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The effect of vitamin D levels on lipid, glucose profiles and depression in perimenopausal women

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Abstract. – OBJECTIVE: Vitamin D deficiency is a significant problem that affects the population living in most countries. This issue is independent by place of residence, sex, age or skin color. It is mainly influenced by the environment we live in and by an unhealthy lifestyle, including bad eating habits.

The aim of this study was to evaluate lipid profile, glucose levels, and vitamin D levels, considering sociodemographic variables, smoking and alcohol consumption in perimenopausal women. Depressive mood was also assessed considering sociodemographic variables and vitamin D levels.

PATIENTS AND METHODS: The study was conducted on a group of 191 women and performed in two stages. The first of them was carried out using a diagnostic survey with the use of a technique questionnaire. The applied research instruments were the author's questionnaire (concerning sociodemographic and selected medical data), and the Beck Depression Inventory. The second stage of the study involved the collection of peripheral blood from each respondent, in order to determine lipid profile, glycemia and serum vitamin D levels.

RESULTS: The age of the female respondents ranged from 45 to 65 years, mean age was 53.1 ± 5.37 years, median 53 years. Vitamin D levels were below normal in 78%; 77% had elevated total cholesterol levels; 91.6% of the respondents had high density lipoprotein (HDL) cholesterol levels within the normal range; 64.4% was characterized by too high (low-density lipoprotein) LDL cholesterol, and 84.8% of the women showed normal triglyceride levels. Among the respondents, 91.1% had normal glycemic levels. Analysis of the collected data showed a weak negative correlation between serum vitamin D levels and the levels of total cholesterol (rho=-0.14; *p*=0.05), LDL cholesterol (rho=-0.16; *p*=0.026), and triglycerides (rho=-0.22; *p*=0.002). Only in the case of HDL cholesterol (*p*=0.067), there was no statistically significant correlation. There were also no statistically significant correlations between serum vitamin D levels and glycemia or severity of depression.

CONCLUSIONS: 1. The majority of the women did not manifest depressive disorders. Of all factors analyzed, only education was associated with the severity of depressiveness. 2. Smoking adversely affected serum vitamin D levels in the studied women. 3. The cessation of menstruation affected carbohydrate metabolism and vitamin D levels. Blood glucose levels increased with the age of the studied women. 4. Relationships were found between the levels of vitamin D and the levels of total cholesterol, LDL cholesterol, and triglycerides. Therefore, it is important to maintain normal vitamin D levels.

Key Words:
Vitamin D, Lipid, Glucose level, Depressiveness, Menopause.

Introduction

Over the years, a scientific study[1] has shown that vitamin D regulates calcium-phosphate metabolism and contributes to bone formation. It also influences the immune system, through proliferation and differentiation of its cells, reduction of oxidative stress and maturation or differentiation of many cells. It is also involved in the initiation of cancer cells death, slowing down the autoimmune response, and thus reducing the risk of numerous autoimmune diseases[2-4]. The role of vitamin D is still being analyzed in terms of prevention, as well as treatment, of many common diseases. These include, among others, systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, diabetes, inflammatory bowel disease and numerous

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dermatological disorders[5]. The vitamin D receptor (VDR) has also been found in cells that build the cardiovascular system. Vitamin D deficiency may indirectly be associated with the formation of atherosclerotic plaques, while it directly affects the development of hypertension[6]. Vitamin D deficiency has been linked to the incidence of cardiovascular diseases (including myocardial infarction, atrial fibrillation, and heart failure). Calcitriol, the active form of vitamin D3, locally produced in the brain tissue, significantly affects the normal development of nervous system tissues, and by normalizing the expression of specific neurotrophins, stimulates neuronal growth[7].

Vitamin D sources can be divided into endogenous, originating from the synthesis occurring in the human skin under the influence of UVB radiation, and exogenous, occurring in food products. The main sources include fatty fish, eggs, milk and dairy products[8]. Within these two groups of sources, sun exposure is the most effective method through which the synthesis of 7-dehydrocholesterol occurs[9]. Vitamin D synthesis in the skin is affected by many factors. Factors that reduce the formation of 7-dehydrocholesterol in the skin include the time of year (autumn, winter), time of day (night), low intensity of sunlight, latitude (above the 37th parallel), high levels of air pollution, dark skin complexion, and too little body surface area exposed to the sun. These factors also include the use of UV filter creams, age over 65, and excessive body weight[9-11]. Approximately 80% of the vitamin D contained in foods is absorbed by the small intestine. Then vitamin D binds with chylomicrons and is distributed together with lymph into the blood, from where this component is absorbed by adipose tissue or muscle tissue. The remaining unabsorbed part of vitamin D goes to the liver[12,13]. Vitamin D deficiency is an important problem that affects the population of most countries, regardless of location, sex, age or skin color[14]. The Polish population in each age group is at particular risk of deficiency of this important vitamin. This is mainly due to the climate in which we live and the unhealthy lifestyle, including bad eating habits[15]. It becomes impossible to establish global standards of vitamin D supplementation, due to different geographical location of individual countries in the world. In Poland, recommendations were established in 2018 by the Polish Society of Pediatric Endocrinology and Diabetology, in consultation with the European Vitamin D Society[16]. The specific prophylactic dose for a healthy adult should be adjusted according to age, body weight, frequency of sun exposure, season, lifestyle/work and dietary habits[17]. In addition, any person who intends to include vitamin D supplementation should perform determinations of liver metabolite 25(OH)D levels, which is a recognized indicator of vitamin D availability in the body[17].

