DOI: https://doi.org/10.53350/pjmhs22161391

ORIGINAL ARTICLE

Frequency of Different Crp Levels in Hemodialysis Patients Having Anemia at Baseline, Taking Erythropoietin for Correction of Anemia

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ABSTRACT

Objectives: To determine the frequency of different C-reactive protein levels in hemodialysis patients having anemia at baseline, taking erythropoietin for the correction of anemia.

Methodology: A cross sectional study was conducted at the Department of Nephrology, Jinnah Hospital Lahore between October 2019 to April 2020. Eighty patients fulfilling the criteria were enrolled after taking informed consent. Demographic information was obtained. Blood samples were taken under aseptic measures. All samples were sent to the laboratory for CRP. The data was analyzed by using SPSS version 20.0.

Results: According to the results of our study, the mean age of patients was 47.50 +16.37 years. With regards to CRP levels, 23.7% patients had CRP < 1.3 mg/l, 22.5% patients had CRP of 1.3-2.04 mg/l, 26.25% had CRP of 2.05-3.21 mg/l and 27.5% patients had >3.21 mg/l. Further analysis showed that CRP was not significantly different in different age groups i.e. p=0.862 but CRP levels were significantly different in males and females(Chi square:7.214) i.e. p value = 0.027.

Conclusion: CRP is high in most CKD anemic patients who are on hemodialysis and taking erythropoietin.

Keywords: Hemodialysis, CRP, Erythropoietin.

INTRODUCTION

Chronic kidney disease (CKD), formerly known as chronic renal failure, is a concept that describes all levels of compromised kidney function, extending from damage-at-risk to mild, intermediate, and profound chronic kidney failure [1]. For patients suffering from end-stage CKD, renal replacement therapy is the only viable approach, and it includes various techniques such as kidney transplants and peritoneal or hemodialysis [2]. One of the prominent characteristics of CKD that is significantly associated with poor prognosis is anemia. This can be treated by recombinant human erythropoietin along with iron-containing medications and diet, to improve the response [4]. However, the use of erythropoiesis-stimulating agents (ESA) in such conditions is linked with increased morbidity and mortality, as per recent experimental studies[3].

Evidence shows the strong association of elevated concentrations of biomarkers such as C- reactive protein (CRP) among the patients of end-stage renal disease (ESRD). CRP in turn results in premature mortality and increased hospital stay in patients who require frequent dialysis [5,6]. As a response to inflammation, tissue injury, or pathogens, CRP is produced in the liver. It is a non-glycated pentagonal peptide, made up of 5 identical noncovalently connected subunits and a have a molecular weight of 105kDa. CRP is found in the healthy population at relatively low levels. Quantities less than 1 mg/dL are classified minor, values between 1 and 10 mg/dL are rated slightly high, and levels greater than 10 mg/dL are considered significantly raised [7].

One study showed that in 25 hemodialysis patients with ESA, 25.8% had CRP< 1.3g/dL, 24.2% had CRP 1.3-2.04g/dL, 25.1% had 2.04-3.21g/dL while 24.8% had >3.21g/dL. In patients with CRP<1.3g/dL, mean Hb was 11.71g/dl, in patients with CRP 1.3-2.04g/dL, mean Hb was 11.68g/dL, in patients with CRP 2.04-3.21g/dL, the mean Hb was 11.78g/dL while in patients with CRP>3.21g/dL, mean Hb was 11.6g/dL. The difference was significant . It was determined that inflammation is independently associated with increased ESA dosage when evaluated by a greater CRP concentration. Despite correcting potential confounders, individuals with increased CRP levels required considerably greater ESA doses to acquire equivalent Hb levels. [8]. One further study shows that lower average CRP values were associated with better Hb control (P < 0.0001) [9].

The aim of this study is to determine the frequency of patients in different C-reactive protein level ranges in hemodialysis patients having anemia at baseline taking erythropoietin for correction of anemia. Literature has shown that in dialysis patients, the CRP levels increase due to inflammation and Hb level decreases which leads to anemia and both of these are the major factors for mortality and dialysis failure in CKD patients. Addition of ESA in the treatment of dialysis patients is beneficial for another reason as it can help in the reduction of CRP and improvement of Hb level [10]. There is no local data available which has studied the relationship between CRP and ESA in dialysis patients. We conducted this study to find the local data which could help us understand the effect of CRP on the ESA dose and resistance, that anemia in dialysis can be managed better, which will ultimately help to improve the morbidity and mortality.

METHODS AND MATERIALS

A cross sectional study was conducted at the Department of Nephrology, Jinnah Hospital, Lahore between October 2019 to April 2020. The study was conducted after

obtaining ethical approval from the institutional review board. Sample size was 80 patients. It was calculated with 95% confidence interval, 9.5% margin of error and taking expected percentage of CRP,1.3-2.04mg/L i.e. 24.2% in hemodialysis patients having anemia [8].

A non probability consecutive sampling was used to recruit the participants in the study. Patients of age 16-60 years of either gender on hemodialysis for at least 6 months with anemia were included in the study while those who were dialyzed from a venous catheter/line, had a bleeding disorder (PT >20 sec, aPTT >35sec), abnormal liver function tests (ALT >40 IU, AST >40 IU) were excluded from the study. Informed consent from all patients were procured.

