Original Research Paper

Volume - 14 | Issue - 11 | November - 2024 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Nephrology

UNDERSTANDING CHRONIC RENAL FAILURE: THE IMPACT OF ACUTE PHASE REACTANTS

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ABSTRACT The progressive loss of kidney function over time is the hallmark of chronic kidney disease. Millions of people worldwide suffer from chronic kidney disease, which is a serious public health concern due to its high prevalence, morbidity, and mortality rates. The rising prevalence of chronic kidney disease is mostly due to the two primary causes of renal sickness, diabetes and hypertension, which are becoming more widespread globally. Thus, the goal of the current study was to assess chronic renal failure using demographic information, clinical symptoms and acute phase reactants, and correlation with estimated-glomerular filtration rate (eGFR) of chronic kidney disease (CKD) by staging it based on eGFR. Several acute phase reactants (C- reactive Protein, Erythrocyte Sedimentation Rate, Fibrinogen, Ferritin, D-dimer, and Procalcitonin) are used in this study as independent inflammatory markers and to assess the severity of chronic kidney disease.

KEYWORDS : Chronic kidney disease, eGFR, Hemodialysis, Inflammatory markers

INTRODUCTION

Chronic kidney disease (CKD) is a non-communicable disease that includes a range of different physiological disorders that are associated with an abnormal renal function and progressive decline in glomerular filtration rate (GFR) [1]. The progressive loss of kidney function over time is the hallmark of chronic kidney disease (CKD). Due to its high rates of prevalence, morbidity, and mortality, chronic kidney disease (CKD) affects millions of people globally and is a major public health concern. The two main causes of renal illness, diabetes and hypertension, are becoming more common worldwide, which is largely to blame for the growing burden of chronic kidney disease (CKD) [2]. As end-stage renal disease (ESRD) can develop from chronic kidney disease (CKD), early detection and routine monitoring are essential to halting the illness's progression [3]. A key component in the development of renal damage is inflammation, which also contributes to the deterioration of kidney function and the emergence of concomitant diseases like cardiovascular disease [4]. As a result, CKD patient's Acute phase reactant levels can provide important prognostic information and aid in directing therapeutic measures [5]. Hence aim of this study was to assess the levels of different acute phase reactants in patients with chronic renal failure, including ferritin, D-Dimer, procalcitonin, Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and fibrinogen.

MATERIALS AND METHODS:

The present study was carried out on 98 adult patients of chronic renal failure following approval from the ethics committee.

I) Inclusion Criteria:

a) Patient with evidence of chronic renal failure (>18 years of age)
b) Patient in whom these tests (C-Reactive Protein, Erythrocyte sedimentation rate, D-dimer, ferritin, Procalcitonin, Fibrinogen) are prescribed by practicing physician
c) Patient willing to give informed consent

II) Exclusion Criteria:

a) Pregnancy
b) Patients with shock or severe sepsis
c) Patients with multiorgan failure

A detailed history and thorough clinical examination were done with emphasis on the chronic kidney disease. At admission, GFR was measured using CKD EPI equation and ultrasonography of abdomen and pelvis was performed. Patients were graded in CRF as per K/DOQI criteria 2002).

Quantitative assessment of C-reactive protein was done with Chem Ultra machine (Aspen). D-dimer was calculated using Neph plus-1 machine (Aspen). ESR measured using Westergren tube. Chemiluminescence immunoassay (CLIA) detection kit was used to measure ferritin levels in a sample. Fibrinogen was calculated using Clauss fibrinogen assay. Procalcitonin was measured with enzyme-linked fluorescent assay (ELFA) method.

Statistical Analysis

Descriptive and inferential statistical analysis has been carried out in the present study. The statistical software namely STATISTICAL PACKAGE FOR THE SOCIAL SCIENCES 20 (SPSS 21.0) was used for the analysis of the data. Analysis of variance (ANOVA) has been used to find the significance of mean difference of parameters between three or more groups of patients.

