronic inflammatory conditions like bacterial, viral, or fungal infections, rheumatic and other inflammatory diseases, malignancy, tissue injury and necrosis.[32] In each of these conditions, interleukin-6 and other cytokines are released, which triggers the liver to produce CRP and fibrinogen. CRP binds to phosphocholine on bacteria. It is thought to facilitate opsonin-mediated phagocytosis by macrophages, which have a CRP receptor, and help complement adhere to foreign and seriously injured cells. Innate immunity uses it as a first line of defence against infections.[33]

CRP is mostly utilized as an indicator of inflammation. There are only a few known conditions that prevent the formation of CRP, other from liver failure. The interferon alpha-induced suppression of CRP generation from liver cells may account for the relatively low levels of CRP observed during viral infections compared to bacterial infections. In kidney diseases, CRP is highly expressed by many inflammatory cells, presumably macrophages, and intrinsic kidney cells including tubular cells and

endothelial cells.[34]

So, the present study has been planned to study the severity of chronic kidney disease with serum CRP.

2.Aims and objectives

The aim of the study was to assess the serum CRP in CKD and to study the correlation between eGFR (which is a marker of severity of CKD) and serum C-reactive protein in CKD.

3.Materials and Methods

For serum CRP testing, all blood samples taken in plain vacutainer tubes were sent to the Biochemistry laboratory of the Biochemistry Department, AIMSR. The investigation lasted six months (October 2022 to March 2023) after receiving clearance from the AIMSR Research Committee and the Ethics Committee of Biomedical and Health Research, Adesh University, Bathinda.

3.1 Inclusion criteria

All the diagnosed cases of chronic kidney disease (all the patients were evaluated for chronic kidney disease as per the K/DOQI criteria by National Kidney foundation for diagnosis of CKD) [35]

3.2 Exclusion criteria

1. All HIV positive individuals.
2. All the patients having history of gout and /or hyperuricemia.
3. Patients who are taking anti tubercular drugs and thiazide diuretics.

3.3 Methodologies and experimental strategy

3.3.1 Serum preparation

Blood samples were obtained in Becton Dickinson's commercially available red capped tubes vacutainers (BD). After that, blood samples were left undisturbed at room temperature for 15-30 minutes to coagulate. For 5 minutes, the tubes were centrifuged at 3000 rpm. After centrifugation, the sample solution (serum) was transferred to a fresh polypropylene tube with a Pasteur pipette.

3.3.2 Specimen storage and handling during testing

During testing, the temperature of the specimens was kept between 20 and 25 degrees Celsius. Specimens were kept at 4-8°C for a maximum of 8 days. If the samples required to be preserved for a longer amount of time, they were put in a deep freezer at -20°C.

3.3.3 Procedure

All the samples were collected from the patient attending IPD and OPD Department of Adesh Institute of Medical Science and Research, Bathinda. Serum creatinine was done on fully automated SYSMEX BX-3010 and CRP were done on fully auto-analyzer NANOLAB 200.

Parameters	Methods	Biological reference
Creatinine	Jaffe's method	0.9-1.3mg/dL (for males) 0.6-1.1mg/ dL (for females)
CRP	Turbilatex method	Up to 6mg/dL

3.4 Statistically Analysis

The data analysis was done by using suitable software like MS EXCEL 2021.t-test was used for enumeration data which were expressed as mean and standard deviation. Pearson's analysis was employed for correlation analysis between variables. Statistical method $P<0.05$ was considered to indicate a statistically significant.

4.Results

This study was conducted in Adesh Institute of Medical Sciences and Research, Bathinda. During a six-month period ,180 serum samples of chronic kidney disease patients were tested for serum C-reactive protein.

The five stages of CKD were determined by the estimated glomerular filtration rate (eGFR). The eGFR was calculated using the level of creatinine. In the present study, males and females were distributed in the stages based on the eGFR because of their different biological reference of serum creatinine in males and females.

The study's finding are as follows.

Table 2 Age distribution amongst chronic kidney disease patients

Age Group	No. of Patients	%
20-30	13	7.2
31-40	25	13.8
41-50	26	14.4
51-60	51	28.3
61-70	65	36.1
TOTAL	180	100
Range	20-70	
Mean ± SD	52.8 ± 12.8	

Above table shows the age distribution among 180 chronic kidney disease patients. The age of patients ranged from 20-70 years. The mean± SD for age was 52.8±12.8 years. Only 7.2% of patients were in the age group of 20-30 years.13.8% of the patients were having the age between 31-40 years and 28.3% of the patients were having the age between 51-60. The patients who were having their age between 41-50 years were 14.4%. Maximum patients, that is, 36.1% were in the age group between 61-70 years.

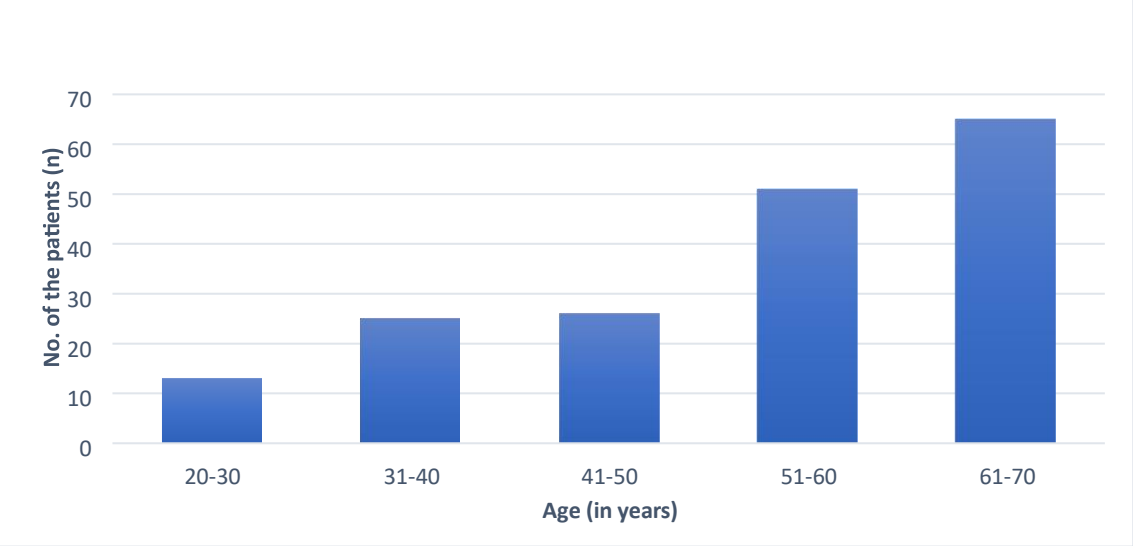

Figure 1- Age distribution in chronic kidney disease patients

Table 3 - Gender distribution amongst chronic kidney disease patients

Gender	**No. of Patients**	**%age**
Male	126	67.7
Female	54	32.2
Total	180	100

As evident from the above table, there were 126 males (67.7%) and 54 females (32.2%) among total of 180 chronic kidney disease patients. So, in the present study, the analysis according to the gender showed marked male preponderance.