In recent years, the association between the occurrence of depressive disorders and vitamin D levels has been highlighted[18-20]. The World Health Organization has recognized depression as the leading cause of mental disorders in the modern world. In Europe, the problem affects about 40 million people. In Poland, depression affects approximately 5% of the population, which is over 1.8 million people. Depression affects mostly women[19]. This may be due to decreasing estrogen levels in the female central nervous system related to the gradual cessation of ovarian hormonal function in the perimenopausal period[21]. Menopause, occurring around the age of 50, is associated with several changes in both the physical and psychological domains[22]. In the psychological domain, increased irritability, problems with concentration and decision-making, memory impairment, emotional instability, sleep disturbances, and lowered mood are registered[20,23]. Unfounded guilt, lack of self-confidence, anxiety symptoms, and eventually suicidal thoughts can also be considered[24]. Depressed patients often develop appetite disorders and altered eating patterns, including avoidance of consumption of certain foods. This can consequently lead to dangerous nutritional deficiencies[25]. Additionally, depressed individuals are often less physically active and spend more time indoors, compared to healthy individuals. These factors may further potentiate serum vitamin D deficiency, which in turn leads to an increase in depressive disorders[18]. It is important to note a significant difference between the severity of a depressive state as perceived by the patient and depression as a diagnosable medical entity, recognized by a physician. The severity of depressiveness can be assessed using standardized tools for assessing well-being, such as the Beck Depression Inventory[26]. Lifestyle, including diet, may have an impact on preventing or accelerating the onset of many chronic conditions associated with vitamin D deficiency, including depressive disorders[27].

The aim of this study was to evaluate lipid profile, glucose levels, vitamin D levels, considering sociodemographic variables, smoking and alcohol consumption in perimenopausal women. Depressive mood was also assessed taking into account sociodemographic variables and vitamin D levels.

Patients and Methods

The study was conducted in a group of 191 women living in northwestern Poland. Information on recruitment for the study was placed on posters in primary health care centers and published on social media; respondents applied for the study by phone.

The project involved 191 respondents. The following study inclusion criteria were adopted:
- perimenopausal age (45-65 years);
- female sex;
- no vitamin D supplementation;
- voluntary willingness to participate in the study;
- signing an informed consent for participation in the project.

The study was performed in two stages. The first of them was carried out using a diagnostic survey which implied the use of a questionnaire technique. The applied research instruments were: the author's questionnaire concerning sociodemographic and selected medical data, and the Beck Depression Inventory.

The Beck Depression Inventory I-II is the most popular scale used for self-assessment of the occurrence and severity of depressive symptoms[28]. This standardized research tool was developed by Aaron Beck and co-authors in 1961, while in recent years this scale has been modernized and the second expanded part has been created[29-31].

According to the established interpretation of the scores, individuals who obtained:
- 0-11 points showed absence of depressive symptoms;
- 12-26 points showed mild depressive symptoms;
- 27-49 points showed moderate depressive symptoms;
- 50-63 points suggested the presence of severe depressive symptoms[32].

The second stage of the study involved collecting peripheral blood from each respondent to determine lipid profile, serum glycemia and vitamin D levels. The tests related to lipid profile measured total cholesterol, HDL, LDL and triglyceride levels. Carbohydrate metabolism was assessed by venous blood glucose test. When analyzing the results, we took into account the range of biological reference values of laboratory tests adopted in the laboratory center "Diagnostics":

Glucose:
- normal fasting blood glucose: 60.00-99.00 mg/dl;
- abnormal fasting blood glucose: 100-125 mg/dl [Oral Glucose Tolerance Test (OGTT) - test indicated];
- diabetes mellitus: ≥126 mg/dl, result obtained on duplicate testing.

