

**MALNUTRITION, INFLAMMATION AND ATHEROSCLEROSIS COMPONENTS IN
ENDSTAGE RENAL DISEASE PATIENTS UNDERGOING HEMODIALYSIS OR
PERITONEAL DIALYSIS****Raji R.P. and M.K. Mohan Das***¹Assistant Professor, Nephrology, ²Additional Professor, Nephrology
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ABSTRACT

Introduction: Malnutrition, inflammation and atherosclerosis are associated with significant morbidity and mortality in ESRD patients undergoing renal replacement therapy. In this study we tried to find out the prevalence of malnutrition, atherosclerosis and inflammation in ESRD patients undergoing hemodialysis or peritoneal dialysis. We also studied factors influencing the development of malnutrition, inflammation and atherosclerosis. The prevalence of malnutrition, inflammation and atherosclerosis was compared between the two dialysis modalities. **Methods:** Total 150 dialysis patients were studied (114 HD patients and 36 CAPD patients). Malnutrition was assessed by BMI. Serum albumin and cholesterol. Inflammation was assessed with CRP. Atherosclerosis was assessed with carotid intima media thickness using B mode ultrasound. **Findings:** Out of 150 patients in our studying population 74.67 % patients had malnutrition, 62 % had inflammation and 74.67 % had atherosclerosis. Among patients who are undergoing hemodialysis 72.8 % had malnutrition. Where as 80.56 % of CAPD patients had malnutrition. Inflammation was seen in 66.67 % of patients undergoing HD and 47.22 % of patients undergoing CAPD and the difference was statistically significant. Atherosclerosis was seen in 78.07% of patients undergoing HD and 63.89 % of patients undergoing CAPD. There was no statistically significant difference in the prevalence of malnutrition and atherosclerosis between HD and CAPD patients. **Discussion:** Prevalence of malnutrition, inflammation and atherosclerosis is significantly high in ESRD patients undergoing renal replacement therapy.

KEYWORDS: Malnutrition, atherosclerosis, inflammation, ESRD.**INTRODUCTION**

Patterns, pathophysiology, treatment, and complications in chronic kidney disease (CKD) have changed considerably over the past few decades. Most of the patients starting dialysis are already having signs of advanced atherosclerosis, and the risk factors for cardiovascular morbidity and mortality seen in patients with CKD develop with the disease progression. So, the predialysis period is the ideal time to start therapeutic interventions. Traditional risk factors alone cannot adequately predict cardiovascular disease (CVD) outcome in patients with end stage renal disease ESRD. Inflammation is identified as playing a key role in atherosclerotic CVD. Proinflammatory cytokines are important in inflammation that is associated with malnutrition and atherosclerosis in ESRD. Malnutrition often worsens patient outcome by exacerbating existing inflammation and heart failure, accelerating atherosclerosis and increasing susceptibility to infection. Atherosclerosis is itself a major risk factor for CVD mortality. Above all, inflammation is associated with cardiac failure. Malnutrition, inflammation, and

atherosclerosis are producing significant problems in patients on dialysis. As these three conditions often occur concomitantly in dialysis patients, they have been referred together as 'malnutrition-inflammation-atherosclerosis syndrome' to emphasize the important association with atherosclerotic cardiovascular disease.

The three factors contributing to the pathophysiology of malnutrition in these patients are dialysis related nutrient loss, increased protein catabolism and hypoalbuminemia. Inflammation in CKD is the most important factor in the genesis of several complications in renal disease. Pro-inflammatory cytokines play a major role in the onset of metabolic alterations in CKD patients (1). Atherosclerosis is a very frequent complication in uremia. Each component of MIA syndrome predicts outcomes in ESRD patients. It could be speculated that suppression of the vicious cycle of malnutrition, inflammation and atherosclerosis could improve survival in dialysis patients.

A better understanding of the pathogenetic processes involved in MIA syndrome can help to reduce the unacceptably high morbidity and mortality rates in ESRD. So identifying MIA components in dialysis patients is important. Preventing and addressing correctable parameters of MIA components are equally important as optimal drug intake and adequate dialysis. Usually MIA syndrome seems to be an ignored entity. More studies are required before the interrelationship between malnutrition, inflammation, cytokines, oxidative stress, endothelial dysfunction, and heart disease in patients with ESRD can be established more accurately. Still there are many missing pieces in the puzzle. In this cross-sectional study, we aimed to estimate the prevalence and compare both dialysis modalities for MIA syndrome components. This study is expected to show light on the existence of MIA syndrome which may help to manage CKD patients more effectively.

METHODOLOGY

Study Design

Cross section study

Study Population

ESRD patients on maintenance hemodialysis from dialysis unit of department of nephrology Government Medical College Thiruvananthapuram and patients on CAPD initiated and followed up in the department of nephrology Government medical college Thiruvananthapuram.

INCLUSION CRITERIA

*Chronic kidney disease patients on maintenance Hemodialysis or CAPD for at least 3 months.

*Age between of 18 -70 years

EXCLUSION CRITERIA

*Patient not providing consent

ESTIMATED STUDY PERIOD

1.5 years period (1-04-2018 to 30-09-2019)

SAMPLE SIZE

The sample size was estimated based on evidence from study Malgorzata Maraj et al (2), From the study it was observed that the average prevalence of mia components is 40 % sample size = $N \frac{pq}{d^2}$

P= prevalence

q= 1-P

d = precision (20 % of p)

substituting the values sample size comes as 150 procedure

ESRD Patients on hemodialysis or CAPD schedule satisfying the inclusion and exclusion criteria were selected for the study. The patients were interviewed during their routine hemodialysis sessions an outpatient basis using a predesigned proforma.

To determine malnutrition in ESRD patients serum albumin, serum cholesterol and anthropometric me

asurements are used. For inflammation, serum C-reactive protein was measured. Mean-carotid artery intima media thickness was used to determine atherosclerosis.