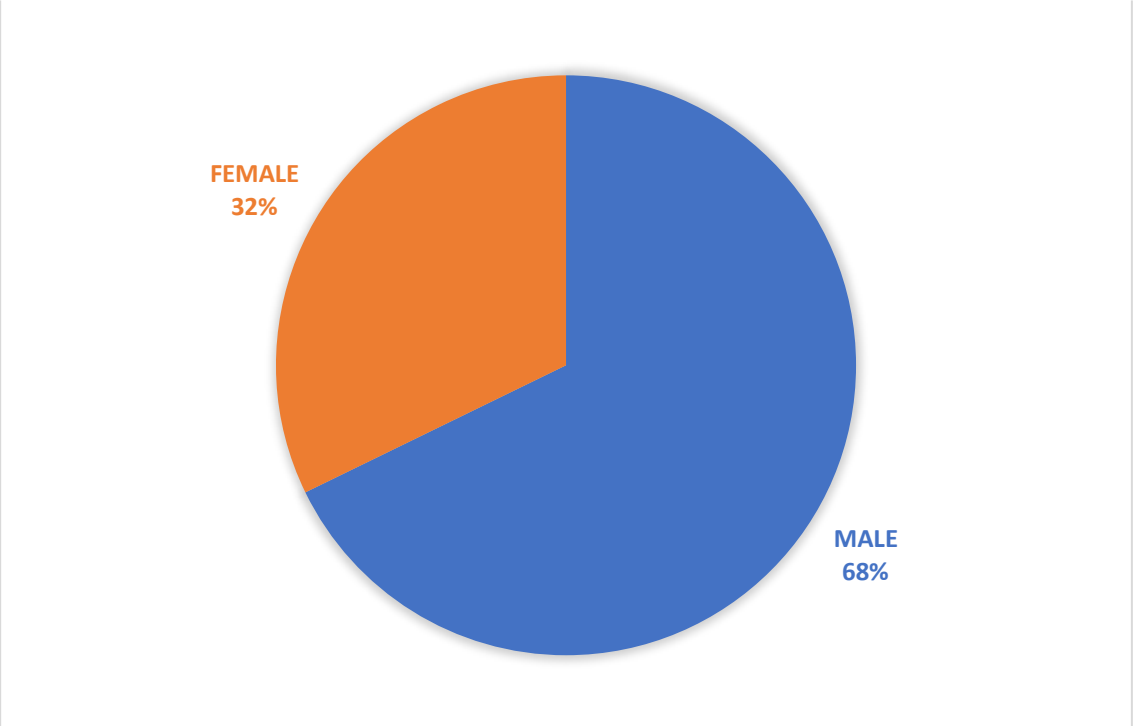

Figure 2- Gender distribution in chronic kidney disease patients

Table 4 - OPD/IPD wise distribution

OPD/IPD	No. of Patients	%
OPD	32	17.7
IPD	148	82.2
TOTAL	**180**	**100**

IPD patients had a higher proportion of cases (82.2%) than IPD patients (17.7%).

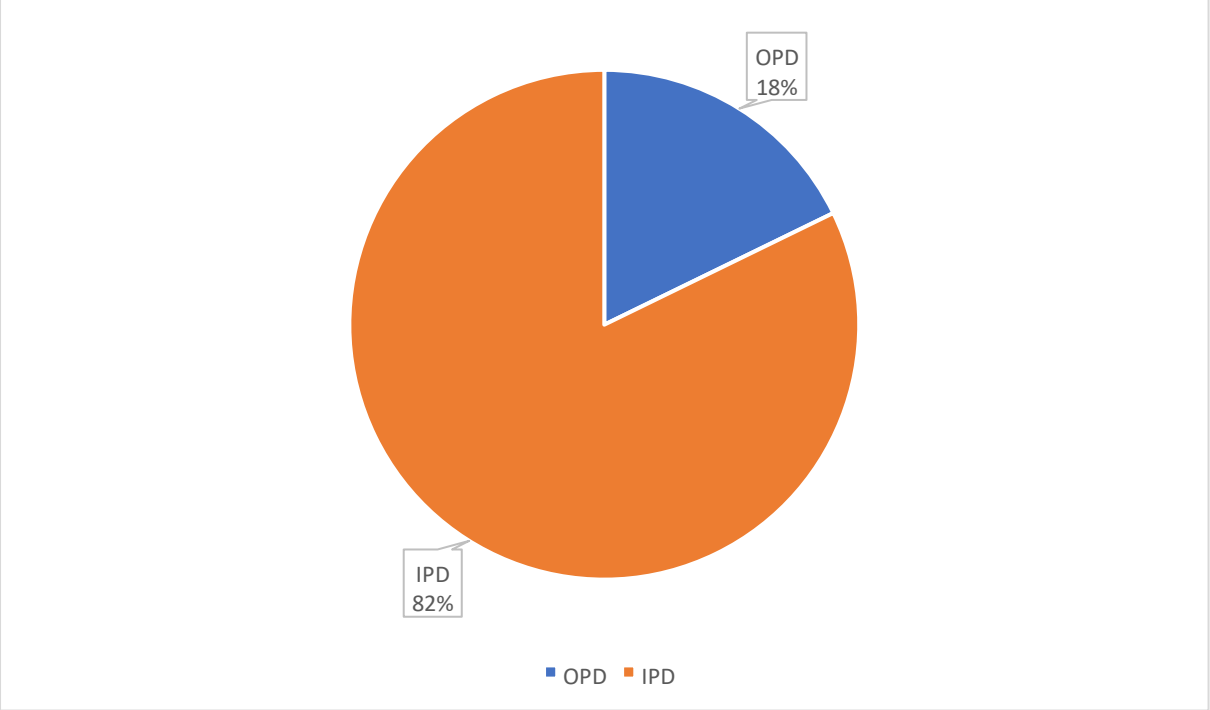

Figure 3 - OPD/IPD wise distribution of chronic kidney disease patients

Table 5 - Patients distribution in the stages of chronic kidney disease based on eGFR

Stages	eGFR value ml/ min/1.73m2	No. Patients of	Male	Female
I	>90	10	7	3
II	60-89	21	13	8
III A	45-59	18	13	5
III B	30-44	27	20	7
IV	15-29	46	32	14
V	<15	58	41	17

Above table shows the distribution of patients in the stages of chronic kidney disease. There were minimum number of male and female present in the stage I and maximum number of male and female present in the stage V.