Total cholesterol:
- normal result: 115.00-190.00 mg/dl, according to Polish Cardiac Society and Polish Society of Laboratory Diagnostics recommendations;
- decreased result: <115.00 mg/dl;
- elevated result: >190.00 mg/dl.

HDL:
- normal result: ≥45 mg/dl, according to the Polish Cardiac Society and the Polish Society of Laboratory Diagnostics recommendations.

LDL:
- normal result in healthy subjects and those with moderate or low cardiovascular risk: <115 mg/dl, as recommended by the Polish Cardiac Society and the Polish Society of Laboratory Diagnostics recommendations.

Triglycerides:
- ≤150 mg/dl, according to the recommendations of the Polish Cardiac Society and the Polish Society of Laboratory Diagnostics.

Vitamin D metabolite 25-OH D:
- deficiency: <10 ng/ml;
- subnormal result: 10-29.99 ng/ml;
- normal result: 30-80 ng/ml;
- result above normal: 80.10-99.99 ng/ml;
- toxicity: >100 ng/ml.

Biological material was collected in the morning by a qualified nurse in an appropriately equipped treatment room, using the rules associated with blood collection and transport to the laboratory. The subjects were fasted on the day of the study. Each patient's blood was drawn into two 4 ml tubes from an accessible peripheral venous vessel in a closed Vacutainer-type system. The extracted material was transported to the medical laboratory, where laboratory analysis was performed, following the material transport procedure. The material was collected from October to November – the period of the study was selected according to the season of the year.

The research project was approved by the Bioethics Committee of the Pomeranian Medical University in Szczecin (KB-0012/119/17).

All responses obtained from the survey part and laboratory results were coded and transferred to the Microsoft Office Excel, Redmond, WA, USA spreadsheet (version 2016).

The collected data were initially evaluated using descriptive statistical methods. Depending on the type of the measurement scale on which the

Table I. Characteristics of the individual components of the lipid profile of the women studied.

Lipid profile	n	M±SD	Mdn	Mini-Max	CV [%]
Total cholesterol [mg/dl]	190	221.5±42.95	218.6	121.4-483.1	19.4
Cholesterol HDL [mg/dl]	190	68±17.44	67.6	31.1-133.1	25.6
Cholesterol LDL [mg/dl]	188	130.1±35.1	127.7	54.9-223.2	27
Triglycerides[mg/dl]	189	110.8±82.82	92.9	42.1-1024	74.7
Glucose [mg/dl]	190	85,6±111,3	82,5	66.7-194.4	18.4

n - number of responders; M±SD - arithmetic mean and standard deviation; Mdn - median, Min-Max - minimum and maximum; CV - coefficient of variation.

variables were expressed, two types of descriptive statistics parameters were essentially used:

- for quantitative variables, the measures of central tendency (mean and median) and dispersion (standard deviation and coefficient of variation) were determined, and the minimum and maximum values were given;
- for non-metric variables (qualitative and ordinal), a measure of structure (abundance and frequency) was determined[33].

The correlation between quantitative variables was determined using Spearman's rank correlation coefficient (rho-Spearman's).

Calculations were performed using the Statistica, Palo Alto, CA, USA (version 13.3) statistical software (TIBCO Software Inc.). For all analyses, verification of the null hypothesis was conducted with an assumed a priori level of statistical significance of 0.05.

Results

A total of 191 perimenopausal women were included in the study. The age of the studied women ranged from 45 to 65 years, the mean age was 53.1±5.37 years, and the median was 53 years.

Among the respondents, more than half (55%) had higher education, 38.7% had secondary education. Most of the women (77.5%) lived in a city with more than 100,000 residents, 10.5% lived in a city with 10,000-100,000 residents, 8.9% lived in rural areas, and the smallest group (3.1%) lived in a city with up to 10,000 residents. Most of the research group declared being in a formal relationship (71.2%). The vast majority of the respondents were employed (88%). More than half of the examined women were menstruating (62.3%), 37.7% were not menstruating.

We analyzed the level of vitamin D, individual components of lipid profile and blood glucose. The lowest serum vitamin D concentration registered was 7.2 ng/ml, while the highest was 49.7 ng/ml. The median was 23 ng/ml, and the arithmetic mean was 23.4 ng/ml. The coefficient of variation was 34.6%. The mean total cholesterol was 221.5±42.95 mg/dl, HDL fraction cholesterol was 68±17.44 mg/dl, LDL fraction was 130.1±35.1 mg/dl, and triglycerides were 110.8±82.82 mg/dl. The median total cholesterol was 218.6 mg/dl. The highest result recorded for triglycerides was max = 1024 mg/dl, and the median was 92.9 mg/dl. The mean peripheral blood glucose level was 85.6 mg/dl, the median was 82.5 mg/dl, the lowest result was 66.7 mg/dl, and the highest was 194.4 mg/dl. The coefficient of variation was 18.4% (Table I).