RESULTS

In present study mean CRP of CRF patients was 1.81±1.04, in which Stage I was 0.2, Stage II was 0.30±0.11, Stage III was 1.3±0.61, Stage IV had 1.81±0.39 and Stage V had 2.86 ± 1.18 CRP level. There was statistically significant ($p < 0.05$) difference of raised mean CRP of patients in increased CRF stages. (Table 1)

Table 1: CRP According To Stage Of CKD

Stage of CKD	C-reactive protein					P Value
	N	Minimum	Maximum	Mean	Std. Deviation	
1	1	0.20	0.20	0.2000		< 0.05
2	9	0.20	0.50	0.3000	0.11180	
3	23	0.60	2.30	1.3000	0.61200	
4	39	1.00	2.60	1.8128	0.39013	
5	26	1.20	5.70	2.8577	1.18226	
Total	98	0.20	5.70	1.8143	1.04881	

Table 2: ESR According To Stage Of CKD

Stage of CKD	C-reactive protein					P Value
	N	Minimum	Maximum	Mean	Std. Deviation	
1	1	0.20	0.20	0.2000		< 0.05
2	9	0.20	0.50	0.3000	0.11180	
3	23	0.60	2.30	1.3000	0.61200	
4	39	1.00	2.60	1.8128	0.39013	
5	26	1.20	5.70	2.8577	1.18226	
Total	98	0.20	5.70	1.8143	1.04881	

Minimum ESR was 7.8 and maximum was 66.8, mean ESR of CRF patients was 36.39 ± 14.8, in which Stage I was 7.8, Stage II was 14.310 ± 3.88, Stage III was 26.24 ± 2.48, Stage IV had 35.42 ± 5.65 and Stage V had 55.57 ± 10.2 CRP level. There was statistically significant (p <0.05) difference of raised mean ESR of patients in increased CRF stages. (Table 2)

Minimum D-dimer was 2.5 and maximum was 6.18, mean D-dimer of CRF patients was 4.4 ± 1.47, in which Stage I was 2.5, Stage II was 2.71 ± 0.30, Stage III was 3.38 ± 0.84, Stage IV had 4.24 ± 0.99 and Stage V had 6.18 ± 1.48 D-dimer level. There was statistically significant (p <0.05) difference of raised mean D-dimer of patients in increased CRF stages. (Table 3)

Table 3: D-Dimer According To Stage Of CKD

Stage of CKD	D-Dimer					P Value
	N	Minimum	Maximum	Mean	Std. Deviation	
1	1	2.50	2.50	2.5000		< 0.05
2	9	2.50	3.40	2.7111	0.30596	
3	23	2.50	4.90	3.3826	0.84027	
4	39	3.00	6.50	4.2436	0.98590	
5	26	4.30	7.50	6.1808	0.87545	
Total	98	2.50	7.50	4.3969	1.46741	

In present study, minimum ferritin was 156 and maximum was 1600, mean ferritin of CRF patients was 952.28 ± 411.48, in which Stage I was 156, Stage II was 257.33 ± 28.72, Stage III was 555.26 ± 54.79, Stage IV had 1042.59 ± 146.54 and Stage V had 1439.19 ± 133.68 ferritin level. There was statistically significant (p <0.05) difference of raised mean serum ferritin of patients in increased CRF stages. (Table 4)

Table 4: Serum Ferritin According To Stage Of CKD

Stage of CKD	Serum ferritin					P Value
	N	Minimum	Maximum	Mean	Std. Deviation	
1	1	156.00	156.00	156.0000		< 0.05
2	9	215.00	298.00	257.3333	28.72281	
3	23	465.00	761.00	555.2609	54.78571	
4	39	823.00	1326.00	1042.5897	146.53628	
5	26	1187.00	1600.00	1439.1923	133.68351	
Total	98	156.00	1600.00	952.2755	411.47975	