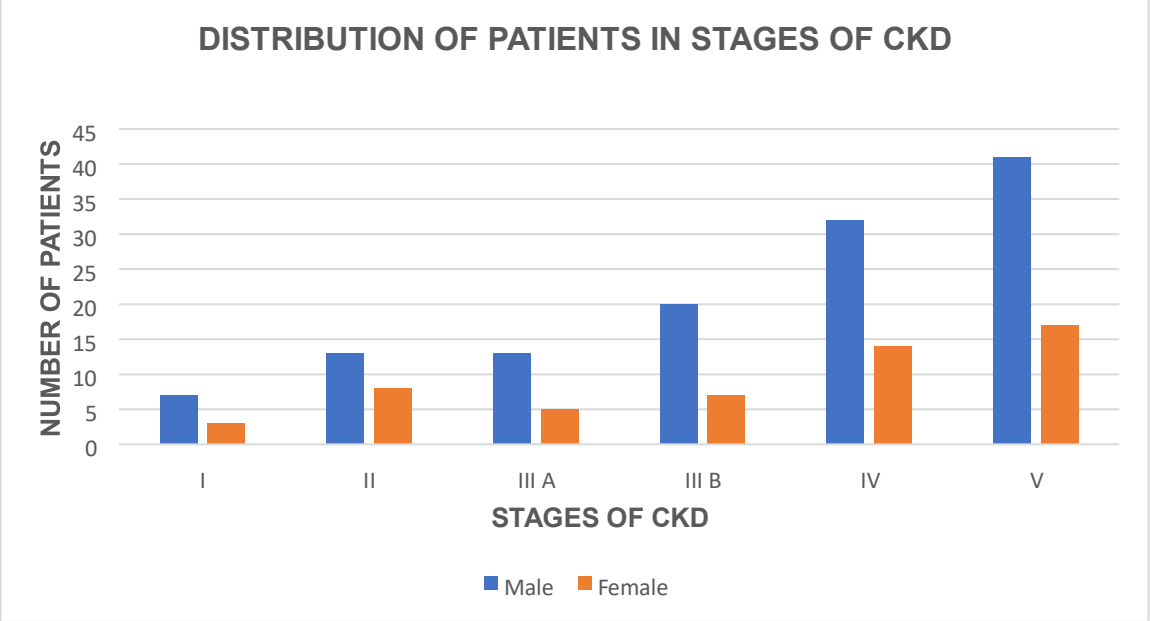

Figure 4 - Patients distribution in the stages of chronic kidney disease

Table 6 Distribution of CRP in the various stages of chronic kidney disease and their mean and standard deviation with p value

Stages	Mean ± Standard deviation in males	Mean ± Standain deviation females	p value
Stage I	5.93±0.66	6.22±0.42	=0.5096
Stage II	62.37±8.44	70.27±5.23	=0.0286*
Stage III A	71.43±6.01	72.4±3.28	=0.7399
Stage III B	72.69±3.60	73.46±4.28	=0.6464
Stage IV	79.14±3.93	79.93±4.75	=0.5592
Stage V	82.96±15.50	86.63±14.02	=0.4028

*(p<0.05) =significant

Table 6 showing mean and standard deviation of CRP with p value between males and females in the different stages of chronic kidney disease which shows a statistically significant difference in stage II (p=0.0286).

Table 7

Stages	Parameters	r value male	p value	r value female	p value
I	eGFR vs CRP	-0.89369	=0.006785*	-0.93296	=0.236125
II	eGFR vs CRP	-0.53992	=0.057337	-0.50444	=0.202835
III A	eGFR vs CRP	-0.81289	=0.000747*	-0.84498	=0.072208
III B	eGFR vs CRP	-0.62469	=0.003278*	-0.6132	=0.143285
IV	eGFR vs CRP	-0.63615	=0.000091*	-0.69594	=0.005797*
V	eGFR vs CRP	-0.84373	<0.00001*	-0.79986	=0.000119*

Correlation of eGFR with CRP in the stages of CKD

*(p<0.05) =significant

Table 7 shows the correlation of eGFR with CRP in the stages of CKD. The correlation of eGFR with CRP in males was found to be significant with p value 0.006785, 0.000747, 0.003278, 0.000091 and <0.00001 respectively in the stage I, III A, III B, IV and V whereas correlation of eGFR with CRP in females was found to be significant with p value 0.005797 and 0.000119 in the stage IV and V.