78% of the subjects had vitamin D levels below normal. Only 21.5% of the examined women had results at the normal level. 77% of the examined women had elevated levels of total cholesterol, and 22.5% had results within the normal range. The HDL cholesterol level was within normal limits in 91.6% of the respondents. More than half of the study group (64.4%) had too high levels of LDL cholesterol. In 84.8% of the women triglyceride levels were normal, in slightly above 14% they were high. Elevated fasting peripheral blood glucose levels were found in 8.4% of the respondents, while up to 91.1% of the women had normal blood glucose levels (Table II).

The severity of the respondents' depression was also assessed; the lowest score was 0 points, while the highest was 40 points. The arithmetic mean was 7.8 points, and the standard deviation was 6.82 points. The coefficient of variation was 87%. Most of the examined women (75.9%) did not show any signs of depression. None of the respondents had severe depressive episodes, only 22.5% had mild depressive episodes, and 1.6% had moderate depressive episodes (Table III).

Assessment of Depression with Sociodemographic Variables and Effect of Vitamin D Concentration

Sociodemographic variables that may have contributed to depression among the studied women were analyzed.

Table II. Characteristics of the study group by laboratory findings.

Variable		n	%
Vitamin D level			
deficiency		1	0.5
belownormal		149	78
normal		41	21.5
Lipid profile			
Total cholesterol	normal	43	22.5
	elevated	147	77
	missing data	1	0.5
HDL cholesterol	belownormal	15	7.9
	normal	175	91.6
	missing data	1	0.5
LDL cholesterol	normal	65	34
	elevated	123	64.4
	missing data	3	1.6
Triglycerydes	normal	162	84.8
	elevated	27	14.1
	missing data	2	1
Glucose level			
normal		174	91.1
elevated		16	8.4
missing data		1	0.5

n - number of respondents; % - percentage of the total number of respondents.

The data analysis revealed statistically significant differences (p<0.041) in the severity of depression, as measured by the Beck Depression Inventory, depending on the level of education of the studied women (η^2=0.023) (Table IV).

There were no statistically significant differences in the severity of depression, according to the Beck Depression Inventory, depending on sociodemographic variables, such as age, place of residence, marital status, and employment status (**Supplementary Tables I, II**).

The analysis also did not show a statistically significant effect of vitamin D serum concentration on the severity of depression, according to the Beck Depression Inventory (p=0.152) (Table V).

Laboratory Test Results with Sociodemographic Variables

Then, the effect of sociodemographic factors on the laboratory test results was analyzed. Among the sociodemographic factors, age was weakly positively correlated with serum glucose levels (rho=0.26; p=0.000). However, there was no statistically significant effect (p>0.05) of the respondents' age on the levels of vitamin D, total cholesterol, HDL fraction cholesterol, LDL fraction cholesterol, and triglycerides (Table VI).

There were also no statistically significant differences in laboratory test results depending on education, place of residence, marital status, and employment status (**Supplementary Tables III, IV, V, VI**).

Laboratory Test Results in Relation to Cigarette Smoking and Alcohol Consumption

There were statistically significant differences in serum vitamin D levels depending on cigarette smoking ↓ it was higher in the group of women who did not smoke (Mdn=23.6 *vs.* 17.8; p=0.002; η^2=0.047). For the other parameters, no statistically significant differences were found between the compared groups (Table VII).

There was also a statistically significant difference in the level of HDL cholesterol depending on alcohol consumption. The level of this parameter was higher in the group declaring alcohol consumption compared to the group not using this substance (Mdn=70.8 *vs.* 65.5; p=0.013; η^2=0.033).

Table III. Severity of depressiveness among female respondents (N=191).

Depressive	n	%
no depressive episode (0-11)	145	75.9
mild depressive episode (12-26)	43	22.5
moderate depressive episode (27-49)	3	1.6
severe depressive episode (50-63)	0	0

n - number of respondents; % - percentage of the total number of respondents

Table IV. Severity of depressive mood according to Beck's Scale in relation to the level of education of female respondents.

Educational level	primary (n=12)		secondary (n=74)		higher (n=104)		H	*p*	η^2
	Mdn	IQR	Mdn	IQR	Mnd	IQR			
Depression severity according to Beck Scale	11	10	7	9	5	7	6,381	**0.041**	0.023

n - number of respondents; Mdn - median; IQR - interquartile range; H - value of statistic; *p* - test probability (Kruskal-Wallis rank ANOVA); η^2 - (eta-square) effect size

For the other parameters no statistically significant differences were found between the compared groups (Table VIII).

