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ESTIMATION OF SERUM FERRITIN AND MALONDIALDEHYDE LEVEL IN CHRONIC KIDNEY DISEASE PATIENTS UNDERGOING DIALYSIS TO DELINEATE OXIDATIVE STRESS, A KEY FACTOR IN THE PROGNOSIS

Biochemistry

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ABSTRACT

Chronic kidney disease is a condition characterized by gradual loss of kidney function over the time. CKD is defined as kidney damage or glomerular filtration rate (GFR) <60 mL/min/1.73 m 2for 3 months or more, irrespective of cause Dialysis typically needed in patients with CKD when GFR <15 mL/min/1.73 m2 or there is development of signs of uremia. It has been observed in various studies that hemodialysis itself causes oxidative stress which may become a limiting factor of this process. In this Scenario we want to see the levels of ferritin and Malondialdehyde to make out how much stress the dialysis creates its own thus formulate the strategy to combat this. Present study was aimed to evaluate whether serum ferritin level reflects the development of pathogenic mechanisms across the spectrum of chronic kidney disease (CKD) particularly with dialysis

Further, the study was intended to investigate whether deranged iron level and the occurrence of oxidative stress (by measuring malondialdehyde) are putatively associated mechanism among the individuals with CKD with dialysis as compared patients with CKD waiting for Dialysis. After the results come out we become astonished to find that Oxidative stress certainly rose in patients with dialysis as compared to patients waiting for dialysis. Serum ferritin and Iron also supports the pathogenesis with loss of many vital blood components during dialysis. So that from this study we can conclude that both CKD and Dialysis have their roles in the pathogenesis and oxidative stress generation. Hence forth a more powerful combat strategy is to be developed with addition of anti-oxidant in the armor so to make better future

KEYWORDS

CKD, Malondialdehyde, Ferritin, Oxidative Stress

INTRODUCTION

Chronic kidney disease is a condition characterized by gradual loss of kidney function over the time. CKD is defined as kidney damage or glomerular filtration rate (GFR) <60 mL/min/1.73 m ^{2}for 3 months or more, irrespective of cause [1, 2].Dialysis typically needed in patients with CKD when GFR <15 mL/min/1.73 m^2 or there is development of signs of uremia.

Ferritin:

The major protein concerned with iron storage. Ferritin is a hollow globular protein of 474 kDa consisting of 24 subunits that is present in every cell type. Typically it has internal and external diameters of about 8 and 12 nm, respectively the blood ferritin level serves as an indicator of the amount of iron stored in the body [3, 4], and it can become elevated due to the presence of condition featuring significant inflammation [5, 6].

Malondialdehyde is an organic compound with the formula CH2(CHO)2, and a byproduct of lipid metabolism in the body. Malondialdehyde, a highly reactive compound, is one of the many reactive electrophile species that cause toxic stress in cells and form covalent protein adducts, called advanced lipoxidation end products (ALE).

Due to decrease synthesis of erythropoietin and loss of transferrin (iron transport protein) through urine, there may be iron deficiency anemia which is reflected by decreased serum ferritin (storage form of iron) [7, 8].

The degree of oxidative stress is related to endothelial dysfunction. These factors may be important with respect to the high morbidity and mortality of CVD found in patients with CRF.[9-10]

In this scenario we have tried to estimate the oxidative stress in between two groups to delineate whether the hemodialysis itself causing deleterious effect by producing more free radicle as compared to other CKD patients waiting for dialysis.

Objectives Of The Study

1) Present study was aimed to evaluate whether serum ferritin level reflects the development of pathogenic mechanisms across the spectrum of chronic kidney disease (CKD) particularly with dialysis

2) Further, the study was intended to investigate whether deranged iron level and the occurrence of oxidative stress (by measuring malondialdehyde) are putatively associated mechanism among the individuals with CKD with dialysis as compared patients with CKD waiting for Dialysis

METHODOLOGY

This is a case control study
Ethical committee clearance: taken
Duration of study:1 and half years

Inclusion Criteria:

Chronic kidney disease patients having GFR less than 15 ml/minute, age more than 18 years but < 60 years were enrolled in the present study and grouped into with dialysis and waiting for dialysis cases.