Complete blood counts and serum biochemistry tests were performed as a part of routine monitoring of patients. Additional aliquots of sera were collected to measure C-reactive protein (CRP.).To measure the carotid intima-media thickness, ultrasonography of the common carotid artery, carotid bifurcation, and internal carotid artery will be performed with B-Mode ultrasonography (7 -14 MHZ probe) using USG machine Mindray. The primary investigator herself does the USG Doppler. The primary investigator was trained in doing USG Doppler and personally did it. On a longitudinal 2 dimensional ultrasound image of the carotid arteries, the anterior (near) and the posterior (far) walls of the carotid artery were displayed as two bright white lines separated by a hypoechogenic space. The distance between the leading edge of the first bright line of the far wall (lumen-intima interface) and the leading edge of the second bright line (media adventitia interface) indicate the intima media thickness. For the near wall, the distance between the trailing edge of the first bright line and the trailing edge of the second bright line at the near wall provided the best estimate of the near wall intima media thickness. CIMT was measured at the common carotid artery, carotid bifurcation, and the initial tract of the internal carotid artery on both sides. Measurements were performed 0.5, 1, and 2 cm below and above the bifurcation (six measurement on each side) in a plaque-free arterial segment. Final measurement was an average of three measurements and all measurements were done by a single observer. The highest measurement of the obtained values was taken as CIMT.

DATA COLLECTION

Data was collected using predesigned proforma.

OPERATIONAL DEFINITIONS

Malnutrition

Malnutrition was defined by the presence of BMI < 18.5 or serum albumin < 3.5g/dl (2) or serum cholesterol < 150mg/dl.

Inflammation

Inflammation was defined by CRP > 0.5 mg /dl

Atherosclerosis

Atherosclerosis was defined by CIMT > 0.9 mm

STATISTICAL ANALYSIS

Data was entered in Microsoft excel spread sheet. Continuous data were expressed as means + SD, Kolmogorov-Smirnov test was used to test normally when sample size was more than 50 and Shapiro-Wilk test when less than 50. Means of two groups of continuous variables with normal distribution were compared by independent sample test and non normal

distribution by mann Whitney U test. For correlation between two variables, Pearson correlation was used for normally distributed variables and Spearman's rank correlation coefficient when non normally distributed. To find the significance of association between categorical variables chi square test was used. Fischer exact test was

used when expected count was less than 5 in any cell. Various risk factors of malnutrition, inflammation and atherosclerosis were analysed using binary logistic regression. Analysis were done using SPSS software version 18.0 P value <0.05 was taken as significant.

RESULTS

1. Mode of dialysis

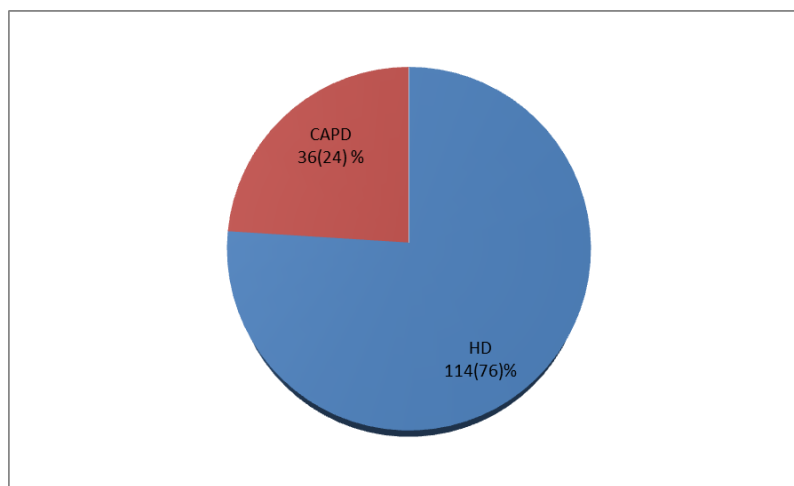


Figure 4: Mode of dialysis.

Among the total 150 cases 114 (76 %) patients were undergoing hemodialysis and 36(24 %) patient were undergoing CAPD.

Table 6: Mode of dialysis.

Mode of Dialysis	Number	Percentage
HD	114	76
CAPD	36	24
Total	150	100

2. Baseline characteristic

Table 7: Baseline characteristics.

	HD (N=114)	CAPD(N=36)	P value
Age (mean-year)	52.76 ± 11.5	52.7 ± 16.5	0.991
Sex Female	23(20.18%)	11(30.56%)	0.195
Male	91(79.82%)	25(69.44%)	
Aetiology of CKD			0.207
ADPKD	5(4.39%)	1(2.78%)	
CGN	27(23.68%)	5(13.89%)	
CTID	1(0.88 %)	1(2.78%)	
Diabetic Nephropathy	72(63.16%)	21(58.33%)	
Ischaemic Nephropathy	3(2.63%)	2(5.56%)	
Others	1(0.88%)	1(2.78%)	
Reflex Nephropathy	2(1.75%)	4(11.11%)	
Stone disease	3(2.63%)	1(2.78%)	
Dialysis Vintage(months)	23.90 ± 21.72	11.66 ± 8.24	0.001<
BMI	21.55 ± 3.15	21.29 ± 2.98	0.664
Hemoglobin-g/dl	8.41 ± 1.48	8.96 ± 1.83	0.067
Albumin-g /dl	3.65 ± 0.38	3.12 ± 0.58	0.001<
Cholesterol-mg/dl	146.59 ± 42.01	171.44 ± 31.86	0.001
Calcium -mg /dl	8.44 ± 0.75	8.25 ± 0.93	0.225
Phosphorous -mg/dl	5.42 ± 1.48	6.11 ± 1.83	0.022
PTH	861.67 ± 612.01	974.33 ± 677.06	0.363
CRP-mg/dl	1.17 ± 3.03	1.09 ± 2.32	0.900
CIMT -mm	0.97 ± 0.14	0.93 ± 0.16	0.104

