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Fund “Nauka” Project № 20005 Resume – Competition-based Session 2020:

“Methylmalonic acid and 25-hydroxy vitamin D3 as new biomarkers for determining functional deficiencies of vitamin B12 and vitamin D3 during pregnancy”

Project leader: Assoc. prof. Daniela Ivanova Gerova, MD, PhD

Aim: study of vitamin D3 and vitamin B12 status of pregnant women with normal and pathological pregnancy with the help of routine and new biomarkers that reliably reflect the functional deficiencies of vitamin D3 and vitamin B12, and to investigate the relationships with clinical characteristics and laboratory parameters assessing the course of pregnancy and fetal development.

A balanced diet containing a variety of micronutrients such as vitamins and minerals is essential for the optimal course of pregnancy. As a result of changing lifestyles, the prevalence of vitamin D and vitamin B12 deficiency or insufficiency is increasing in various population groups, including pregnant women.

In Bulgaria, data on the vitamin D and vitamin B12 status of pregnant women are very scarce, which attracted our research interest. Therefore, the aim of this study was to determine the vitamin D and vitamin B12 status of pregnant women with normal and pathological pregnancies and to assess the role of their deficiency and/or insufficiency on the course and outcome of pregnancy.

Objectives:

1. Development of a new chromatographic method with mass-selective detection for quantification of serum methyl malonic acid (MMA);
2. Examination of established and new biomarkers and development of a new algorithm for early assessment of functional deficiencies of vitamins D3 and B12 in pregnant women in the first and third trimesters of pregnancy.

Patients: this 3-year study will include 300 pregnant women over the age of 18, selected according to inclusion and exclusion criteria.

An innovative, original combination of **methods** will be used:

1. Clinical methods – assessment of the course of pregnancy and fetal development;
2. Immunochemical methods – determination of total vitamin B12 and holotranscobalamin;
3. Chromatographic methods – determination of MMA and 25-hydroxy-vitamin-D3;
4. Questionnaires – assessment of diet and medical history.

Expected results:

1. A new modern chromatographic method with mass-selective detection for quantification of serum MMA will be developed;
2. A new data will be collected on the role of functional deficiencies of vitamins B12 and D3 for the occurrence of pregnancy complications, affecting both mother and newborn, insufficiently studied in Bulgaria and worldwide;
3. Through statistical modelling the diagnostic reliability of a new algorithm for a combination of biomarkers will be established, allowing early detection of functional deficiencies of vitamins B12 and D3 in pregnant women.

An important contribution of the project activities is the development of a modern liquid chromatography method with mass spectrometric detection for the analysis of methylmalonic acid (MMA) in blood serum, characterized by high analytical performance, which can be used as a functional biomarker for the assessment of vitamin B12 status.

Main results:

Vitamin D status:

1. The vitamin D status of Bulgarian pregnant women is comparable to that of women with higher social status in developed countries around the world.
2. A seasonal dependence of serum 25(OH)D levels was found, with optimal levels in the summer half-year and suboptimal levels in the winter half-year.
3. Increased BMI was an adverse factor regarding vitamin D status in the pregnant women studied.
4. More than two-thirds of the women studied supplemented with vitamin D, with almost 22% taking doses many times higher than the 600 IU/ day recommended by health authorities, which significantly improved their vitamin D status.
5. Women with pre-eclampsia and obesity were less likely to supplement with vitamin D, which predicted their significantly worse vitamin D status.
6. The highest incidence and risk of preterm birth was found in women with pre-eclampsia, correlating with serum 25(OH)D levels.
7. The highest incidence and risk of low birth weight was found in women with pre-eclampsia, with vitamin D intake being a significant predictor of low birth weight.

Vitamin B12 status:

8. The prevalence of vitamin B12 deficiency/ insufficiency is comparable to that in developed countries.
9. The winter season is more favorable for vitamin B12 status.
10. Two-thirds of the women studied were taking vitamin B12 supplements, and about half of them were taking doses exceeding the recommended daily intake.
11. In women with pre-eclampsia, there was no significant difference between serum concentrations of active vitamin B12 and those of healthy controls, but there was a trend towards a statistical difference for MMA.

12. In women with pre-eclampsia, there was a statistically significant increase in the risk of having a low-birth-weight baby with a worsening of the vitamin B12 status.

Important achievements:

13. The vitamin D and vitamin B12 status of a representative sample of pregnant women from Northeastern Bulgaria was determined.
14. The role of their deficiency and insufficiency in the occurrence of complications during pregnancy was studied.
15. The role of vitamin supplementation in improving the vitamin status of pregnant women was established.

In conclusion, the results of the study warrant a change in the standard of care for pregnant women, adding serum vitamin D and vitamin B12 testing to the mandatory panel of laboratory tests, and recommending supplementation with these vitamins when necessary to prevent possible adverse pregnancy complications.