Laboratory Test Results in Relation to Menstruation

The data analysis showed statistically significant differences in the levels of glucose and vitamin D depending on the presence of menstruation. The levels of both parameters were higher in the non-menstruating than in the menstruating group. The mean glucose level was Mdn = 83.8 *vs.* 80.8; p=0.004; η^2=0.045, while the mean vitamin D level was Mdn = 23.3 *vs*. 21.4; p=0.048; η^2=0.018. For the other parameters, there were no statistically significant differences between the groups compared (Table IX).

Laboratory Test Results Concerning the Influence of Vitamin D Levels

Then we analyzed the influence of serum vitamin D levels on individual components of the lipid profile. There was a weak negative correlation between serum vitamin D levels and the levels of total cholesterol (rho=-0.14; p=0.05), LDL cholesterol (rho=-0.16; p=0.026), and triglycerides (rho=-0.22; p=0.002). Only HDL cholesterol (p=0.067) and glucose levels showed no statistically significant correlations (Table X).

Discussion

Vitamin D deficiency is recognized as the most common medical condition in the world[34]. An epidemiological study conducted in 18 countries at different latitudes, which assessed plasma 25-hydroxyvitamin D [25(OH)D] levels in postmenopausal women found low levels in 64% of the respondents[35]. Studies[36-38] suggest a role of vitamin D deficiency in various non-communicable chronic diseases, such as obesity, hypertension, diabetes, and consequently metabolic syndrome (MetS) and cardio-vascular syndrome (CVD). In a meta-analysis of 28 studies, elevated serum 25(OH)D levels were associated with a 55% reduction in the prevalence of diabetes, a 51% lower risk of MetS, and a 33% lower risk of CVD (38). Measurement of 25(OH)D levels in blood samples can be used to assess and monitor nutritional status, as serum vitamin D levels are a major indicator of body reserves[39].

According to the Institute for Health Metrics and Evaluation (IHME) data from 2017, approximately one million people (2.8%) in the Polish population suffered from depression. Against the background of European Union countries, this was one of the lower results, as depressive disorders affected almost 21 million Europeans, or 4.2% of the total population. It is worth noting that it is the second most common mental disorder in the world[40], most often affecting women[41]. The risk of depressive symptoms significantly increases in the perimenopausal period[42]. Freeman[43] conducted a review of epidemiological studies on depression developing in the premenopausal period. According to this review, the increase in depressive symptoms during menopause was mainly due to changes in the hormonal system. Perimenopausal women were 30% more likely to experience depressed moods than premenopausal women. What is more, women who had a history of depressive episodes were at risk of another di agnosis of depression in the perimenopausal peri-

Table V. Effect of vitamin D concentration on the severity of depression according to Beck Scale of the examined women.

Correlation	N	rho–Spearman's	t	*p*
Vitamin D and depression severity according to Beck Scale	191	-0.1	-1.438	0.152

n - number of respondents; rho-Spearman's rank correlation coefficient; t - value of the statistic; *p* - test probability.

Table VI. Influence of age of the respondents on the results of serum laboratory tests.

Age	n	rho – Spearman's	t	p
Glucose [mg/dl]	190	0.26	3.668	**0.000**
Total cholesterol [mg/dl]	190	0.08	1.137	0.257
HDL cholesterol [mg/dl]	190	0.01	0.122	0.903
LDL cholesterol [mg/dl]	188	0.06	0.825	0.410
Triglycerides [mg/dl]	189	0.12	1.623	0.106
Vitamin D [ng/ml]	191	0.12	1.659	0.099

n - number of respondents; rho-Spearman's - rank correlation coefficient; t - value of the statistic; *p* - test probability.

od. The study conducted by Willi et al[44] focused on biopsychosocial factors influencing the health of perimenopausal Swiss women, and mainly assessed the relationship between depressive disorders and prevailing body changes.