The mean age of our study population was 52.7 ± 11.5 in HD patients and 52.7 ± 16.5 in CAPD patients. In HD 20.18% were females and 79.82% were males. In CAPD 30.56% were females and 69.44% were females. Among the aetiology of CKD diabetic nephropathy was the most common cause in both groups which accounts for 63.16% in HD patients and 58.33% in CAPD patients. The mean dialysis vintage was more in HD group (26.90 ± 21.72) compared to CAPD group (11.56 ± 8.24) which showed a statistically significant difference (p value < 0.001). The mean BMI in both groups were comparable (21.55 ± 3.15 in HD group and 21.29 ± 2.98 in CAPD group). The mean hemoglobin was 8.41 ± 1.48 in HD group and 8.96 ± 1.83 in CAPD group. The mean albumin in CAPD group was 3.12 ± 0.58 which was significantly lower than HD patients (3.62 ± 0.38) (p value < 0.001). The mean cholesterol was low in HD group (146.59 ± 42.01) compared to CAPD group (171.44 ± 31.86) and the difference was statistically significant (p value = 0.001). The mean calcium was 8.44 ± 0.75 in HD group and 8.25 ± 0.93 in CAPD group and both were comparable. The mean phosphorous was high in CAPD group (6.11 ± 1.83) compared to HD group (5.42 ± 1.47) and the difference was statistically significant (p value = 0.022). The mean PTH was 964.67 ± 612.01 in HD group and 974.33 ± 677.06 in CAPD group. The mean CRP was $1.17 \pm$ in HD group and 1.09 ± 2.32 in CAPD group. The mean CIMT (carotid intima media thickness) in mm was 0.97 ± 0.14 in HD group and 0.93 ± 0.16 in CAPD group.

3. Malnutrition, inflammation and atherosclerosis

Table 8: Total prevalence of malnutrition, inflammation and atherosclerosis.

	Number	Percentage
Malnutrition	112	74.67 %
Inflammation	93	62 %
Atherosclerosis	112	74.67 %

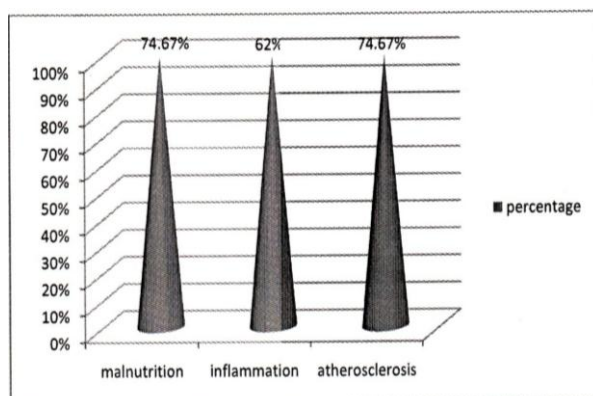


Figure 5: Total prevalence of malnutrition, inflammation and atherosclerosis.

Out of 150 patients in our study population 112 (74.67 %) patients had malnutrition, 93(62 %) had inflammation and 112 (74.67 %) had atherosclerosis.

4. Prevalence of malnutrition, atherosclerosis and inflammation in HD vs CAPD

Table 8: Total prevalence of malnutrition, inflammation and atherosclerosis.

	HD	CAPD	P Value
Malnutrition	83	29	0.351
Inflammation	76	17	0.036
Atherosclerosis	89	23	0.088

Among patients who are undergoing hemodialysis 72.8% had malnutrition. Where as 80.56% of CAPD patients had malnutrition. Inflammation was seen in 66.67% of patients undergoing HD and 47.22% of patients undergoing CAPD and the difference was statistically significant (p value 0.036). Atherosclerosis was seen in 78.07% of patients undergoing HD and 63.89% of patients undergoing CAPD. There was no Statistically significant difference in the prevalence of malnutrition and atherosclerosis between HD and CAPD patients

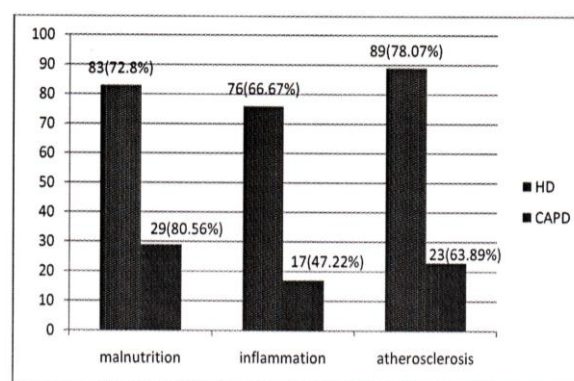


Figure 6: Prevalence of malnutrition and inflammation in HD vs CAPD.

5. Relation between inflammation and atherosclerosis

Table 10: Relation between inflammation and atherosclerosis.

		atherosclerosis		
		No	Yes	
Inflammation	No	13	44	57
	Yes	25	68	93
		38	112	150

P value = 0.578

In our study there was no statistically significant relation between inflammation and atherosclerosis.

6. Relation between malnutrition and atherosclerosis

Table 11: Relation between malnutrition and atherosclerosis.

		atherosclerosis		
		No	Yes	
Malnutrition	No	12	26	38
	Yes	26	86	112
		38	112	150

P value = 0.306

In our study there was no statistically significant relation between Malnutrition and atherosclerosis.

7. Relation between malnutrition and inflammation

Table 12: Relation between malnutrition and inflammation.

Malnutrition		atherosclerosis		
		No	Yes	
	No	12	26	38
	Yes	45	67	112
		57	93	150

P value =0.345

In our study there was no statistically significant relation between Malnutrition and inflammation.

8. Correlation of CIMT with various variables.

Table 13: Correlation of CIMT with other variables.

Parameters	Coefficient of correlation	P value
Age	0.172	0.036
BMI	0.193	0.018
CRP	0.017	0.833
PTH	-0.090	0.274
Cholesterol	-0.200	0.014
Albumin	0.020	0.811
Hemoglobin	-0.089	0.280
Vintage	0.076	0.357

Correlation of CIMT with other various variables were analyses and shown in table 8. Statistically significant positive correlation was seen with age (coefficient of correlation 0.172 and p value 0.036) and BMI (coefficient of correlation 0.193 and p value 0.018). Statistically significant negative correlation was seen with serum cholesterol (correlation coefficient -0.200 and p value 0.014).

