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CORRELATION BETWEEN ATTITUDES AND EATING HABITS AND SERUM LEVEL OF PHOSHPATES IN HEMODIALYSIS PATIENTS

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Nutritional problems in hemodialysis (HD) patients are frequently associated with poor control of serum phosphorus what may lead to chronic kidney disease-metabolic bone disease. Hyperphosphatemia is an important risk factor for extraskeletal and vascular calcifications and is associated with cardiovascular morbidity and mortality. Increased ingestion of phosphorus is an important factor in development of hyperphosphatemia.

We investigated nutritional habits and attitudes of HD patients and determined their correlation with serum phosphate levels in 57 patients treated in Clinical centre Montenegro. Twenty-two patients were male (38.6%), with average age 57 (range, 30-73 years). Statistically significant correlation was found between red meat or milk ingestion and serum phosphate, as well as between educational level and serum phosphate. In our population, socioeconomic level was directly correlated with serum phosphate. Conclusion: a serum phosphate level is determined by socioeconomic level, ingestion of red meat and milk, and depends on educational level in HD population of the capital of Montenegro.

Key words: end-stage renal disease; hemodialyisis; hyperphosphatemia; nutritional status

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INTRODUCTION

Hyperphosphatemia is an significant and common disorder in patients with chronic kidney disease and occurs as a result of reduced renal elimination of phosphates and disordered bone remodeling, with simultaneous continuous intestinal absorption of phosphate and it is often associated with poor clinical outcome[(1)]. Hormonal regulation of serum phosphate includes activation of 1.25 dihydroxy vitamin D(1,25(OH)^2 vitamin D), fibroblast growth factor 23 (FGF-23), with the cofactor Klotho, and parathyroid hormone (PTH)[(2)]. The system of FGF-23 Klotho has a significant role in the regulation of homeostasis of phosphate. Klotho is a co-receptor for phosphatiuric hormone FGF-23. FGF-23 is secreted by osteocytes and osteoblasts in response to increased oral intake of phosphate and increased serum levels of 1,25 (OH)^{2}D3. Phosphate retention is a critical moment in the pathophysiology of chronic kidney disease (CKD). Hyperphosphatemia occurs early in the third stage of CKD, and it's evidenced by increased serum FGF-23, which precedes the increased concentration of PTH and serum phosphate concentration[(3)].

There is correlation between hyperphosphatemia and increased risk of CKD and mortality in the general population, and an increased risk of mortality in patients with CKD who are undergoing chronic intermittent hemodialysis. Hyperphosphatemia is an independent risk factor for increased mortality in patients with CKD, whether

they are on chronic dialysis programme or not[4]. The high rate of mortality in patients with CKD is associated with cardiovascular disorders (CVD), which are responsible for over 50% of deaths among patients in the terminal stage of CKD. Sudden cardiac death, heart failure, ischemic heart disease and peripheral artery disease are the primary cause of cardiovascular mortality in those patients[5]. Those cardiovascular diseases are directly associated with vascular calcifications, which are pathological disorder that occurs as a result of hyperphosphatemia. The main characteristic of vascular calcification is the deposition of calcium phosphate in the form of hydroxyapatite in arteries, myocardium and heart valves. Calcification of blood vessels is an active process regulated by inhibitors and promoters of calcification[6]. Hyperphosphatemia leads to worsening of CKD-MBD (bone mineral disorder in chronic kidney disease). Continuous stimulation of the parathyroid glands with increased concentrations of extracellular phosphate, especially when it is associated with a reduced extracellular concentrations of ionized calcium and significantly reduced serum concentrations of calcitriol leads to increased production of PTH. As a result of all this pathophysiologycal mechanisms polyclonal diffuse hyperplasia of parathyroid glands accompanied by monoclonal nodular hyperplasia is common in those patients. Severe form of secondary hyperparathyroidism may exacerbate hyperphosphatemia by turning out phosphorus from the bones. In some cases, the PTH-induced bone changes can progress to Brown's tumors, which are a product of the rapid destruction of bone reabsorption, with the bleeding and replacement of the normal bone tissue, with granulation tissue[7]. Increased serum phosphate level is also associated with endothelial dysfunction and elevated FGF-23, what contribute to left ventricular hypertrophy as an independent risk factor for mortality in CKD[8].

