ISSN 1857-9345
UDC: 613.2:616.61-008.64-78-052

ASSESSMENT OF MALNUTRITION INFLAMMATION SCORE IN DIFFERENT STAGES OF CHRONIC KIDNEY DISEASE

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ABSTRACT

Background: Protein-energy wasting (PEW) is common in patients with chronic kidney disease (CKD), and is associated with high morbidity and mortality. Malnutrition-Inflammation Score (MIS) has significant correlations with prospective hospitalization and mortality, as well as measures of anemia, inflammation, and nutrition in dialysis patients.

Material and Methods: The study was conducted on 100 adult patients of CKD selected from K&D clinic PGIMS, Rohtak. All the patients went under detailed socioeconomic, clinical, biochemical and radiological examination. The average of three measurements of body weight, height, triceps skin fold thickness (TST), and mid-arm muscle circumference (MAMC) were measured in all patients. MIS was calculated for all the patients.

Results: Out of total 100 patients, 64 were male and 36 were female. Overall, the prevalence of malnutrition was 60%. A total of 42%, 16% and 2% patients had mild, moderate and severe malnutrition respectively. Our study also shows significant association between staging of CKD (3 to 5-D) and MIS. A significant negative correlation was found between MIS and factors such as BMI, eGFR, serum calcium and hemoglobin levels. A significant positive correlation of this score was found with blood urea serum creatinine, serum uric acid, serum potassium and serum phosphate. Multivariate analysis showed significant association between MIS and serum albumin, TIBC, BMI, family income and hs-CRP.

Conclusion: Assessment of key components of malnutrition and inflammation early in disease course will help to identify high risk subjects in whom modifying these predictors will help in providing active and healthy life for CKD patients.

Keywords: Malnutrition Inflammation Score, chronic kidney disease

INTRODUCTION

Progressive and irreversible loss of renal function over a period of at least months to many years is characteristic feature of Chronic Kidney Disease (CKD). With increased availability of resources and care, the last two decades have seen an increase in longevity; hence the prevalence of CKD is bound to increase. Various epidemiologic studies suggests a prevalence of

CKD of approximately 10% to 14% in the general population in developed countries. [1] In absence of exact data and large population based studies, the exact prevalence is not known, but problem is likely to be much more in developing countries like India. Patients with chronic kidney disease constitute a significant social and economic burden, both in terms of resource utilization and indirectly through loss of productivity and impaired quality of life.

The concept of protein-energy wasting (PEW) was proposed by the International Society of Renal Nutrition and Metabolism (ISRNM) in 2007 and it refers to the multiple nutritional and catabolic alterations that occur in CKD and associated with increased morbidity and mortality. [2] Multiple mechanisms which are inherent to CKD including hormonal derangements, co-morbidities, under nutrition, dialysis procedure, inflammation, and other consequences of uremic toxicity lead to PEW. PEW may cause infection, CVD, frailty and depression. These complications may also further increase the extent of PEW. [3] According to many western and Indian studies there is high prevalence of PEW in patients with CKD and in patients with end stage renal disease (ESRD) on dialysis. [4, 5] Due to use of different diagnostic tools in various studies, the prevalence of malnutrition ranges widely from 20-50% at different stages of CKD. [6]

Several clinical, nutritional, and biochemical parameters have been used to assess the PEW in CKD patients. Since there is still lack of single method to reliably diagnose the nutritional status of CKD patients, various tools with use of objective and/or subjective markers have been recommended. [7] The Subjective Global Assessment (SGA) and the Malnutrition-Inflammation Score (MIS) are commonly used nutritional scoring system for PEW assessment. [2] The Malnutrition-Inflammation Score (MIS) developed by Kalantar-Zadeh is a combination of anthropometric data, biochemical data and SGA. MIS has significant correlations with prospective hospitalization and mortality, as well as measures of anemia, inflammation, and nutrition in dialysis patients. [8]

PEW and inflammation are common and usually concurrent in CKD patients. [6] Higher levels of inflammatory markers are associated with accelerated rate of CKD progression and disease related complications. [9] The nutritional condition of CKD and ESRD patients remains a significant cause for concern despite the better understanding of the pathophysiologic mechanisms of PEW. Whenever the first sign of malnutrition is observed, strategies with multimodal targets like dietary supplements, nutritional counselling and psychosocial interventions should be considered as early diagnosis and treatment can improve the prognosis for CKD patients and reduce economic costs connected with treatment. [10]

The purpose of assessing malnutrition and inflammation is to identify patients at risk for complications and poor clinical outcome because these two are major prognostic determinant factors in patients with CKD and these two conditions often coexist in Indian patients with CKD. There is paucity of data from developing countries like India and most of the available data is from western countries. Hence the present study was done at our tertiary care centre to study the Malnutrition Inflammation Score and its relationship with inflammatory markers associated with chronic kidney disease.