Minimum fibrinogen was 3.4 and maximum was 5.5, mean fibrinogen of CRF patients was 4.12 ± 0.61, in which Stage I was 3.4, Stage II was 3.43 ± 0.16, Stage III was 3.62 ± 0.3, Stage IV had 4.18 ± 0.42 and Stage V had 4.75 ± 0.51 fibrinogen level. There was statistically significant (p <0.05) difference of raised mean fibrinogen of patients in different CRF stages. (Table 5)

Table 5: Fibrinogen According To Stage Of CKD

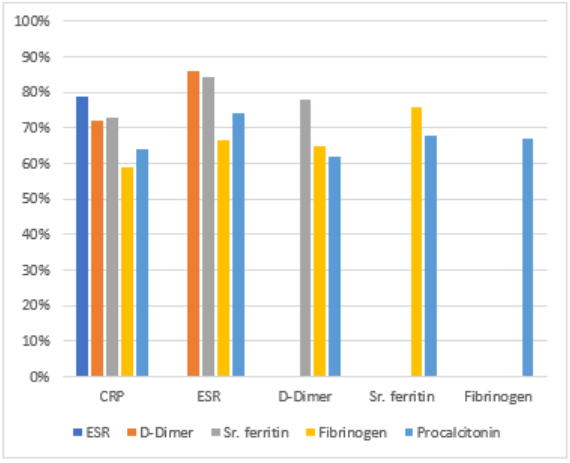
Stage of CKD	Fibrinogen					P Value
	N	Minimum	Maximum	Mean	Std. Deviation	
1	1	3.40	3.40	3.4000		< 0.05
2	9	3.30	3.70	3.4333	0.15811	
3	23	3.40	4.50	3.6217	0.29689	
4	39	3.50	5.00	4.1769	0.41705	
5	26	3.90	5.50	4.7538	0.50615	
Total	98	3.30	5.50	4.1235	0.61086	

Table 6: Procalcitonin According To Stage Of CKD

Stage of CKD	Procalcitonin					P Value
	N	Minimum	Maximum	Mean	Std. Deviation	
1	1	0.04	0.04	0.0400		< 0.05
2	9	0.05	0.11	0.0789	0.01833	
3	23	0.07	0.21	0.1270	0.05013	
4	39	0.06	0.32	0.1923	0.06297	
5	26	0.12	0.92	0.4773	0.22764	
Total	98	0.04	0.92	0.2406	0.19330	

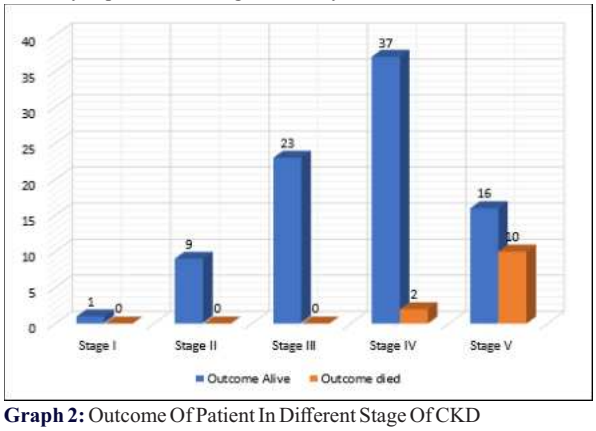
In present study, minimum procalcitonin was 0.04 and maximum was 0.92, mean fibrinogen of CRF patients was 0.24 ± 0.19, in which Stage I was 0.04, Stage II was 0.078 ± 0.018, Stage III was 0.127 ± 0.05, Stage IV had 0.192 ± 0.062 and Stage V had 0.477 ± 0.227 procalcitonin level. There was statistically significant (p <0.05) difference of raised mean procalcitonin of patients in different CRF stages. (Table 6)

Current study showed that there was overall positive co-relation between the different acute phase reactants. In patient with raised CRP had 79% co-relation to ESR, 72% co-relation to D-Dimer, 73% co-relation to serum ferritin, 59% co-relation to fibrinogen and 64% co-relation to procalcitonin. In patients with raised ESR had 86% co-relation to D-Dimer, 84.5% co-relation to sr ferritin, 66.5% co-relation to fibrinogen and 74% co-relation to procalcitonin. In patients with raised D-dimer had 78% co-relation to serum ferritin, 65% co-relation to fibrinogen levels and 62% co-relation to procalcitonin levels. In patients with raised Serum ferritin the co-relation with fibrinogen and procalcitonin was 75.7% and 67.7% respectively.



