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# Indicators of carbohydrate metabolism and vitamin D levels in pregnant women with metabolic syndrome

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***The objective:*** to assess the level of vitamin D and its relationship with carbohydrate metabolism in women with metabolic syndrome in the I trimester of pregnancy.
***Materials and methods.*** 120 pregnant women were examined, of which 60 patients were diagnosed with metabolic syndrome before pregnancy (main group) and 60 patients without this pathology (control group). All women were measured for fasting blood glucose, glycated hemoglobin, immunoreactive insulin, HOMA-IR index, and serum vitamin D levels.
***Results.*** In women in the main group, the average level of vitamin D was 15.76±3.77 ng/ml, in the control group – 17.20±3.76 ng/ml. The concentration of vitamin D less than 20 ng/ml in the main group was found in 70.0% of patients, in the control group – in 51.7%, 20–30 ng/ml – in 30.0% and 48.3%, respectively ($p<0.05$). The mean body mass index was significantly higher in women of the main group relative to the control group ($p=0.041$) and in patients with metabolic syndrome did not differ from the values in women with vitamin D deficiency and insufficiency. However, body mass index was significantly higher in the presence of vitamin D deficiency between patients with and without metabolic syndrome ($p=0.001$).
There was a significant difference in the concentration of immunoreactive insulin and the value of the HOMA-IR index between pregnant women with vitamin D deficiency and metabolic syndrome ($p=0.040$) and without it ($p=0.023$). Serum 25(OH)D levels in early pregnancy in persons with metabolic syndrome positively correlated with glucose ($r=0.361$; $p>0.05$), HbA1c ($r=0.355$; $p>0.05$) and HOMA-IR ($r=0.239$; $p>0.05$) in vitamin D deficiency and negative in 25(OH)D insufficiency: $r=-0.795$ ($p<0.05$), $r=-0.464$ ($p>0.05$) and $r=-0.500$ ($p>0.05$), respectively.
***Conclusions.*** Pregnant women with metabolic syndrome and vitamin D deficiency, compared with pregnant women without this syndrome, may have higher levels of immunoreactive insulin and HOMA-IR index. Between the women with the deficiency and insufficiency of vitamin D and the parameters of carbohydrate metabolism in the metabolic syndrome a multidirectional correlation was revealed.
***Keywords:*** *metabolic syndrome, pregnancy, vitamin D, carbohydrate metabolism, correlation.*

## Показники вуглеводного обміну та рівень вітаміну D у вагітних із метаболічним синдромом

***Є.М. Ахундова***

***Мета дослідження:*** оцінювання рівня вітаміну D та його взаємозв'язку з показниками вуглеводного обміну у жінок із метаболічним синдромом у I триместрі вагітності.
***Матеріали та методи.*** Проведено обстеження 120 вагітних, з них у 60 пацієнток до вагітності діагностовано метаболічний синдром (основна група) та 60 пацієнток без даної патології (контрольна група). Усім жінкам визначали рівні глюкози у крові натще, глікованого гемоглобіну, імунореактивного інсуліну, індекс HOMA-IR та рівень вітаміну D у сироватці крові.
***Результати.*** У жінок в основній групі середній рівень вітаміну D становив 15,76±3,77 нг/мл, у групі контролю – 17,20±3,76 нг/мл. Концентрація вітаміну D менше 20 нг/мл в основній групі встановлена у 70,0% пацієнток, у групі контролю – у 51,7%, 20–30 нг/мл – у 30,0% та 48,3% відповідно ($p<0,05$). Середній показник індексу маси тіла був достовірно вищий у жінок основної групи щодо контрольної ($p=0,041$) та у пацієнток із метаболічним синдромом не відрізнявся від значень у жінок з дефіцитом вітаміну D та його недостатністю. Однак індекс маси тіла був достовірно вищий на тлі дефіциту вітаміну D між пацієнтками з метаболічним синдромом і без метаболічного синдрому ($p=0,001$). Виявлено значну відмінність показників концентрації імунореактивного інсуліну та величини індексу HOMA-IR між вагітними з дефіцитом вітаміну D та метаболічним синдромом ($p=0,040$) і без нього ($p=0,023$). Рівні 25(OH)D у сироватці крові на ранніх термінах вагітності при метаболічному синдромі позитивно корелювали з вмістом глюкози ($r=0,361$; $p>0,05$), HbA1c ($r=0,355$; $p>0,05$) та величиною індексу HOMA-IR ($r=0,239$; $p>0,05$) при дефіциті вітаміну D і негативно – при недостатності 25(OH)D: $r=-0,795$ ($p<0,05$), $r=-0,464$ ($p>0,05$) та $r=-0,500$ ($p>0,05$) відповідно.
***Висновки.*** Вагітні з метаболічним синдромом та дефіцитом вітаміну D порівняно з вагітними без цього синдрому можуть мати більш високі показники рівнів імунореактивного інсуліну та індексу HOMA-IR. Між дефіцитом та недостатністю вітаміну D і параметрами вуглеводного обміну при метаболічному синдромі виявлено різноспрямований кореляційний зв'язок.
***Ключові слова:*** *метаболічний синдром, вагітність, вітамін D, вуглеводний обмін, кореляція.*