MATERIAL AND METHODS

The study was conducted on 100 adult patients of chronic kidney on regular follow up of Kidney and Dialysis (K & D) clinic at Pt. B.D. Sharma PGIMS, Rohtak, India. After taking written informed consent and a thorough history, each participant went under detailed clinical, biochemical and radiological examination. All the patients were assessed for education level, occupation and family income per month as per revised Kuppuswamy's model. [11] Patients with pre-existing gastrointestinal disease, pregnancy, chronic liver and inflammatory disease, HIV/AIDS, with any malignancy and refusal to cooperate with the study were excluded. The study was approved by ethical committee of Pt. B.D. Sharma University of Health Sciences.

All the included patients were equally divided into four groups: Group A, B, C and D based on CKD staging.

Group A consisted of 25 patients with eGFR between 30-59 ml/min/1.73m^2 (CKD Stage 3).

Group B consisted of 25 patients with eGFR between 15-29 ml/min/1.73m^2 (CKD Stage 4).

Another 50 patients of eGFR < 15 ml/min/1.73m^2 (stage 5) were recruited and divided into two groups on the basis of dialysis:

Group C consisted of 25 patients with of eGFR <15 ml/min/1.73m^2 not on hemodialysis (CKD stage 5).

Group D consisted of 25 patients with of eGFR <15 ml/min/1.73m^2 on hemodialysis (CKD stage 5-D).

Morning blood samples were taken after an overnight fasting for generation of plasma and serum for biochemical parameters analysis. Blood hemoglobin, blood urea, random blood sugar, serum creatinine, uric acid, sodium, potassium, calcium, phosphate, total protein and creatinine were analyzed using certified methods at the department of biochemistry at PGIMS, Rohtak. Creatinine clearance was calculated using MDRD formulae. Serum ferritin, hs-CRP and serum lipoprotein (a) were used to assess the inflammatory state of the patient. High-sensitivity C-reactive protein (hs-CRP) was measured by immuno-turbidimetry assay, albumin was measured by colorimetry assay, total iron binding capacity (TIBC) was measured by automated DTIBC assay, serum lipoprotein[Lp(a)] was measured by enzyme-linked immunosorbent assay and serum ferritin was measured by enzyme immunoassay. Serum ferritin >200 µg/L, hs-CRP >3 mg/L or serum lipoprotein(a) >30 mg/dL was taken as presence of inflammation.

The average of three measurements of body weight, height, triceps skin fold thickness (TST), and mid-arm muscle circumference (MAMC) were measured in all patients. Body mass index (BMI) was calculated in all patients.

Each patient was assessed for nutritional status by using Malnutrition Inflammation Score (MIS). [8, 12] Grading of MIS was done (Table 1) and patients were divided into 4 subgroups on the basis of score for further analysis.

Group 1 consisted of patients with MIS 0-2, indicating normal nutritional status

Group 2 consisted of patients with MIS 3-5, indicating mild malnutrition

Table 1. *Components of the "Malnutrition-Inflammation Score" (MIS)*

MIS Components	Score			
	0	**1**	**2**	**3**
(A) Medical history:				
1. Change in end dialysis dry weight (overall change in the past 3–6 months)	<0.5 Kg	0.5–1.0 Kg	≥1 Kg but <5%	≥ 5%
2. Dietary intake	Good appetite, no deterioration of dietary intake	Sub-optimal solid dietary intake	Moderate overall decrease to full liquid diet	Hypo-caloric liquid to starvation
3. Gastrointestinal symptoms	No symptoms with good appetite	Mild symptoms, poor appetite or nauseated occasionally	Occasional vomiting or moderate GI symptoms	Frequent diarrhea or vomiting or sever anorexia
4. Functional capacity (nutritionally related functional impairment)	Normal to improved functional capacity, feeling fine	Occasional difficulty with baseline ambulation, or feeling tired frequently	Difficulty with otherwise independent activities (e.g. going bathroom)	Bed/chair ridden, or little to no physical activity
5. Co-morbidity *	No comorbidity	Mild comorbidity (excluding MCC**)	Moderate comorbidity (including one MCC*)	Any sever multiple comorbidity (≥2 MCC*)
(B) Physical exam:				
6. Decreased fat stores or loss of subcutaneous fat (below eyes, triceps, biceps, chest)	No change	mild	moderate	sever
7. Signs of muscle wasting (temple, clavicle, scapula, ribs, quadriceps, knee, interosseous)	No change	mild	moderate	sever
(C) Body size				
8. Body mass index (kg/m^2)	≥ 20	18–19.9	16–17.99	<16
(D) Laboratory parameters				
9. Serum albumin (g/L)	≥4	3.5–3.9	3.–3.4	<3.0
10. Serum total iron binding capacity (mg/dL)	≥ 250	200–249	150–199	<150
Total MIS = sum of the above 10 components, ranging from 0 (no malnutrition) to 30 (severely malnourished)				