Graph 1: Co-relation Between Different Acute Phase Reactants

In present study in stage V 10 patient out of 26 died, and in stage IV 2 patients out of 39 patients died while all patient survived in stage I, II, III There was statistically significant (p <0.05) difference of increased mortality of patients with higher severity of CKD.



Graph 2: Outcome Of Patient In Different Stage Of CKD

DISCUSSION:

In present study of 98 CKD patients indicate a greater risk of mortality and morbidity particularly cardiovascular diseases in CKD patients as the acute phase reactants increases. Acute phase reactants as inflammatory markers have proposed to be independent risk of mortality and severity of CKD. Hence, the present study assessed various acute phase reactants (CRP, ESR, fibrinogen, ferritin, D-dimer, Procalcitonin) as an independent inflammatory marker and to determine the severity of CKD.

Distribution of patient according to eGFR, it was found that 1 patient (1%) had Stage I, 9 patients (9.2%) had Stage II CKD, 23 patients (23.5%) had Stage III, 39 patients (39.8%) were in Stage IV and 26 patients (26.5%) were in Stage V. This is probably because of CKD patients in higher stages (IV & III) were enrolled in our study as only patients with advanced stages were referred in tertiary hospital like our hospital. The finding is consistent with finding by Hill *et al.* (2016) who noted in their metanalysis that majority of individuals at early stages of CKD remained undiagnosed and untreated [6].

In our study, it is found that there is progressive decline in GFR as CKD progresses and having negative significant correlation, similar findings of negative correlation in GFR and stage of CKD is found in study by Khunte *et al*. (2019) [7]. There was statistically significant ($p < 0.05$) difference of raised mean CRP of patients in increased CRF stages. In CKD patients there is also positive correlation between CRP and other acute phase reactants which is consistent with findings of Li *et al* (2023). So, there was statistical significance with increased CRP and increased severity of CKD stage [8]. Moreover, Singh et al. showed that elevated CRP levels are associated with worse outcomes in CKD patients, making it a valuable tool for early detection and control of inflammation [9].

In present study, there was statistically significant ($p < 0.05$) difference of raised mean ESR of patients in increased CRF stages which was consistent with the findings by Farha Khan *et al*. (2022) in which it was found that ESR increases dramatically as CKD advances [10]. Fibrinogen has negative corelation with renal function but was a particularly powerful predictor of CKD development, with each standard deviation rise associated with a greater chance of fast renal function deterioration. The results demonstrate the importance of fibrinogen as a crucial inflammatory marker in the context of CKD [11].

Also, it was found that as ferritin level increased there was decrease in renal function that is negative correlation between ferritin and renal function, this finding was consistent with the findings of Hur *et al.* (2014) in which there was a substantial negative connection between baseline ferritin levels and RRF (residual renal function) decrease rate [12]. Study concluded that in CKD patients, serum D-dimer levels correlate negatively with GFR and as the stage of CKD progressed the PCT level increased indicating there was negative correlation between procalcitonin and renal function which was consistent with the findings of Sun et al. (2017) [13].

CONCLUSION

In present study CRP, ESR, D-dimer, ferritin, fibrinogen, and procalcitonin were found to positively correlate with age, creatinine, and potassium, but negatively correlate with urine output, eGFR, sodium, and calcium showing a positive correlation between increase in level of the acute phase reactants with the stage severity of the CKD. There was quantitative and qualitative increase in number of acute phase reactants as severity of CKD progressed. Further research can be done for assessment of other phase reactants which are responsible for late-stage CKD.

Financial Support And Sponsorship
Nil.

Conflicts Of Interest
There are no conflicts of interest.

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