Diabetes patients and smokers are not excluded.

Sample Size:

sample size was 90. Number of cases (CKD patients with undergoing dialysis) =45,
Number of controls (CKD patients waiting for dialysis to commence)=45

Exclusion Criteria

1) Presence of any renal carcinoma.
2) Congenital haemolytic anaemia
3) Acute infective disorder
4) Known liver disorder
5) Pregnancy

GFR Calculation

GFR is calculated using MDRD(modification of diet in renal disease) study equitation.

MDRD Study Equation:

eGFR =175 x (SCr)-1.154 x(age)-0.203 x0.742 [if female] x1.212 [if Black]

Abbreviations / Units

eGFR (estimated glomerular filtration rate) = mL/min/1.73 m2
Scr (standardized serum creatinine) = mg/dL
age = years

Parameters Measured

1) Serum malondialdehyde
2) Serum ferritine
3) Serum iron
4) Serum total iron binding capacity
5) Serum transferrin saturation
6) Serum creatinine
7) Serum urea

RESULTS

Distribution Of Mean Ferritin (ng/ml) In
Distribution Of Mean Of Ferritin 1 Is Described With Table No 1 And Diagram No 1

	Number	Mean	SD	Minimum	Maximum	Median	p-value
Case	45	470.3978	341.4121	54.9000	1626.0000	358.0000	<0.0001
Control	45	142.0667	57.9080	67.0000	310.0000	120.0000	<0.0001

In case, the mean ferritne (mean± s.d.) of patients was 470.3978 ± 341.4121 ng/ml. In control, the mean ferritne (mean± s.d.) of patients was 142.0667 ± 57.9080 ng/ml. Difference of mean ferritne vs. group was statistically significant (p<0.0001) depicted in Diagrams as well

Diagram No 1

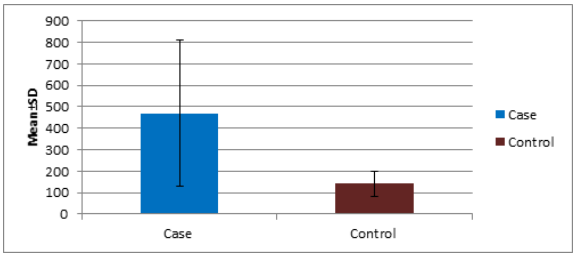

Table 2: Distribution Of Mean Of MALONDIALDEHYDE

	Number	Mean	SD	Minimum	Maximum	Median	p-value
Case	45	4.3333	1.4663	1.8000	7.7000	4.1000	<0.0001
Control	45	1.9316	.3825	1.2000	2.9200	1.8900	

Distribution Of Mean MDA Is Described With Tabie No2 And Diagram No 2

In case, the mean MDA (mean± s.d.) of patients was 4.3333 ± 1.4663. In control, the mean MDA (mean± s.d.) of patients was 1.9316 ± .3825. Difference of mean MDA vs. group was statistically significant (p<0.0001).

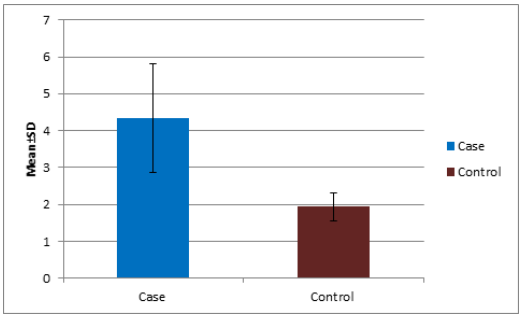

Diagram 2

Table 3: Distribution Of Mean Iron

	Number	Mean	SD	Minimum	Maximum	Median	p-value
Case	45	8.5778	2.8404	5.0000	18.0000	8.0000	<0.0001
Control	45	18.6889	3.9590	12.0000	30.0000	18.0000	

Distribution Of Mean Iron Is Described With Tabie No 3 And Diagram No 3

In case, the mean Iron (mean± s.d.) of patients was 8.5778 ± 2.8404 µg./dL. In control, the mean Iron (mean± s.d.) of patients was 18.6889 ± 3.9590 µg./dL. Difference of mean Iron vs. group was statistically significant (p<0.0001).