The relationship between vitamin D levels and menopausal symptoms in postmenopausal women has also been sought. According to LeBlanc et al[45], vitamin D levels are not associated with menopausal symptoms in women (mean age 66 years). However, they did not rule out such an association in younger women who are just entering the perimenopausal period. The role of vitamin D in the treatment of patients diagnosed with depression has also been not fully understood. The results of various randomized controlled trials are not consistent[46]. Hoogendijk et al[47] conducted study of 1,282 Dutch residents was conducted to determine the association between depression and altered vitamin D and parathormone levels. They found that depression severity was associated with decreased serum vitamin D levels and with increased parathormone levels in individuals aged between 65-95 years. Similar conclusions were reached by Stewart and Hirani[48], who examined depressive symptoms and measured 25-hydroxyvitamin D blood levels in a group of more than 2,000 respondents over the age of 65. An analogous study was conducted by Brouwer-Brolsma et al[49] among Dutch residents being over 65 years of age, providing the same observations. Similarly, in Switzerland[50], the severity of depressive symptoms was assessed, and serum vitamin D levels were measured in 380 patients hospitalized for depressive disorders. Low 25-OH D levels were found in these patients and this factor was associated with increased severity of depressive symptoms. The association ~~of~~ between serum 25-hydroxyvitamin D levels and depressed mood was evaluated in 80 elderly subjects. It was shown that less than 60% had very low vitamin D levels (<20 ng/ml), which in turn was strongly associated with lowered mood in these patients[51]. Similar findings were obtained by Imai et al[52], when they analyzed the AGES-Reykjavik study and confirmed the association between vitamin D levels and depression. However, long-term observations are still lacking to determine whether biological changes occurring in the body (e.g., vitamin D deficiency) are the cause of depression or its consequence. To determine the link between vitamin D deficiency and depression, a study[53] of 31,424 respondents was conducted using a meta-analysis of observational studies and randomized control trials. Patients with clinically confirmed depression had lower vitamin D levels compared to controls. A cross-sectional study found an increased rate of depression for the lowest vitamin D levels. This analysis was consistent with the hypothesis that

Table VII. Laboratory test results in relation to cigarette smoking among female respondents.

Cigarette smoking / Laboratory tests	Yes (n=25)		No (n=165)		Z	p
	Mdn	IQR	Mdn	IQR		
Glucose [mg/dl]	84.7	13.1	82.1	13.3	0.993	0.322
Total cholesterol [mg/dl]	218.5	42.1	219.9	51.5	-0.174	0.861
HDL cholesterol [mg/dl]	65.6	12.5	68.3	22.9	-1.194	0.234
LDL cholesterol [mg/dl]	128.8	31.1	127.2	48.3	0.491	0.624
Triglycerides [mg/dl]	103.8	47.8	92.1	54.6	0.787	0.434
Vitamina D [ng/ml]	17.8	8	23.6	11.4	-2.988	**0.002**

n - number of respondents; Mdn - median; IQR - interquartile range; Z - value of the statistic; *p* - test probability (Mann-Whitney U test).

Table VIII. Results of laboratory tests in relation to alcohol consumption among the examined women.

Alcohol consumption / Laboratory tests	Yes (n=58) Mdn	Yes (n=58) IQR	No (n=132) Mdn	No (n=132) IQR	Z	*p*
Glucose [mg/dl]	82.3	10.8	82.7	13.5	-0.514	0.607
Total cholesterol [mg/dl]	220.3	44.3	217.2	51.2	1.005	0.315
HDL cholesterol [mg/dl]	70.8	18.9	65.5	22.2	2.484	**0.013**
LDL cholesterol [mg/dl]	128.9	49.5	126.9	45.2	0.411	0.681
Triglycerides [mg/dl]	90.6	60	95.3	53.5	-1.56	0.119
Vitamin D [ng/ml]	22.8	8.5	23	13.6	0.179	0.858

n - number of respondents; Mdn - median; IQR - interquartile range; Z - value of the statistic; *p* - test probability (Mann-Whitney U test).

low vitamin D concentrations are associated with depression. It also highlighted the need for randomized, controlled trials of vitamin D in the prevention and treatment of depression to determine whether this association is causal.

Analysis of the data in our study showed that the female respondents overwhelmingly did not show signs of depression. There was also no statistically significant relationship between serum vitamin D levels and severity of depression.

Similar results were obtained by Norwegian researchers[54] conducting a randomized control trial with vitamin D supplementation, which showed no significant relationship between vitamin D levels and depression. A different trend was observed in the study[55] of the relationship between serum 25-hydroxyvitamin D levels and depression severity in overweight and obese individuals aged 21-70 years. An association was found between 25-(OH) D and increased depressive symptoms in this study group.

Some researchers[56-58] argue that the severity of depression in menopause is determined by sociodemographic factors.

Our study did not show a relationship between most of the analyzed sociodemographic factors and severity of depression. However, the influence of education on the severity of depressive symptoms in the study group was demonstrated.

Many researchers[59-62] have demonstrated the positive impact of higher education, which is associated with better knowledge, cognitive development, and greater social support, on the occurrence of depressive symptoms.

