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Biochemical Assessment of Malnutrition in Sudanese Patients with Chronic Renal Failure on Hemodialysis Maintenance Therapy

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Authors' contributions

This work was carried out in collaboration between all authors. Author MSM designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author OFI is the supervisor of the study. Author SA managed the analyses of the study. Author AEAA is the co-supervisor of the study. All authors read and approved the final manuscript.

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ABSTRACT

Background: Malnutrition in Chronic Kidney Disease Patients on Hemodialysis remains one of the major causes of morbidity and mortality characterized by changes in circulating levels of plasma albumin, pre-albumin and transferrin.

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Purpose: The aim of this study was to determine the serum levels of albumin, pre-albumin, transferrin, highly sensitive C-reactive protein (hs-CRP) and BMI as markers for malnutrition.
Materials and Methods: A total of one hundred patients with Chronic Kidney Disease on hemodialysis maintenance therapy and one hundred sex and age-matched healthy control subjects were enrolled in this study; After informed consent six milliliters of venous blood Were collected from each patient of the study group and the control group after dialysis session in the morning, after an overnight fasting in a plain container from which serum is separated and then stored in Eppendorf tubes at -80°C.
Results: In our study: significant decrease in the mean level of serum albumin (3.12±0.39) (P. value >0.001), pre-albumin (24.76±6.46) (P. value >0.001), transferrin (278.66±59.47) (P. value 0. 04), hs-CRP (20.13±5.70) (P. value >0.001) and BMI (20.3±5.5) (P. value >0.001) among the Chronic Kidney Disease patients on maintenance hemodialysis therapy when compared to the control group.
Furthermore, the results showed that there was a negative correlation between serum highly sensitive C-reactive protein with plasma albumin (rho= -.812, p<0.02), pre-albumin (rho= -0.752, p<0.02) and no correlation between serum hs-CRP with transferrin level (rho= -0.062, p=0.385).
Conclusion: In conclusion, a significant decreased in the mean level of serum albumin, pre-albumin, transferrin and BMI among Sudanese Patients with Chronic Kidney Disease on hemodialysis maintenance therapy place them at risk of developing Malnutrition.
The significant negative correlation between albumin and pre-albumin with hs-CRP proofed that Albumin and pre-albumin were negative acute phase reactants that tended to decreased during inflammation and these negative correlations linked between chronic systemic inflammation and malnutrition in chronic kidney disease patients on hemodialysis maintenance therapy.

Keywords: Chronic kidney disease (CKD); hemodialysis (HD); protein–energy malnutrition (PEM); body mass index (BMI).

1. INTRODUCTION

Patients undergoing hemodialysis have a high prevalence of protein-energy malnutrition and inflammation. Those conditions often occur together in CKD patients on maintenance hemodialysis therapy, they have been referred together as the malnutrition-inflammation-atherosclerosis syndrome (MIA syndrome) to confirm their important association with atherosclerotic cardiovascular disease.

Chronic kidney disease is an effective disease command by multiple factors that affect its progression and prognosis. The prevalence of CKD in Sudan is 0.7% of the adult population and, the estimated incidence of new cases of CKD patients is 70–140 per million inhabitants/year.

1.1 Definition of Protein–energy Malnutrition

Protein–energy malnutrition (PEM) known as protein–calorie malnutrition it refers to a form of malnutrition where there is an inadequate supply of protein that is not enough to meet the body's metabolic demands due to either an inadequate dietary intake of protein or increased demands due to disease, or increased protein losses.

1.2 Epidemiology

Recent studies report about 20–50% of CKD Patients on maintenance haemodialysis therapy suffer from PEM. In the majority of dialysis patients, malnutrition extends from mild to moderate and only 10% of CKD Patients on maintenance haemodialysis therapy severe PEM can be found.

In spite of its high prevalence, malnutrition was rarely listed as a cause of death in CKD patients on maintenance hemodialysis therapy due to the fact that malnourished patients die from cardiovascular disease. A strong association between malnutrition, inflammation and arteriosclerosis (MIA-syndrome) has been found in CKD patients on maintenance hemodialysis therapy, suggesting that chronic inflammation participates in the acceleration of atherosclerosis and the development of malnutrition [1].

