Doctoral School of Interdisciplinary Medicine

MICRONUTRIENT SUPPLEMENTATION AMONG HUNGARIAN PREGNANT WOMEN WITH A SPECIAL FOCUS ON VITAMIN D

Summary of PhD Thesis

Evelin Oltean-Polanek

Supervisor:

Dr. Andrea Szabó

Department of Public Health

Albert Szent-Györgyi Medical School

University of Szeged

Szeged

2025

INTRODUCTION

Pregnancy is a physiologically demanding period in which maternal nutrition must simultaneously support the mother's health and the growth and development of the fetus. Insufficient intake of critical micronutrients has been associated with maternal complications, impaired fetal development, and long-term health risks for the offspring. Despite clear national and international guidelines, deficiencies in essential nutrients remain widespread.

Among the key micronutrients, folic acid (FA), vitamin D (VD), omega-3 fatty acids (O3), and prenatal multiple micronutrient supplements (PMM) play particularly important roles. FA supplementation is well established in the prevention of neural tube defects and has been linked to reduced risks of congenital anomalies, preterm birth, and autism spectrum disorders. Guidelines recommend 400 µg daily beginning before conception and continuing through the first trimester. However, adherence is often suboptimal, as many women initiate supplementation only after recognizing pregnancy.

VD has crucial functions beyond bone metabolism, including immune regulation, placental activity, and insulin sensitivity. Deficiency in pregnancy has been linked to gestational diabetes, preeclampsia, low birth weight, impaired uterine contractions, and preterm delivery. While sufficiency is generally defined as serum 25(OH)D >50 nmol/L, many experts recommend ≥75 nmol/L. Worldwide, an estimated 50% of the population presents with VD insufficiency, and 6–20% suffer from deficiency (<30 nmol/L). The determinants of VD deficiency are multifaceted. Dietary intake of VD is typically insufficient to meet daily requirements (including Hungary), with average intakes often below 5 µg/day, making supplementation essential. Most guidelines suggest 10–15 µg (400–600 IU) VD daily, although some scientific societies, including the Hungarian one, recommend that higher intakes (37.5–50 µg/day) are necessary to achieve sufficiency.

O3 fatty acids, particularly DHA and EPA, are vital for fetal brain development and maternal cardiovascular health. Their intake is associated with lower risk of preeclampsia, improved lipid profiles, better fetal neurocognitive development, and prolonged gestation. European Food Safety Authority (EFSA) recommendations suggest a daily intake of 250 mg EPA + DHA, supplemented with an additional

100 mg DHA, starting around the 20th gestational week Nonetheless, adherence to recommendations remains poor in many countries, including Hungary.

PMM provide a broad range of nutrients, combining FA, VD, iron, and others. The WHO recommends their use particularly in low- and middle-income countries, though their role is increasingly emphasized elsewhere. The recommended duration of PMM intake is not explicitly defined, but given the health benefits of their individual components, continued use across the entire course of pregnancy is generally advised. Despite their availability, PMM use does not guarantee correct intake of individual micronutrients, as awareness of composition and timing often remains limited.

Previous Hungarian studies have primarily focused on FA, showing very low rates of preconceptional use. Information on VD, O3, and PMM is scarce, and adherence to timing and dosage guidelines has not been assessed comprehensively. Moreover, biomarker data confirming vitamin D status in pregnancy are lacking.

This dissertation therefore addresses these knowledge gaps by integrating self-reported intake and adherence data with serum vitamin D concentrations, while also examining predictors and maternal–neonatal outcomes.

AIMS

To bridge these gaps, the present work was designed to provide a comprehensive overview of micronutrient supplementation among Hungarian pregnant women. By combining intake data with biological validation and clinical outcomes, the study aimed to generate evidence that could inform both public health policies and clinical practice. The specific objectives were as follows:

1. To assess prevalence and patterns of FA, VD, O3, and PMM supplementation among Hungarian pregnant women.
2. To evaluate adherence to guideline-recommended timing and duration of supplementation for each micronutrient, and to develop a composite adherence score.

3. To identify sociodemographic, obstetric, and lifestyle predictors of correct supplementation.
4. To analyze dietary intake of vitamin D and compare it with supplement intake.
5. To measure maternal serum 25(OH)D concentrations and classify vitamin D status.
6. To explore associations between supplementation and adherence with pregnancy, delivery, and neonatal outcomes.