*In the original MIS dialysis treatment age (vintage) contributes to the comorbid condition scoring: 0 if vintage <1 year, 1 if vintage 1 to 4 years, and at least 2 if vintage >4 years.

**Major co-morbid conditions (MCC) include CHF class III or IV, full blown AIDS, severe coronary artery disease, moderate to severe chronic obstructive pulmonary disease, major neurological sequelae, metastatic malignancy or recent chemotherapy

Group 3 consisted of patients with MIS 6-8, indicating moderate malnutrition

Group 4 consisted of patients with MIS 9-30, indicating severe malnutrition

All the four groups were further analyzed for their correlation with renal function and other specific investigations and results were recorded and analyzed.

Statistical analysis

At the end of the study, the data was expressed as mean±1SD or range. Probability values of <0.05 were considered to be significant in all the analyses. ANOVA test and all other appropriate tests were used to analyze differences in quantitative variables between the groups. The correlations were tested using Pearson correlation coefficient analysis. All statistical calculations were carried out using SPSS 20.0 software.

RESULTS

Out of total 100 patients, 64 were male and 36 were female. Majority of patients (74%) were above 45 years of age and were equally distributed in all groups. The mean age of study population was 53 years, ranging from 25 to 81 years. The most common cause of CKD in all groups was diabetes mellitus (38%) followed by hypertension (24%) and chronic glomerulonephritis (12%). Most of the patients were farmers (29%) as most of the study population was from rural area. In our study majority of patients were educated upto secondary school, 27 patients studied upto higher secondary school and 9 patients were graduate. Most of the patients were from lower and middle family income class. There was no statistically significant difference between all CKD groups regarding age, sex, education, occupation and primary etiology. General characteristics of the studied population are summarized in Table 2. On the basis of MIS, malnutrition was present in 60 patients (60%) with mild, moderate and severe malnutrition present in 42, 16 and 2 patients respectively. It was seen that as the CKD stage advances the number of patients without malnutrition decreased and the severity of malnutrition increased gradually (Table 3). The percentage of patients with malnutrition increased in a step wise fashion as GFR declines.

All the inflammatory markers were mostly elevated in group D patients indicating high prevalence of inflammation in ESRD patients (Table 4). Table 5 shows Pearson correlation coefficients (r) between the patients' MIS and nutritionally relevant parameters. Pearson cor-

