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# MALNUTRITION INFLAMMATION COMPLEX SYNDROME IN MAINTENANCE HAEMODIALYSIS PATIENTS

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A b s t r a c t: Malnutrition inflammation complex syndrome (MICS) occurs in maintenance haemodialysis (MHD) patients and is a strong predictor of morbidity and mortality in these patients. The aim of our study was to evaluate the influence of inflammation on the biochemical and anthropometrical parameters of the nutritional status in MHD patients.

Our study was made on 154 patients (93 men and 61 women, mean age = 54.7 yrs. and mean time on dialysis 84 months) over a period of 6 months. The indicator of inflammation, C-reactive protein (CRP), was measured monthly at the central laboratory by nephelometry. The assessment tools used to evaluate the influence of inflammation on the nutritional status in MHD patients were: serum albumin and cholesterol level, midarm circumference (MAC), midarm muscle circumference (MAMC), triceps skin fold thickness (TSF) and body mass index (BMI). Student's t-test was used for group mean comparison between men and women. Person's correlation r was used to determine the significance and the strength of associations.

The CRP level was significantly greater in men than in women (12.9 vs. 7.97, $p < 0.04$). The CRP level showed a strong correlation only with the serum concentration of cholesterol ($r = 0.49$, $p < 0.000$), and did not correlate with the serum albumin of the MHD patients. There was no correlation between the CRP level and the anthropometrical parameters of the MHD patients in our study.

Two separate processes, inflammation and reduced protein intake, each separately contributed to causing a decrease in serum albumin concentration and anthropometrical measurements. The levels of acute phase proteins vary widely as opposed to

the serum albumin level; for that reason, changes in the albumin catabolic rate or synthesis require a considerable time to become visible. The average value of the protein catabolic rate of the patients in our study was 1.01 g/kg/d, a value that showed adequate protein intake. These findings would suggest that clinical attention to the maintenance of adequate nutrition could blunt the effects of inflammation on both somatic and visceral protein stores.

**Key words:** malnutrition, inflammation, nutritional status, maintenance haemodialysis patients.

## *Introduction*

Malnutrition and inflammation are common occurrences in maintenance haemodialysis (MHD) patients and they are strong predictors of morbidity and mortality in these patients. These observations, made by different researchers, have led to the coinage of the term malnutrition inflammation complex syndrome (MICS) [1, 2]. The apparent causes of MICS are anorexia, muscle wasting, hypoalbuminemia, refractory anaemia and, possibly, accelerated atherosclerosis [3, 4]. Malnutrition is caused by inadequate dietary intake, gastrointestinal disturbances, psychosocial and socioeconomic factors or increased nutritional requirements due to concomitant diseases, namely cardiovascular disease and sepsis [5]. Indicators of malnutrition in MHD patients include decreased dietary protein and energy intake, reduced serum albumin and cholesterol, decreased body mass index, reduced midarm muscle mass and skin fold thickness [6]. There is evidence that inflammation is much more common in dialysis patients than in the general population. A common underlying mechanism can be an elevated level of inflammatory markers (positive acute phase proteins, including C-reactive protein) that is associated with reduced renal function, oxidative stress, or other proinflammatory conditions in dialysis patients such as frequent contact with dialysis membranes, vascular accesses or dialysis fluid [7, 8]. Inflammation causes decreased albumin gene expression, resulting in a decreased albumin synthetic rate with a consequence of reduced albumin concentration [9]. Hypoalbuminemia is a potent risk factor for mortality and morbidity in MHD patients and in other populations [10]. Inflammation also has an important role in mediating loss of muscle mass through ubiquitin-mediated proteolysis of muscle mass. Although inadequate nutritional intake can result in a decrease of the serum albumin level and muscle protein wasting, malnutrition alone has very little effect on the nutritional status of MHD patients. It is the combination of both malnutrition and inflammation that effect the greatest change [9].

The aim of our study was to evaluate the influence of inflammation on the biochemical and anthropometrical parameters of the nutritional status in maintenance haemodialysis patients.