Phosphate intake from food is an important factor which contributes to the development of hyperphosphatemia, but its bioavailability depends on various factors such as the origin of food (animal or plant) and the types of food (organic or inorganic phosphates). The organic phosphates are generally found in food rich in proteins, including animal and vegetarian sources of proteins and dairy products[9]. Inorganic phosphates are used as feed additives in the form of additives that improve the color and flavor of food, and their bioavailability is almost 100%[10]. The organic phosphates from dairy products, meat, poultry and fish can become easily available as inorganic phosphates after a many hydrolytic processes what is reason why diet rich in animal protein associated with the development of hyperphosphatemia in patients with CKD. On the other hand phosphates plant origins are in the form of phytic acid or phytate and because there is no human form of the enzyme phytase bioavailability of this source of phosphate is low (20-40%)[11]. Group of foods that are rich in phosphates include: red meat, milk and dairy products (cheese, goat's milk, sheep's milk), grains (wheat germ, bran, soybean meal, rice), soups made with additives that are rich in phosphate, mushrooms, fish, mainly sea fish, a moderate proportion of phosphate containing chocolate, ice cream, carbonated beverages, pasta, snacks[12].

Man with weight 70 kg contains 700 g of phosphorus , of which 85% goes to the bones and teeth , 14% of the soft tissues, and 1% in the blood and extracellular fluids. 40-80% of phosphate entered by nutrition will be absorbed in the digestive tract. During hemodialysis, can be removed and 600 mg of phosphorus. According to the recommendations of the European Renal Best Practice (ERBP) daily protein intake must be at 1.1 g/kg "dry" weight[13].

Modern therapeutic approaches in controlling of hyperphosphatemia in patients who are on chronic hemodialysis programme include multiple modalities: 1. Regulation of phosphate intake through nutrition, which involves reducing intake of foods rich in phosphates. This type of regulation of phosphate homeostasis in recent times is in the focus of interests[14], 2. More intensive dialysis processes, which require longer and more frequent dialysis improves phosphate homeostasis[15], 3. Usage a phosphate binder can also contribute to the regulation of serum phosphate concentration. Studies have shown that the usage of a phosphate binders is associated with a substantial reduction in the risk of mortality in the multivariate analyzes[16]. The benefits are related to the basic values of serum phosphate and lowering the concentration of FGF-23 which has been increased up to 100 times in patients with untreated form of hyperphosphatemia, who are undergoing hemodialysis programme[17]. Applicable KDIGO (Kidney disease-Improving Global Outcome) guidelines recommend the use of phosphate binder for the treatment of hyperphosphatemia of III-V stages of CKD[18].

However, a reduced intake of protein foods rich in phosphates may disturb the nutritional status by type PEW (protein-energy malnutrition) which represents a significant risk factor for increased mortality in these patients. PEW is the "short term killer" in those patients[19]. Inflammation and oxidative stress are important factors that lead to protein-energy malnutrition, which consecutively leads to increased mortality of these patients[20].

Nephrologists have a key role, who in team with a nutritionist and medical technicians should participate in the education of patients with CKD treated with hemodialysis about the types of foods that can be consumed, eating habits in order to achieve an adequate intake of foods rich in phosphates and consecutive better regulation of serum phosphate levels[21].

AIM

The aim of this study was to investigate attitudes and eating habits of patients who has been treated by the hemodialysis and to determine the correlation between attitudes and habits of patients on chronic hemodialysis, and serum phosphorus in those patients.

PATIENTS AND METHODS

The survey was conducted in March 2015. It was conducted among the patients at the Center for hemodialysis, Clinic for Urology and nephrology, Clinical Center of Montenegro. The study incuded patients who are on chronic hemodialysis programme, two to three times a week, lasting 4 hours or 4.5h. The subjects were informed about the objectives of the research, after which they voluntarily agreed to participate. The sample included 57 patients who were at the time of the survey the chronic hemodialysis program at the Center for Hemodialysis, Clinical Center of Montenegro. Eight patients (12.30%) were refused participation in the study. The rate of inclusion of the patients was 87.69%.