Table 2. *Baseline Demographic and Clinical Parameters*

Parameter (Mean±SD)	Group A (n=25)	Group B (n=25)	Group C (n=25)	Group D (n=25)	p value**
Age (years)	54.56±13.81	54.28±12.68	56.92±9.08	45.72±16.91	>0.05
Weight (kg)	66.72±11.41	61.12±9.57	58.68±9.17	58.16±9.86	<0.05
BMI* (kg/m^2)	23.72±3.55	22.4±2.91	22.08±1.93	21.56±2.98	>0.05
SBP*(mmHg)	132.08±18.74	128.32±21.91	142.44±24.99	128±15.69	>0.05
DBP*(mmHg)	83.6±17.11	79.76±11.85	85.64±11.10	78.64±8.48	>0.05
MAP*(mmHg)	99.72±16.56	95.92±14.67	104.6±14.77	95.12±9.88	>0.05
Haemoglobin (g/dL)	11±1.73	10.4±2.23	8.48±1.38	8.28±1.51	<0.001
Blood sugar (mg/dL)	122.44±28.14	120.92±47.08	130.8±38.02	127.8±40.59	>0.05
Blood urea (mg/dL)	83.96±33.61	111.6±36.37	160.68±64.08	232±69.61	<0.001
Serum creatinine (mg/dL)	2.2±0.81	2.92±0.6	6.16±1.81	8.88±2.72	<0.001
Serum uric acid (mg/dL)	5.92±1.75	7.6±2.36	7.64±2.87	8.6±2.76	<0.05
Serum Sodium (mEq/L)	139.56±3.30	139.88±2.96	142.72±5.02	139.2±3.92	<0.05
Serum potassium (mEq/L)	4.4±0.64	4.2±0.5	4.36±0.63	4.12±0.6	>0.05
Serum calcium (mg/dL)	9.28±0.89	9.08±0.95	8.72±0.54	8.68±1.24	>0.05
Serum phosphate (mg/dL)	3.88±1.30	4.64±1.68	6.16±1.37	6.52±2.25	<0.001
eGFR ($ml/min/1.73m^2$)	42.76±8.06	23.04±4.55	10.04±3.43	7.16±2.19	<0.001
Serum protein (g/dL)	6.56±1.08	6.92±0.95	6.68±0.85	6.28±0.73	>0.05
Serum albumin (g/dL)	3.64±0.49	3.76±0.52	3.52±0.51	3.48±0.58	>0.05
Serum ferritin (µg/L)	431.76±308.16	476.16±380.76	390.84±461.34	646.04±442.58	>0.05
TIBC (µg/dL)	285.88±70.54	285.84±87.25	255.08±81.37	270.48±79.29	>0.05
hs-CRP (mg/L)	0.76±0.77	1.4±1.29	2.28±1.30	2.96±1.56	<0.05
Serum lipoprotein(a) (mg/dL)	23.96±11.46	23.12±11.65	27.8±9.57	31.84±13.22	<0.05

*BMI – Body Mass Index, SBP– Systolic Blood Pressure, DBP– Diastolic Blood Pressure, MAP– Mean Arterial Pressure
**Analyzed by ANOVA

Table 3. *Relationship between CKD staging and MIS*

MIS score grading	Group A (n=25)	Group B (n=25)	Group C (n=25)	Group D (n=25)	Total (n=100)
Normal (0-2)	18	12	6	4	40
Mild (3-5)	6	10	14	12	42
Moderate (6-8)	1	3	5	7	16
Severe (9-30)	0	0	0	2	2
P value <0.01					

Table 4. *Prevalence of inflammatory markers in study population*

	Group A (n=25)	Group B (n=25)	Group C (n=25)	Group D (n=25)	Total(n=100)
S ferritin (>200 µg/L)	15	16	11	20	62%
hs-CRP b(>3 mg/L)	0	5	7	10	22%
S lipoprotein (a) (>30 mg/dL)	8	8	11	13	40%

relation coefficients (r) between the malnutrition score and other parameters were highly significant (P<0.01) for income (r=-0.773), weight (r=-0.346), BMI (r=-0.343), Hb (r=-0.383), urea (r=0.364), eGFR (r=-0.471), serum albumin (r=-0.439), TIBC (r=−0.466), hs-CRP (r=0.784) and lipoprotein(a) (r=0.673). The malnutrition score was also significantly correlated (P<0.05) with serum potassium (r=0.253) and calcium (r=-0.204). However, no significant correlation was found between the malnutrition score and gender or other laboratory parameters.

Table 6 describes general patient characteristics according to the severity of MIS. Across increasing scores, patients were more often with low family income, low BMI and also had a lower GFR. Whereas urea, creatinine, phosphorus, hs-CRP and lipoprotein(a) were increased, the levels of hemoglobin, serum protein, albumin and TIBC were incrementally reduced across increasing MIS groups. Additionally, there was a progressive worsening of all indicators of nutritional status analyzed.

Table 5. *Correlation between parameters and Malnutrition Inflammation Score (MIS)*

Parameter	Correlation coefficient	p value*
Age (years)	0.038	>0.05
Sex	-0.151	>0.05
Education level	-0.12	>0.05
Income(RS per month)	-0.773	<0.01
Weight (kg)	-0.346	<0.01
BMI (kg/m^2)	-0.343	<0.01
MAP(mmHg)	-0.143	>0.05
Haemoglobin (g/dL)	-0.383	<0.01
Blood urea (mg/dL)	0.364	<0.01
Blood sugar (mg/dL)	0.155	>0.05
Serum creatinine (mg/dL)	0.345	<0.01
Serum uric acid (mg/dL)	0.410	<0.01
Serum Sodium (mEq/L)	0.077	>0.05
Serum potassium (mEq/L)	0.253	<0.05
Serum calcium (mg/dL)	-0.204	<0.05
Serum phosphate (mg/dL)	0.395	<0.01
eGFR (ml/min/1.73m^2)	-0.471	<0.01
Serum protein(g/dL)	-0.324	<0.01
Serum albumin(g/dL)	-0.439	<0.01
Serum ferritin(µg/L)	-0.106	>0.05
TIBC(µg/dL)	-0.466	<0.01
hs-CRP(mg/L)	0.784	<0.01
Serum lipoprotein(a)(mg/dL)	0.673	<0.01

