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Original Article

Serum C-reactive Protein & Ferritin Level in Patients with Maintenance Hemodialysis

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Abstract

Background: Hemodialysis is the widely used renal replacement therapy for end stage renal disease. Chronic inflammation is very common in patients with maintenance hemodialysis. There are several markers to assess the inflammatory status. Some of these markers strongly predict the mortality & morbidity among these patients.

Objectives: This study was carried out to determine serum C-reactive protein and ferritin level inpatients with maintenance hemodialysis (MHD).

Methods: This cross-sectional study was carried out in the Department ofBiochemistry, Dhaka medical college, Dhaka from the period of July 2018 to June2019. In this study, thirty patients on MHD were taken from the dialysis unit,Department of Nephrology, Dhaka Medical College Hospital, Dhaka. For betterassessment another age and sex matched thirty healthy individual were also taken.SerumCRP and ferritin level of all participants were measured and all values wereanalyzed statistically.

Results: Serum C-reactive protein level was found to be higher than normal in 70%of MHD patients. Median CRP level was significantlyhigher in hemodialysis group (13.9 mg/L) when compared with controls (1.74 mg/L). 80% MHD patient had serum ferritin value >500 µg/L. Median serum ferritin level was alsosignificantly higher in hemodialysis patients compared with controls (1342 µg/L vs 51 µg/L). Serum CRP had significant positivecorrelation with serum ferritin in high CRP group of MHD patients (r= 0.658, p= 0.001).

Conclusion: Serum CRP and ferritin level were higher in MHD patients than control. Serum CRP had linear positive relation with serum ferritin in MHD patients having high CRP value.

Keywords: Maintenance hemodialysis, C-reactive protein, Ferritin

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Introduction

The rapidly increasing number of patients with end-stage renal disease (ESRD) is a matter of concern worldwide especially in Asia. Patients with ESRD undergo regular dialysis. Data indicates that at least 2.9 million people need dialysis in Asia.[1] Patients undergoing hemodialysis have an extremelyhigh risk of developing cardiovascular diseases (CVD). They also have 10-30 times higher mortalityrate due to CVD than general population which can be explained by both traditional risk factors of atherosclerosis likediabetes mellitus, hypertension, dyslipidemia and the other non-traditional factorslike persistent inflammation, oxidant stress, anemia etc.[2] Chronic inflammation has a substantialcontribution in the pathogenesis of atherosclerosis, vascular calcification and other causes of cardiovascular diseases as well as morbidity andmortality in hemodialysis patients.

Several studies have showed that chronicinflammation is highly prevalent in maintenance hemodialysis (MHD) patients. Thecauses of inflammation in hemodialysis patients are multifactorial. Non-dialysisrelated factors of inflammation in these patients are increased pro-inflammatory cytokines, oxidative stress, chronic and recurrent infections, altered metabolism of adipose tissue

and intestinal dysbiosis.[3,4,5] Inflammatory activationin CKD is also influenced by genetic and epigenetic conditions.[6] Dialysis related factors such as- use of catheters for vascular access, poor dialyzermembrane biocompatibility, dialysate contamination, exposure to endotoxins, andback-leak of dialysate across the dialysis membrane in hemodialysis may promote apersistent, low-grade inflammatory response. Biomaterial-induced contact activationof proteins within the plasma cascade system occurs during hemodialysis and leads tolocal generation of inflammatory mediators on the biomaterial surface.[7]

There are many biochemical markers for the evaluation of inflammation. Among them C-reactive protein (CRP) is commonly measured. This acute-phase proteinsynthesized by the liverfollowing interleukin-6 secretion by macrophages and T cells in response.It makes a widerange of acute and chronic inflammatory conditions. High level of CRP is a strong predictor ofoverall and cardiovascular mortality in hemodialysis patients.[8-11]

Ferritin is the representativeprotein that stores and releases iron. Serum ferritin concentration is among the mostcommonly used markers of iron status in maintenance hemodialysis patients. It is influenced by body iron and also by various inflammatory conditions. Lowerserum ferritin level typically indicates iron deficiency but higher level of serumferritin in hemodialysis patient may be due to iron excess or inflammation. Some study showed that patients devoid of iron therapymay also have high serum ferritin level caused solely by inflammation.[12,13] High serum ferritin level is also associated with high mortality rate in MHD patients.[14,15,16]

This study was aimed to determine serum C-reactive protein and ferritin level inpatients with maintenance hemodialysis.