The survey instrument was a questionnaire. The questionnaire consists of 31 questions. It contains basic socio-demographic information about patients, data on nutritional habits, attitudes and knowledge about nutrition, information on physical activity and other habits. The survey was anonymous and there were no issues that would be used for identification purposes. The response rate to the questions amounted to 99.79%.

Also, in this study we used the laboratory data on serum levels of phosphorus, which is under regular control laboratory findings do several times a month. Laboratory analyzes are conducted at the Center for Clinical Laboratory Diagnostics, Clinical Center of Montenegro.

The data were processed in the software program SPSS (Statistical Package for Social Science) version 20.

RESULTS

The study included 57 patients undergoing chronic intermittent hemodialysis in Center for haemodialysis , Clinical Center of Montenegro. The parameters of reasarch are presented in Table 1 (age and serum phosphorus (PO_4)), while the distribution of values in relation to the categories is presented in Table 2 (gender, level of education and informing patients about the specifics of diet on hemodialysis. Also , the distribution of serum phosphate (PO_4) is listed in Table 2 and causes of terminal stage of CKD in those group of patients (Fig. 1).

Table 1.

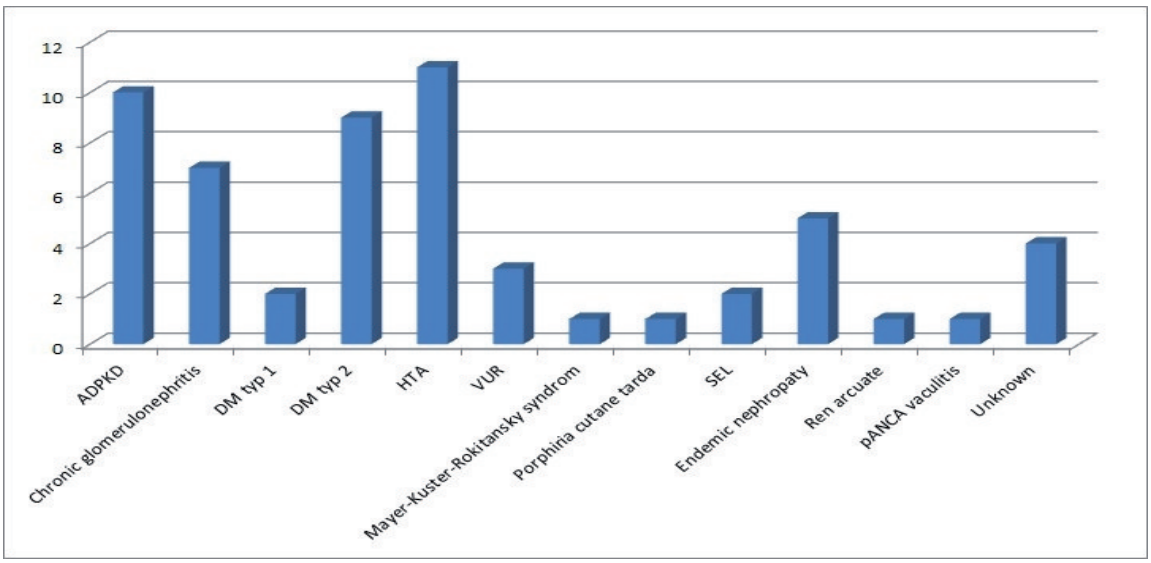
Parameter	**Mean** (std.dev.) minimum - maximum
Age	**57.07** (9.71) 30 - 73
PO_4	**2.18** (0.61) 1.22 - 3.77

Table 2.

Parameter	Category	Number of patients (%)
Gender	Male	21 (37.50%)
	Female	35 (62.50%)
Level of education	Elementary school	13 (23.64%)
	Secondary school	31 (56.36%)
	Higher education	4 (7.27%)
	Faculty	7 (12.73%)
Awareness about special food treatments	Yes	34 (59.65%)
	No	1 (1.75%)
	Partially	22 (38.59%)
Serum level of phosphate (PO_4)	Normal	11 (19.29%)
	Cat1	23 (40.35%)
	Cat2	20 (35.09%)
	Cat3	3 (5.26%)

Figure 1.