*Analyzed by Pearson correlation coefficient

Table 6. *Association of baseline parameters and MIS*

Parameter	(Group 1) MIS (0-2) (n=40)	(Group 2) MIS (3-5) (n=42)	(Group 3) MIS (6-8) (n=16)	(Group 4) MIS (9-30) (n=2)	p value**
Age (years)	52.18±14.04	54.26±12.26	52.31±15.98	42±32.52	>0.05
Weight (kg)	64.7±10.79	60.4±9.54	55.06±9.40	55.5±6.36	<0.05
BMI* (kg/m^2)	23.68±3.26	21.93±2.42	21.06±2.54	19.5±0.70	<0.05
MAP*(mmHg)	101.28±12.95	98.33±16.20	95.56±13.42	87±5.65	>0.05
Haemoglobin (g/dL)	10.43±2.11	9.12±1.97	8.63±1.66	8±0	<0.05
Blood urea (mg/dL)	117.73±69.99	154.12±72.72	188.69±78.13	252.5±61.51	<0.05
Blood sugar (mg/dL)	110.95±30.33	128.69±47.55	118.75±41.17	115.5±30.40	>0.05
Serum creatinine (mg/dL)	3.78±2.93	5.81±3.27	5.75±2.56	8.5±2.12	<0.05
Serum uric acid (mg/dL)	6.63±1.87	7.31±2.62	9.69±3.13	8.5±2.12	<0.05
Serum Sodium (mEq/L)	139.93±3.69	140.45±4.31	141.19±4.65	139.5±2.12	>0.05
Serum potassium (mEq/L)	4.38±0.58	4.39±0.52	3.88±0.71	4±0	<0.05
Serum calcium (mg/dL)	9.13±0.96	8.88±0.88	8.63±1.08	9±1.41	>0.05
Serum phosphate (mg/dL)	4.53±1.56	5.64±2.12	6.19±2.10	6.5±0.70	<0.05
eGFR (ml/min/1.73m^2)	29.45±15.99	15.79±11.57	13.94±9.82	5.5±0.70	<0.05
Serum protein (g/dL)	6.88±0.99	6.57±0.83	6.06±0.85	6.5±0.70	<0.05
Serum albumin (g/dL)	3.85±0.42	3.52±0.50	3.19±0.54	3.5±0.70	<0.05
Serum ferritin (µg/L)	484.4±399.42	520.4±436.98	375.25±293.00	691.5±917.11	>0.05
TIBC (µg/dL)	320.75±58.72	257.02±77.04	216.56±70.10	171±56.56	<0.05
hs-CRP (mg/L)	0.73±0.84	1.98±0.92	4±1.21	4.5±0.70	<0.05
Serum lipoprotein(a) (mg/dL)	19±8.78	27.74±9.35	40.69±8.28	46±9.89	<0.05

*BMI – Body Mass Index, MAP– Mean Arterial Pressure
**Analyzed by ANOVA

A multivariate analysis using linear regression was done to find the covariates of MIS score. On preparing a model including only the objective components of MIS score (BMI, Serum Albumin, and TIBC) it was found that the model is statistically significant (p<0.001), had a predictive value of 42% (R2=0.420) and each covariate had a statistically significant effect on the MIS score [Table 7(a)]. This was in concordance with the existing validation of the MIS score which depends on these three key objective parameters. To improve the predictive value of the linear regression model above, additional covariate variables were included based upon the univariate analysis. Three additional covariates– income, eGFR and hs-CRP were added to the model [Table 7(b)]. The predictive value of the model increased to 78.6% (R2=0.786), with income and hs-CRP significantly affecting the MIS score (p<0.001). Overall, this model was also statistically significant (p<0.001).