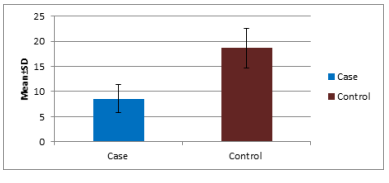

Diagram 3

Table 4: Distribution Of Mean Total Iron Binding Capacity

	Number	Mean	SD	Minimum	Maximum	Median	p-value
Case	45	52.8444	13.2784	31.0000	81.0000	52.0000	<0.0001
Control	45	67.9333	9.0287	46.0000	81.0000	69.0000	

In case, the mean TIBC (mean± s.d.) of patients was 52.8444 ± 13.2784. In control, the mean TIBC (mean± s.d.) of patients was 67.9333 ± 9.0287. Difference of mean TIBC vs. group was statistically significant (p<0.0001). Distribution of mean TIBC is described with table no 4 and diagram no 4

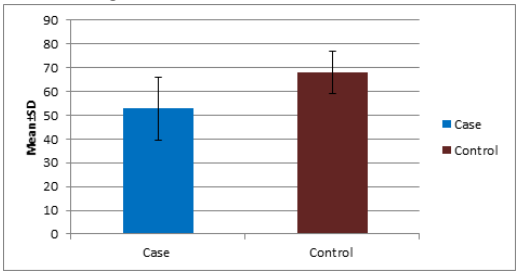

Diagram4

Table 5: Distribution Of Mean Transferrin Saturation

	Number	Mean	SD	Minimum	Maximum	Median	p-value
Case	45	17.0222	8.1895	6.0000	38.0000	15.0000	<0.0001
Control	45	28.3111	10.1463	15.0000	62.0000	24.0000	

In case, the mean TR SAT (mean± s.d.) of patients was 17.0222 ± 8.1895. In control, the mean TR SAT (mean± s.d.) of patients was 28.3111 ± 10.1463. Difference of mean TR SAT vs. group was statistically significant (p<0.0001). Distribution of mean TR saturation is described with table no 5 and diagram no 5

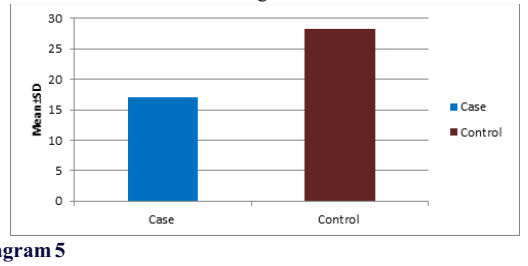

Diagram 5

Table 6: Distribution Of Mean Ferritin In Males And Females

	Number	Mean	SD	Minimum	Maximum	Median	p-value
Case Female	22	449.3136	288.1421	54.9000	1050.0000	340.0000	<0.0001
Control Female	21	94.4762	15.6033	67.0000	121.0000	97.0000	
Case Male	23	490.5652	391.1556	128.0000	1626.0000	359.0000	
Control Male	24	183.7083	48.2291	81.0000	310.0000	184.0000	

In case female, the mean ferritin (mean± s.d.) of patients was 449.3136 ± 288.1421. In control female, the mean ferritin (mean± s.d.) of patients was 94.4762 ± 15.6033. In case male, the mean ferritin (mean± s.d.) of patients was 490.5652 ± 391.1556. In control male, the mean ferritin (mean± s.d.) of patients was 183.7083 ± 48.2291. Difference of mean ferritin vs. group was statistically significant (p<0.0001). Distribution of mean mean ferritin is described with table no 6 and diagram no 6

DISCUSSION

Next we have studied the levels of Ferritin among them, we have found that in cases serum ferritin level shows a mean value of 470.39ng/ml and sd value of 341ng/ml among cases and a mean of 142ng/ml and a sd of 57.9 ng/ml among controls. Thus we can say among the patients

with CKD undergoing dialysis shows a significantly greater value with respect to their serum ferritin level as compared to age matched control individuals as shown in literature Serum Ferritin in Chronic Kidney Disease: Reconsidering the Upper Limit for Iron Treatment Steven Fishbane KamyarKalantar-Zadeh Allen R. Nissenson which also stated that therapy was indicated in terms of hemodialysis or iv erythropoietin therapy in CKD patient with raised ferritin level.