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The increase in the prevalence of metabolic syndrome (MS), especially among the female population, has become a serious problem in the health care system. Metabolic syndrome is a set of interrelated pathological conditions characterized by central obesity, hypertension, insulin resistance and atherogenic dyslipidemia. More and more data are emerging that link individual components of MS with the growing prevalence of women's dysfunctional reproductive health [1–3].

Significant links have been established between the main components of MS, namely dyslipidemia, insulin, glucose metabolism, obesity, body mass index (BMI), blood pressure (BP) and vitamin D levels [4]. Studies have shown that vitamin D3 deficiency plays a role in the pathogenesis of MS [5, 6].

Vitamin D deficiency (25 (OH)D) is a global health problem that increases the risk and severity of many diseases in all age groups [7, 8]. There is a frequent prevalence of MS among women of fertile age, which is attributed to the risk factor for gestational complications [9]. Worldwide, the prevalence of vitamin D deficiency and insufficiency among pregnant women ranges from 5 to 84% [10]. The relationship between MS and reproductive changes is not excluded [11].

Vitamin D deficiency is currently being proposed as one of the possible risk factors for MS.

**The aim** of the study was to assess the level of vitamin D and its relationship with the parameters of carbohydrate metabolism in women with metabolic syndrome in the first trimester of pregnancy.

## MATERIALS AND METHODS

120 pregnant women were examined: 60 women were diagnosed with MS before pregnancy (the main group) and 60 patients did not suffer from MS (the control group). The criteria for inclusion in the study were: I trimester of gestation, single pregnancy, over 18 years of age, actual residence in Baku and the suburbs for at least 6 months before pregnancy; women suffering from MS before pregnancy.

Exclusion criteria: multiple pregnancies, HIV infection, a history of parathyroid, kidney or liver diseases, chronic malabsorption syndromes, age under 18, known (or suspected) drug or alcohol abuse, patients with acute or chronic diseases, patients who received vitamin D or calcium supplements in the previous 3 months. Informed consent was obtained from the patients. The study was conducted in accordance with the principles of the Helsinki Declaration.

Body mass index (BMI) was calculated using the following formula:

$$BMI = \frac{m}{height^2},$$

where: m is body weight in kilograms, height in meters.

The state of carbohydrate metabolism was assessed by the level of glycated hemoglobin (HbA1c) in blood serum, which was determined by direct photometric method using the Glycohemoglobin (HbA1c liquidirect) kit (Human GmbH, Germany). Insulin was determined by immunochemiluminescence analysis, glucose by photometric method. To determine insulin resistance, the HOMA-IR index (Homeostasis Model Assessment of Insulin Resistance) was calculated using the formula:

$$HOMA\text{-}IR = \frac{fasting\ insulin\ (mcED/ml)\ x\ fasting\ plasma\ glucose\ (mmol/L)}{22,5}$$

Total 25-hydroxyvitamin D (25(OH)D) analyzed using electrochemoluminescent immunoassay on a Roche Cobas ® analyzer (Roche Diagnostics, Basel, Switzerland). Detection range: 3.0–70.0 ng/ml for 25(OH)D; above 15 ng/ml, coefficient of variation between assays: 11.5% and coefficient within the assay: 6.5% [12]. According to the recommendations of the Endocrine Society [13], women with a concentration of 25(OH)D in serum <20 ng/ml were considered deficient in vitamin D. Women with a concentration of 25(OH)D in serum >20 ng/ml were considered non-deficient (including both insufficient (from 20 to 30 ng/ml) and sufficient (above 30 ng/ml) [14].

Statistical analysis was carried out in Microsoft System Excel 2016 using statistical software SPSS (USA). The differences between the groups were compared using the t-test and Pearson's chi-square test. The Spearman correlation coefficient is calculated. The value of $p<0.05$ was considered statistically significant.

## RESULTS

The average concentration of vitamin D in the total sample (n=120) was 16.5±0.6 ng/ml (6.25–28.7 ng/ml). In the main group, the average vitamin D level was 15.76±3.77 ng/ml (6.25–25.4 ng/ml). In the control group, vitamin D levels ranged from 9.74 to 28.7 ng/ml, which averaged 17.20±3.76 ng/ml. There was no significant difference between the values of vitamin D in the main and control groups – p=0.787 (t=0.27). At the same time, the level of vitamin D<20 ng/ml in the main group was determined in 42 (70.0%) patients, in the control group – in 31 (51.7%) patients.