MATERIALS AND METHODS

Study Design and Participants

This dissertation is based on data from the Quantifying Maternal Non-Obstetrical Risk Factors for Preterm Birth—Retrospective and Prospective Study (MANOR study), conducted at the University of Szeged in 2019. After excluding multiple pregnancies, 100 mothers consented to participate and were enrolled as cases (<37 gestational weeks). For each case, two mothers with term deliveries were selected as controls, matched by age and date of delivery, resulting in a control group of 200, and a final study population of 300 women. For the purposes of this dissertation, both groups were analyzed together. Instead of preterm birth as the primary outcome, the focus was shifted to micronutrient supplementation practices, adherence to recommendations, and VD status.

Data Collection and Variables

Information was collected from multiple sources:

Questionnaire: captured demographic data (age, education, residence, relationship status), obstetric history (parity, miscarriages, previous preterm birth, timing of first antenatal care visit [≤12 or >12 weeks of gestation]), conception-related factors (contraceptive use, infertility treatment, mode of conception, pregnancy planning), lifestyle factors, (lifestyle counseling received during pregnancy, the sources of such information, and whether participants had adopted more conscious dietary habits, gestational weight gain) and supplementation practices for FA, VD, O3, and PMM. Product names, dosages, and timing were recorded.

Dietary assessment: dietary VD intake was estimated using a validated food frequency questionnaire (FFQ) focusing on vitamin D-rich foods (fish, milk, yogurt, margarine).

Medical documentation: maternal health records provided data on gestational complications (gestational diabetes mellitus, hypertension), mode of delivery, inadequate uterine contraction, cephalopelvic disproportion, and premature rupture of membranes. Neonatal records included birth weight and preterm status.

Biological samples: maternal venous blood was collected after delivery and serum 25-hydroxyvitamin D [25(OH)D] concentrations were measured by chemiluminescent microparticle immunoassay.

Supplement use was classified as appropriate, inappropriate, or non-use according to guideline-based timing and duration. Correct FA use meant initiation before conception and continuation to at least the 12th week. Correct VD and PMM use meant initiation by the 9th week and continuation until delivery. Correct O3 use was defined as initiation by the 20th week and continuation until delivery. A composite adherence score (0–6) was calculated for FA, VD, and O3 combined, based on the appropriateness of their intake.

VD status was defined according to the Institute of Medicine (2009) and Hungarian consensus (Takács et al., 2022): deficiency (<30 nmol/L), insufficiency (30–50 nmol/L), sufficiency (≥50 nmol/L), and optimal (≥75 nmol/L).

Ethical approval for the study was obtained. Participation in the study was voluntary, and all participants provided written informed consent before enrollment

Statistical Analysis

Descriptive statistics were used to characterize the cohort. Chi-square or Fisher's exact test compared categorical variables, while Mann–Whitney U and Kruskal–Wallis tests were applied for non-normally distributed continuous data. Correlations between dietary/supplemental VD intake and serum levels were assessed using Spearman's coefficients. Logistic regression models were used to identify predictors of supplementation and adherence, expressed as odds ratios (OR) and adjusted odds ratios (AOR) with 95% confidence intervals. Associations between adherence categories and maternal/neonatal outcomes were also evaluated by logistic regression. A p-value <0.05 was considered significant.

RESULTS

Study Population

The mean maternal age was 32 years; 42% were ≥35 years. University degree was held by 41.5% of mothers, while 8.5% had only primary education. Most lived with a partner (97.6%) and 45% resided in county towns. Planned pregnancy was reported by 80.8%, and 41.6% were primiparas. 11.8% participated in fertility treatment. A previous miscarriage was noted by 23.2%. Early antenatal care (≤12 weeks) was reported by 83.7%, 73.3% received professional advice on lifestyle, while 77.6% reported paying more attention to diet during pregnancy. Excessive weight gain was observed in 39.3%. GDM was diagnosed in 15.2% and gestational hypertension in 10.8%. Cesarean section occurred in 53.7%, preterm birth in 33.3%, and low birth weight in 21.6%. 31.6% of the pregnant women experienced inadequate uterine contractions, 7.5% cephalopelvic disproportion, and 35.5% abnormal rupture of membranes.

Supplementation Prevalence

PMM use was reported by 69%. FA was used by 88.7%, VD by 77.6%, and O3 by 60.1%. Many women combined products: 23.7% took FA from PMM and other sources, 13.5% took VD from both, and 10.8% took O3 from both. A small proportion relied solely on single supplements: 21.3% for FA, 8.8% for VD, and 13.5% for O3. Interestingly, only 25.9% of women who consumed prenatal vitamins were aware that these products contained VD.