9. Correlation of CRP with other variables

Table 14: Correlation of CRP with other variables.

Parameters	Coefficient of correlation	P value
Age	0.089	.277
BMI	-0.103	.209
PTH	-0.084	.306
Cholesterol	-0.108	.186
Albumin	-0.121	.141
Hemoglobin	0.020	.806
Vintage	-0.042	.607

12. Risk factors of atherosclerosis

Table 17: Risk factors atherosclerosis.

Risk factors	Odds ratio	95 % Confidence interval		P value
		Lower	Upper	
Age	1.025	.992	1.058	0.139
Dialysis vintage	.993	.975	1.011	0.434
BMI	1.055	.923	1.206	0.434
CRP	1.162	.856	1.578	0.336
PTH	1.000	.999	1.000	0.506
Cholesterol	.991	.982	1.001	0.076
Albumin	.961	.398	2.322	0.929

Age, dialysis vintage, BMI, CRP, PTH, cholesterol and albumin were analysed as risk factors of atherosclerosis using univariate logistic regression method. Results are

Correlation of CRP with other variable were analysed and shown in table no 9 No statistically significant correlation was obtained.

10. Correlation of cholesterol with other variables

Table 15: Correlation of Cholesterol with other variables.

Parameters	Coefficient of correlation	P value
Age	0.016	0.846
BMI	-0.069	0.402
PTH	0.001	0.988
Albumin	0.112	0.171
Hemoglobin	0.116	0.157
Vintage	-0.077	0.347

Correlation of cholesterol with other variables were analysed and shown in table NO.10 statistically significant correlation was obtained.

11. Correlation of albumin with other variables

Table 16: Correlation of albumin with other variables.

Parameters	Coefficient of correlation	P value
Age	-0.059	0.473
BMI	0.093	0.259
PTH	0.165	0.044
Hemoglobin	0.125	0.127
Vintage	0.246	0.002

Correlation of albumin with other variables were analysed and shown in table no.11. Statistically significant positive correlation was seen with dialysis vintage (coefficient of correlation 0.246 and p value 0.002) and PTH (coefficient of correlation 0.165 and p value 0.044).

shown in table no.12. None of them were found as statistically significant risk factor for development of atherosclerosis.

13. Risk factors of inflammation

Table 18: Risk factors inflammation.

Risk factors	Odds ratio	95 % Confidence interval		P value
		Lower	Upper	
Age	.997	.968	1.026	0.617
Dialysis vintage	1.003	.985	1.021	0.77
BMI	1.058	.941	1.191	0.345
PTH	1.000	.999	1.000	0.103
Cholesterol	0.988	.980	.997	0.009
Albumin	1.742	.815	3.726	0.152

Age, dialysis vintage, BMI, PTH, cholesterol and albumin were analysed as risk factors of inflammation using univariate logistic regression method. Results are shown in table no.13. Increase in cholesterol was found

as statistically significant protective factor In the development of inflammation (odds ratio=0.988, 95% confidence interval 0.980-0.997, p value=0.009)

14. Risk factors of malnutrition.

Table 19. Risk factors malnutrition.

Risk factors	Odds ratio	95 % Confidence interval		P value
		Lower	Upper	
Age	.988	.946	1.031	0.574
Dialysis vintage	1.016	.990	1.042	0.229
BMI	.768	.656	.901	0.001
PTH	1.000	.999	1.001	0.759
Cholesterol	.966	.953	.980	<0.001
Albumin	.095	.024	.371	0.001
CRP	.884	.755	1.035	0.125

Age, dialysis vintage, BMI, PTH, cholesterol, albumin and CRP were analysed as risk factors of malnutrition using univariate logistic regression method. Results are shown in table no.14. Increase in cholesterol was found as a statistically significant protective factor in the development of malnutrition (odds ratio=0.966, 95% confidence interval 0.953-0.980, p value=<0.001). Increase in albumin was also statistically significant protective factor in the development of malnutrition (odds ratio=0.095, 95% confidence interval 0.024-0.371, p value=0.001).

15. Malnutrition and dialysis adequacy.

Table 20: Malnutrition and dialysis adequacy.

Malnutrition		Adequacy		
		No	Yes	
	No	5	33	38
	Yes	24	88	112
		29	121	150

P value =0.265

There was no statistically significant association between dialysis adequacy and malnutrition

16. Inflammation and dialysis adequacy

Table 21: Inflammation and dialysis adequacy.

		Adequacy		
		No	Yes	
Inflammation	No	11	46	57
	Yes	18	75	93
		29	121	150

P value =0.993

There was no statistically significant association between dialysis adequacy and inflammation

17. Atherosclerosis and dialysis adequacy

Table 22 atherosclerosis and dialysis adequacy.

		Adequacy		
		No	Yes	
Atherosclerosis	No	8	30	38
	Yes	21	91	112
		29	121	150

P value =0.756

There was no statistically significant association between dialysis adequacy and atherosclerosis

18. Comparison of Albumin between HD and CAPD

Table 23: Comparison of Albumin between HD and CAPD.

Albumin	HD (N=114)	CAPD (N=36)	Total (N=150)	P- Value
>3.5	71(62.3%)	8(22.2%)	79(52.7%)	0.000
<3.5	43(37.7%)	28(77.8%)	71(47.3%)	
Mean \pm SD	3.62 \pm 0.38	3.12 \pm 0.58	3.50 \pm 0.48	

In this study, almost 52.7% of the cases have albumin >3.5 and 47.3% of the cases have albumin <3.5. in patients 37.7 % patients has hypoalbuminemia where as in CAPD 77.8 % patients had hypoalbuminemia. Here the p – value (<0.05) suggest that the difference in albumin between HD and CAPD is significant. The mean albumin reveals that albumin is significantly higher in HD (3.36 ± 0.38) compared to CAPD (3.12 ± 0.58).