Changes associated with the perimenopausal period are considered to be one of the causes of the development of atherosclerotic disease. It has been noted that premenopausal women are significantly less likely to be affected by cardiovascular disease due to atherosclerosis than men. The incidence of cardiovascular disease among women increases sharply after menopause[63]. Hormonal fluctuations, prior to the cessation of menstruation, occurring during the perimenopausal period are thought to influence the changes occurring within the lipid profile[64]. A retrospective study[65] evaluating the lipid profile from perimenopausal to postmenopausal period and the association of lipid profile with menopausal status, was conducted in a group of 275 women. It was observed that levels of total cholesterol, LDL fraction cholesterol, and triglycerides were significantly higher in postmenopausal women than in perimenopausal women.

Table IX. Results of laboratory tests according to the occurrence of menstruation in the studied women.

Occurrence of menstruation / Laboratory tests	Menstruate (n=71) Mdn	Menstruate (n=71) IQR	Not menstruating (n=119) Mdn	Not menstruating (n=119) IQR	Z	*p*
Glucose [mg/dl]	80.8	11.9	83.8	13.8	-2.914	**0.004**
Total cholesterol [mg/dl]	215	48.6	220.9	49.5	-1.415	0.157
HDL cholesterol [mg/dl]	68.3	23.7	67.6	20.2	-0.004	0.997
LDL cholesterol [mg/dl]	124.9	44.9	129.9	48	-1.07	0.285
Triglycerides [mg/dl]	89.9	51.1	96.9	54	-0.968	0.333
Vitamin D [ng/ml]	21.4	13.1	23.3	10.8	-1.98	**0.048**

n - number of respondents; Mdn - median; IQR - interquartile range; Z - value of the statistic; *p* - test probability (Mann-Whitney U test).

Table X. Correlation between vitamin D level and particular components of lipid profile and glucose.

Vitamin D	n	rho – Spearman's	t	p
Total cholesterol [mg/dl]	190	-0.14	-1.977	**0.05**
HDL cholesterol [mg/dl]	190	0.13	1.839	0.067
LDL cholesterol [mg/dl]	188	-0.16	-2.247	**0.026**
Triglycerides [mg/dl]	189	-0.22	-3.132	**0.002**
Glucose [mg/dl]	190	-0.13	-1.851	0.066

n - number of respondents; rho-Spearman's - rank correlation coefficient; t - value of the statistic; *p* - test probability

Cho et al[66] conducted a study in which they measured quantitative changes in lipoprotein and lipid levels of women from premenopausal to postmenopausal and identified parameters that are related to changes in the perimenopausal period. Their analysis showed that total cholesterol and LDL fraction cholesterol both increased during the perimenopausal period, and this was due to the modification of female sex hormones. HDL cholesterol, as well as triglyceride levels, remained unchanged. A meta-analysis by Akbari et al[67] showed that vitamin D supplementation could lead to improvements in the Homeostasis Model Assessment of insulin resistance (HOMA-IR), Quantitative Insulin Sensitivity Check Index (QUICKI), and LDL cholesterol levels, but did not affect the Fasting Plasma Glucose (FPG), insulin, Glycated hemoglobin (HbA1c), triglycerides, total cholesterol, and HDL cholesterol levels. However, vitamin D supplementation can increase the Homeostatic Model Assessment of beta-cell function (HOMA-B) index. Similarly, a study by Lee et al[68] did not confirm the effect of vitamin D supplementation among diabetes mellitus patients on blood glucose levels. Korean researchers[67] observed elevated levels of total cholesterol in 77% and LDL cholesterol in about 65% of the studied women. Similar results were obtained by Pinkas et al[69], comparing vitamin D levels, lipid profile components and BMI in female respondents aged 44-66 years. The women were divided into three groups: early perimenopausal, late perimenopausal, and postmenopausal. Less than 10% of the respondents had optimal vitamin D levels, most women had normal HDL cholesterol levels (93%), and more than half of them were overweight or obese. Blood vitamin D levels were found to be associated with the lipid profile and the degree of obesity in a group of pre- and postmenopausal women who did not do physical work. Similar conclusions were reached in a study[70] of nearly 4,000 adult respondents living in northern China. The researchers found that vitamin D deficiency was strongly associated with dyslipidemia.

Our study showed that most of the respondents had normal HDL cholesterol (about 92%), triglycerides (about 85%), and glycemic levels (91%). The analysis showed no association between vitamin D levels and the subjects' lipid profile or blood glucose levels.

Furthermore, our study confirmed a relationship between alcohol consumption and the level of HDL cholesterol. HDL levels were higher in the group declaring alcohol consumption compared to the group not using this stimulant.

Similar findings were obtained in a study[71] conducted on 1,676 patients with at least one >75% coronary artery stenosis on angiography. Moderate alcohol consumption has been found to be associated with higher HDL-C levels. However, even if there is a causal relationship between alcohol consumption and higher HDL cholesterol levels, it is suggested that efforts to reduce the risk of coronary heart disease should focus on controlling other risk factors.