Materials and Methods

This cross-sectional study was carried out in the Department ofBiochemistry, Dhaka medical college, Dhaka from the period of July 2018 to June2019. In this study, thirty patients on maintenance hemodialysis (MHD group) were selected by purposive sampling technique from the dialysis unit,Department of Nephrology, Dhaka Medical College Hospital, Dhaka. All the patients took at least 2 dialysis sessions per week regularly for minimum 3 months. For betterassessment another thirty healthy individual (control group) were also selected. Written informed consent was taken from all the participants. Demographic and clinical data were collected from the participants by structured questionnaire. All the required investigation findings were recorded in a predesigned checklist / data collection sheet.

Data analysis of continuous variables were presented as means ± SD or median (interquartile range). Student's t-test and Mann Whitney U test were used to compare variables between groups. Discrete variables were presented as frequency and percentages. Chi-square test was used to determine the significance between categorical variable. Pearson's correlation and Spearman's correlation test was used to determine correlation between variables where appropriate. All the data were analyzed statistically by using SPSS software for windows (version 20). All p value significance was defined as $p < 0.05$ at the level of 95% confidence interval.

Results

Table 1: Comparison of demographic profile between MHD (maintenance hemodialysis) and control (N=60)

	MHD (n=30) Mean±SD	Control (n=30) Mean±SD	p value
Age (years)	46.60±11.67	45.13±10.47	0.610
Gender			
Male f(%)	21 (70.0)	19 (63.3)	0.584
Female f(%)	9 (30.0)	11 (36.7)	

Table 1 shows that, the mean age of MHD patients is 46.60 years and 70% of MHD patients are male whereas only 30% are female.

Table 2: CKD related information of MHD(maintenance hemodialysis) patients (n=30)

Attributes	Mean±SD	Min-max
Age of onset of CKD (years)	42.97±11.56	23.00-64.00
Duration of CKD (months)	30.67 20.18	8.00-84.00
Duration of hemodialysis (months)	26.10±18.76	7.00-78.00
Mode of correction of anemia		
Blood transfusion	25	83.3%
Iron therapy	5	16.7%

Table 2 shows, the mean age of onset of CKD is 42.97 years, mean duration of CKD & hemodialysis are 30.67 and 26.10 months respectively. It also shows that about 83% MHD patients took blood transfusion at varying interval.

Table 3: Distribution of respondents according to C-reactive protein level (N=60)

Serum C-reactive proteinvalue (mg/L)	MHD group (n=30) f (%)	Control group (n=30) f (%)	p value
< 5.0	9 (30.0)	25 (83.3)	<0.001
5.0-20.0	21 (40.0)	5 (16.7)	
>20.0	9 (30.0)	0	

Table 3 shows, 30% of MHD patients have serum CRP level >20 mg/L and total 70% patients have higher than normal CRP indicating high inflammation rate. The difference between two groups is significant.

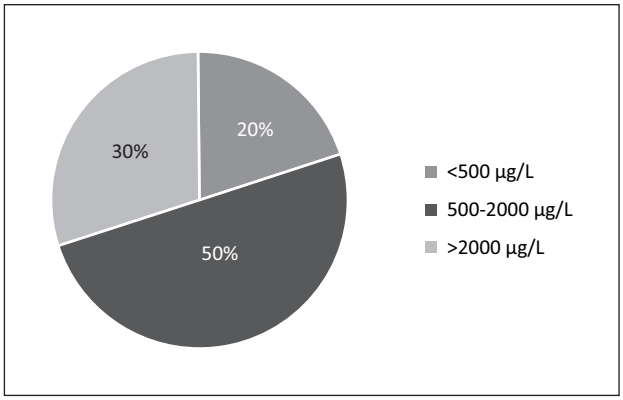

Figure 1: Distribution of MHD (maintenance hemodialysis) patients according to serum ferritin level.

Figure 1 shows that, 30% of MHD patients have ferritin level >2000 µg/L while 50% have ferritin level between 500-2000 µg/L.

Table 4: Comparison of lab parameters between MHD & control group (N=60).

Parameters	MHD group (n=30)	Control group (n=30)	p value
	[Median (IQR)]	[Median (IQR)]	
Serum CRP (mg/L)	13.9 (16.98)	1.74 (2.06)	<0.001
Serum ferritin (µg/L)	1342.9 (1320.15)	51.85 (60.29)	<0.001

Table 4 shows, serum C-reactive protein & ferritin level is significantly higher in MHD patients than control group. The differences between two groups are significant.

Table 5: Correlation between serum CRP and ferritin level in MHD group (n=30)

	r value	p value
All MHD patients	0.258	0.168
High CRP (≥5.0 mg/L) group	0.658	0.001

Table 5 shows, correlation between serum CRP & ferritin level in MHD group. There is weak positive correlation in all MHD patients but strong positive correlation is present in high CRP group which is statistically significant.