Causes of terminal stage of CKD

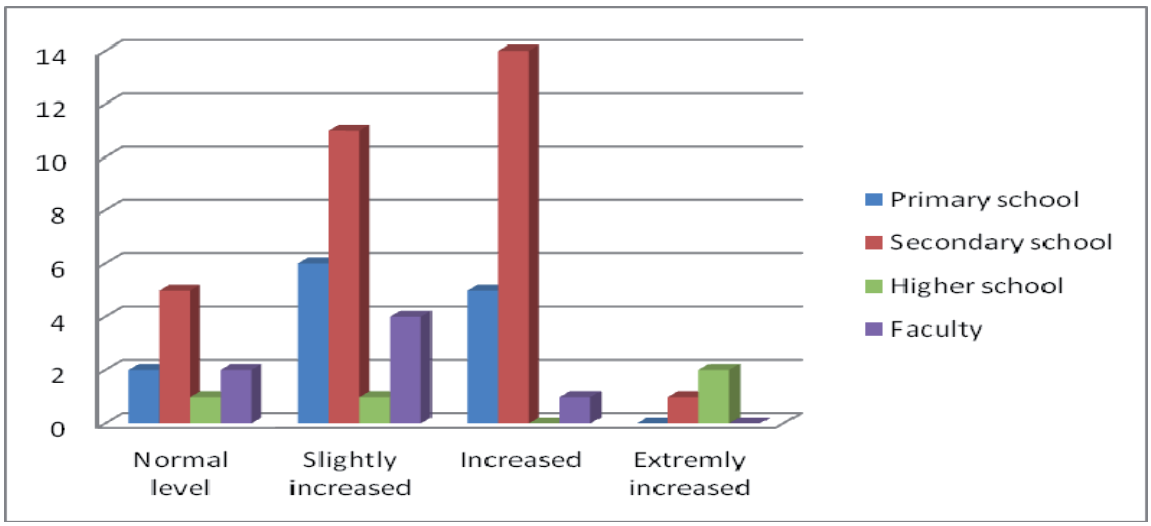


Below are the results of an analysis comparing the differences between the groups in relation to the category of serum phosphate (PO_4).

χ^2 test showed that there is a statistically significant difference between the serum levels of phosphate and education of patients (χ^2 (9,55) = 20.569, p = 0.014 <0.005). Among the patients with normal serum levels of phosphate most of them has finished secondary school while those with extremely elevated serum phosphate values are mostly in category with higher education (Fig. 2).

Figure 2.

Level of education and serum level of phosphate



Regarding the consumption of red meat χ^2 test results show that there is a statistically significant difference in the values of the increased serum level of phosphate (χ^2 (9,55) = 18.703, p = 0.036 <0.05). Among the patients with extremely elevated serum levels of phosphate most of them used to consume red meat more than five times a week (Fig. 3).

χ^2 test results show that there is a statistically significant difference in the values of the extreme values of serum phosphate regarding to consumption of milk and milk products (χ^2 (9,50) = 16.019, p = 0.05 $\leq$0.05). Among patients with extremely elevated serum phosphate most of them used to consume milk and dairy products more than five times a week (Fig. 4).

Figure 3.