Table 7 (a). *Predictive value of the linear regression model*

Model		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		Beta			Lower Bound	Upper Bound
1	(Constant)		9.110	.000	14.113	21.976
	BMI	-0.289	-3.674	.000	-0.336	-0.100
	Albumin	-0.305	-3.873	.000	-2.683	-0.865
	TIBC	-0.418	-5.340	.000	-0.016	-0.007

Table (b)

Model		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		Beta			Lower Bound	Upper Bound
2	(Constant)		3.490	0.001	2.477	9.017
	BMI	-0.089	-1.708	0.091	-0.145	0.011
	Albumin	-0.034	-0.635	0.527	-0.821	0.423
	TIBC	-0.012	-0.200	0.842	-0.004	0.003
	Income	-0.339	-5.369	0.000	-0.278	-0.128
	eGFR	-0.036	-0.596	0.552	-0.023	0.013
	hs-CRP	0.570	7.427	0.000	0.666	1.152

DISCUSSION

Chronic kidney disease is an emerging health problem in both developed and developing countries. It is a progressive and life-long condition with multiple co-morbidities of which malnutrition is important health related issue.

PEW is common in patients with CKD especially in those with ESRD and it is associated with high morbidity and mortality. Dietary restrictions and insufficient food intake due to poor appetite leads to malnutrition, but the pathophysiology of PEW cannot be fully explained by these factors alone and many other factors must be present for PEW to develop. Endocrine disorders, chronic inflammation, metabolic acidosis, uremia-induced alterations such as increased energy expenditure that lead to hypermetabolism like state and result in excess muscle and fat catabolism are the other factors which have been shown to play an important role in pathophysiology. In addition, many comorbid conditions which are commonly prevalent in CKD patients also contribute to the development of PEW. [3]

PEW and inflammation are common and usually occur concurrently in maintenance dialysis patients and they are potential candidates for the high rate of hospitalization and mortality in CKD patients, collectively termed as malnutrition inflammation complex syndrome (MICS). [13] Several markers are used for the detection of inflammatory status in patients with CKD. CRP, high sensitivity CRP (hs-CRP), TNF-α, adiponectin, ESR, hepcidine and serum ferritin all are increased in chronic renal failure while serum albumin, LDL and HDL cholesterol levels decreased. [14]

Although there is a lack of a single measure that can reliably assess the nutritional status of CKD patients, the MIS represents an advance over single measures in the assessment of nutritional status. MIS was first used in 2001 as a complete and quantitative tool. It correlated significantly with prospective hospitalizations, morbidity and mortality in MHD patients. [8]

The prevalence of malnutrition was found using the MIS. The prevalence in our study (60%) was found to be slightly higher than reported from the western world (10–54%). [15] A total of 42%, 16% and 2% patients had mild, moderate and severe malnutrition, respectively. Prakash et al. also found a high prevalence of malnutrition (65%) in CKD patients in India. [16] Ebrahimzadehkor et al. reported in their study that 25% of patients on hemodialysis were normal nourished, 54.3% of patients were mild malnourished, 20.8% were moderately malnourished, and no one of them was severe malnourished. [17] These findings can be explained by the facts that in Indian population most of the people have low income status, low level of education with poor approach to a good medical facility leading to negative effect on health status. In our study no difference in MIS score was found on the basis of age <55 year and ≥55 year and gender of the patients. The correlation between MIS and family income was calculated and it was found to be statistically significant ($p<0.001$), indicating higher prevalence of malnutrition in lower income groups. Poverty and under nutrition seems to be very significant factors for malnutrition in India like in other developing nations. High education level results in better nutrition knowledge and higher general socio-economic condition of family, both these factor increase the food purchasing power and improve the nutritional status. However, our study – failed to find any correlation.

Patients with malnutrition had higher level of blood urea and serum creatinine indicating that advanced renal failure leads to higher prevalence of malnutrition in comparison to early stage renal failure. Renal insufficiency is a catabolic and inflammatory state and it is evidenced by the fact that independent of relevant demographic, social, and medical condition, renal insufficiency was strongly associated with malnutrition. In the present study, we observed that eGFR of patients with malnutrition was much lower in comparison to non-malnourished cases ($p<0.001$). eGFR progressively decreased from group 1 to 4. Similarly the MIS impaired progressively and significantly across the groups with the highest scores seen in group D of CKD patients. This confirms that as CKD stage advances the nutrition of patients gets worse. Our study also shows significant association between staging of CKD (3 to 5-D) and MIS ($p<0.01$). Our findings were consistent with other studies which have shown significant association between CKD stages (3 to 5) and MIS ($p<0.001$). [18] Garg et al. reported that one third of individuals with malnutrition had GFR <60 mL/ min/1.73m^2 and in a multivariate analysis, after adjustment for relevant demographic, social, and medical conditions, low GFR was independently associated with malnu-

trition suggesting that decreased renal functions are an important independent risk factor for malnutrition. [19]