1.3 Malnutrition in Patients with MIA Syndrome

It has been recently reported that a systemic inflammatory response may participate in developing hypoalbuminemia in CKD patients on maintenance hemodialysis [2].

The systemic inflammatory process stimulated by many factors as a uremic state, dialysis membranes, dialysis solution and infection, causing down regulation of the cellular metabolism and reduction of the protein synthesis causing acceleration in the negative balance and protein degradation [3].

Malnutrition in CKD patients on maintenance hemodialysis caused by uremic syndrome, comorbid conditions and inflammation [4].

Malnutrition is frequently present in early stages of chronic renal failure which characterised by a loss of skeletal muscle mass but a preservation of fat mass [5], This loss result from uraemia, or from inflammation, metabolic acidosis and nutritional deficiency and supposedly hyperleptinemia [6].

During the evaluation of chronic renal failure, malnutrition can appear when glomerular filtration assessed by creatinine clearance becomes lower than 40 ml/min/1.73 m and there was different mechanism can explain this state of malnutrition as reduction in protein and caloric intakes, deterioration of the renal function, disorders in metabolism of the main nutrients and increased protein catabolism due to acidosis, infections and inflammations [7].

The various aspects of the pathophysiology of malnutrition in HD patients are (schematically presented in Fig. 1 [8].

1.4 Laboratory Parameters

Laboratory techniques depend on the determination of the plasma protein levels mainly the negative acute phase reactant. The evaluation of nutritional status depends on an assessment of biochemical laboratory parameters combined with biophysical markers, both will help to identify the onset of nutritional disorders and rapid assessment of ongoing treatments.

1.5 Serum Albumin (Half-life 20 Days)

Serum albumin levels have been used extensively to assess the nutritional status of an individual with and without chronic renal failure (CRF). Serum albumin concentration is a long-term marker of nutritional status (half-life 3 weeks), Malnutrition and hypoalbuminemia were common in CKD patients on maintenance hemodialysis therapy due to a group of pathological conditions such as hypertension, cardiovascular disease, inflammation, infection, low nutrient intake, dialysis protein loss and systemic inflammatory response [9].

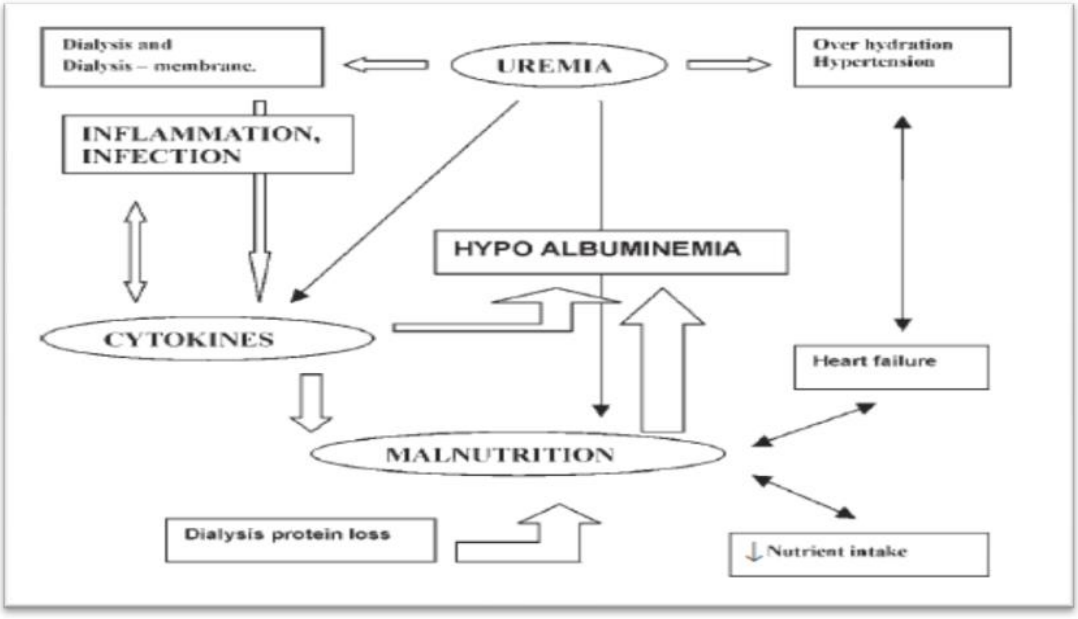

Fig. 1. Pathophysiology of malnutrition in patients with MIA syndrome [8]