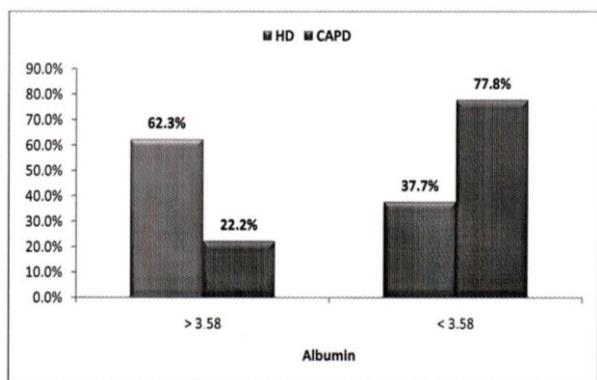


Figure 7: Comparison of Albumin between HD and CAPD.

19. MIA syndrome

Total 49(32.67 %) had all the components of MIA syndrome. Co occurrence of malnutrition and inflammation was seen in 18(12%) patients. Co occurrence of malnutrition and atherosclerosis was seen in 36(24 %) patients. Co occurrence of inflammation and atherosclerosis was seen in 20(13.33 %) patients.

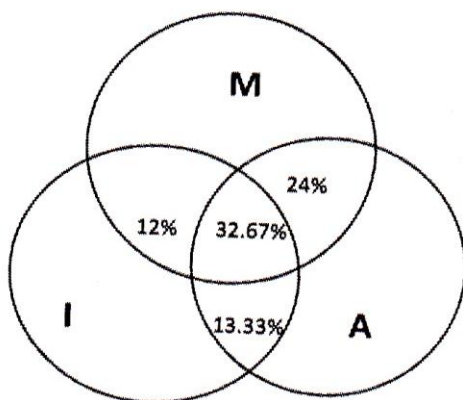


Figure 8: MIA syndrome.

DISCUSSION

We studied prevalence of malnutrition, atherosclerosis and inflammation in HD and CAPD patients. Among 150 cases 114(76%) patients were undergoing haemodialysis and 36(24%) patients were undergoing CAPD.

The mean age of our study population was 52.7 ± 11.5 in HD patients and 52.7 ± 16.5 in CAPD patients. In HD 20.18% were females and 79.82% were males. In CAPD 30.56% were females and 69.44% were females. In a study by B.B. Kirushnan et.al (125) the mean

age was 61 ± 11.3 years and 69% were males. Among the aetiology of CKD diabetic nephropathy was the most common cause in both groups which accounts for 63.16% in HD patients and 58.33% in CAPD patients. The mean dialysis vintage was more in HD group (26.90 ± 21.72) compared CAPD group (11.56 ± 8.24) which showed a statistically significant difference (p value<0.001). In a study by B.B. Kirushnan et.al (125) the mean dialysis vintage was 34 ± 29.3 months in HD patients. In a study by Seid Kazem et al (129). The mean dialysis vintage was 26.12 ± 25.42 months in CAPD patients. The mean BMI in both groups were comparable (21.55 ± 3.15 in HD group and 21.29 ± 2.98 in CAPD group).

The mean haemoglobin was 8.41 ± 1.48 in HD group and 8.96 ± 1.83 in CAPD group. The mean albumin in CAPD group was 3.12 ± 0.58 which was significantly lower than HD patients (3.62 ± 0.38) (p value<0.001). In HD patients 37.7% patients had hypoalbuminaemia where as in CAPD 77.8% patients had hypoalbuminaemia. Here the p-value(<0.05) suggests that the difference in albumin in between HD and CAPD is significant. In a study by H. Zeki Tonbul et al (130). 16% CAPD patients and 3% HD patients were hypoalbuminaemic. The mean cholesterol was low in HD group (146.59 ± 42.01) compared to CAPD group (171.44 ± 31.86) and the difference was statistically significant (p value=0.001). The mean calcium was 8.44 ± 0.75 in HD group and 8.25 ± 0.93 in CAPD group and both were comparable. The mean phosphorous was high in CAPD group (6.11 ± 1.83) compared to HD group (5.42 ± 1.47) and the difference was statistically significant (p value=0.022). The mean PTH was 864.67 ± 612.01 in HD group and 974.33 ± 677.06 in CAPD group. The mean CRP was 1.17 ± 3.03 in HD group and 1.09 ± 2.32 in CAPD group. The mean CIMT in mm was 0.97 ± 0.14 in HD group and 0.93 ± 0.16 in CAPD group.

Out of 150 patients in our study population 112(74.67%) patients had malnutrition, 93(62%) had inflammation and 112(74.67%) had atherosclerosis. Among patients who are undergoing haemodialysis 72.8% had malnutrition. Where as 80.56% of CAPD patients had malnutrition. Inflammation was seen in 66.67% of patients undergoing HD and 47.22% of patients undergoing CAPD and the difference was statistically significant (p value0.036). Atherosclerosis was seen in 78.07% of patients undergoing HD and 63.89% of patients undergoing CAPD. There was no statistically significant difference in the prevalence of malnutrition and atherosclerosis between HD and CAPD patients. In a study by B.B. Kirushnan et. al (125) in HD patients malnutrition was seen in 32% patients, inflammation was seen in 78.5% patients and atherosclerosis was seen in 78.5% patients. In a study by H. Zeki Tonbul et al (130) HD and CAPD groups were similar for inflammation and mean-CIMT was higher in HD patients than CAPD patients.

There was no statistically significant relation among malnutrition, atherosclerosis and inflammation. Correlation of CIMT showed statistically significant negative correlation was seen with serum cholesterol. When risk factors of inflammation were assessed, increase in cholesterol was found as statistically significant protective factor in the development of inflammation. Risk factors of malnutrition were analysed. Increase in cholesterol was found as a statistically significant protective factor in the development of malnutrition. When risk factors of atherosclerosis were analysed there was no statistically significant risk factor for the developments of atherosclerosis. Dialysis adequacy did not show any statistically significant association with malnutrition, inflammation or atherosclerosis.

Total 49 (32.67%) had all the components of MIA syndrome. Co occurrence of malnutrition and inflammation was seen in 18 (12%) patients. Co occurrence of malnutrition and atherosclerosis was seen in 36 (24%) patients. Co occurrence of inflammation and atherosclerosis was seen in 20 (13.33%) patients. In a study by B.B. Kirushnan et. al (125) showed that 45% patients had all the three components of MIA syndrome, 33% had co occurrence of malnutrition and inflammation, 40% had malnutrition and atherosclerosis and 10% had atherosclerosis and inflammation.