The concentration of 25(OH)D 20-30 ng/ml in the main and control groups was determined in 18 (30.0%) and 29 (48.3%; p<0.05) patients, respectively. Depending on the concentration of vitamin D, the main and control groups were divided into subgroups: patients with a vitamin D level of less than 20 ng/ml and with a level of 20-30 ng/ml. Average level 25(OH)D in patients of the main group with deficiency and insufficiency vitamin content was 13.87±2.77 ng/ml and 21.73±1.81 ng/ml, respectively, in the control group – 15.24±2.75 ng/ml and 22.51±2.08 ng/ml.

The general characteristics and parameters of carbohydrate metabolism in patients with different concentrations of vitamin D in the main and control groups are presented in Table.1.

From the table.1 it follows that the age groups were comparable. In the main group of patients with a deficiency of 25(OH)D. The number of pre-pregnant women was significantly lower than in the control group ($\chi^2$=5,777; p=0.017). There were no significant differences in parity.

The average BMI, as expected, in patients with MS exceeded this indicator in the control group (p=0.041). Normal BMI in the main group was observed only in 1.7% of cases (n=1), in the control group – in 31.7% of cases ($\chi^2$=19.440; p<0.01). In the main group, the average BMI did not differ significantly in patients with vitamin D deficiency and insufficiency (t=0.80; p=0.425). A comparative analysis of BMI in pregnant women with MS and vitamin D deficiency with patients without MS with vitamin deficiency revealed a significant difference (t=3.50; p=0.001).


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There was also a significant difference between BMI in patients with and without MS with vitamin D deficiency (t=2.58; p=0.013). There was no significant difference in blood glucose levels between the groups, although it was higher in patients with MS. In patients of the main group with deficiency and insufficiency of 25(OH)D in comparison with the same indicator in the control group was higher by 10.2% (t=0.94; p=0.349) and by 14.9% (t=1.42; p=0.163), respectively.

Fasting glucose level in the group of patients with 25(OH)D deficiency and MS in 7.1% of cases, and in the group with vitamin insufficiency in 12.9% of cases exceeded the norm. In the control group in patients with deficiency and deficiency of 25(OH)D glucose levels did not exceed normal values. The maximum level of HbA1c was observed in pregnant women of the main group with vitamin D deficiency, which exceeded that in patients with vitamin insufficiency by 9.4% (t=0.75; p=0.455). When comparing patients of the main and control groups with deficiency and insufficiency of 25(OH)D revealed an increase in HbA1c by 18.3% (t=1.84; p=0.069) and 4.3% (t=0.38; p=0.706), respectively.

In the main group of patients with deficiency and insufficiency of 25(OH)D in 7.1% and 5.6% of cases, the level of HbA1c exceeded 6.5%, in the control group, the value of glycated hemoglobin was within the normal range. The average level of immunoreactive insulin in all study groups was within the normal range. In patients with MS and vitamin D deficiency compared with pregnant women of the control group with a deficiency of 25(OH)D it was higher by 24.4% (t=2.09; p=0.040). There was a significant increase in the NOMA-IR index between these groups of patients (t=2.32; p=0.023).

Correlation analysis between vitamin D and carbohydrate metabolism indicators showed multidirectional relationships and, mainly, statistically insignificant (Table 2).

As follows from the data in Table 2, the glucose value correlated with 25(OH)D strong feedback ($p<0.05$) in patients of the main group with vitamin D insufficiency and moderate direct feedback ($p>0.05$) with its deficiency. In the control group, the relationship between these indicators was also reversed, but weak ($p>0.05$). Glycated hemoglobin correlated with 25(OH)D with its deficiency in the main and control groups with moderate and weak connections, respectively, but with insufficient vitamin D content, this connection was somewhat strengthened, especially in patients without MS ($p<0.05$).

There was a weak association of insulin and HOMA index in the main group and a moderate association in the control group.