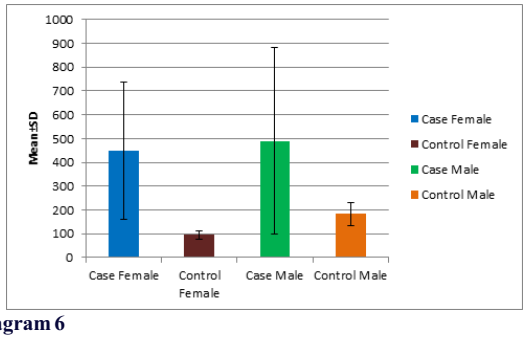

Diagram 6

Next we look for the levels of MDA in our study settings. The results shows mean value of 4.33nmol/ml and a sd value of 1.46nmol/ml among patients with CKD undergoing dialysis and a mean value of 1.93nmol/ml , sd value of .38nmol/ml among CKD patients showing a statistically significant p value. From this result we can say that among cases MDA value were higher and in the pathogenesis of CKD it is quite clear that oxidative stress holds an important cornerstone of the disease process and particularly the patients undergoing dialysis. We also know that MDA is the marker of oxidative stress hence our result corroborating with the findings ofMargusAnnuk, MihkelZilmer, Lars Lind, Torbjörn Linde and Bengt FellströmJASN December 2001, 12 (12) 2747-2752;Oxidative Stress and Endothelial Function in Chronic Renal Failure.

We then shifted our focus to the analysis of serum Fe which again showed a statistically significant lower value among cases over controls which describes the role of iron as a marker to denote any cases of CKD. In the study by G Tsagalis on Renal anemia: A Nephrologists view, it was seen that anemia is common among CKD. So the findings we found are consistent with this result.

In our analysis we noted that in the cases mean TIBC level was 52.8 µmol/L and sd of 13.28µmoi/L whereas in the control group mean value was 67.93µmol/L with a sd of 9.07µmol/L so we can say that TIBC level was significantly lower in control group as supported by the G Tsagalis on Renal anemia: A Nephrologists view.

In our analysis we noted that in the cases mean TIBC level was 52.8 µmol/L and sd of 13.28µmoi/L whereas in the control group mean value was 67.93µmol/L with a sd of 9.07µmol/L so we can say that TIBC level was significantly lower in control group as supported by the G Tsagalis on Renal anemia: A Nephrologists view**.**

From our study we have found that the CKD cases undergoing dialysis are having significantly low serum transferrin saturation comparing control group as supported byG. Chinnapu Reddy, Ramakrishna Devaki, and PragnaRao Iron Indices in Patients with Functional Anaemia in Chronic Kidney Disease.

SUMMARY& CONCLUSION

Chronic kidney disease is a condition characterized by gradual loss of kidney function over the time. Due to decrease synthesis of erythropoietin and loss of transferrin (iron transport protein) through urine, there may be iron deficiency anemia which is reflected by decreased serum ferritin(storage form of iron) .On the other hand CKD with haemodialysis may aggravate chronic inflammatory disease caused by CKD itself where inflammatory mediator IL-6 is increased resulting in increased hepcidin synthesis. Hepcidin prevents release of iron in serum from intestinal epithelial cell and tissue. Situation is getting complicated when due to Hemodialysis there is loss of transferrin resulting in free iron mediated oxidative stress which is reflected by serum malondialdehyde. In this scenario We have measured serum ferritin and malondialdehyde in an observational case control study taking 45 cases and 45 controls. We have also measured additional factors influencing iron status and defining CKD like serum Urea, creatinine, TIBC, Transferrin saturation. Serum ferritin is measured by ELISA, Iron and TIBC are measured by MgCO3 and FerroZine method. Urea and creatinine are measured in auto analyzer.

In result We have found positive correlation for serum ferritin and malondialdehyde in CKD patients undergoing dialysis as compared to CKD patients waiting for hemodialysis to begin with .We can thus conclude that in CKD patients going for dialysis should be supplemented with anti-oxidant and regularly monitored for this generation of free radicle which can complicate the condition as seen in our study.

Conflict Of Interest If Any: No such

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