CONCLUSION

In our study 74.67% patients had malnutrition, 62% inflammation and 74.67% atherosclerosis. Among patients who underwent haemodialysis and CAPD malnutrition was seen in 72.8% and 80.56% respectively. Inflammation was seen in 66.67% of patients undergoing HD and 47.22% of patients undergoing CAPD and the difference was statistically significant. Atherosclerosis was seen in 78.07% of patients undergoing HD and 63.89% of patients undergoing CAPD. There was no statistically significant difference in the prevalence of malnutrition and atherosclerosis between HD and CAPD patients. But inflammation was significantly high in HD patients. There was no statistically significant relation among malnutrition, atherosclerosis and inflammation. 32.67% had all components of MIA syndrome. Co occurrence of malnutrition and inflammation was seen in 12% patients. Co occurrence of malnutrition and atherosclerosis was seen in 24% patients. Co occurrence of inflammation and atherosclerosis was seen in 13.33% patients. Correlation of CIMT with other various variables were analysed and statistically significant negative correlation was seen with serum cholesterol. When risks of inflammation were assessed, increase in cholesterol was statistically significant protective factor in the development of inflammation. Increase in cholesterol was found as a statistically significant protective factor in the development of malnutrition. Increase in albumin was also statistically significant protective factor in the development of malnutrition. When risk factor of atherosclerosis were analysed there

was no statistically significant risk factor for the development of atherosclerosis. Dialysis adequacy did not show any statistically significant association with malnutrition, inflammation or atherosclerosis. Our study showed that malnutrition, atherosclerosis and inflammation components are alarmingly high in dialysis patients and appropriate measures have to be taken to reduce those factors.

REFERENCES

1. Pragna Rao, G C Reddy and A S Kangasabapathy et al. Malnutrition-inflammation- atherosclerosis syndrome in chronic kidney disease. Indian Journal of Clinical biochemistry, 2008; 23(3): 209-217.
2. Malgorzata Maraj 1, Beata Ku'sneirz-Cabala 2, Paulina Dumnicka et al malnutrition, Inflammation, Atherosclerosis Syndrome (MIA) and Diet Recommendations among End-Stage renal Disease patients Treated with maintenance Haemodialysis. Nutrients, 2018; 10: 69. doi: 10.3390 /nu 1001 0 069.
3. Stenvinkel, P. Inflammatory and atherosclerotic interactions in the depleted uremic patient. Blood purify, 2001; 19: 53-61.
4. Gerasimoula, K.; Lefkothea, L.; Maria, L.; Victoria, A.; Paraskevi, T.; Maria, P. Quality of life in haemodialysis patients Mater. Sociomed, 2015; 27: 305-309.
5. Oliveria, A.P.B.; Schmidt, D.B.; Amatneeks, T.M.; Santos, J.C.; Cavallet, L.H.; Michel, R.B. Quality of life in haemodialysis patients and the relationship with mortality, hospitalizations and poor treatment adherence. J. Bras. Nefrol, 2016; 38: 411-420.
6. Mollaglu, M. Quality of life in patients undergoing haemodialysis. In Haemodialysis; Suzuki, H., Ed.: In Tech: Rijeka, Croatia, 2013; 823-841.
7. Kraut, J.A.; Madias, N.E. Metabolic acidosis of CKD: An update. Am. J. Kidney Dis., 2016; 67: 307-317.
8. Kopple, J.C.; Kalantar-Zadeh, K.; Meharotra, R. Risks of chronic metabolic acidosis in patients with chronic kidney disease, Kidney Int., 2005; 95: 21-27.
9. Pickering, W.P.; Price, S.R.; Bricher, G.; Marinovic, A.C.; Mitch, W.E.; Walls, J. Nutrition in CAPD: Serum bicarbonate and the ubiquitin-proteasome system in muscle. Kidney Int., 2002; 61: 1286-1292.
10. Piccoli, G.B.; Molo, M.R.; Fois, A.; Sofronie, A.; Gendrot, L.; Cabiddu, G.; D'Alessandro, C.; Cuplsti, A. The diet and haemodialysis dyad: Three eras, four open questions and four paradoxes. A narrative review, towards a personalized, patient-centered approach. Nutrients, 2017; 9: 372.
11. Malnutrition, Inflammation, atherosclerosis in haemodialysis patients zespól mia u pacjentów haemodializowanych. A. Jeznach-Steinhagen, R. Stotwinski, B. Szczygiel. Roczn. Pzh, 2007; 58(Zo 1): 83p88.
12. Lim VS. Thyroid function in patients with chronic renal failure. Proceedings of the second international