Albumin has been considered as negative acute phase protein because it is level fall actually with inflammation, thus it serves as an indicator of chronic inflammation.

Hypoalbuminemia in CKD patients on maintenance hemodialysis therapy patients can be a consequence of a combination of malnutrition and inflammatory reactions [10].

Serum albumin concentration is negatively correlated with mortality in patients on maintenance dialysis [11].

Many studies have classified the diverse levels of malnutrition by using serum albumin the shows that serum albumin levels of 3.5 g/dL or greater are considered normal, serum albumin levels of 2.7 g/dL indicate moderate malnutrition, and levels serum albumin level of less than 2.1 g/dl indicate severely depleted levels [12].

1.6 Prealbumin (Half-life 2–3 Days)

Serum pre-albumin (transthyretin) is a precursor of serum albumin with a short half-life (2-3 days), thus it is an earlier nutritional marker compared with serum albumin and more sensitive marker to immediate changes in nutritional status than albumin. In spite of Pre-albumin is a negative acute phase reactant serves as an indicator of chronic inflammation, a few studies support that pre-albumin is a reliable marker of inflammation [13].

Many studies showed that pre-albumin level <30 mg/dl was associated with increased risk of PEM in dialysis patients [14].

Furthermore, recent studies reported that serum pre-albumin like that of serum cholesterol tends to be higher in patients on peritoneal dialysis (PD) than on hemodialysis (HD), despite the substantial loss of protein during PD [15].

1.7 Transferrin (Half-life 8 Days)

Serum Transferrin has also been identified as markers of nutrition status (half-life 8 days). Because transferrin is involved with iron transport, its levels are influenced by iron Status [16].

Iron deficiency can cause increased transferrin levels due to increased iron absorption and is often used as an indirect method of determining total iron binding capacity, therefore, Transferrin is not a specific indicator of nutritional status. It is catabolized in the kidneys and is elevated with renal failure [17].

1.8 Highly Sensitive C-reactive Protein (hs-CRP)

Is a positive acute-phase reactant whose levels are elevated with both acute and chronic inflammation. It has a short half-life of 19 hours [18]. In spite of the fact that CRP is not an indicator of nutritional status, many studies reported that serum albumin and pre-albumin were correlated negatively with hs-CRP during an acute phase reaction, thus CRP was helpful in interpreting levels of other visceral proteins [19].

1.9 Anthropometry

Anthropometry is a semi quantitative quantification of the various body compartments, particularly bone, muscle and fat. Anthropometric assessment includes besides body weight, height and skeletal frame size, the measurement of skin fold thickness (fat mass) and mid-arm muscle circumference (muscle mass) [20].

Body mass index (BMI)/ The Quetelet-Index is calculated from a subject's height and weight is widely used for assessment of malnutrition and obesity. BMI <18 kg/m^2 considered as malnutrition, the threshold of 18 kg/m^2 is an indicator of malnutrition and should not be used alone as an indicator of nutritional status [20].

2. MATERIALS AND METHODS

This is a case control study conducted at Ahmed Gasem Hospital, Omdurman Teaching Hospital, Khartoum Teaching Hospital and Ibn Sina Specialized Hospital from December 2014 to December 2016, these hospitals represent all the three cities of tricipital Khartoum. Sudanese patients with CKD whom routinely attend to dialysis centre at all above-mentioned hospitals during the period of the study were randomly recruited for this study.