This study showed low BMI in the malnourished groups of patients in comparison to the non-malnourished group and this difference was statistically significant ($p<0.05$). Serum total protein and albumin levels in patients with CKD were also significantly ($p<0.05$) lower in the malnourished groups of patients in comparison to the non-malnourished group. Prakash et al. also reported that serum total protein and albumin were higher in the non-malnourished CRF patients in comparison to malnourished patients (5.74 ± 0.38 mg/dL vs. 5.50 ± 0.40 mg/dL, $p<0.05$; 3.68 ± 0.55 mg/dL vs. 3.18 ± 0.58 mg/dL, $p<0.05$). [16] Serum albumin level is an indicator of visceral protein stores and low level of albumin is suggestive of malnutrition or inflammation. It is a strong predictor of mortality in hemodialysis patients. [10]

The correlation of MIS with various other parameters was calculated using Pearson correlation to determine the significance and strength of associations. A significant negative correlation was found between malnutrition inflammation score and factors such as BMI ($r=-0.343$, $p<0.01$), eGFR ($r=-0.471$, $p<0.01$), serum calcium ($r=-0.204$, $p<0.05$) and hemoglobin levels ($r=-0.383$, $p<0.01$). It indicates that patients with low BMI, low eGFR and decreased hemoglobin tend to have high score and worse nutritional status. This means that patient's health perception is not only related to the renal function, but also to other conditions like anemia and bone mineral disorder which are commonly found in patients of CKD. A significant positive correlation of this score was found with blood urea serum creatinine, serum uric acid, serum potassium and serum phosphate. This correlation suggested that high levels of blood urea, creatinine, uric acid and phosphate were associated with poor nutritional status. By screening for these parameters already from an early stage, the possibility for treatment and secondary prevention may increase and contribute to improved well-being and function. Even by multivariate analysis significant association was found between MIS and serum albumin, TIBC, BMI, family income and hs-CRP. By adding income and hs-CRP, predictive value increased significantly. The findings suggested that along with MIS, family income and inflammatory markers like hs-CRP, added more value for early diagnosis and screening of these patients. Similar results were also found by Ho et al. and Kalantar-Zadeh et al. [8, 20]

Multiple factors affect the prevalence of inflammation such as geographies, genetic differences, residual renal function, co-morbidities, dialysis therapy and various markers used in diagnosis of inflammation. The prevalence of inflammation varies from 30–75% in CKD patients. Variety of factors like oxidative stress, decreased clearance of cytokines, infectious complications and dialysis-related factors leads to persistence of low grade inflammation in CKD patients. [21] In general, iron deficiency anemia is associated with low serum ferritin levels. Serum ferritin which is used as a marker of iron status is also an inflammatory marker. As already described that prevalence of inflammation is high in CKD. Hence, it is quite possible that high levels of serum ferritin are procreated by inflammation independently of iron stores and the higher ferritin level in the patients with severe MIS may suggest more severe inflammatory status instead of better iron store. Kalantar-Zadeh et al. observed that both high serum ferritin and low serum albumin were significant markers of dialysis mortality. [22] In this study serum ferritin levels were higher in the malnourished CKD patients in comparison to non-malnourished patients but difference was not statistically significant. In CKD patients, hyperferritinemia and refractory anemia including EPO hyporesponsiveness is associated with MICS which also leads to poor clinical outcome including a high rate of mortality and hospitalization and diminished quality of life. [23]

The mean value of serum hs-CRP and lipoprotein(a) showed an increasing trend from group 1 to 4 and this was statistically significant ($p<0.05$). Patients with higher levels of hs-CRP and lipoprotein(a) had high MIS. There was a strong positive correlation between hs-CRP, serum lipoprotein(a) and MIS with values of correlation coefficient, $r=0.784$ ($p<0.01$) and 0.673 ($p<0.01$) respectively for hs-CRP and lipoprotein(a). Haemodialysis patients are at greater risk of cardiovascular disease. Dyslipidaemia as well as inflammation have been associated with higher cardiovascular morbidity and mortality in these patients. High Lp(a) in blood is a risk factor for coronary heart disease (CHD), cardiovascular disease (CVD), atherosclerosis, thrombosis, and stroke. [24] Higher troponin levels were

associated with higher mortality in hemodialysis patients with history of coronary artery disease as compared to those without coronary disease. While in patients without history of CAD, hs-CRP >3mg/L was associated with significantly higher mortality. [25]

