ORIGINAL ARTICLE

Relationship of Anti-HCV Positivity and Malnutrition among Patients on Maintenance Hemodialysis: A Case Control Study

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ABSTRACT

Background: The nutritional status of patients on maintenance hemodialysis has a direct impact on their morbidity and mortality. Periodic nutritional assessment coupled with timely intervention has significant role in improving quality of life of those patients.
Aim: To study the relationship of serum anti-HCV positivity and levels of serum Albumin (marker of malnutrition) among patients of ERSD who are on maintenance hemodialysis (MHD).
Study design & duration: Case Control Study Data was collected during 2016.
Study setting: Department of Nephrology, Allama Iqbal Medical College/Jinnah Hospital Lahore.
Methods: A Case Control Study was conducted with total of 128 patients (Cases=35 Anti-HCV positive, Controls=93 Anti-HCV negative) participating in study. Purposive sampling was done. Standardized Questionnaire was used to collect data after taking their informed consent. Following serum markers were measured in both groups; Albumin, Calcium, Phosphate, Parathyroid Hormone, Uric Acid and Hemoglobin. SPSS version 20.0 was used to analyze the data.
Result: 35 Anti-HCV positive and 93 Anti-HCV negative patients were included in the study. There is statistically significant difference in albumin and hemoglobin levels between case and control groups, but no difference was found in rest of the serum markers. Average albumin in case group is 3.5579 and in control group is 3.7732 (p=0.055).
Conclusion: Anti-HCV positive patients have lowalbumin levels in serum as compared to control group. However, Hemoglobin levels are better controlled in Anti-HCV negative patients as compared to control group.
Keywords: Anti-HCV positivity, Malnutrition, Maintenance Hemodialysis, Serum albumin

INTRODUCTION

A case control study was done to find out a cause-effect relationship between anti-HCV positivity and below normal levels of serum Albumin (serum marker of malnutrition) among patients of End Stage Renal Disease (ERSD) who are on maintenance hemodialysis (MHD).

Malnutrition is of great concern as it is a marker of poor prognosis in hemodialysis patients. Epidemiological studies have shown a strong inverse association of nutritional status with increased risk of hospitalization and direct association of nutritional status with functional activity and patients' quality of life. Prevalence of malnutrition is highin hemodialysis patients ranging from 20% - 50%. Morbidity and mortality in hemodialysis patients with malnourishment remain unacceptably high despite continuous improvement in treatment of hemodialysis patients. Therefore it is crucial to diagnose, treat and prevent conditions associated with malnutrition.

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S. Chung *et al*. states that malnutrition exists in patients on hemodialysis due to several factors such as disorders of protein metabolism, lipid metabolism, and carbohydrate metabolism; chronic inflammation, metabolic acidosis, oxidative stress, dialysis related problems and hormonal derangements.[1]*Pifer et al.* states that several nutritional indicators which can be readily measured are good predictors of mortality in hemodialysis patients[2].

Several nutritional assessment scores and serum markers are used in clinical practice to diagnose malnutrition and predict mortality risk in patients on MHD. But serum Albumin has surfaced as most reliable and readily measured serum marker for nutritional assessment in literature. *Camiel L.M. de Roij van Zuijdewijn et al.* stated that out of the eight investigated nutrition-related tests such as Malnutrition-Inflammation Score (MIS), Subjective Global Assessment (SGA), composite score of protein-energy nutritional status (cPENS), normalized protein nitrogen appearance (nPNA), BMI, creatinine, Geriatric Nutritional Risk Index (GNRI) and albumin; MIS and albumin predict mortality best in hemodialysis patients[3]. *Leinig et al* also stated that SGA, albumin, and PEW were the only nutritional markers which were significantly associated with

mortality in peritoneal dialysis patients. In this cohort, only patients with hypoalbuminemia were at a higher mortality risk at follow up[4].