The study included one hundred CKD patients on regular hemodialysis maintenance therapy and one hundred age and sex matched healthy controls, the sample size was derived by using the Fleiss formula for cross sectional study using the following information [21]:

Confidence interval = 95%, power of study = 80%, the ratio of cases to control of 1:1, the

percentage of control exposed: 8.7% and percentage of cases exposed: 26%, this formula gave a minimum sample size of 75 for cases and 75 for control.

None of the patients suffered from any symptoms of infections or presented with clinical signs of infection (Hepatitis B, Hepatitis C and HIV), malignancy, congestive heart failure and active immunological disorders. Furthermore, the patients did not receive any medications known to affect immune functions and Overhydrated patients or patient with ascites or eclampsia were excluded from the study.

All participants gave informed consent before enrolling in the study and the study was approved by Alneelain University Ethical Committee.

The patients' information such as age, sex, height, weight and clinical history were recorded.

Blood samples (6 ml) were collected from patients in plain containers from which serum is separated and then stored in Eppendorf tubes at -80°C. Before analysis, frozen specimens were thawed and allowed to reach room temperature for various measurements.

Serum albumin was measured by Bromo cresol green method using Cobas C 311 analyser (Roche Diagnostics, Germany).

Serum pre-albumin, transferrin and hs-CRP were measured by sandwich Enzyme-Linked Immunosorbent Assay using Stat Fax Microstrip Reader (Awareness Technology, USA).

BMI calculated from a subject's height and weight.

2.1 Statistical Analysis

The student's t-test was employed to compare differences between the mean concentration of study parameters and Pearson's correlation for the association between study variables. P-value 0.05 was considered statistically significant. Data were analysed by SPSS (Version 16.0; SPSS Inc).

3. RESULTS

This is a case–control study, included 100 patients with chronic renal failure, 54% of them were males and 46% were females, their ages ranged between 16-81 years and the mean age was 43 years.

The results obtained revealed that hypertension was the primary cause of CKD (35.0% of respondents) while diabetes mellitus accounted for 30.0% of cases. However, UTI and glomerulonephritis were identified to be the primary cause in 8.0% and 7.0% of cases, respectively. Other identified causes, were Lupus Nephritis (4.0%), Autosomal Dominant Polycystic Kidney Disease (3.0%), Gout (4.0%), Renal Stone (5.0%) and Obstructive uropathy (4.0%) (Fig. 1).

The result in Table 1 showed that the mean of albumin level (3.116 g/dl) was lower in CKD patients compared to the control group (4.70 g/dl) with a significant difference between the two groups (P. value >0.001).

The result in Table 1 also revealed that the mean level of the pre-albumin level (24.76 mg/dl) was lower among CKD patients in comparison to the control group (71.36 mg/dl) with a significant difference between the two groups (P. value >0.001).

The result in Table 1 also showed that the mean level of the hs-CRP level (20.13 mg/dl) was higher among CKD patients in comparison to the control group (3.22 mg/dl) with a significant difference between the two groups (P. value >0.001).

The result in Table 1 showed that the mean level of transferrin was 278.66 mg/dl among CKD patients, while it was 290.47 mg/dl in healthy control group showing a significant difference between the two groups (P. value 0.049).

Furthermore, the result in Table 1 showed that the mean level of BMI 20.3 Kg/m^2 was lower among CKD patients in comparison to the healthy control group 26.1 Kg/m^2 with a significant difference between the two groups (P. value 0.049).

4. DISCUSSION

Chronic kidney disease is a dynamic disease governed by multiple factors that affect its progression and prognosis. The prevalence of CKD in Sudan in different communities is 0.7% of the adult population, In Sudan, the estimated incidence of new cases of CKD patients is 70–140 per million inhabitants/year [22].