- congress on uremic research, Nasa, Japan 2001: Metabolic dysfunction in Uremia. *Am J Kidney Dis.*, 2001; 35: 580-84.
13. Chung SH, Lindholm B, Lee HB, influence of initial nutritional status on continuous ambulatory peritoneal dialysis patient survival. *Perit Dial Int.*, 2000; 20: 19-26.
 14. Stenvinkel P, Heimbürger O, Lindholm B, Kaysen GA, Bergström J. Are there two types of malnutrition in chronic renal failure? Evidence for relationships between malnutrition, inflammation and atherosclerosis (MIA) syndrome. *Nephrol Dial Transplant*, 2000; 15: 953-60.
 15. O'Sullivan AJ, Larsson JA, Chan M, Kelly JJ. Body composition and energy metabolism in chronic renal insufficiency. *Am J Kidney Dis.*, 2002; 39: 369-75.
 16. Roelfsema V, Clark RG. The growth hormone and insulin like growth factor axis. Its manipulation for the benefit of growth disorders in renal failure. *J Am Soc Nephrol*, 2001; 12: 297-306.
 17. Goodman HM, Tai LR, Ray J, Cooke NE, Leibhaber SA. Human growth hormone variant produces insulin-like lipolytic responses in rat adipose tissue. *Endocrinol*, 1991; 129: 1779-83.
 18. Barany P, Eriksson LC, Hultcrantz R, Pettersson E, Bergström J. Serum ferritin and tissue iron in anaemic dialysis patients. *Miner Electrolyte Metab*, 1997; 23: 273-6.
 19. Mitch WE. Insights into the abnormalities of chronic renal disease attributed to malnutrition. Pathophysiology of chronic renal failure and complications. *J Am Soc Nephrol*, 2002; 13: s22-27.
 20. Odumaki M, Furuya R, Yoneyama T, Nishikino M, Hibi I, Miyaji K, et al. Association of serum leptin concentration with weight loss in chronic haemodialysis patients. *Am J Kidney Dis.*, 1999; 33: 361-8.
 21. Lkizier TA, Wingard RL, Sun M, Harvell J, Parker RA, Hakim RM. Increased energy expenditure in haemodialysis patients. *A Am Soc Nephrol*, 1996; 7: 2646-53.
 22. Yaker S, Liu J, Le Roith D. The growth hormone/insulin like growth factor spectrum; Implications for organ growth and development. *Paediatric Nephrol*, 2000; 52: 39-44.
 23. Jacob V, Le Carpentier JE, Saizano S, Naylor V, Wild G, Brown CB, et al. IGF-1, a marker of under nutrition in haemodialysis. *Trans Am J Clin Nutr.*, 1990; 52: 39-44.
 24. Kopple JD, Swendseid ME, Shinaberger JH, Umezawa CY. The free and bound amino acid removed by haemodialysis. *Trans Am Soc Artif Inter Organs*, 1973; 19: 309-13.
 25. Kopple JD. Pathophysiology of protein-energy wasting chronic renal failure. *J Nutr.*, 1994; 129: s147-251.
 26. Alfonso Martin Cueto manzano. Hypoalbuminaemia in dialysis patients. A malnutrition or an inflammatory marker? *La Revista de Investigación Clínica*, 2001; 52: 152-8.
 27. Moshage HJ, Janssen JA, Franssen JH, Hafkenseld JC, Yap SH. Study of the molecular mechanisms of decreased liver synthesis of albumin in inflammation. *J Clin Invest*, 1987.
 28. Luger A, Kovarik J, Stummvoll HK, Urbanska A, Luger TA. Blood membrane interaction in haemodialysis leads to increased cytokine production. *Kidney Int.*, 1987; 32: 84-8.
 29. Ikizier TA, Hakim RM. Nutrition in end-stage renal disease. *Kidney Int*, 1996; 50: 343-57.
 30. Blackburn GL, Thornton PA. Nutritional assessment of the hospitalized patients. *Med Clin North Am*, 1979; 63: 1103-15.
 31. Klahr S, Levey AS, Beck GJ, Cagglula AW, Hunsicker L, Kusek JW, et al. The effects of dietary protein restriction and blood control on the progression of renal diseases: Modification of diet in renal diseases study group. *N Engl J Med.*, 1994; 330: 877-84.
 32. Mears A. Outcomes of continuous process improvement of a nutritional care program incorporating serum pre-albumin measurements. *Nutrition*, 1996; 12: 479-84.
 33. Chertow GM, Ackert K, Lew NL, Lazarus JM, Lowrie EG. Pre-albumin is as important as albumin in the nutritional assessment of haemodialysis patients. *Kidney Int.*, 2000; 58: 2512-7.
 34. Bologna RM, Levine DM, Parker TS, Cheigh JS, Serur D, Stenzel KH, et al. Interleukin-6 predicts. Hypoalbuminaemia, hypocholesterolemia, and mortality in haemodialysis patients *J Am J Kidney Dis.*, 1998; 32: 107-14.
 35. Qureshi AR, Alvestrand A, Divino-Filho JC, Gutierrez A, Helmsberger O, Lindholm B, et al. Inflammation, malnutrition, and cardiac diseases as predictors of mortality in haemodialysis patients. *J Am Soc Nephrol*, 2002; 13(1): S28-36.
 36. Poole S, Bird TA, Selkirk S, Gaines-Das RE, Choudry Y, Stephenson SL, et al. Fate of injected interleukin-1 in rats: sequestration and degradation in the kidney. *Cytokine*, 1990; 2: 416-22.
 37. Descamps-Latscha B, Herbelin A, Nguyen AT, Roux-Lombard P, Zingarff J, Moynot A, et al. Balance between IL-1 beta, TNF-alpha, and their specific inhibitions in chronic renal failure and maintenance dialysis. Relationship with activation markers of T-cells, B-cells, and monocytes. *J Immunol*, 1995; 154: 882-92.
 38. Schindler R, Boenisch O, Fischer C, Frei U. Effect of the haemodialysis membrane on the inflammatory reaction in vivo. *Clin nephrol*, 2000; 53: 452-9.
 39. Miyata T, Hori O, Zhang J, Yan SD, Ferran L, Iida Y, et al. The receptor for advanced glycation and products (RAGE) is a central mediator of the interaction AGE-beta 2 microglobulin with human mononuclear phagocytes via an oxidant sensitive pathway: Implications for the pathogenesis of dialysis-related amyloidosis. *Clin Invest*, 1996; 98: 1088-94.