Red meat and serum level of phosphates

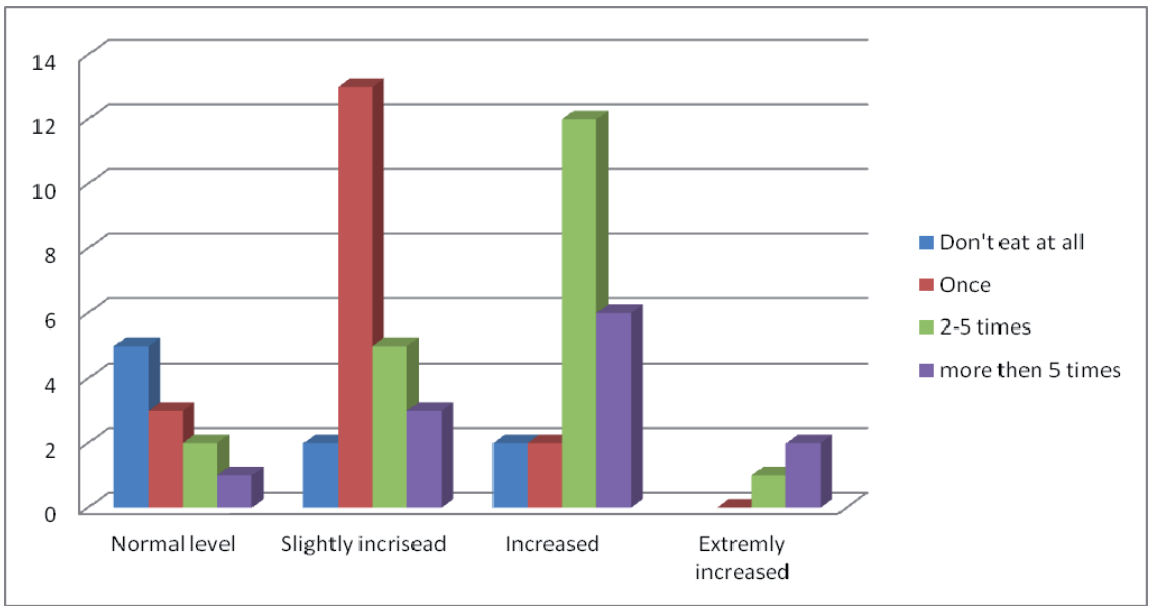
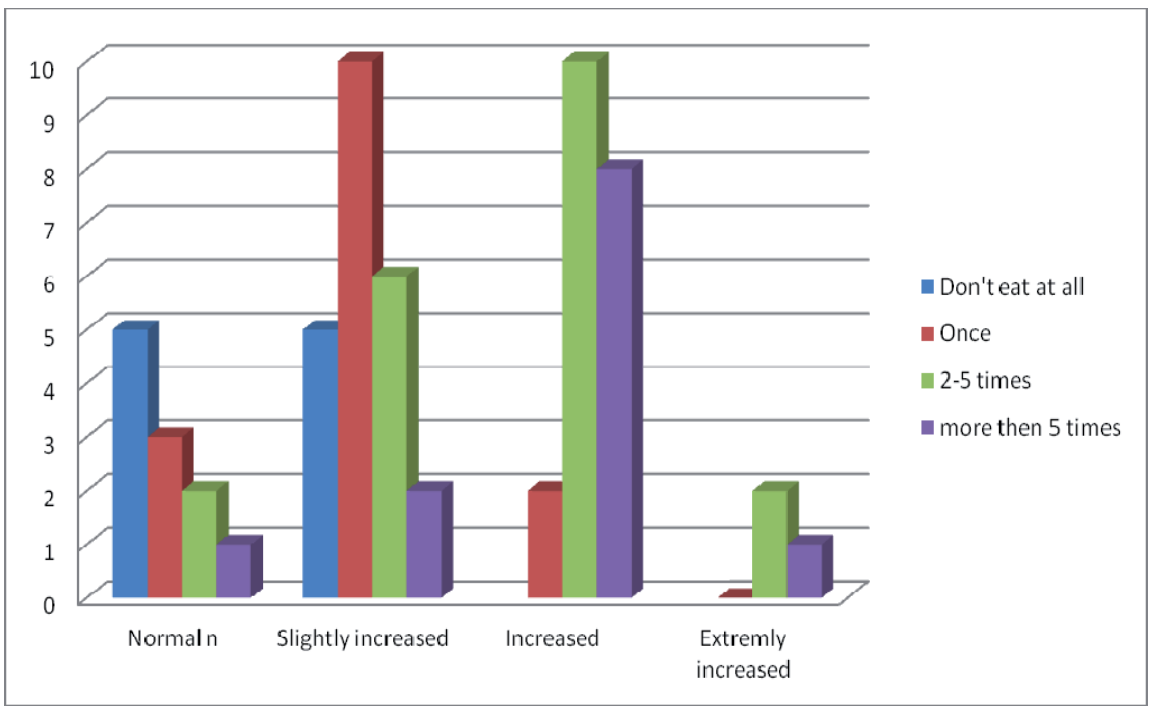


Figure 4.