Adherence

Adherence was highest for VD (41.1%), followed by O3 (37.5%), PMM (36%), and FA (31%). Inappropriate use was most common for FA (58%), while non-use was highest for O3 (41.3%). Using the composite adherence score, 30.4% were categorized as high, 50.2% as moderate, and 19.4% as low/non-users.

Characteristics of women according to adherence levels

Among population characteristics, planned pregnancy was associated with higher adherence across all micronutrients. Higher maternal education ($p=0.005$) and older age ($p=0.032$) were positively related to FA, O3, and combined adherence, whereas paternal education and marital status showed no effect. Living in the county town appeared to result in high adherence, in the case of FA ($p=0.007$).

Predictors of Supplementation and Adherence

Parity was a consistent determinant: primiparas had higher odds of correct PMM (AOR ≈2.1, borderline significant), correct VD (AOR 3.37, p=0.004), correct O3 (AOR 2.66, p=0.005), and correct FA use (AOR 3.16, p=0.04). Previous miscarriage predicted appropriate O3 use (AOR 2.21, p=0.043). Early antenatal care strongly increased adherence: correct VD (AOR 2.75, p=0.023), correct FA (AOR 4.70, p=0.009), and correct combined use (AOR 3.75, p=0.012). Women with normal gestational weight gain during pregnancy were significantly more likely to be in the appropriate or near-appropriate adherence groups (AOR 3.18, p= 0.02), compared with those whose weight gain was below the recommended levels.

Dietary VD Intake and Supplement Use

Mean dietary VD intake was 2.08 µg/day, mainly from milk, fish, margarine, and yogurt, in order. More than half did not consume fish, and only 8% consumed it ≥2 times/week. This intake was far below recommendations, and no sociodemographic associations were identified. Total VD intake (dietary + supplemental) averaged 19.3 µg/day. While 44.5% reached ≥15 µg/day, only 11% reached ≥50 µg/day. Higher intake was observed among women with higher education, contraceptive use before conception, and ART.

Maternal Serum VD

Mean serum 25(OH)D was 52.8 nmol/L (median 52.4). Deficiency was found in 13.1%, sufficiency in 55.6%, and optimal status in 12.1%. Higher levels were associated with early antenatal care, ART, and receiving advice from a gynecologist. No associations were observed with sociodemographic or obstetric parameters. Serum VD correlated with supplement use ($r \approx 0.26$, $p<0.001$) but not with dietary intake.

Associations with Outcomes

Pregnancy complications: Appropriate O3 use was associated with lower odds of GDM (OR 0.06, p=0.047). Total VD intake above recommendations was protective against gestational hypertension (OR 0.44, p=0.043) and showed a borderline protective effect against GDM (OR 0.56, p=0.083).

Delivery outcomes: Inappropriate O3 use increased the risk of inadequate uterine contraction (OR 4.24, p=0.005). FA supplementation, both appropriate and inappropriate, reduced the risk

of cesarean section (OR 0.25–0.31, p≈0.036–0.038). No associations were observed for preterm birth, cephalopelvic disproportion, or abnormal membrane rupture.

Serum VD and outcomes: Insufficiency was associated with increased odds of inadequate uterine contractions (OR 2.95, p=0.030), while optimal levels were linked to higher likelihood of abnormal rupture of membranes (OR 5.59, p=0.002).

DISCUSSION

This dissertation provides the first comprehensive overview of micronutrient supplementation among Hungarian pregnant women, integrating intake and adherence data with serum VD levels and clinical outcomes. The results highlight a paradox: while the majority of women reported taking supplements, adherence to guideline-based recommendations was poor, and biological sufficiency, particularly for VD, was achieved only by a minority.

Intake and Adherence Patterns

The prevalence of supplement use was high: nearly 90% reported FA, 78% VD, 60% O3, and 69% PMM. However, correct adherence ranged from 31% for FA to 41% for VD. Inappropriate use was especially frequent for FA (58%), reflecting late initiation. These findings mirror earlier Hungarian data and international studies where supplementation prevalence was high but adherence remains limited. Population-based studies from North America and Northern Europe have similarly shown that although most women use supplements, only a minority follow recommendations regarding timing and duration.

O3 supplementation was the least common in our cohort, consistent with global patterns despite growing evidence of benefits for neurodevelopment and metabolic outcomes. The underuse of O3 may reflect limited awareness, cost, or lack of clear national guidelines. PMM use was common but varied widely in composition, and many women were unaware of their precise nutrient contents, raising concerns about dose adequacy.

Predictors of Adherence

Parity and antenatal care timing emerged as the most consistent predictors of correct use. Primiparas and women who began care ≤12 weeks were significantly more likely to use supplements correctly. Planned pregnancy, older maternal age, and higher education were also positive determinants, while paternal education and marital status had no influence. These results underline the importance of early pregnancy counselling and the role of health literacy in shaping behaviors.