The effect of smoking on serum levels of vitamin D metabolites was assessed in 510 healthy perimenopausal women. The analysis indicated that smoking had a significant effect on vitamin D metabolism, as women who smoked cigarettes had significantly reduced serum levels of vitamin D metabolites [25 (OH) D, 1,25 (OH) D, and 2D][72]. Reduced vitamin D levels due to cigarette smoking are probably caused by increased liver enzyme activity in the body. Analogous results were obtained in the SAMINOR 2 clinical trial. Cigarette smoking and excessive body weight were associated with decreased 25 (OH) D levels[73]. Another study[74] showed that non-smoking respondents had higher serum vitamin D levels compared with smokers regardless of their sex. Also, a study[75] conducted in Japan among 9,084 participants aged 40-74 years confirmed relationships between vitamin D deficiency and demographic, environmental and lifestyle factors. The results indicated that only 9% of the subjects had normal 25 (OH) D levels. It was found that the lifestyle modification may contribute to sufficient vitamin D levels in the body. A study[76] of 1,952 Bulgarian respondents demonstrated that cigarette smoking and higher education in the case of men, and obesity in the case of women, were variables that influenced low vitamin D levels. An analysis by Jääskeläinen et al[77], who studied almost 6,000 individuals from the Finnish population, showed an association of serum vitamin D levels with a number of sociodemographic and lifestyle factors. One finding was that non-smokers had higher blood 25 (OH) D concentrations.

Our study confirmed this relationship. It was shown that women who smoked cigarettes had lower serum vitamin D levels than non-smoking ones. Our study also showed the relationship between vitamin D levels and menstruation in the studied group of women. Non-menstruating women were characterized by higher vitamin D levels.

This has not been confirmed by other authors. Perimenopausal women are at risk of vitamin D deficiency due to hormonal changes. Decreased estrogen levels tend to produce low serum vitamin D levels. Vázquez-Lorente et al[78] studied 78 postmenopausal women residing in Granada, Spain. Their analysis showed that at least 80% of the respondents were vitamin D deficient. Similar results were obtained in a study by Li et al[79], and vitamin D deficiency was observed in approximately 72% of healthy postmenopausal women.

Menopause is characterized by a significant decrease in endogenous estrogen levels and is associated with changes in body weight, fat distribution, and energy expenditure. There is also a decrease in insulin secretion, sensitivity, and activity, which may predispose to the development of type 2 diabetes, independent ~~of~~ from the aging process[80,81]. According to Ren et al[82], postmenopausal status may be a stable and significant risk factor for type 2 diabetes. Our study showed higher serum glucose levels in non-menopausal women.

The perimenopausal period is a difficult time for most women, full of not only hormonal but also social, family, and work-related changes. A strong point of our study was the elimination of interfering factors in the assessment of vitamin D saturation levels. These included not taking supplementation and seasonally dependent differences in vitamin D levels. A limitation of the study is the changing criteria for assessing serum vitamin D levels, which are updated from time to time and may differ in different parts of the world. However, when comparing the results, an attempt was made to collate data from different female populations to illustrate the widespread problem of vitamin D deficiency throughout the world (despite differences in the criteria for assessing vitamin D levels). Another limitation was undoubtedly the cross-sectional type of the study, which made it only possible to assess a small percentage of a concrete population of women. This difficulty, however, does not affect the credibility of the results of the present study, but emphasizes the importance of expanding the research sample.

Conclusions

1. The majority of the women did not manifest depressive disorders. Of all factors analyzed, only education was associated with the severity of depressiveness.
2. Smoking adversely affected serum vitamin D levels in the studied women.
3. The cessation of menstruation affected carbohydrate metabolism and vitamin D levels. Blood glucose levels increased with the age of the studied women.
4. Relationships were found between the levels of vitamin D and the levels of total cholesterol, LDL cholesterol, and triglycerides. Therefore, it is important to maintain normal vitamin D levels.

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Authors' Contributions

Conceptualization, D.K., K.B. and E.G.; Methodology D.K., P.U. and M.S.; Analysis, D.K., M.Sz., P.U., J.B. and E.G.; Investigation, D.K., M.S. and M.Sz.; Data Curation, D.K., B.K. and M.Sz; Writing – Original Draft Preparation, D.S.M., J.B. and E.G.; Writing – Review& Editing, D.S.M., P.U., and E.G.; Visualization, D.K., and B.K.; Supervision, E.G.; Funding Acquisition, E.G.

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Conflicts of Interest

Authors declare no conflict of interest.

Ethical Approval

Not applicable.

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