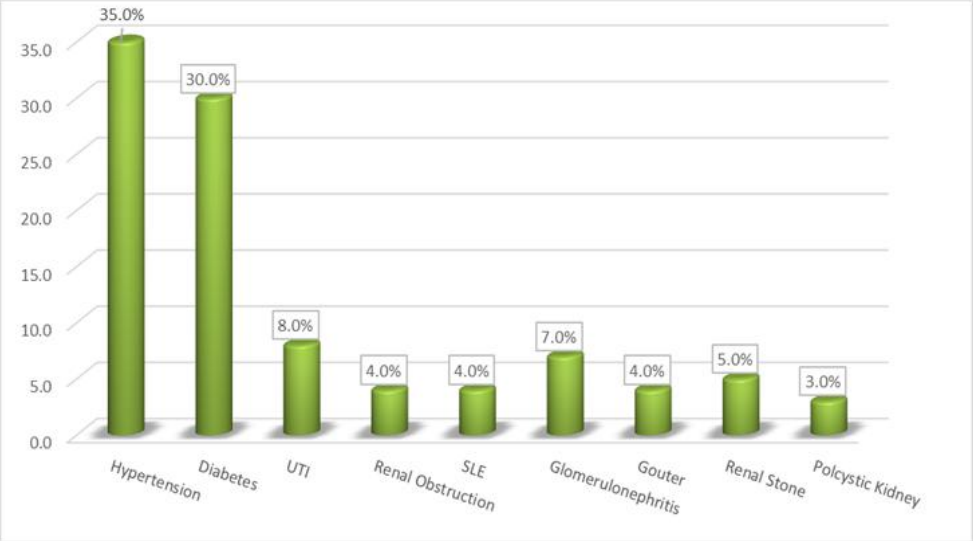

Fig. 2. The main causes of chronic kidney disease in Sudan

Table 1. The levels of albumin, pre-albumin and transferrin in CKD patients group and the control group

Study groups / Parameters	CKD patients (Case group)		Healthy Individuals (Control group)		P. value
	Mean	SD	Mean	SD	
Albumin g/dl	3.116	0.3897	4.703	0.3883	>0.001
Prealbumin mg/dl	24.76	6.458	71.36	19.558	>0.001
Transferrin mg/dl	278.66	40.827	290.47	34.305	0.049
hs-CRP mg/dl	20.13	5.704	3.22	1.277	>0.001
BMI Kg/m^2	20.3	5.5	26.1	6.2	>0.001

Table 2. Pearson correlations of high sensitive C-reactive protein (h-CRP) with the level of malnutrition marker serum albumin

Malnutrition markers albumin / h-CRP	Albumin g/dl	
	Pearson correlation (r)	P. value
h-CRP ng/ml	-.812	0.00

Table 3. Pearson correlations of high sensitive C-reactive protein (h-CRP) with the level of Malnutrition marker serum prealbumin

Malnutrition marker prealbumin / h-CRP	Prealbumin mg/dl	
	Pearson correlation (r)	P. value
h-CRP ng/ml	-0.752	0.00

Table 4. Pearson correlations of high sensitive C-reactive protein (h-CRP) with the level of malnutrition marker serum transferring

Malnutrition marker transferrin / h-CRP	Transferrin mg/dl	
	Pearson correlation (r)	P.Value
h-CRP ng/ml	-0.062	0.385