Stage I

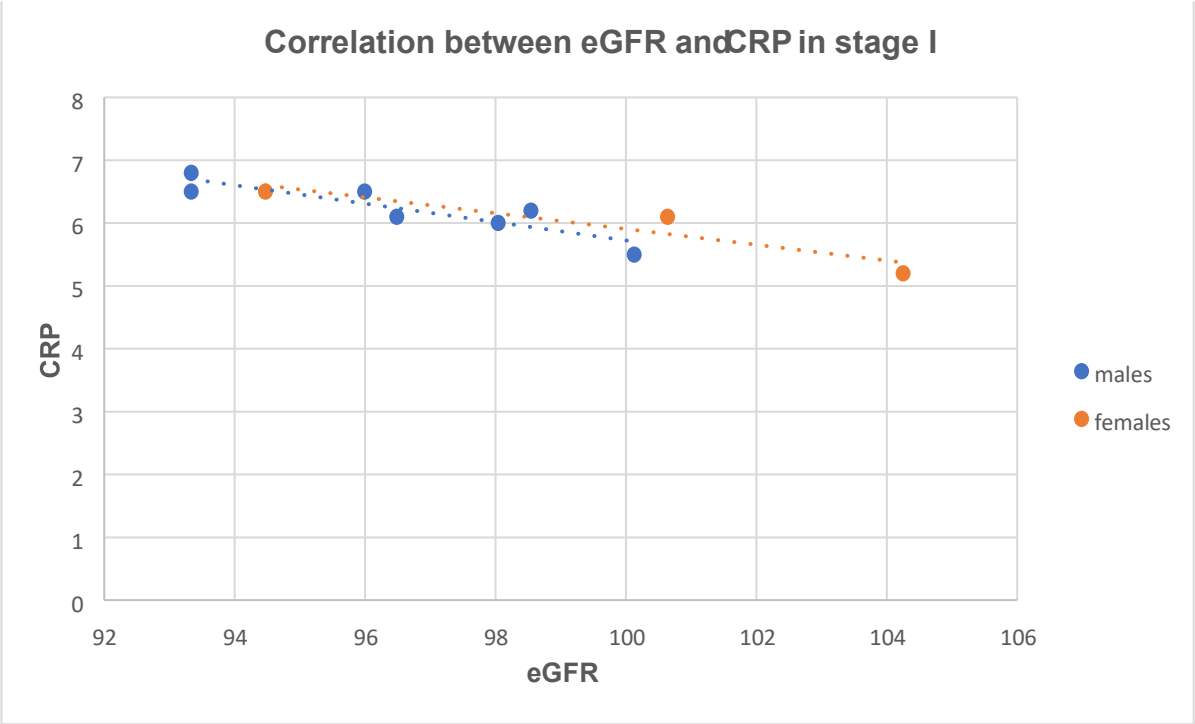

Figure 5 – Showing correlation of eGFR and CRP in stage I

Stage II

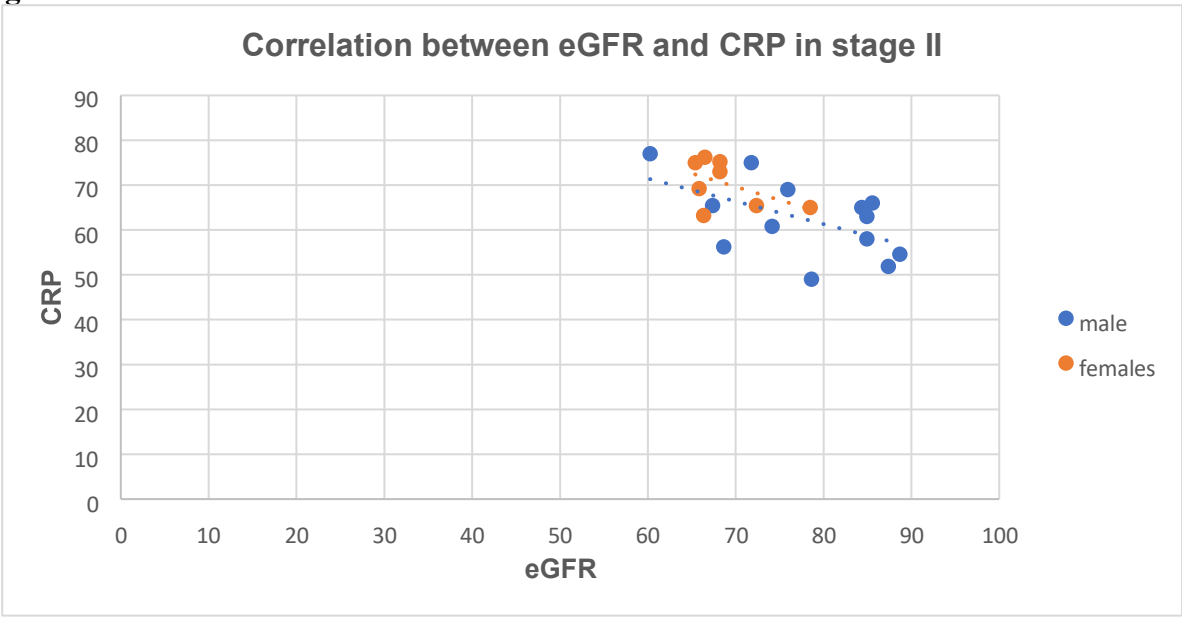

Figure 6 – Showing correlation of eGFR and CRP in stage II

Stage III A

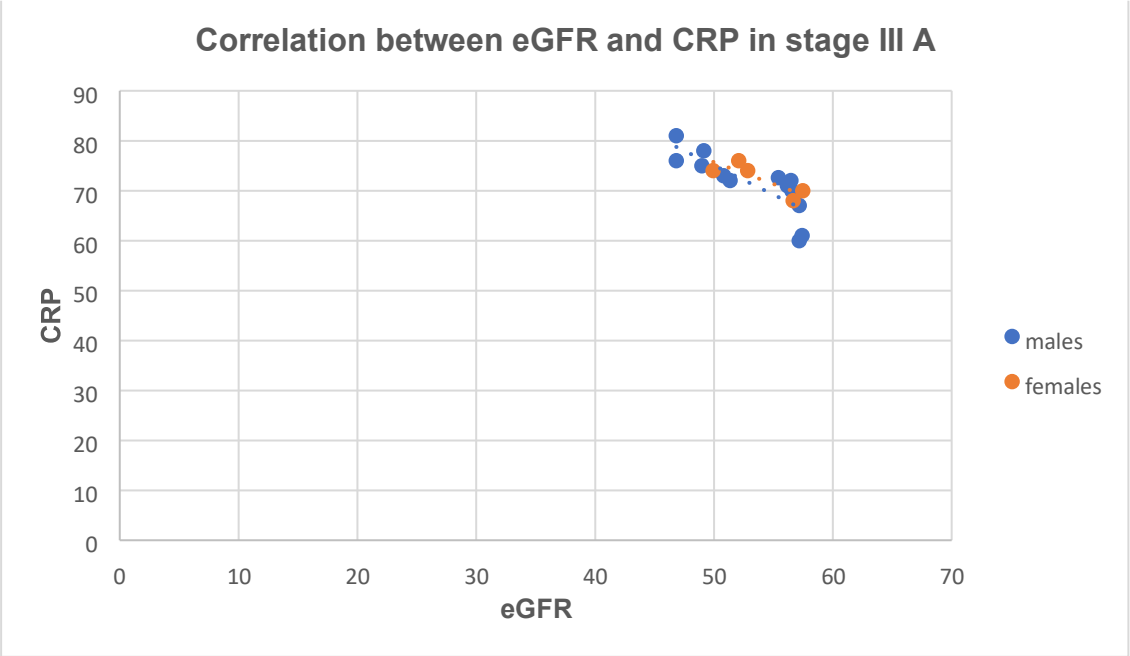

Figure 7 – Showing correlation of eGFR and CRP in stage III A

Stage III B

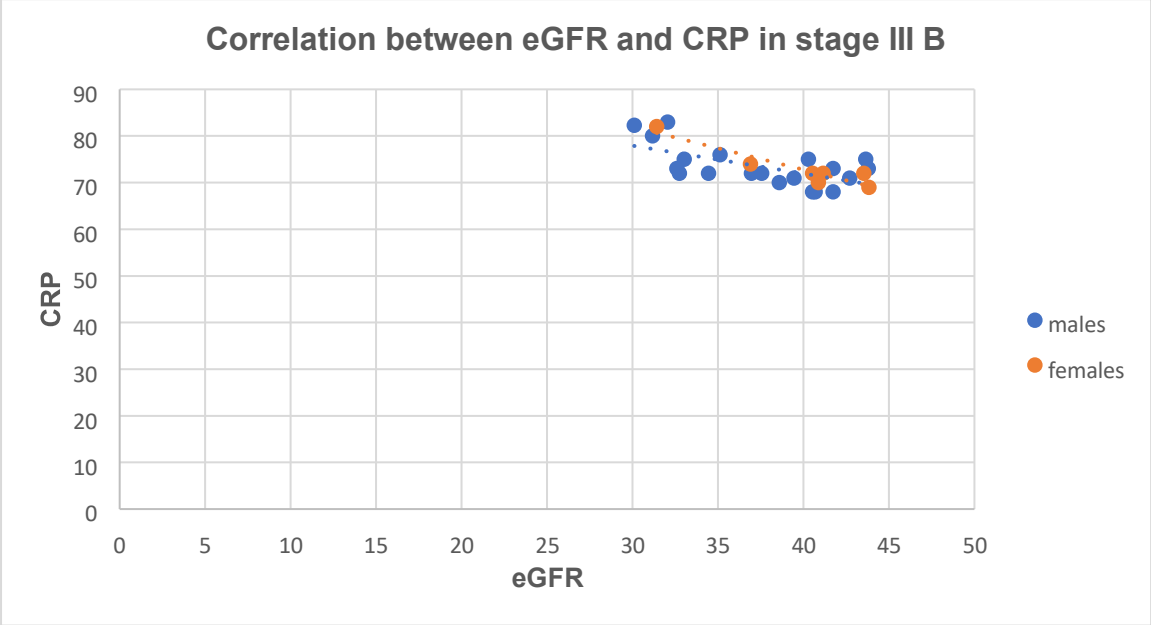

Figure 8 – Showing correlation of eGFR and CRP in stage III B

Stage IV

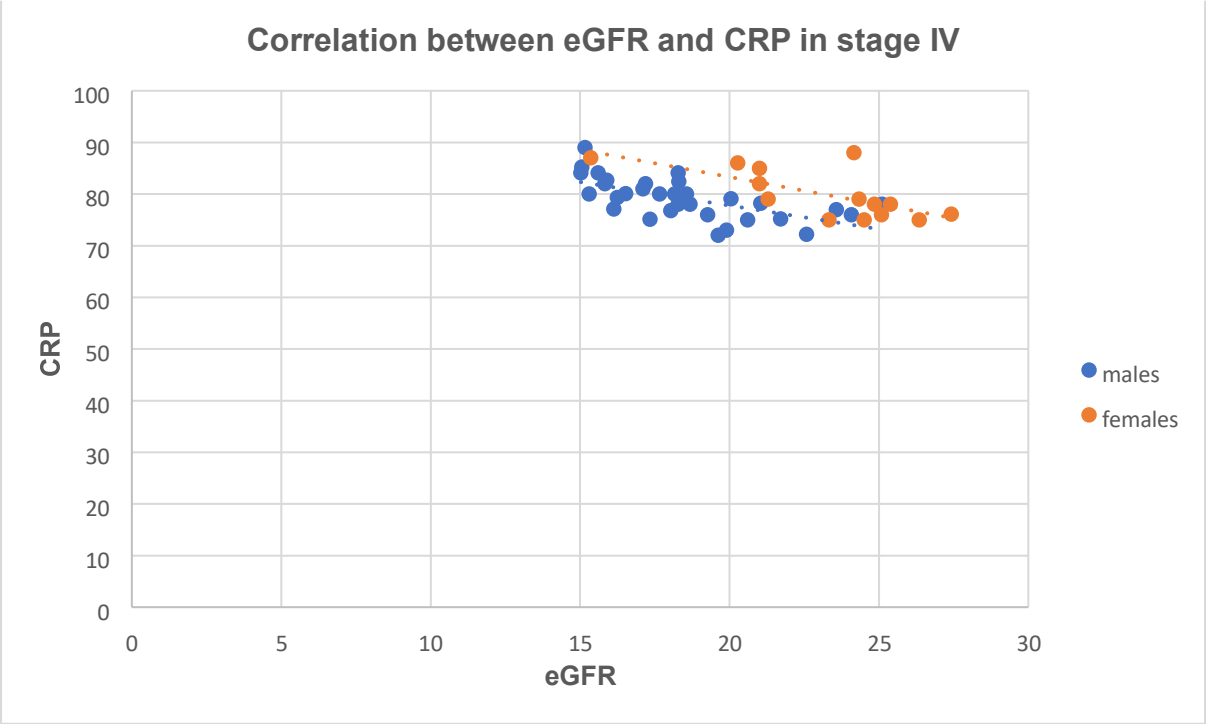

Figure 9 – Showing correlation of eGFR and CRP in stage IV

Stage V

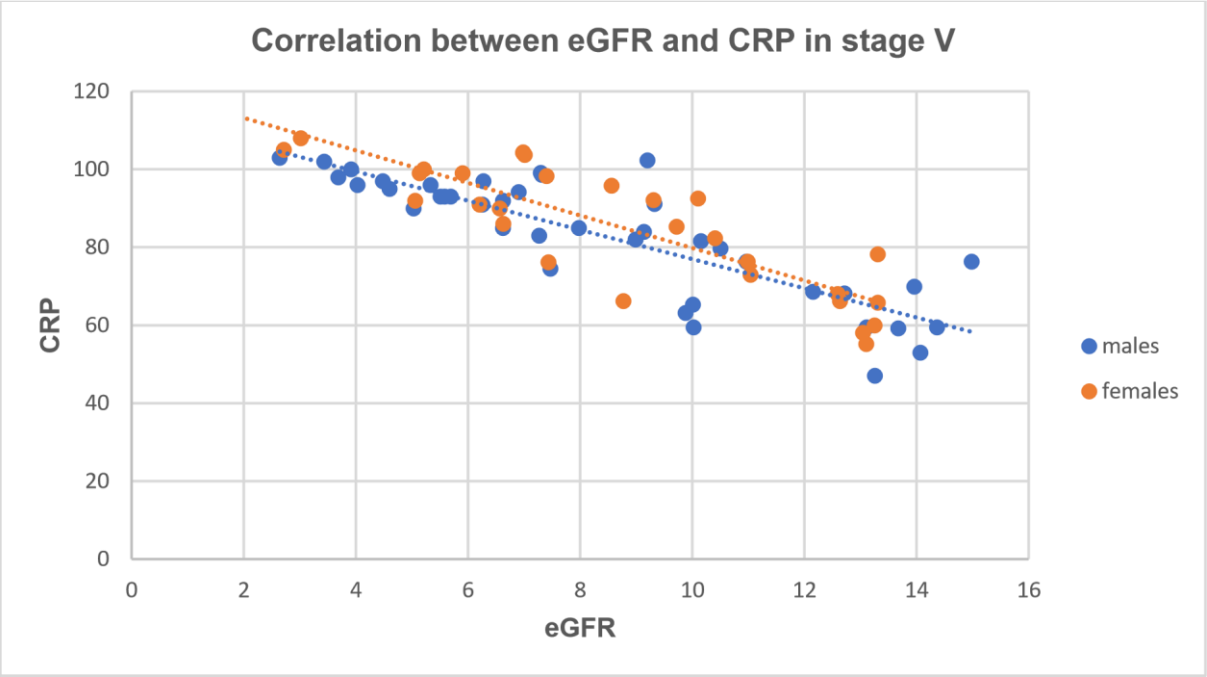

Figure 10 – Showing correlation of eGFR and CRP in stage V

4.Discussion

Chronic kidney disease (CKD) is a prevalent health condition that affects millions of individuals worldwide.[36] It is a progressive and irreversible disease that results in the gradual deterioration of kidney function over time. CKD can have various causes, the most common being diabetes and high blood pressure.[37] The progression of CKD occurs in stages, each characterized by the level of kidney function and the presence of symptoms. The five stages of CKD are determined by the estimated glomerular filtration rate (eGFR) which measures how well the kidneys are filtering waste. Diagnosing CKD involves various tests and assessments. The eGFR mentioned earlier is calculated

using a blood test that measures the level of creatinine, a waste product produced by muscle metabolism.[38]