Although three-fourths of women reported receiving advice from health professionals, this was not associated with adherence, raising concerns about the effectiveness of communication during counselling. This is consistent with international studies highlighting barriers such as limited awareness, forgetfulness, or poor quality of advice. Successful interventions reported elsewhere, including structured education, SMS reminders, and free provision of supplements, could be adapted to Hungary.

Vitamin D Intake and Serum Status

Dietary VD intake was extremely low (≈2 μg/day, reflecting that of the general population), and only supplementation contributed meaningfully to total intake. Yet even with supplementation, only 12% of women reached the Hungarian consensus threshold of ≥75 nmol/L. This discrepancy highlights the inadequacy of typical supplement doses and confirms that dietary strategies alone cannot ensure sufficiency.

Serum VD was correlated with supplement intake but not with diet. Higher levels were observed among women with ART, early antenatal care, and gynecologist advice. Nonetheless, more than 40% remained insufficient. This emphasizes the urgent need for stronger supplementation recommendations, consistent with RCTs showing that higher daily doses are both safe and effective.

Associations with Outcomes

Micronutrient use was linked to several maternal and delivery outcomes. Correct O3 supplementation was associated with reduced odds of GDM, in line with evidence that O3 improves insulin sensitivity and reduces inflammation. Conversely, inappropriate O3 use increased the risk of inadequate uterine contractions, possibly due to altered prostaglandin activity.

FA supplementation was associated with a reduced risk of cesarean section, regardless of whether use was strictly appropriate. While direct evidence on FA and delivery outcomes is limited, indirect benefits through improved placental function and reduced complications are plausible.

Unexpectedly, higher VD serum concentrations were associated with increased risks of certain labor complications, such as uterine contractility disorders, and abnormal membrane rupture. Nevertheless, they highlight the complexity of interpreting serum VD in pregnancy. By contrast, higher VD intake (≥ recommendations) was protective against gestational hypertension and suggested a reduced risk of GDM, consistent with supplementation trials.

Implications

The findings have significant public health and clinical implications. Although most Hungarian women take supplements, inappropriate timing and insufficient dosing undermine their effectiveness. Early antenatal care, targeted education, and tailored counselling are crucial to improving adherence. For VD, supplementation guidelines should be revised to reflect higher physiological needs, and routine counselling should emphasize timing and dosage. Public health campaigns and digital interventions may also help address persistent knowledge gaps.

CONCLUSIONS

This dissertation provides the first comprehensive analysis of FA, VD, O3, and PMM supplementation among Hungarian pregnant women, integrating self-reported intake and adherence data with biomarker measurements of VD and maternal–neonatal outcomes. The results clearly demonstrate that although supplementation is widespread, correct adherence to guideline-based recommendations remains suboptimal.

The prevalence of use was high, yet adherence to recommended timing and duration was low, with only 30–40% of women classified as appropriate users. Inappropriate use was most common for FA, largely due to late initiation, while O3 supplementation remained underutilized. These findings highlight a gap between knowledge and practice that persists despite decades of recommendations.

Sociodemographic and obstetric predictors strongly influenced supplementation behaviors. Primiparity, planned pregnancy, higher education, and early antenatal care were associated with better adherence. Conversely, younger age, lower education, and unplanned pregnancies were linked to poor adherence. Advice from health professionals, although frequently received, did not translate into correct practices, suggesting ineffective communication strategies.

Dietary VD intake was very low, and supplementation was the only meaningful source. Nevertheless, maternal serum concentrations showed that sufficiency was not achieved in the majority of women, with only 12% reaching the optimal Hungarian consensus threshold of ≥75 nmol/L. This demonstrates that current supplementation practices are inadequate for ensuring biological sufficiency.

Associations with outcomes underscored the clinical importance of adherence. Correct O3 use was linked to reduced odds of GDM, while inappropriate O3 use increased the risk of inadequate uterine contractions. FA supplementation, regardless of strict appropriateness, reduced the likelihood of cesarean delivery. Unexpectedly, higher VD serum levels were associated with certain intrapartum complications, although these findings likely reflect confounding and warrant further research. By contrast, higher total VD intake was protective against gestational hypertension and showed a tendency to reduce GDM risk.

Overall, the findings highlight a paradox: while most pregnant women in Hungary use supplements, few do so in accordance with evidence-based guidelines, and biological sufficiency is rarely achieved. To improve outcomes, antenatal care must prioritize early counselling, effective communication, and individualized supplementation strategies. Updated national recommendations, particularly regarding VD dosing, are urgently needed.