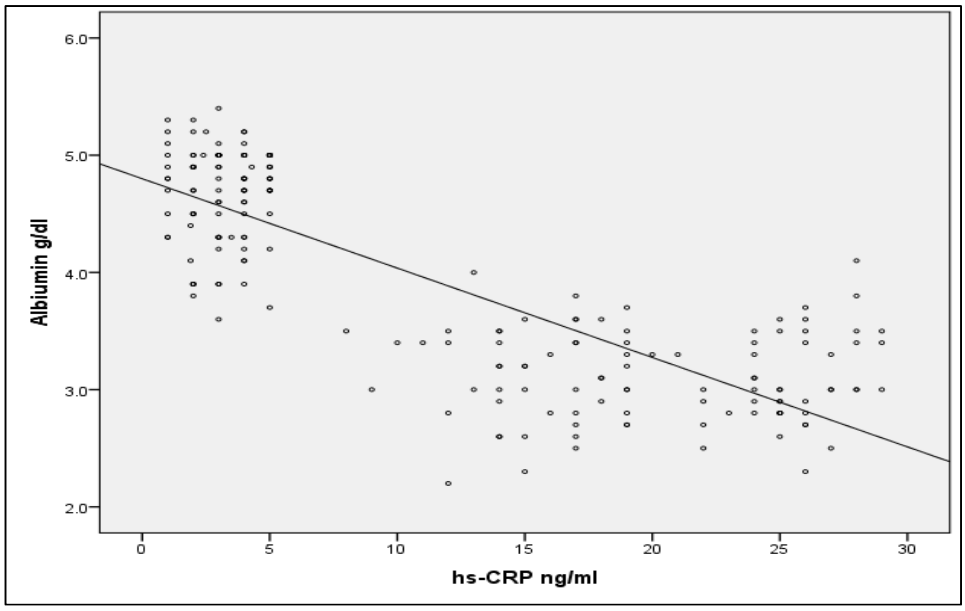

Fig. 3. Correlation between serum hs-CRP and albumin levels in in CKD patients group (n=100, r= -.812, p<0.02)

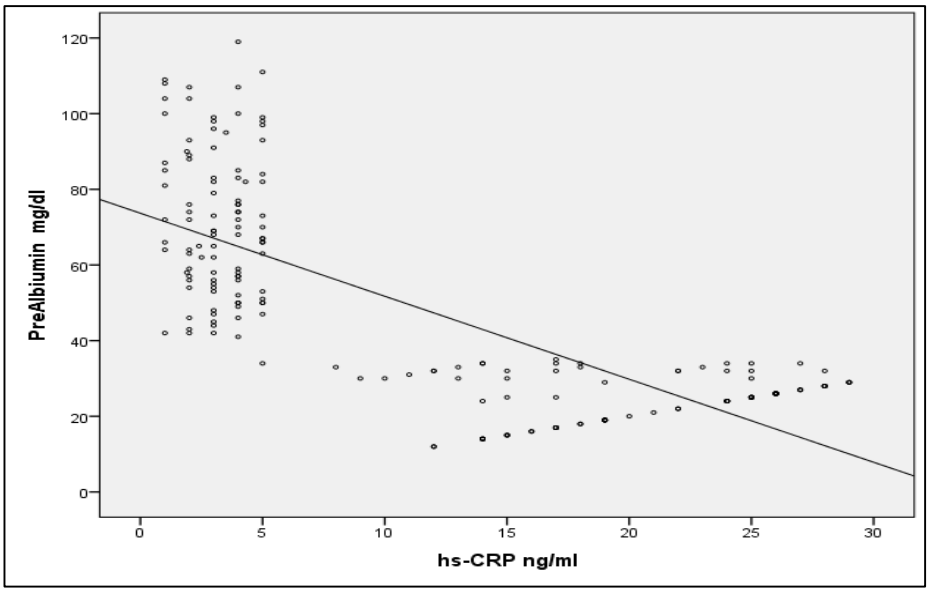

Fig. 4. Correlation between serum hs-CRP and prealbumin levels in in CKD patients group (n=100, r= -0.752, p<0.02)

The principal aim of the present study was to determine the association of malnutrition with chronic kidney disease patients on maintenance hemodialysis.

The finding of this study supported the effects of malnutrition in CKD patients on maintenance hemodialysis which confirmed by the decrease in the mean level of serum albumin, pre-albumin and transferrin among the CKD patients when compared to the control group and our findings were similar to those reported by Sathishbabu, et al. [23] who showed that there was a strong correlation between serum pre-albumin with other biochemical parameters of malnutrition in hemodialysis patient.