This might be the first observational study conducted to assess the serum uric acid, serum C-reactive protein and lipid levels in the chronic kidney disease patients. To achieve the objectives of this study, 180 participants attending to outpatient departments (OPD) and inpatient department (IPD) of medicine, AIMSR Hospital, Bathinda were enrolled. The participants were further classified into the stages of chronic kidney disease for correlation and to identify status of biochemical parameters.

Chronic Kidney Disease (CKD) can develop at any age and various conditions can lead to CKD (Mary Mallappallil et al., 2014) [39]. Previously study, Ji Cheng Lv et al., 2019 [40] have reported, CKD becomes more common with increasing age. For every decade above age 40 years, GFR declines by 10 ml/min such that by age 70 years, the GFR has declined by about 30 ml/min. The aging process compounded by risk factors as well as well as hemodynamic and nonhemodynamic consequences of activation of the renin angiotensin system make the elderly susceptible to CKD. Therefore, in this present study, in order to verify the impact of age for the outcomes of chronic kidney disease participants were categorized into different age groups, which indicate;7.2% of cases were in the age groups of 20 to 30 years,13.8% of cases were in the age groups of 31 to 40 years,14.4% of cases were in the age groups of 41 to 50, 28.3% of cases were in age groups of 51 to 60 years, while 36.1% of the cases were in the age groups of 61 to 70 years suggested that highest number of cases were in the older age groups (Table 4). This clearly indicated that increase in the age may have direct impact on the chronic kidney disease. The age of patients in the present study ranged from 20-70 years. The mean± SD for age was 52.8±12.8 years. Maximum patients, that is, 36.1% were in the age group between 61-70 years. The other studies like those done by Vandana Menon et al., 2003[41], Madero et al., 2009[42] and Zhibin li et al., 2013[43] were having the age of the patients as 52±12, 52±12 and 58.7± 12 respectively which was almost similar to the present study. On the contrary, study by Kentaro Kohagura et al., 2013[44] was having mean± SD of the age of patients as 42.4± 18.5 which was lesser than the present study and that by Liu et al., 2021[45], Sebastjan bevc et al., 2017[46], Ailing zahang et al., 2021[47] and Yin et al., 2013[35] was having mean± SD of age as 63.5 ±13.5, 72.5± 5, 73.63 ±10.26, 73.63 ±10.26 respectively which was higher than the present study group.

In the present study, there were 122 males (67.7%) and 58 females (32.2%) among total of 180 chronic kidney disease patients. So, in the present study, the analysis according to the gender showed marked male preponderance. As the enrolment of patients in the present study was random so a greater number of males could be due to high prevalence of kidney disease in males as compare to females because of differences in hormones levels. Higher testosterone levels in men may cause a loss in kidney function. On the other hand, men's kidney may not be protected by estrogen, which is higher in women until menopause. This was in accordance with other studies by Mohamed E. Suliman et al., 2006[74] and Oluseyi A. Adejumo et al., 2016[86] who were also having a greater number of males in their studies in their studies as compared to females. Also H.K. Aggarwal et al., 2018[112] were having a greater number of males as was there in the present study. Only the study by Sebastjan Bevc et al., 2017[109] were having a greater number of females as compare to males.

Biomarkers of inflammation, including CRP are increased even in early stages of CKD and have been linked to CKD progression. Moreover, recent studies show association between certain CRP polymorphisms and CKD progression (Koray uludag et al., 2021).[81] Yet, longitudinal studies assessing CRP role in predicting long term risk for CKD in the general population are lacking. Previous cross-sectional studies suggested a possible association between CRP and decreased kidney function (Eitan kugler et al., 2015) [125] demonstrated an independent association between CRP and diminished filtration rate on subjects without renal disease or diabetes. In another cross-sectional studies, Wachtell et al., 2009[126] explored the association between CRP levels and the decline of renal function in patients with type 2 diabetes. It found that elevated CRP levels were predictive of renal function decline, Yi wen tsai et al.,2018[82] examined the relationship between CRP and the development of hypertension, which is a common comorbidity in CKD and Georgi Abraham et al.,2009[83] investigated the role of CRP as a predictor of CKD progression in patients with type 2 diabetes. It suggested that CRP levels were associated with an increased risk of CKD progression. In

this study, we investigated variations in CRP levels across different CKD stages and examined potential gender-based differences in these levels. Our findings demonstrate varying trends in CRP levels as CKD progresses through its stages. Notably, Stage II exhibited a significant increase in CRP levels compared to earlier stages (Stage I) (Table 14). This suggests a potential association between advanced CKD stages and elevated CRP levels, indicating a potential connection between CKD progression and inflammation. In agreement to these statements, CM Lora et al.,2009[127] investigated the role of inflammation, including CRP levels, in the progression of kidney disease using data from the Chronic Renal Insufficiency Cohort (CRIC) Study. It found that higher CRP levels were associated with an increased risk of CKD progression and Besarab et al., 2011[128] assessed the relationship between CRP levels and the risk of end-stage renal disease (ESRD) in patients with CKD. It found that elevated CRP levels were associated with a higher risk of ESRD. Elevated CRP levels are often indicative of systemic inflammation and have been associated with adverse outcomes, including cardiovascular diseases and CKD progression. The significant increase in CRP levels observed in Stage II could reflect an underlying inflammatory process triggered by renal dysfunction. Our study also explored gender-based differences in CRP levels within each CKD stage. While variations were observed, statistical significance was achieved only in Stage II. This suggests that, within the scope of this study, gender might not consistently influence CRP levels in CKD patients. Elevated CRP levels could indicate a heightened state of inflammation that could contribute to the progression of both CKD and cardiovascular diseases. This underscores the need for strategies that address both inflammation and CKD management in patients, particularly in advanced CKD stages.
In this study, we explored the correlations between eGFR and CRP in Stages of CKD patients. Our findings indicate a negative correlation between eGFR and C-reactive protein (CRP) levels indicate that lower eGFR values are associated with higher CRP levels in both males ($r = -0.89369$, $p = 0.006785$) and females ($r = -0.93296$, $p = 0.236125$). This suggests a potential link between reduced renal function and increased inflammation in Stages of CKD.
It's important to acknowledge some limitations of our study, including the relatively small sample size and the observational design. The observational design restricts our ability to establish causal relationships between serum CRP and CKD progression. Additionally, our study did not consider factors such as dietary habits, lifestyle, infections, comorbidities and medication use, which could influence serum CRP. Future research could benefit from longitudinal designs that track changes in serum CRP and lipid levels as CKD progresses.