Consumption of milk and milk products and serum level of phosphates



χ^2 test results show that there is a statistically significant difference in the values of the extreme values of serum phosphate in subjects with respect to the consumption of carbonated drinks (χ^2 (9,55) = 23.000, p = 0.001 <0.05). Among patients with extremely elevated serum phosphate most of those who consume soft drinks more than five times a week (Fig. 5).

χ^2 test results show that there is a statistically significant difference between the extreme values of serum phosphorus in patients in relation to the place of food consumption among 19 patients who had previously responded to have meals outside the home (χ^2 (6,19) = 13.242 , p = 0.039 <0,05). Among patients with extremely elevated serum phosphorus values most of them used to eat in bakeries,

while a slightly lower value of serum phosphate concentration is found in those patients who eat in restaurants and fast food markets. Respondents with normal serum concentrations of phosphate used to eat exclusively in restaurants (Fig. 6).

Figure 5.

Carbonated drinks and serum level of phoshates

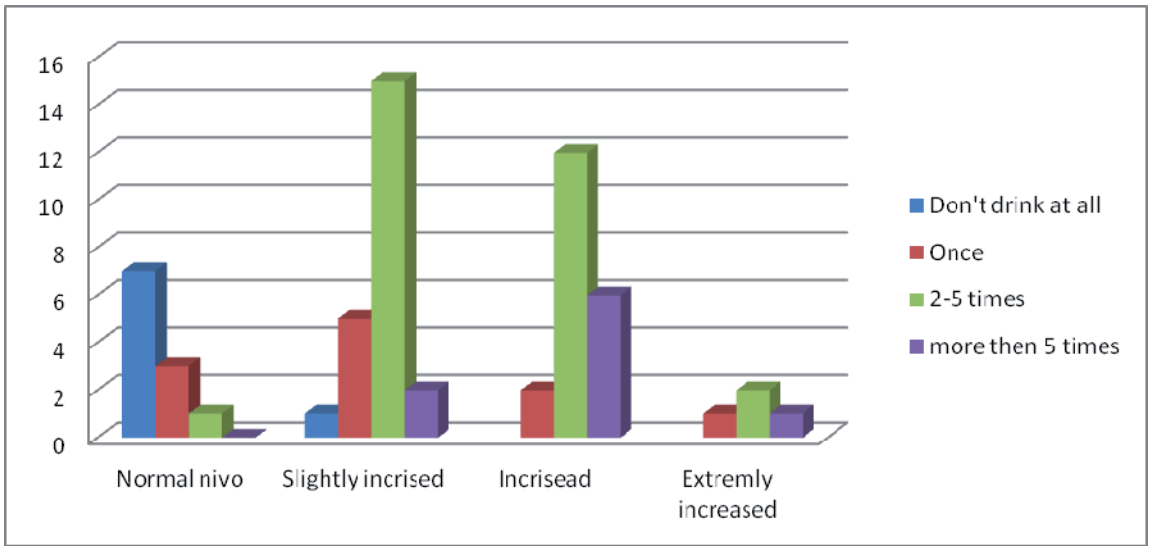
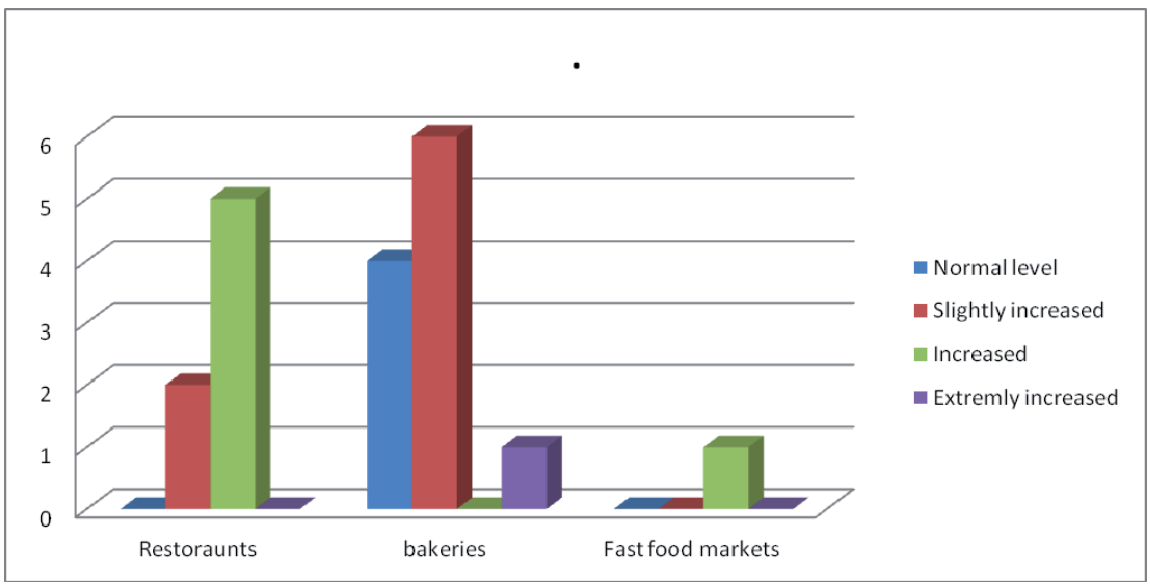