S. Chung et al. states that in CKD patients, inflammation which can occur in response to various internal or external stimulants; can influence the body through various physiologic, immunologic, and metabolic effects and it is the most important factor associated with malnutrition[1]. Hepatitis C virus infection in body is a chronic inflammatory condition which worsens the malnutrition status, already present due to maintenance hemodialysis. Studies have established a strong independent cause-effect relationship between HCV infection and malnutrition–inflammation complex syndrome (MICS)[6]. *Chong V H et al* stated that almost one-third of maintenance hemodialysis patients tested positive for anti-HCV in their follow-up. HD was responsible for 13.6% of the etiologies among all HCV-infected patients. So HCV infection is a common entity among HD patients. [7]It is important to determine the quantitative nutritional status in anti-HCV positive hemodialysis patients, before starting the nutritional intervention,

In order to identify an increased risk of complications and poor clinical outcome due to anti-HCV positivity, inflammation and malnutrition status of anti-HCV positive and anti-HCV negative HD patients was compared. *A. Zumrutdal et al* found out that there was no significant difference in MIS (Malnutrition-Inflammation Score) of two groups[8].

MATERIALS AND METHODS

A case-control study was done in Department of Nephrology, Jinnah Hospital Lahore. We took informed consent from patients after explaining risk and benefits. It was also made sure that the personal information of participants be kept confidential. Sample size was calculated to be 128 (CI = 95%). Study subjects were divided into two groups with ratio of 1:2.6;35 cases (anti-HCV positive) and 93 controls (anti-HCV negative).Purposive sampling was done.

Anti-HCV positivity: Anti-HCV antibodies are typically identified by using enzyme-linked immunosorbent assay (ELISA). A reactive or positive antibody test means patient has been infected with the Hepatitis C virus in past (cleared the infection) or still is infected[10]. Worldwide accepted definition of maintenance hemodialysis is dialysis sessions done thrice weekly with four hours daily[11].

All stable patients on maintenance dialysis for past 12 months were included. Thirty five (35) out of 128 total patients were anti-HCV antibody positive. Patients with untreated active infection (HCV RNA positive) and patients with early cirrhosis were included as well. Patients with decompensated CLD were excluded. Following serum markers were measured in both groups; Albumin (ALB), Calcium (Ca++), Phosphate (PO_4), Parathyroid Hormone PTH), Uric Acid (Uric Acid) and Hemoglobin(HB). SPSS version 20.0was used to analyze the data. P value<0.05 was considered as significant. Test of significance was also applied. Quantitative variables like age were described by mean and SD.

RESULTS

Thirty five hepatitis C positive and 93 hepatitis C negative patients were included in the study. 28% of cases were females and 72% were males. Mean age of cases was 39 years. 25% of controls were females and 75% were males. There is statistically significant difference in albumin and hemoglobin level between case and control groups, but no difference was found in rest of the serum markers. Average albumin in case group is 3.5579 and in control group is 3.7732 (p=0.055). Average hemoglobin in case group is 10.6254 and in control group is 10.0257 (p=0.043).

Table 1

Group		Age	Duration (month)	ALB	PO_4	Ca++	PTH	Uric Acid	HB	URR
HCV	N	35	34	35	33	35	29	33	35	27
	Mean	51.8571	35.6471	3.5579	5.5423	8.3249	864.2462	6.8209	10.6254	64.6248
	Std. Deviation	13.68585	28.93868	.34901	1.39447	.61264	706.17326	1.24373	.92676	12.18150
	Minimum	25.00	6.00	2.60	3.30	6.84	22.10	4.35	8.73	36.00
	Maximum	82.00	96.00	4.13	8.80	9.70	2623.00	9.93	12.13	88.42
Control	N	93	91	84	70	90	63	87	90	62
	Mean	47.2043	26.7143	3.7732	5.2520	8.2638	684.3776	6.8179	10.0257	176.4044
	Std. Deviation	16.13433	29.32965	.61485	1.42977	.62228	818.83385	6.74299	1.63589	849.90892
	Minimum	16.00	6.00	2.70	2.89	6.48	8.74	2.70	5.90	26.56
	Maximum	76.00	120.00	8.40	9.50	10.11	5125.10	68.00	14.90	6760.00
Total	N	128	125	119	103	125	92	120	125	89
	Mean	48.4766	29.1440	3.7098	5.3450	8.2809	741.0753	6.8188	10.1936	142.4937
	Std. Deviation	15.59021	29.37953	.55742	1.41825	.61774	785.69527	5.76846	1.49311	709.52870
	Minimum	16.00	6.00	2.60	2.89	6.48	8.74	2.70	5.90	26.56
	Maximum	82.00	120.00	8.40	9.50	10.11	5125.10	68.00	14.90	6760.00
t test		1.523	1.521	-1.942	.969	.495	1.020	.003	2.042	.498
P value		.133	.131	.055	.335	.662	.310	.998	.043	.305