## *Patients and methods*

The study was made on 154 patients on the maintenance haemodialysis programme at the Department of Nephrology, Clinical Centre, Skopje, over a period of 6 months. Data on sex, age, vintage (duration of dialysis therapy), dialysis membrane, protein catabolic rate (PCR), vascular access and primary renal disease were recorded and presented in Table 1.

Table 1 – Табела 1

*Patients' characteristics for sex, age, vintage, dialysis membrane, protein catabolic rate (PCR), vascular access, and primary renal disease*

*Податоци за пол, возраст, дијализен стаж, мембрана за дијализа, интензитет на катаболизамот на протеини (PCR), васкуларен пристап и основна бубрежна болест кај испитуваните пациенти*

| **Number of patients (pts)** | **154** | **Primary renal disease** | **pts** |
|---|---|---|---|
| female vs. male | 61 vs. 93 | | |
| age (years) | 54.7 ± 12.8 | glomerulopaties | 27 |
| vintage (months) | 84 (7 do 288) | renal ischemic disease | 23 |
| hours on HD (weekly) | 12 | diabetic nephropathy | 21 |
| membrane | polysulfone | polycystic kidney disease | 14 |
| PCR (g/kg/d) | 1.01 ± 0.17 | pyelonephritis | 16 |
| | | obstructive nephropathy | 7 |
| **vascular access** | **pts** | nephropathy in systemic diseases | 7 |
| A-V fistula | 146 | nephrolithiasis | 5 |
| A-V graft | 1 | hypoplasio renis | 2 |
| central venous cathetre | 7 | unknown | 32 |

The assessment tools used to evaluate the influence of inflammation on nutritional status in MHD patients were: serum albumin and cholesterol level, midarm circumference (MAC), midarm muscle circumference (MAMC), triceps skin fold thickness (TSF) and body mass index (BMI).

The indicator of inflammation, C-reactive protein (CRP), was measured monthly by nephelometry, at the Institute of Clinical Biochemistry, Clinical Centre, Skopje. The lower limit of detection by the assay was 6 mg/l [13]. Predialysis serum albumin (ref. value 35–50 g/l) and cholesterol (ref. value till 5.5 mmol/l) concentrations were determined monthly by nephelometry, at the same Institute [14]. Anthropometrical measurements were performed immediately after the termination of a haemodialysis treatment, twice during the study. Body mass index (kilograms per square metre) was calculated from the patients' height obtained at study entry and post dialysis weight. Triceps skin fold thickness was measured using a conventional skin fold caliper, described elsewhere [12]. Midarm circumference was measured with a plastic tape. All anthropometrical measurements were performed three times on the non-access-containing arm of each patient, and the three measurements were averaged to give the final result. Midarm muscle circumference was calculated from the formula:

$$MAMC = MAC - (3.14 \times TSF) \quad (12)$$

Student's t-test was used for a group mean comparison between men and women. Person's correlation r was used to determine the significance and the strength of associations.

## *Results*

Table 2 shows clinical data, CRP, laboratory values of serum albumin and cholesterol, and anthropometrical measurements of all 154 MHD patients and a comparison between men and women. Sixty-one patients were women. The mean age of all patients was 54.7 ± 12.8 years and vintage (duration of dialysis therapy) from 7 to 288 months. Dry body weight (63.4 ± 12.9 kg) was the average oedema-free weight immediately at the end of a haemodialysis session.

Table 2– Табела 2

*Clinical, laboratory and anthropometrical data of all 154 MHD patients and a comparison between men and women*

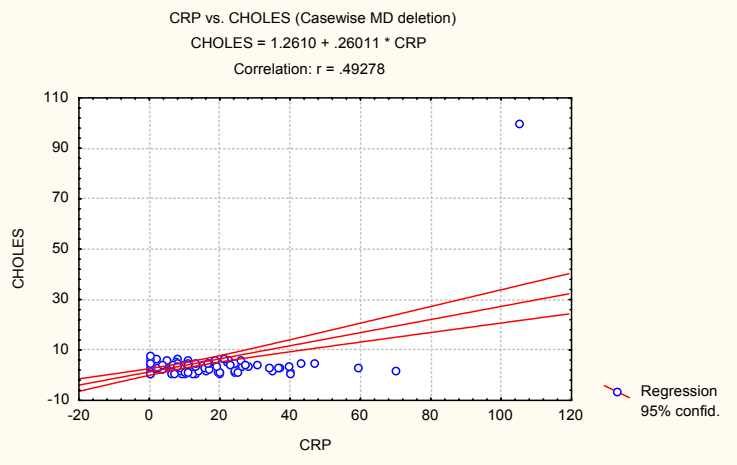
*Приказ на резултатите од клиничките, лабораториските и антропометриските иследувања кај сите 154 испитаници, како и споредба помеѓу мажите и жените*