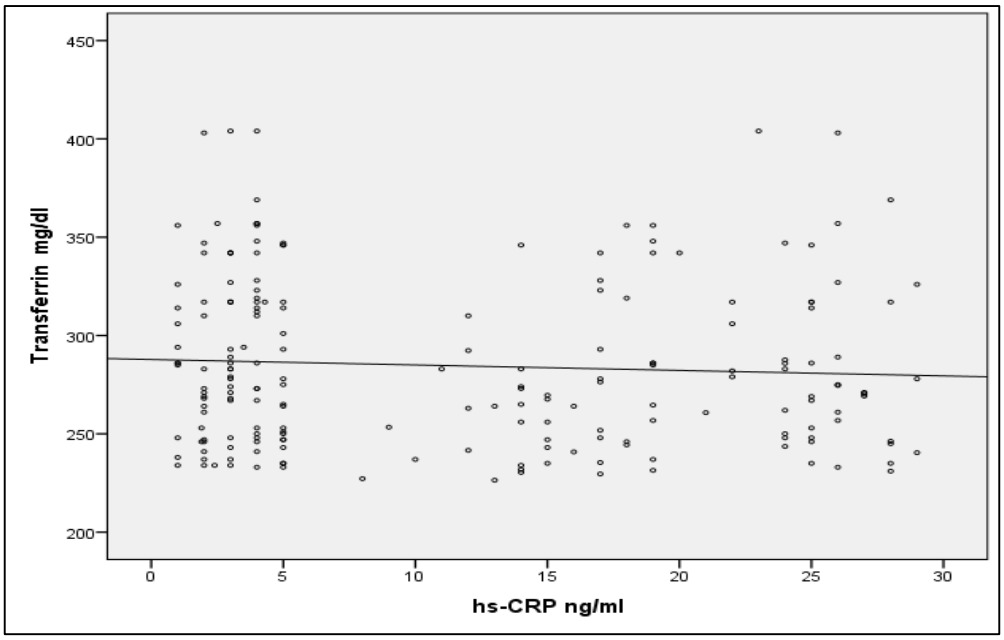

Fig. 5. Correlation between serum hs-CRP and transferrin levels in in CKD patients group (n=100, r= -0.062, p=0.385)

Our findings also showed that the BMI levels were decreased among the CKD patients on maintenance hemodialysis when compared to the control group and these findings were in agreement with the study done on Saudi patients conducted by Alharbi K, et al. [24] who showed that Malnutrition is Prevalent among Hemodialysis Patients.

Furthermore, the study correlated the level of plasma proteins markers of malnutrition (albumin, pre-albumin and transferrin) with the level of the acute phase proteins hs-CRP to evaluate whether the reduced level of plasma proteins in CKD patients was due to the effect of malnutrition only or accompanied with inflammation. The results obtained showed that there was a significant negative correlation between albumin and pre-albumin with hs-CRP and these findings were agreed with results published by Kelleher et al. [25], who reported that British patients on maintenance hemodialysis had a significant negative correlation between albumin, pre-albumin and transferrin with hs-CRP.

Our findings showed that there was no correlation between transferrin and hs-CRP which disagreed with the results of Kelleher, et al. [25] and this conflict in the results was due to fact that not only the chronic inflammation affected the transferrin level but also malnutrition and anemias alter the result of plasma Transferrin and both of them were uncommon in British patients thus the variation of the results could be attributed to life style, racial, socioeconomic and environmental factors. Our findings proofed that Albumin, pre-albumin and transferrin were negative acute phase reactants that tended to decreased during inflammation, also chronic systemic inflammation is the main cause of malnutrition in chronic kidney disease patients .

5. LIMITATION OF THE STUDY

Although the research has reached its aims, there were unavoidable limitations. The absence of funds made us conducting the research only on chronic renal failure patients on Hemodialysis Maintenance Therapy. Therefore, to generalize the results of our study for larger groups, the study should have involved more participants at different chronic renal failure stages.

6. CONCLUSION

In conclusion, a significant decreased in the mean level of serum albumin, pre-albumin, transferrin and BMI among Sudanese Patients with Chronic Kidney Disease on hemodialysis

maintenance therapy place them at risk of developing Malnutrition.

The significant negative correlation between albumin and pre-albumin with hs-CRP proofed that Albumin and pre-albumin were negative acute phase reactants that tended to decreased during inflammation and these negative correlations linked between chronic systemic inflammation and malnutrition in chronic kidney disease patients on hemodialysis maintenance therapy.

7. RECOMMENDATIONS

We recommend that further studies should be done particularly focus on the balance between pro-inflammatory and anti-inflammatory cytokines relating to nutrition status to improve the diagnosis of immune disorders, expecting the outcome and developing the best treatment strategy in chronic kidney disease patients on hemodialysis maintenance therapy.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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