DISCUSSION

Dialysis patients are commonly depleted of protein and energy stores. Approximately 20% - 50% of dialysis patients are malnourished and it is evident by the loss of protein stores, which is reflected clinically as lean body mass. In this case, levels of viscera proteins such as serum albumin, prealbumin and transferrin go low. Protein loss in urine and removal of amino acids during dialysis also play a role. In addition, negative nitrogen balance is also created by metabolic acidosis in CKD patients[1].

The assessment of nutritional status is a routine part of the care of maintenance dialysis patients in order to allow early recognition and treatment of malnutrition. Among the markers of nutrition, Serum Albumin is the strongest predictors of morbidity and mortality in ESRD patients. Serum albumin <3.8g/dL is a suggested diagnostic criterion for PEW syndrome or malnutrition. The serum albumin levels are widely accepted diagnostic tool to assess the nutritional status of patients, with or without chronic kidney disease (CKD). A low serum albumin is one of the strongest predictors of outcomes in CKD and dialysis patients. However, serum albumin levels may also fall due to non-nutritional factors including inflammation, acute or chronic stress, over hydration, urinary or peritoneal losses, and academia. Serum albumin is more commonly measured by either bromocresol green method or bromocresol purple method. Among ESRD patients, albumin estimation by bromocresol green method more closely estimates values obtained by nephelometry, whereas the bromocresol purple method underestimates the albumin concentration[12].

International Society of Renal Nutrition and Metabolism (ISRNM) recommends performing monthly nutritional assessments of all hemodialysis patients including a dietary assessment, physical examination, and laboratory examination so that timely intervention can be done.[13] In developing countries like Pakistan, We suggest that only serum Albumin levels should be used to assess the nutritional status of patient and to predict the morbidity and mortality, as it is not possible to do routine dietary assessment and physical examination.

A nutritional test should be quick, easy, cheap, have a good intra-observer and inter-observer reproducibility, an adequate and sufficient discrimination. Camiel L.M. deRoij van Zuijdewijn et al suggested that SGA, which is the recommended screening tool by American Society for Parenteral and Enteral Nutrition (ASPEN), should not be used now due to lack of objectivity, inadequate discrimination, calibration or a lower predictive value for mortality.[3]Malnutrition-Inflammation Score (MIS) proved to be the excellent predictor of malnourishment in hemodialysis patients but got no added value over serum albumin.[3]BMI got no significance in predicting malnourishment in hemodialysis patients. Fatin A M et al found 47% of hemodialysis patients with severe malnutrition had normal BMI[14]. Sensitivity and applicability of anthropometric measurements such as skin fold thickness, mid arm circumference (MAC) and mid arm muscle circumference (MAMC) has not been convincing.[15]Assessing anthropometric variables by methods like dual-energy X-ray absorptiometry, bioelectric impedance analysis, and total body protein is an expensive, cumbersome and impractical process for routine use[15].

A study on Taiwanese Maintenance Hemodialysis Patients demonstrated that HCV infection is a strong independent predictor of Malnutrition-Inflammation Complex Syndrome in maintenance hemodialysis patients. They used Malnutrition-Inflammation Score to evaluate the prognosis of Maintenance Hemodialysis patients with active HCV infection.[7]We suggest prompt treatment of patients with Anti-HCV positivity especially those on maintenance hemodialysis in order to improve their nutritional status and clinical prognosis.

The reason for elevated hemoglobin in hepatitis C positive patients is unclear. The average dose of erythropoietin stimulating agents (ESA) used was higher in these patients. This could be, in part, secondary to increased incidence of fatigue encountered in hepatitis C positive patients requiring the nephrologists use higher dose of ESA and hence higher hemoglobulin.

Main limitations of this study have been smaller sample size and limitation of serum Albumin in predicting the etiology of malnutrition.

CONCLUSION

Patients on maintenance Hemodialysis with positive anti-HCV antibodies have statistically significant low serum albumin levels as compared to patients on maintenance dialysis with negative anti-HCV antibodies. Hence any dialysis center should include routine nutritional assessment and prompt treatment of HCV infection in their guidelines.

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