VIII. Streszczenie w języku angielskim.

Vitamin D, a fat-soluble derivative of cholesterol, is found both in plant and fungal organisms and in animal organisms. The two main sources of vitamin D in the body are dermal synthesis from cholesterol (the source of 80-90% of vitamin D) and food products (daily diet, vitamin preparations), which cover only 10-20% of its daily requirement. Synthesized in the skin or absorbed from the gastrointestinal tract, vitamin D is converted to 25-hydroxyvitamin D_3 ($25(OH)D_3$) through hydroxylation by 25-hydroxylase in the liver. Determination of serum $25(OH)D_3$ levels is used in the diagnosis of vitamin D deficiency, whether in the elderly, children or those with malabsorption or osteoporosis. In recent years, there has been a kind of renaissance of interest in the role of vitamin D in the development of risk factors for cardiometabolic diseases, especially hypertension and type 2 diabetes. Vitamin D deficiencies are associated with an increase in the incidence of cardiovascular incidents and an increase in overall mortality. Results of epidemiological studies indicate that the incidence of hypertension, type 2 diabetes and coronary artery disease increases with increasing distance from the equator (latitude) and UVB exposure. The effects of the active metabolite of vitamin D on the heart and blood vessels are multidirectional. The hormone has the ability to regulate the renin-angiotensin-aldosterone system (RAAS), and also inhibits the proliferation of vascular myocytes and cardiomyocytes (reduction of left ventricular hypertrophy). The role of vitamin D in the pathogenesis of hypertension is not entirely clear. There are reports in the literature that UVB exposure, causing an increase in serum $25(OH)D_3$ levels, was associated with a reduction in blood pressure in patients with mild hypertension.

Vitamin D Binding Protein (VDBP),which belongs to the albumin group and is a monomeric glycoprotein, binds and transports vitamin D and its metabolites in the blood. There are few reports in the available literature on vitamin D binding protein (VDBP) concentrations and its correlation with other parameters in hypertensive patients.

The aim of the present study was:

- to evaluate vitamin D and vitamin D binding protein (VDBP) concentrations in patients diagnosed with primary hypertension and to compare vitamin D and vitamin D binding protein concentrations in hypertensive patients and reference subjects.

- evaluation of the correlation of vitamin D concentration and vitamin D binding protein in patients with hypertension in relation to selected clinical or laboratory parameters and comorbidities.
- to evaluate the concentration of vitamin D receptor (VDR) and active metabolite of vitamin D- 1.25 $(OH)_2D_3$ in the study group and the reference group.
- to evaluate the correlation of vitamin D receptor (VDR) and active vitamin D - 1,25$(OH)_2D_3$ metabolite levels in patients in the study group against selected clinical and laboratory parameters and comorbidities.
- to evaluate the correlation of vitamin D levels and vitamin D binding protein in patients in the study group taking vitamin D supplementation.

The prospective analysis included a group of 185 patients with primary hypertension under the care of the Academic Practice of Family Medicine in Bialystok in 2019. The median age of patients in the study group was 59 years. Men accounted for 45.7% of the total study population, while women accounted for 54.3%. The median history of hypertension in the study population was 8 years (min 0.01; max 34). Patients were treated nonpharmacologically (1%) or received nonpharmacologic treatment in combination with hypotensive drugs (99%). During the patient visit blood pressure measurements were taken, home blood pressure control was recommended, and laboratory tests were performed. The reference group consisted of 56 subjects without hypertension and not receiving treatment for cardiovascular disease. In both the study and reference groups, blood was drawn from a peripheral vein to determine total vitamin D , 1,25-dihydroxyvitamin D_3, vitamin D binding protein (VDBP), vitamin D receptor (VDR) serum levels by ELISA, and to perform basic laboratory tests. In all patients, blood pressure values were assessed by office measurements. In addition, clinical parameters, comorbidities, drug treatment and vitamin D supplementation were analyzed. Statistical analysis of the obtained results was performed using Statistica 10.

Among the patients in the study group, almost 33% had diabetes or pre-diabetes co-morbidities with hypertension and 62% had lipid disorders, while 29% had heart failure.

Compared to the reference group, patients with hypertension had significantly lower plasma vitamin D levels (Me= 19.4 ng/mL vs Me= 23.08 ng/mL, p=0.007). When gender was included in the statistical analysis, significantly lower vitamin D concentrations were observed among women in both the study and reference groups (p=0.01 and p=0.008). During

statistical analysis, a significant negative correlation was observed between serum vitamin D levels in patients in the study group and heart rate, body weight, BMI, glucose and triglyceride levels and also significantly lower vitamin D levels in the subgroup among patients with co-morbid heart failure. We observed statistically significant lower VDBP concentrations among men in the study group , also in the case of co-morbid diabetes or heart failure, and a negative correlation between VDBP concentrations and systolic blood pressure, glucose levels and age of patients in the study group. In contrast, $25(OH)D_3$ and VDBP s concentrations were found to be positively correlated with HDL cholesterol levels.

Based on the study, the following conclusions were drawn:

- Vitamin D deficiency is common in the population of patients with primary hypertension, including among patients using oral supplementation.
- The serum concentration of vitamin D and vitamin D-binding protein in hypertensive patients is dependent on the gender of the patient. Statistically significantly lower vitamin D concentrations were observed among both female patients in the study group and the reference group, so additional recommendations for vitamin D supplementation should be considered in this particular population. On the other hand, in the case of VDBP, lower concentrations were observed among men in the study group, which may suggest that there is no effect of changes in VDPB concentrations on "free hormone" levels.
- The concentration of vitamin D-binding protein in the serum of hypertensive patients negatively correlates with the values of systolic blood pressure in relation to the values in the reference group. No similar relationship has been described in the available literature to date. VDBP concentration may be a parameter to facilitate therapeutic decision-making and treatment control.
- Both vitamin D and VDBP concentrations, as well as vitamin D receptor and its active metabolite, do not differ significantly among patients with hypertension and carbohydrate metabolism disorders
- Lower concentrations of vitamin D and vitamin D-binding protein among patients with hypertension and co-morbid heart failure may affect the increased risk of cardiovascular complications.

- Vitamin D and VDBP levels in hypertensive patients positively correlate with serum HDL cholesterol levels. We also observed a negative correlation between vitamin D concentration and triglyceride levels in the study population, which may influence the increased risk of residual cardiovascular complications.
- Vitamin D concentrations are lower in the serum of patients taking beta-blocker drugs. Lower vitamin D, VDBP and VDR concentrations were observed in the serum of patients taking drugs from the mineralocorticoid receptor antagonist group.
- Further studies are needed on changes in vitamin D and vitamin D-binding protein concentrations and their clinical consequences, as well as the possible benefits of supplementation on a larger population of hypertensive patients.