ORIGINAL FINDINGS

This dissertation contributes several new insights to the field of maternal nutrition in Hungary and internationally.

- First, it is the first Hungarian study to examine FA, VD, O3, and PMM supplementation simultaneously, evaluating both prevalence and adherence. Previous Hungarian research focused mainly on FA, with little information on other micronutrients or on the

appropriateness of timing and duration. By analyzing all designated nutrients together, this study provides a more complete picture of maternal supplementation behaviors.

- Second, it is the first to integrate intake data with biomarker evidence of VD status in a Hungarian pregnant population. The combination of self-reported supplement use, dietary assessment, and serum 25(OH)D measurements allowed for an objective evaluation of adequacy. This revealed that despite widespread use, most women failed to achieve optimal VD levels, highlighting the limitations of current supplementation practices.
- Third, the study introduced a composite adherence score for FA, VD, and O3, providing a multidimensional measure of supplementation behavior. This approach identified that fewer than one-third of women achieved high adherence, despite high prevalence of supplement use, offering a novel way to capture real-world behaviors beyond simple prevalence rates.
- Fourth, the analyses identified parity, education, pregnancy planning, and early antenatal care as the strongest predictors of adherence. These associations confirm some international findings but are documented here for the first time in Hungary. They also provide actionable targets for public health interventions.
- Fifth, the dissertation demonstrated clinically relevant associations between supplementation and outcomes. Correct O3 use was linked to reduced GDM risk, inappropriate O3 use was associated with inadequate uterine contractions, and FA supplementation was associated with reduced cesarean rates. These findings extend current knowledge in Central and Eastern Europe and highlight the importance of adherence, not just prevalence.
- Finally, unexpected associations were observed between higher maternal VD serum levels and certain intrapartum complications. Although likely influenced by confounding or sample size limitations, these paradoxical results are novel and point to the complexity of interpreting serum VD in pregnancy. At the same time, higher total VD intake was protective against gestational hypertension, underlining the importance of distinguishing between intake behaviors and serum concentrations.

In summary, the originality of this dissertation lies in its integrated approach, combining prevalence, adherence, predictors, biomarker validation, and clinical outcomes in one study. It documents both progress and persistent shortcomings in maternal supplementation practices in Hungary, offering new evidence to inform clinical guidelines and public health policy.

ACKNOWLEDGMENTS

First and foremost, I would like to express my deepest gratitude to my supervisor, **Dr. Andrea Szabó**, who has not only guided me with her professional expertise but has also supported me with her positive personality throughout this journey.

I would also like to thank **Professor Dr. Edit Paulik** for her professional advice and continuous encouragement, which were invaluable for the completion of this dissertation.

My thanks further go to the members of the PhD and residents' room, **Gordi, Gyöngyi, Marci, Bence, and Jakka**, for their friendship, support, and the many discussions that helped me both academically and personally during these years.

Last but certainly not least, I am profoundly grateful to my family. To my parents, for always believing in me and providing unconditional love and encouragement. To my husband, for his patience, understanding, and unwavering support during the most challenging periods of this work. And to my little son, whose presence brought light and joy even on the most difficult days, reminding me of the true purpose behind all my efforts. Without their love and encouragement, this dissertation would not have been possible.

Finally, I wish to extend my gratitude to everyone who may not be mentioned by name here, but whose support, encouragement, and kindness contributed in countless ways to the realization of this dissertation.

LIST OF PUBLICATIONS

Publications related to the thesis

I. **Polanek, Evelin**; Rárosi, Ferenc; Béky, Csenge Fruzsina; Molnár, Regina; Németh, Gábor; Orvos, Hajnalka; Paulik, Edit; Szabó, Andrea. Beyond the Pill: Unveiling the Characteristics of Prenatal Micronutrient Consumption Among Hungarian Pregnant Women According to Different Levels of Adherence NUTRIENTS 17: 17 Paper: 2732, 27 p. (2025)
SJR indicator: D1; IF: 5.

II. **Polanek, Evelin**; Sisák, Anita; Molnár, Regina; Máté, Zsuzsanna; Horváth, Edina; Németh, Gábor; Orvos, Hajnalka; Paulik, Edit; Szabó, Andrea. A Study of Vitamin D Status and Its Influencing Factors among Pregnant Women in Szeged, Hungary: A Secondary Outcome of a Case–Control Study NUTRIENTS 16: 10 p. 1431, 16 p. (2024)
SJR indicator: D1; IF: 5.