*Table 1*

**General characteristics and indicators of carbohydrate metabolism in patients with different levels of vitamin D**

| Indicator | Main group, n=60 | | Control group, n=60 | | |
|---|---|---|---|---|---|
| | Vitamin D level <20 ng/ml, n=42 | Vitamin D level 20–30 ng/ml, n=18 | Vitamin D level <20 ng/ml, n=31 | Vitamin D level 20–30 ng/ml, n=29 | |
| Age, years | 29,79±4,43 | 28,43±4,94 | 27,53±4,03 | 24,33±3,67 | p1=0,838<br>p2=0,707<br>p3=0,509 |
| Pregnancy, n (%):<br>first<br>repeated | <br>8 (19,0)<br>34 (81,0) | <br>6 (33,3)<br>12 (66,7) | <br>14 (45,2)<br>17 (54,8) | <br>13 (44,8)<br>16 (55,2) | p1=0,231<br>p2=0,017<br>p3=0,436 |
| Primiparous, n (%) Repeat-generative | 28 (66,7)<br>14 (33,3) | 10 (55,6)<br>8 (44,4) | 19 (61,3)<br>12 (38,7) | 19 (65,5)<br>10 (34,5) | p1=0,414<br>p2=0,636<br>p3=0,495 |
| BMI, kg/m$^2$ | 36,73±2,57 | 34,11±2,01 | 24,09±2,54 | 26,28±2,28 | p1=0,425<br>p2=0,001<br>p3=0,013 |
| Glucose, mmol/l | 5,02±0,48 | 5,56±0,56 | 4,51±0,25 | 4,73±0,17 | p1=0,467<br>p2=0,349<br>p3=0,163 |
| Glycated hemoglobin,% | 6,17±0,55 | 5,59±0,54 | 5,04±0,27 | 5,35±0,33 | p1=0,455<br>p2=0,069<br>p3=0,706 |
| Insulin, MkEd/ml | 17,1 ±1,31 | 15,76±1,58 | 12,92±1,51 | 12,67±0,93 | p1=0,516<br>p2=0,040<br>p3=0,098 |
| HOMA-IR | 4,25±0,63 | 3,50±0,58 | 2,59±0,34 | 2,72±0,25 | p1=0,385<br>p2=0,023<br>p3=0,223 |

*Note:* p is the statistical significance of the differences in indicators:
p1 – between the level of vitamin D <20 and the level of 20–30 ng/ml of the main group;
p2 – between the level of vitamin D <20 of the main and control groups;
p3 – between the level of vitamin D 20–30 ng/ml of the main and control groups



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*Table 2*

**Correlation relationship of vitamin D with carbohydrate metabolism indicators**

| Indicator | Main group | | | | Control group | | | |
|---|---|---|---|---|---|---|---|---|
| | Vitamin D level <20 ng/ml, n=42 | | Vitamin D level 20–30 ng/ml, n=18 | | Vitamin D level <20 ng/ml, n=31 | | Vitamin D level 20–30 ng/ml, n=29 | |
| | r | p | r | p | r | p | r | p |
| Glucose | 0,361 | >0,05 | -0,795 | <0,05 | 0,133 | >0,05 | -0,271 | >0,05 |
| HbA1c | 0,355 | >0,05 | -0,464 | >0,05 | 0,268 | >0,05 | -0,629 | <0,05 |
| Insulin | -0,011 | >0,05 | 0,241 | >0,05 | 0,430 | >0,05 | 0,271 | >0,05 |
| HOMA-IR | 0,239 | >0,05 | -0,500 | >0,05 | 0,404 | >0,05 | -0,157 | >0,05 |

Low vitamin D levels during pregnancy are common and can negatively affect health. Vitamin D deficiency is associated with various diseases, including MS, which is clinically determined by a complex of metabolic and vascular disorders [14].

In this study, we found a reduced concentration of vitamin D in serum in the MS group compared with the control group, which is consistent with the literature data [4, 15–17].

In our study, the relationship between vitamin D and such metabolic parameters as glucose, glycated hemoglobin, insulin, HOMA-IR was determined. There was a statistically significant difference in BMI, immunoreactive insulin and HOMA-IR between pregnant women with vitamin D deficiency with and without MS. This study showed that levels of 25(OH)D in blood serum in early pregnancy in women with MS positively correlated with glucose and HbA1c with vitamin deficiency and negatively – with an insufficiency of 25(OH)D. In the current study, fasting insulin concentrations were higher in women with vitamin D deficiency than in women without MS.

Nevertheless, there were no significant differences in the concentration of fasting glucose and glycated hemoglobin between the group with and without MS. Similar studies have shown that vitamin D has been associated with MS, including insulin resistance and obesity [18–22]. Insulin resistance during pregnancy can lead to termination of pregnancy [23–25].

Thus, our study suggests that vitamin D deficiency may be associated with immunoreactive insulin and insulin resistance involved in the development and progression of MS.

## CONCLUSION

Pregnant women with MS with vitamin D deficiency in comparison with pregnant women without MS may have higher levels of immunoreactive insulin and HOMA-IR. There is a multidirectional correlation between vitamin D deficiency and insufficiency and parameters of carbohydrate metabolism in MS. Well-planned studies are needed to determine if there is a link between 25(OH)D and immunoreactive insulin and HOMA-IR in early pregnancy with MS characteristic of pregnant women.

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