| | all pts | men | women | p< |
|---|---|---|---|---|
| No. of pts | 154 | 93 | 61 | |
| age (yr) | 54.7 ± 12.8 | 54.5 ± 12.3 | 55.4 ± 13.2 | NS |

| | | | | |
|---|---|---|---|---|
| vintage (months) | 83.8 ± 68.2 | 79 ± 66.3 | 89.6 ± 70.7 | NS |
| dry weight (kg) | 63.4 ± 12.9 | 66.7 ± 10.8 | 58.7 ± 12.5 | 0.00004 |
| CRP (mg/l) | 10.8 ± 14.8 | 12.9 ± 16.9 | 7.97 ± 10.9 | 0.04 |
| albumin (g/l) | 39.6 ± 3.9 | 40.2 ± 4.0 | 38.8 ± 3.7 | 0.02 |
| cholesterol (mmol/L) | 3.5 ± 1.5 | 3.7 ± 1.4 | 3.2 ± 1.5 | NS |
| TSF (cm) | 1.1 ± 0.5 | 0.96 ± 0.3 | 1.37 ± 0.6 | 0.000001 |
| MAC (cm) | 26.7 ± 3.6 | 26.3 ± 2.7 | 27.3 ± 4.4 | NS |
| MAMC (cm) | 23.2 ± 2.8 | 23.27 ± 3.1 | 23.03 ± 3.5 | NS |
| BMI (kg/m2) | 23.4 ± 3.9 | 23.03 ± 3.2 | 23.7 ± 4.7 | NS |

The CRP level was significantly greater in men than in women (12.9 vs. 7.97, $p < 0.04$). The serum concentration of albumin was significantly greater in men than in women (40.2 vs. 38.8, $p < 0.02$). The serum cholesterol level was greater in men than in women, but not significantly so. Triceps skin fold measurements were statistically greater in women than in men (1.37 vs. 0.96, $p < 0.000001$). Midarm circumference and body mass index were greater in women, whereas midarm muscle circumference was greater in men, but not statistically.

Figura 1 – Графикон 1




*Correlations between CRP levels and serum concentration of cholesterol (scatter diagram)*

*Корелација помеѓу вредностите на ЦРП и серумската концентрација на холестеролот (прикажана во вид на дијаграм)*

The CRP level showed a strong correlation with the serum concentration of cholesterol ($r = 0.49$, $p < 0.000$), and did not correlate with the serum albumin of the MHD patients. There was no correlation between the CRP level and anthropometrical parameters (TSF, MAC, MAMC, BMI) of the MHD patients in our study.

## *Discussion*

Malnutrition and inflammation complex syndrome are associated with poorer clinical conditions and worse outcomes in the MHD patients, but nevertheless, there is no uniform method of assessing the nutritional and inflammatory status of dialysis patients. We used serum albumin level as a laboratory predictor of visceral protein mass, serum cholesterol level, TSF and BMI as parameters of body fat, and MAMC as a parameter of somatic protein mass.