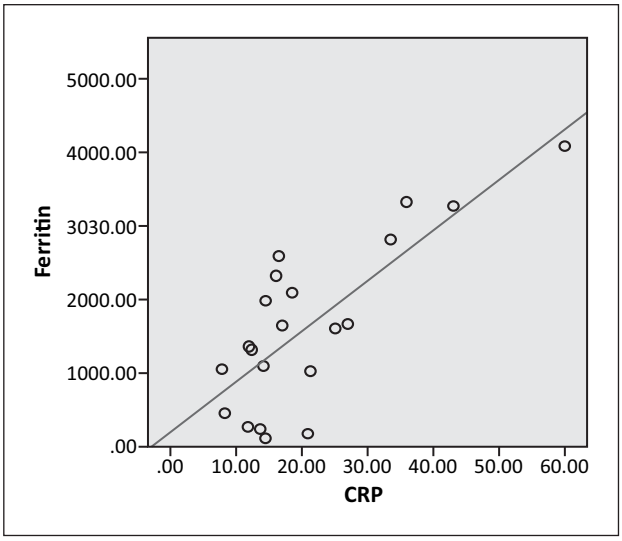

Figure 2: Correlation between serum CRP and ferritin level in high CRP group of MHD (maintenance hemodialysis) patients.

Figure 2 shows, strong positive linear relation between serum CRP and ferritin level in high CRP group of MHD patients.

Discussion

This cross-sectional study was carried out with the aim to evaluate serum CRP and ferritin level in patients with maintenance hemodialysis. In this study, high serum CRP level (>5 mg/L) was found in 70 % of MHD patients and 16.7% of control groups and the difference was statistically significant. Baradari, et al.[17] found 72.8% of 147 hemodialysis patients have high serum CRP level. In another study by Banu, et al.[18] during their assessment of inflammation and malnutrition in 50 MHD patients, they found high serum CRP level in 68% of MHD patients. In a recent study on 112 MHD patients, Kara[19] found 60% patients have increased serum CRP. In our study we observed that a large proportion of MHD patients had very high serum CRP. 30% of MHD patients in this study had serum CRP value >20 mg/L. Baradari, et al.[17] and Lalramenga, et al.[20] found CRP level >10 mg/L in 52.4% and 52.8% of MHD patients respectively. The elevated CRP in a significant number of MHD patients indicates the existence of chronically activated inflammatory response.

Serum CRP greater than 6.2 mg/L is a strong predictor of overall and cardiovascular mortality.[9] In this study, median serum CRP was found 13.9 mg/L in MHD patients which was significantly higher than control group. Baradari, et al.[17] found mean serum CRP 15.8 mg/L. Majoni, et al.[21] and Antunes, et al.[22] found median serum CRP 13.9 mg/L and 10 mg/L respectively. All these study showed increased level of CRP among MHD patients which may be due to both dialysis and non-dialysis related factors.

In this study, 80% MHD patient had serum ferritin level over 500 µg/L. Median serum ferritin level was found to be higher (1342.9 µg/L) in MHD patients than control group (51.8 µg/L). This difference was statistically significant. Similar result was obtained in a study done by Majoni, et al.[21] The study found median serum ferritin level 1022 µg/L in this group of patients. Karaboyas et al.[23] studied on 8510 American patients and found 70% patient had ferritin level >500 µg/L and mean serum ferritin level 774 ng/ml. It was found in other study that 80% MHD patients had hyperferritinemia.[24] In another study by Elmenyawi et al.[25] serum ferritin level was found 825 ng/ml. Yamashita, et al.[26] observed that serum ferritin level increased significantly after iron supplementation for 3 months in MHD patients

The study also observed that there was no significant correlation between serum CRP and ferritin in whole group of MHD patients, but when we studied only patients with high CRP value, we found a statistically significant positive linear relation (r=0.658, p=0.001) between them. This findings clearly indicate that rise in serum ferritin concentration in MHD patients is partly associated with inflammation. Some other study also found positive correlation between serum CRP and ferritin in MHD patients.[13,27] Previous study showed that high serum ferritin level can be also caused by inflammation in MHD patients devoid of iron therapy.[12] High level of serum ferritin in MHD patients may be due to both iron excess caused by blood transfusion and persistent inflammation measured by serum CRP level.

Conclusion

It can be concluded that, both serum CRP and ferritin level was found to be very high in majority of the patients on maintenance hemodialysis. Serum CRP was positively correlated with serum ferritin in only MHD patients with high CRP value. High ferritin level in MHD patients should be evaluated for the presence of chronic inflammation.

Limitations

The study had some limitations like; a single centered study with small sample size that cannot represent the whole population.

Conflict of interest: There is no conflict of interest.

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