Demographic information i.e. name, age, sex, duration of dialysis were obtained. Then blood samples were obtained by using a 3cc BD syringe under aseptic measures. All samples were sent to the laboratory of the hospital for assessment of CRP and Hb level. CRP was recorded as per operational definition. Dialysis treatment was provided as per standard protocols of the hospital. All this information was recorded through proforma.

The data was entered and analyzed using SPSS version 20.0. Mean ± SDs were calculated for quantitative variables like age, duration of dialysis, Hb level at baseline and CRP levels. Frequency and percentages were calculated for qualitative variables like gender and CRP levels. Data was stratified for age, gender and duration of dialysis and post-stratification chi square test was applied by taking $p < 0.05$ as significant.

RESULTS

A total of eighty patients participated in our study. According to the results of our study, 57.5% patients were between ages of 31-60 years whereas 27.5% patients were above 60 years. Mean age of patients was 47.50 +16.37 years (Table 1).

Table 1: Baseline characteristics of Study Participants (n=80)

Characteristics	Number of participants (n)	Percentage of Participants (%)
Age (in years)		
<30 years	12	15.00%
31-60 years	46	57.50%
>60 years	22	27.50%
Gender		
Female	34	42.50%
Male	46	57.50%
Duration of Dialysis		
Upto 4 hours	80	100.00%
> 4 hours	0	0.00%
CRP (mg/l)		
< 1.3	19	23.70%
1.3-2.04	18	22.50%
2.05-3.21	21	26.25%
>3.21	22	27.50%

CRP was not significantly different in different age groups i.e. p=0.862 however, CRP levels were significantly different in males and females i.e. p value = 0.027 (<0.05) (Table 2).

Table 2: Association of C-reactive protein with Age and Gender

Age In years	CRP				P-value
	< 1.3	1.3-2.04	2.05-3.21	>3.21	
<30 years	2 (16.67%)	3 (25.00%)	5 (41.67%)	2 (16.67%)	0.862
31-60 years	14 (30.43%)	9 (19.57%)	8 (17.39%)	15 (32.61%)	
>60 years	3 (13.64%)	6 (27.27%)	8 (36.36%)	5 (22.73%)	
Gender					0.027
Male	11 (23.91%)	13 (28.26%)	10 (21.74%)	12 (26.09%)	
Female	8 (23.53%)	5 (14.71%)	11 (32.35%)	10 (29.41%)	
Duration of Dialysis					
Upto 4 hours	19 (23.75%)	18 (22.50%)	21 (26.25%)	22 (27.50%)	-
>4 hours	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	

DISCUSSION

Globally, CKD is one of the leading causes of morbidities and premature mortalities [11]. It refers to various degrees of renal impairment, ranging from mild to extensive chronic kidney failure. The key method of managing terminally ill CKD patients is renal replacement therapy, for instance, kidney transplant and different techniques of dialysis. Other underlying complications of CKD, such as anemia can be addressed using iron supplements and recombinant human erythropoietin – an ESA [12]. In end-stage renal disease, patients are likely to experience early death or frequent hospital admissions due to elevated concentrations of CRP [13].

In our study, the mean age of patients was 47.50+16.37 years. In one similar study conducted in Iran, the mean age of patients was 53 ±15.8 years [14]. In our study 57.5 % of patients were male. In one similar study conducted in Egypt 66% were male patients [6].

Regarding CRP levels, 23.7% patients had CRP < 1.3 mg/l, 22.5% patients had CRP of 1.3-2.04 mg/l, 26.25% had CRP of 2.05-3.21 mg/l and 27.5% patients had >3.21 mg/l. Similar results were obtained in other studies. One study conducted in India, 25.8% had CRP< 1.3g/dL, 24.2% had CRP 1.3-2.04g/dL, 25.1% had 2.04-3.21g/dL while 24.8% had >3.21g/dL [8]. In another similar study conducted in the USA, it was seen that 37.9% anemic patients had hs-CRP ≥3 mg/L [15]. Results of our study were consistent with other studies as well. Other studies also showed a strong relationship between anemia and chronic inflammation which also showed that chronic inflammation occurs even in early CKD patients with anemia. [16-18]. There was one study from India which showed a significantly high proportion of anemia CKD patients with raised CRP. In this study 67% of patients had elevated CRP (> 6 mg/L) levels. This possible cause for this high number of patients with raised CRP might be severe nutritional deficiency in these patients because all

patients with higher CRP levels also showed lower mean serum albumin levels (3.2 +/- 0.7 gm/dL) (P < 0.01) [19]. Nutritional deficiency can aggravate the pre-existing anemia in CKD patients and we usually have to replace iron in cases where it is necessary.

When we stratified our data according to age, there is no statistically significant difference in hs-CRP in different age groups i.e. p = 0.862. Similar results were obtained in other studies. One study conducted in India showed that hs-CRP was not statistically significant in different age groups i.e. p value was > 0.05 [8]. We further stratified our data according to gender. According to results of our study, CRP levels were significantly different between male and females i.e. p value = 0.027. These results were significant. Results of a similar study conducted in India found that CRP levels were not significantly different in males and females p value > 0.05 [8]. In short we found our findings to be consistent with the existing literature. However, our study was not without limitations. Due to a small sample size the study findings cannot be generalized to a larger population. A long-term follow up of the patients could not be sustained due to a high rate of dropouts.

CONCLUSION

CRP is high in most chronic kidney disease anemic patients who are on hemodialysis and taking erythropoietin for correction of anemia.

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