5.Conclusion

Chronic kidney disease is one of the non-communicable diseases that have had an increase in deaths related to them over the previous two decades. The present study highlights the progressive increase in CRP levels as CKD advances through its stages. This finding shows the increase in CRP levels as CKD progresses through its stages, particularly evident in Stage II in the present study underscores the importance of addressing inflammation in CKD management.

7. Ethics Declaration

This study was approved by AIMSR Research Committee and the Ethics Committee of Biomedical and Health Research, Adesh University, Bathinda.

8. Consent

Written informed consent was obtained from all participants for the use of their blood sample for this research and the publication of any findings in the scientific literature.

9. Source of Funding

None.

10. References

1. Levey, A. S., Eckardt, K. U., Tsukamoto, Y., Levin, A., Coresh, J., Rossert, J., ... & Eknoyan, G. (2005). Definition and classification of chronic kidney disease: a position statement from kidney disease: Improving Global Outcomes (KDIGO). *Kidney international*, *67*(6), 2089-2100.
2. Kovesdy, C. P. (2022). Epidemiology of chronic kidney disease: an update 2022. *Kidney International Supplements*, *12*(1), 7-11.
3. Wanner, C., & Tonelli, M. (2014). KDIGO Clinical Practice Guideline for Lipid Management in CKD: summary of recommendation statements and clinical approach to the patient. *Kidney international*, *85*(6), 1303-1309.
4. Hill, N. R., Fatoba, S. T., Oke, J. L., Hirst, J. A., O'Callaghan, C. A., Lasserson, D. S., & Hobbs,F. R. (2016). Global prevalence of chronic kidney disease–a systematic review and meta-analysis. *PloS one*, *11*(7), e0158765.
5. Mohanty, N. K., Sahoo, K. C., Pati, S., Sahu, A. K., & Mohanty, R. (2020). Prevalence of chronic kidney disease in Cuttack district of Odisha, India. *International Journal of Environmental Research and Public Health*, *17*(2), 456.
6. Vos, T., Allen, C., Arora, M., Barber, R. M., Bhutta, Z. A., Brown, A., ... & Boufous, S. (2016). Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The lancet*, *388*(10053), 15451602.
7. Chaity, B. S. (2022). Treatment and prevention of chronic kidney disease.
8. Wesseling, C., Crowe, J., Hogstedt, C., Jakobsson, K., Lucas, R., & Wegman, D. H. (2013). The epidemic of chronic kidney disease of unknown etiology in Mesoamerica: a call for interdisciplinary research and action. *American journal of public health*, *103*(11), 1927-1930.
9. Yousif, E. A., Ahmed, S. M. S., Alsadig, S. M., Elmukashfi, S. T. A., & Falih, R. E. (2019). Estimation of Salivary Creatinine and Urea as alternative to Plasma Creatinine and Urea in Sudanese Patients with Chronic Kidney Disease in Khartoum State-Sudan. *Int. J. Curr. Res. Med. Sci*, *5*(9), 8-14.
10. Kalantar-Zadeh, K., Lockwood, M. B., Rhee, C. M., Tantisattamo, E., Andreoli,
S., Balducci, A., ... & Li, P. K. T. (2022). Patient-centred approaches for the management of unpleasant symptoms in kidney disease. *Nature Reviews Nephrology*, *18*(3), 185-198.
11. Go, A. S., Chertow, G. M., & Fan, D. (2005). Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *Journal of Vascular Surgery*, *41*(1), 177.
12. Natale, P., Ruospo, M., Saglimbene, V. M., Palmer, S. C., & Strippoli, G. F. (2019). Interventions for improving sleep quality in people with chronic kidney disease. *Cochrane Database of Systematic Reviews*, (5).
13. Ladhani, M., Craig, J. C., Irving, M., Clayton, P. A., & Wong, G. (2017). Obesity and the risk of cardiovascular and all-cause mortality in chronic kidney disease: a systematic review and meta-analysis. *Nephrology Dialysis* Transplantation, *32*(3), 439-449.
14. Mishra, R. K., Yang, W., Roy, J., Anderson, A. H., Bansal, N., Chen, J., ... & Shlipak, M. G. (2015). Kansas City Cardiomyopathy Questionnaire score is associated with incident heart failure hospitalization in patients with chronic kidney disease without previously diagnosed heart failure: chronic renal insufficiency cohort study. *Circulation: Heart Failure*, *8*(4), 702-708.
15. Bansal, N., McCulloch, C. E., Rahman, M., Kusek, J. W., Anderson, A. H., Xie, D., ... & Hsu, C. Y. (2015). Blood pressure and risk of all-cause mortality in advanced chronic kidney disease and hemodialysis: the chronic renal insufficiency cohort study. *Hypertension*, *65*(1), 93-100.
16. Johnson, D. (2011). Chapter 4: CKD Screening and Management: Overview. *Daugirdas, John. Handbook of Chronic Kidney Disease Management. Lippincott Williams and Wilkins*, 32-43.
17. Patel, S. S., Molnar, M. Z., Tayek, J. A., Ix, J. H., Noori, N., Benner, D., ... & Kalantar-Zadeh, K. (2013). Serum creatinine as a marker of muscle mass in chronic kidney disease: results of a cross-sectional study and review of literature. *Journal of cachexia, sarcopenia and muscle*, *4*, 19-29.