The presences of higher levels of inflammatory markers were consistent with the observations done by Prakash et al. They noticed that inflammatory markers serum ferritin and C-reactive protein were elevated significantly in patients with malnutrition in comparison to those without malnutrition (301.2 ± 127.1 mg/dL vs. 212.7 ± 124.9 mg/dL, $p<0.05$; 63% vs. 33%, $p<0.05$). [16]

Considering the worldwide growing prevalence of CKD and increasing importance of malnutrition and inflammation in chronic diseases, improving our knowledge about it and its predictors in CKD patients is important. The deterioration of nutrition and presence of inflammation in CKD is a complex multi-factorial problem which commences early and progresses with the stage of disease. The term protein-energy wasting (PEW) attempts to unite many nutritional and catabolic disorders that occur in CKD and lead to a gradual and progressive loss of both muscle and fat mass. It is a common syndrome particularly from stage 4-5 CKD and is present in 30%-60% of dialysis patients. The MIS is a non-expensive and easy tool for identification of PEW and inflammation in CKD patients. MIS has shown correlation with inflammation, nutritional status, quality of life and mortality. The clinical consequences of PEW may be severe and require rapid and effective treatment. K/DOQI has also published clinical practice guidelines for nutrition in chronic kidney disease. It is important to search actively for malnutrition since early diagnosis and evaluation of nutritional status can improve the prognosis of CKD patients and reduces the monetary costs of treatment. The "management" of malnutrition and inflammation is complicated, as is the "management" of chronic illness. Because of the interaction of these two components, solutions will need to be integrated. It is therefore time to develop and test the clinical and cost-effectiveness of integrated disease management systems for these conditions in CKD.

Limitation of study

The present study was associated with certain limitations. One of the limitations of this study was that it was a cross-sectional study and no follow up was done. No dietary intervention was done in this study. We did not compare the nutritional status of CKD patients according to the etiology of kidney failure, including diabetes and other causes and other markers of inflammation such as CRP, IL-1β, IL-6 or TNF-α were also not measured in this study. In minority of patients adequacy of dialysis could not be maintained due to unwillingness of patients and technical errors. A longitudinal study can assess the association between nutritional markers and long-term outcomes in Indian CKD patients which could influence the dietary policies of CKD patient management.

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Резиме

ПРОЦЕНКА НА ВРЕДНОСТА НА ВОСПАЛЕНИЕТО ПРИ НЕИСХРАНЕТОСТ ВО РАЗЛИЧНИ ФАЗИ НА ХРОНИЧНАТА БУБРЕЖНА БОЛЕСТ

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Историја: Губењето на енергија од протеини (PEW) е често кај пациентите со хронична бубрежна болест (CKD) и е поврзано со висок морбидитет и морталитет. Вредноста на воспалението при неисхранетост (MIS) има значајни корелации со потенцијалната хоспитализација и морталитет, како и мерките за анемија, воспаление и исхрана кај пациентите на дијализа.

Материјал и методи: Студијата беше спроведена на 100 возрасни пациенти со CKD избрани од Клиниката К и Д ПГИМС, Рохтак. Сите пациенти беа под детален социоекономски, клинички, биохемиски и радиолошки преглед. Кај сите пациенти беа измерени просеците од три мерења на телесната тежина, висината, трицепсната дебелина на кожата (TST) и обемот на мускулите во средината на рацете (MAMC). Беше пресметан MIS за сите пациенти.

Резултати: Од вкупно 100 пациенти, 64 беа мажи, а 36 жени. Генерално, преваленцата на неисхранетост изнесуваше 60 %. Вкупно 42 %, 16 % и 2 % пациенти имаа лесна, умерена и тешка неисхранетост, соодветно. Нашата студија, исто така, покажува значајна поврзаност меѓу поставеноста на ХББ (3 до 5-Д) и MIS. Значителна негативна корелација беше пронајдена меѓу MIS и факторите како BMI, eGFR, серумскиот калциум и нивоата на хемоглобин. Значајна позитивна корелација на оваа вредност беше пронајдена кај крвниот уреа-серумски креатинин, серумска уринска киселина, серумскиот калиум и серумски фосфат. Мултиваријантната анализа покажа значајна поврзаност меѓу MIS и серумскиот албумин, TIBC, BMI, семејниот приход и hs-CRP.

Заклучок: Проценката на клучните компоненти на неисхранетост и воспалението на почетокот на болеста ќе помогне да се идентификуваат високоризичните субјекти кај кои модификацијата на овие предиктори ќе помогне во обезбедувањето активен и здрав живот кај пациентите со ХББ.

Клучни зборови: вредност на воспалението при неисхранетост, хронична бубрежна болест