Kaysen G.A. *et al* (2003) showed an association between the CRP levels and reduced albumin levels in MHD patients in the HEMO study, multicentre randomized clinical trial [9]. In the study of Kalantar Zadeh K. *et al* (2001), CRP levels correlated strongly with the serum albumin levels and the anthropometrical measurements (11). Despite the results from these studies, in our study, there was only a strong correlation between the CRP levels and the predialysis serum cholesterol levels and no strong correlation between CRP levels on the one hand and serum albumin and anthropometrical parameters on the other hand. The same authors (Kaysen G. A. *et al*) recently established that inflammation in haemodialysis patients is a dynamic process. The levels of acute phase proteins vary widely, while serum albumin concentration varies on a far smaller scale. For that reason, changes in the albumin fractional catabolic rate or in the rate of albumin synthesis require a considerable time to become visible [9, 10, 15]. The greater range of CRP values may make it a more sensitive clinical indicator of morbidity than is albumin [10]. Two separate processes, inflammation and reduced protein intake, each separately contribute to causing a decrease in the serum albumin concentration. The average value of the protein catabolic rate (PCR) of the patients in our study was 1.01 g/kg/d, a value that showed an adequate protein intake. These findings would suggest that clinical attention to maintenance of adequate nutrition could blunt the effects of inflammation on both somatic and visceral protein stores.

## *Conclusion*

The purpose of assessing malnutrition and inflammation, the two major indicators of poor outcome in dialysis patients, was to identify patients at risk of complications and a poor outcome. Dialysis Outcome Quality Initiative guide-

lines recommended regular and uniform assessments of nutrition for all dialysis patients. We have to use biochemical and anthropometrical parameters for assessment of the nutritional status of all dialysis patients. Also we have to measure the CRP value regularly in all dialysis patients, because it is an indicator of inflammation and, by increasing protein and calorie intake, it might be possible to modulate the effects of inflammation. It is likely that increased attention to a global measure of nutritional and inflammatory could improve patient outcome.

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Резиме

## МАЛНУТРИЦИЈА ИНФЛАМАЦИЈА КОМПЛЕКС СИНДРОМ КАЈ ПАЦИЕНТИ НА ХРОНИЧНА ХЕМОДИЈАЛИЗНА ПРОГРАМА

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Малнутрицијa инфламација комплекс синдромот (MICS) кој е присутен кај пациентите на хронична хемодијализна (ХХД) програма е асоциран со морбидитетот и морталитетот кај овие пациенти. Целта на нашето истражување беше да се испита влијанието на инфламацијата врз биохемиските и антропометриските параметри на нутритивниот статус кај пациентите на ХХД програма.

Во студијата беа вклучени 154 пациенти (93 мажи и 61 жена, со средна возраст 54.7 год. и средно време на дијализа од 84 месеци). Ц реактивниот протеин (ЦРП), како индикатор за инфламација, беше одредуван еднаш месечно во текот на 6 месеци. Влијанието на инфламацијата се испитуваше на следните параметри на нутритивниот статус на пациентите на ХХД програма: предијализна серумска концентрација на албумин и холестерол, обем на надлакотница (МАС), мускулен обем на надлакотница (МАМС), дебелина на трицепсна кожна дипла (TSF) и индекс на телесна маса (BMI). Серумската концентрација на албумините и холестеролот се одредуваше еднаш месечно, а антропометриските параметри беа измерени по дијалиниот третман, два пати во текот на 6 месеци.

Резултатите покажаа дека средната вредност на ЦРП е сигнификантно статистички поголема кај мажите во споредба со жените (12.9 vs. 7.97, $p < 0.04$). ЦРП покажа силна корелација со серумската концентрација на холестеролот ($p = 0.49$, $p < 0.000$), но не и со албумините кај испитуваните па-

циенти. ЦРП не корелираше со измерените вредности на антропометриските параметри на пациентите во студијата.

Два различни процеси, инфламацијата и неадекватната протеинска исхрана, засебно придонесуваат до намалување на серумскиот албумин и антропометриските параметри. Создавањето на протеините на акутната фаза (ЦРП) е динамичен процес, за разлика од катаболизмот и анаболизмот на албуминте, заради што е потребно време да се манифестира хипоалбуминемијата. Средната вредност на интензитетот на катаболизмот на протеините кај испитуваните пациенти беше 1.01 г/кг/д, што покажува адекватен протеински внес од нивна страна. Овие согледувања сугерираат дека со адекватна протеинска исхрана може да се неутрализира дејството на инфламацијата врз висцералните и соматските протеини.

**Клучни зборови:** малнутриција, инфламација, нутритивен статус, хронична хемодијализна програма.

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