Figure 6.

Places for eating food and serum level of phoshates



DISCUSSION

The conducted study was based on determining the relationship of nutritional attitudes and habits , education level in patients undergoing chronic intermittent hemodialysis and their influence on serum phosphate levels. There are many studies that find a correlation between hyperphosphatemia with increased mortality in patients with advanced renal failure or who are undergoing chronic hemodialysis. In one study published in 2004 which included 40.538 patients it was found that high serum level of phosphate are directly associated with increased mortality[22].

Numerous studies dealing with the examination of the most appropriate mechanism for the correction of hy-

perphosphatemia in patients with chronic kidney disease and in patients who are undergoing chronic intermittent hemodialysis. The last few years in the research focus placed phosphate binders and various dialysis modalities that can directly affect the correction of serum phosphate. A small number of studies have examined the eating habits as a significant factor that can influence the regulation of serum phosphate.

The significance of our study is that it demonstrates the enormous influence of the nutrition, with the direct analysis of individual foods on serum level of phosphate, and that the intervention procedures on changing eating habits, can significantly affect the regulation of serum phosphate and the reduction of morbidity and mortality in those patients, what consecutively occurring as a result of the hyperphosphatemia. This fairly simple, affordable and less expensive interventional procedure can reach respectable result in long-term outcome and treatment of these patients. It is a modern and innovative concept that is primarily related to patient education about the specifics of diet in patients with chronic renal failure and chronic dialysis, and the importance of this concept is often curtailed in relation to the application of phosphate binder and adequate dialysis modalities.

Restriction diet for the control of serum phosphorus is generally associated with a reduced daily intake of foods rich in proteins. Decreased intake of foods rich in proteins can, on the other hand, lead to protein-energy malnutrition (PEW) and decreased survival of patients on chronic hemodialysis programme.

Study Sullivan et al. in 2010 showed that education of patients about the specifics of nutrition on chronic hemodialysis is primarily related to the reduction in the intake of foods rich in phosphate, what leads to a statistically significant improvement in serum phosphate[23].

Results of this study showed that 59.6% of respondents, and 34 were well educated about the special food treatmans. The study Poduval et al. from 2003, which was conducted among 117 patients on chronic hemodialysis programme showed that 74% of them did not know to identify foods that are rich in phosphorus, while 61% of respondents did not know the potential clinical complications related to hyperphosphatemia, and the results of this study shows that patients are not educated enough regarding the specifics of nutrition of patients on chronic hemodialysis program, which differs from the results of studies conducted in our patients[24].

The results of this study have shown that excessive consumption of foods rich in phosphates, primarily of red meat and dairy products is directly linked to the extreme increase in serum phosphate. The study Moa and his associates conducted in 2010 among patients of stage 3-5 CKD were monitored serum levels of phosphate in patients who have taken the meat in the diet foods and in patients who were predominantly on a vegetarian diet. The results of this study showed that in patients who were exclusively fed food containing meat there is a significant increase in serum concentration of the phosphate relative to those who had been on a vegetarian diet[25].