40. Stenvinkel P, Inflammation in end-stage renal disease: could it be treated? *Nephrol dial therapy*, 2002; 17: 33-8.
41. Choy EHS, Panayi GS, Cytokine pathways and joint inflammation in rheumatoid arthritis. *N Engl J Med.*, 2001; 344: 907-16.
42. Garibotto G, Russo R, Sofia A, Sala MR, Robaudo C, Moscatellil P, et al. Skeletal muscle protein synthesis and degradation in patients with chronic renal failure. *Kidney Int*, 1994; 45: 432-9.
43. Guarnieri G, toigo G, Flotti N, Clochi B, Situlin R, Glansante C, et al. Mechanism of malnutrition in uremia *Kidney Int.*, 1997; 62: s41-s44.
44. Marette A, Mediators of cytokine-induced Insulin resistance in obesity and other inflammatory settings. *Clin nutri Metab*, 2002; 5: 377-83.
45. Charles A Dinarello, Interleukin -1: A pro-inflammatory cytokine, inflammation, basic principles and clinical correlates, 3rd ed, Lippincott Williams and Wilkins, Philadelphia, 199.
46. Schindler R, Clark BD, Dinarello CA, Disassociation between Interlukin-1pm RNA and protein synthesis in human peripheral blood mononuclear cells. *J Biol Chem.*, 1990; 265: 1232-7.
47. Schindler R, Elchert F, Lepenies J, Frei U. Blood components influence cytokine induction by bacterial substances. *Blood Purif*, 2001; 19(4): 380-7.
48. Miller LC, Isa S, Vannier E, Georgilis K, Steere AC, Dinarello CA, Live Borella burgorferi preferentially activate IL- β gene expression and protein synthesis over the interleukin-1 receptor antagonist. *J Clin Invest*, 1992; 90: 906-12.
49. Haichao Wang, Kevin J. Tracey. Tumour necrosis factor, Interleukin-6, macrophage Migration Inflammatory Factor and macrophage inflammatory protein-1 in InflammationL: basic principles and clinical correlates. 3rd ed, Lippincott Williams and Wilkins, Philadelphia, 1999.
50. Barton BE: IL-6 insights into novel biological activities. *Clin Immunol immunopathoi*, 1997; 85: 16-20.
51. Weiss G, Meusburger, E Radacher G, Garimorth K, Neyer U, mayer G, Effect of iron treatment on circulating cytokine levels in ESRD patients receiving recombinant human erythropoietin. *Kidney Int*, 2003; 64: 572-8.
52. Mastroakos G, Chrousos QP, Webber JS, Cachectin/tumour necrosis factor regulates haepatic acute phase gene expression. *J Clin Invest*, 1986; 78: 1349-54.
53. Gauldie J, Richards C, Harnish D, Lansdrop P, BaumannH. Effects of Interleukin-6 and leukemia inhibitory factor on the acute phase response and DNA synthesis in cultured rat hepatocytes. *Lymphokine Cytokine Res.*, 1991; 10: 23-26.
54. Tracey KJ, Tumour necrosis factor (cachectin) in the biology of septic shock syndrome. *Circ Shock*, 1991; 35: 123-8.
55. Kumins NH, Hunt J, Gamelli RL, Filkins JP, Partial hepatectomy reduces the endotoxin-induced peak circulating levels of tumour necrosis factor in rats. *Shock*, 1989; 338: 225-8.
56. Lindner A, Charra B, Sherrard DJ, Scribner BH. Accelerated atherosclerosis in prolonged maintenance hemodialysis. *N Engl J Med.*, 1974; 290: 697-701.217.
57. Jungers P, massy ZA, Nguyen Khoa T, Fumeron C, Labrunie M, lacour B, et al. Incidence and risk factors of atherosclerosis cardiovascular accidents in predialysis chronic renal failure patients: a prospective study *Nephrol Dial Transplant*, 1997; 12: 2597-602.
58. Moorhead JF, Chan MK, El-Nahas M, varghese Z. Lipid nephrotoxicity in chronic progressive glomerular and tubule interstitial disease. *Lancet*, 1982; 2: 1309-11.
59. Poole S Bird TA, Selkrik S, Gaines-Das RE, Choudary Y, Stephenson SL, et al. Fate of injected Interleukin-1 in rats: sequestration and degradation in the kidney. *Cytikine*, 1990; 2: 416-22.
60. Klein JB, Mc Leish KR, Ward RA. Transplantation, not dialysis corrects azotemia-dependent priming of the neutrophil oxidative burst. *Am J Kidney Dis.*, 1999; 33: 483-91.
61. Himmelfarb J, Stenvinkel P, Ikizier TA, Hakim RM, The elephant in uremia: oxidative stress as a unifying concept of cardiocascular disease in uremia. *Kidney Int*, 2002; 62: 1524-8.
62. Atman PO, Samuelsson O, Alanpovic P, Lipoprotein metabolism and renal failure. *Am J Kidney Dis.*, 1993; 21: 573-92.
63. Savide E, Gibson JC, Crawford GA, Simous LA, Mahony JF. Impaired plasma triglyceride clearance as a feature of both uremic and post transplant triglyceridemia. *Kidney Int.*, 1980; 18: 774-82.
64. Arnadottir M, Thyssel H, Dallongeville J. evidence that reduced lipoprotein lipase activity is not a primary pathogenetic factor for hyper triglyceridemia. *Kidney Int.*, 1995; 48: 779-84.
65. Arnadottir M, thysell H, Dallongeville J, Fruchart JC, Nilsson-Ehle P. Very low density lipoprotein of uremic patients is a poor substrate for bovine lipoprotein lipase in vitro. *Metabolism*, 1996; 17: 3542-56.
66. Packard CJ Shepherd J. Lipoprotein heterogenelty and apoliptrotein B Metabolism, *Arterioscler Thromb Vasc Bio.*, 1995; 17: 3542-56.
67. Van Lenten B J, Hama SY, de Beer FC, Stafforini DM, McIntyre TM, Prescott SM, et al Anti-inflammatory HDL becomes pro-inflammatory during the acute phase responses. Loss of protective effect of HDL against LDL oxidation in aortiv wall cell culture. *J. Clin invest*, 1995; 96: 2758-67.
68. Pruzanski W, Stefanski E, de Beer FC, de Beer MC, Ravandi A, Kuksis A. Comparative analysis of lipid composition of normal and acute-phase high density lipoproteins. *J Lipid Res.*, 2000; 41: 1035-47.

69. Marz W, Beckmann A, Scharnagi H, Siekmeler R, Mondort U, Held I, et al: Heterogenous lipoprotein (a) size isoforms differ by their interaction with the low density lipoprotein receptor and the low density lipoprotein receptor related protein/ α 2 – macroglobulin receptor FEBS Lett., 1993; 325: 271-5.
70. Scanu AM LP(a) lipoprotein – coping with heterogeneity, New Eng J Med., 2003; 349: 2089-90.