18. Myers, G. L., Miller, W. G., Coresh, J., Fleming, J., Greenberg, N., Greene, T., ... & National Kidney Disease Education Program Laboratory Working Group. (2006). Recommendations for improving serum creatinine measurement: a report from the Laboratory Working Group of the National Kidney Disease Education Program. *Clinical chemistry*, *52*(1), 5-18.
19. Drawz, P., & Rahman, M. (2015). Chronic kidney disease. *Annals of internal medicine*, *162*(11), ITC1-ITC16.
20. El Nahas, A. M., & Bello, A. K. (2005). Chronic kidney disease: the global challenge. *The lancet*, *365*(9456), 331-340.
21. Levey, A. S., Eckardt, K. U., Tsukamoto, Y., Levin, A., Coresh, J., Rossert, J., ... & Eknoyan, G. (2005). Definition and classification of chronic kidney disease: a position statement from kidney disease: Improving Global Outcomes (KDIGO). *Kidney international*, *67*(6), 2089-2100.
22. Jha, V., Garcia-Garcia, G., Iseki, K., Li, Z., Naicker, S., Plattner, B., ... & Yang, C. W. (2013). Chronic kidney disease: global dimension and perspectives. *The Lancet*, *382*(9888), 260-272.
23. Charles, C., & Ferris, A. H. (2020). Chronic kidney disease. *Primary Care: Clinics in Office Practice*, *47*(4), 585-595.
24. Lv, J. C., & Zhang, L. X. (2019). Prevalence and disease burden of chronic kidney disease. *Renal fibrosis: mechanisms and therapies*, 3-15.
25. Jha, V., Garcia-Garcia, G., Iseki, K., Li, Z., Naicker, S., Plattner, B., ... & Yang, C. W. (2013). Chronic kidney disease: global dimension and perspectives. *The Lancet*, *382*(9888), 260-272.
26. Nacak, H., van Diepen, M., Qureshi, A. R., Carrero, J. J., Stijnen, T., Dekker, F. W., & Evans, M. (2015). Uric acid is not associated with decline in renal function or time to renal replacement therapy initiation in a referred cohort of patients with Stage III, IV and V chronic kidney disease. *Nephrology Dialysis Transplantation*, *30*(12), 2039-2045.
27. Ye, M., Hu, K., Jin, J., Wu, D., Hu, P., & He, Q. (2018). The association between time-mean serum uric acid levels and the incidence of chronic kidney disease in the general population: a retrospective study. *BMC nephrology*, *19*, 1-10.
28. Xia, X., Luo, Q., Li, B., Lin, Z., Yu, X., & Huang, F. (2016). Serum uric acid and mortality in chronic kidney disease: a systematic review and metaanalysis. *Metabolism*, *65*(9), 1326-1341.
29. Uludag, K., Boz, G., Arikan, T., & Gunal, A. I. (2022). Temporal evolution of Creactive protein levels and its association with the incident hospitalization risk among individuals with stage 3–4 chronic kidney disease. *International Urology and Nephrology*, *54*(3), 609-617.
30. Jeena, J., Manhas, S., Prasad, R., Prasad, S., & Gupta, R. (2022). Direct Relationship Between Uric Acid and C-Reactive Protein and Its Implication in the Chronic Kidney Disease. *Indian Journal of Clinical Biochemistry*, *37*(3), 365-369.
31. Miao, L., Min, Y., Qi, B., Zhu, C. M., Chen, J. H., Deng, G. X., ... & Li, R. S. (2021). Causal effect between total cholesterol and HDL cholesterol as risk factors for chronic kidney disease: a mendelian randomization study. *BMC nephrology*, *22*, 1-9.
32. Zhang, L., Yuan, Z., Chen, W., Chen, S., Liu, X., Liang, Y., ... & Zou, H. (2014). Serum lipid profiles, lipid ratios and chronic kidney disease in a Chinese population. *International Journal of Environmental Research and Public Health*, *11*(8), 7622-7635.
33. Arnold, R., Issar, T., Krishnan, A. V., & Pussell, B. A. (2016). Neurological complications in chronic kidney disease. *JRSM cardiovascular disease*, *5*, 2048004016677687.
34. Cravedi, P., & Remuzzi, G. (2013). Pathophysiology of proteinuria and its value as an outcome measure in chronic kidney disease. *British journal of clinical pharmacology*, *76*(4), 516-523.
35. Nehus, E. (2018). Obesity and chronic kidney disease. *Current opinion in pediatrics*, *30*(2), 241-246.
36. Olsen, E., & van Galen, G. (2022). Chronic renal failure-causes, clinical findings, treatments and prognosis. *Veterinary Clinics: Equine Practice*, *38*(1), 25-46.
37. Kazancioglu, R. (2013). Risk factors for chronic kidney disease: an update. *Kidney international supplements*, *3*(4), 368-371.

38. Zhang, L., Zhang, P., Wang, F., Zuo, L., Zhou, Y., Shi, Y., ... & Wang, H. (2008). Prevalence and factors associated with CKD: a population study from Beijing. *American Journal of Kidney Diseases*, *51*(3), 373-384.
39. Nivedita, A. K., Sinha, A., Mitra, J. K., & Sinha, R. (2021). Uric acid levels in chronic kidney disease-a hospital based cross-sectional study in RIMS, Ranchi, Jharkhand. *International Journal of Research in Medical Sciences*, *9*(2), 569.
40. Kugler, E., Cohen, E., Goldberg, E., Nardi, Y., Levi, A., Krause, I., ... & Krause, I. (2015). C reactive protein and long-term risk for chronic kidney disease: a historical prospective study. *Journal of nephrology*, *28*, 321-327.
41. Menon, V., Wang, X., Greene, T., Beck, G. J., Kusek, J. W., Marcovina, S. M., & Sarnak, M. J. (2003). Relationship between C-reactive protein, albumin, and cardiovascular disease in patients with chronic kidney disease. *American Journal of Kidney Diseases*, *42*(1), 44-52.
42. Son, M., Seo, J., & Yang, S. (2020). Association between dyslipidemia and serum uric acid levels in Korean adults: Korea National Health and Nutrition Examination Survey 2016-2017. *PLoS One*, *15*(2), e0228684.
43. Nakano, T., Tanaka, S., Tsuruya, K., & Kitazono, T. (2021). Relationship between serum lipid concentrations and impaired renal function in patients with chronic kidney disease: the Fukuoka Kidney Disease Registry Study. *Clinical and Experimental Nephrology*, *25*, 385-393.
44. Lamprea-Montealegre, J. A., Shlipak, M. G., & Estrella, M. M. (2021). Chronic kidney disease detection, staging and treatment in cardiovascular disease prevention. *Heart*, *107*(16), 1282-1288.
45. Sonoda, H., Takase, H., Dohi, Y., & Kimura, G. (2011). Uric acid levels predict future development of chronic kidney disease. *American journal of nephrology*, *33*(4), 352-357.
46. Mora-Gutiérrez, J. M., MF, S. R., & Bilbao, C. (2016). Chronic kidney disease in the elderly patient. *Revista Espanola de Geriatria y Gerontologia*, *52*(3), 152158.
47. Streja, E., Norris, K. C., Budoff, M. J., Hashemi, L., Akbilgic, O., & KalantarZadeh, K. (2021). The quest for cardiovascular disease risk prediction models in patients with nondialysis chronic kidney disease. *Current opinion in nephrology and hypertension*, *30*(1), 38-46.