In this study it was found that the increasing level of education of respondents is directly connected with increased level of serum phosphate, and is found in patients with university degrees most of those with extremely elevated serum phosphate values. This does not coincide with the results of other studies. In the study of Gutiérrez and al. From 2010, which included 2.879 patients with chronic kidney disease, it was found that a lower level of education of the patient is directly associated with elevated serum phosphate concentrations (26). This can be explained by the fact that most patients who are on chronic dialysis, and have a high school education are mainly employed and have a wider range of social activities, and despite knowing the specifics of diet in patients undergoing chronic hemodialysis are not able to act in accordance with it.

The research found that the majority of patients with elevated serum levels of phosphate in the food bakeries and fast food shops, where it offers the greatest number of foods rich in inorganic phosphates. These results are consistent with results of other studies. Most studies indicate that the majority of patients treated with the method of chronic renal insufficiency, lower economic status[26], and that usually buy food in places where food is cheaper and they are primarily bakeries and fast food shops and these foods are rich organic and inorganic phosphates[27].

CONCLUSIONS

Diet food rich in phosphates (red meat, milk and dairy products, foods rich in additives, saltwater fish, etc.) in patients on chronic hemodialysis programme is directly associated with increased serum levels of phosphate, which is a significant risk factor for cardiovascular disorders and mineral-bone disorders which consecutively leads to increased morbidity and mortality in these patients.

Attitudes and eating habits in these patients are directly connected with the level of education, and patient's konowladge related to nutrition can significantly affect the regulation of serum phosphate and morbidity and mortality in these patients.

An important role in the consumption of foods rich in phosphates have places where patients are taking food which is usually associated with socioeconomic status of those patients. Serum level of phosphate therefore are extremely elevated in patients who are predominantly taking food in bakeries and fast food shops, and normal serum phosphate occur in those patients who mostly consume food in restaurants.

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SAŽETAK

POVEZANOST IZMEĐU STAVOVA I NAVIKA U ISHRANI I SERUMSKOG FOSFORA U BOLESNIKA NA HEMODIJALIZI

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Poremećaj uhranjenosti bolesnika kojima se bubrežna funkcija nadomješta hemodijalizom (HD) često je povezan s lošom kontrolom serumskog fosfora, što može dovesti do poremećaja metabolizma kosti s posljedičnim razvojem sekundarnog hiperparatireoidizma i poremećajem mineralo-koštanog metabolizma. Hiperfosfatemija je značajan čimbenik rizika za razvoj kalcifikacija mekih tkiva, kao i za pobolijevanje i smrtnost od srčano-žilnih bolesti. Povećan unos hrane bogate fosforom značajan je čimbenik koji dovodi do hiperfosfatemije. Istraživanje ima za cilj ispitati prehrambene navike i stavove bolesnika liječenih HD i utvrditi njihovu povezanost s razinama serumskog fosfora. Istraživanje je provedeno u ožujku 2015. u Centru za hemodijalizu, Kliničkog centra Crne Gore. Istraživanje je provedeno na 57 bolesnika koji su na redovitom programu intermitentne hemodijalize. Muškaraca je bilo 22 (38,6 %). Prosječna dob bolesnika bila je 57 godina (raspon 30-73 godine). Pronađena je statistički značajna povezanost između vrste hrane, osobito crvenog mesa ili konzumiranja mlijeka i mliječnih proizvoda i serumske razine fosfora, kao i između razine obrazovanja ispitanika i razine serumskog fosfora. U našoj je populaciji serumska razina fosfora bila direktno povezana sa socioekonomskim statusom bolesnika. Zaključujemo da je: koncentracija fosfata u serumu određena socijalno–ekonomskom razinom društva, kao i običajem da se u prehrani koriste meso i mlijeko. Nadalje, u konkretnom slučaju vezana je uz prosvjećenost bolesnika koji se dijaliziraju u glavnom gradu Crne Gore.

Ključne riječi: uremija; hemodijaliza; hiperfosfatemija; uhranjenost