Effects of maternal vitamin D status on pregnancy outcomes, health of pregnant women and their offspring

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Abstract

OBJECTIVE: Pregnancy increases the demand for vitamins, including vitamin D. Data on effects of vitamin D deficiency for pregnant woman and fetus available in Poland are scarce. The aim of this study was to evaluate vitamin D3 concentration in pregnant women and its influence on pregnancy course, health of pregnant women and their offspring.

PATIENTS AND METHODS: The study included 102 healthy pregnant women, aged 21 to 40 years, mean 30.5±4.9 years. Women were divided into three groups based on 25(OH)D serum concentration in the third trimester of pregnancy: Group I – with sufficient 25(OH)D serum concentration (>30 ng/ml), Group II – with vitamin D3 insufficiency (20–30 ng/ml), Group III – with serious vitamin D deficiency (<20 ng/ml).

RESULTS: Optimal vitamin D concentrations were found only in 31.2% of women, however in winter months only in 16%. Bacterial vaginosis was significantly more common in women with vitamin D deficiency and insufficiency (p<0.05). In contrast, there were no relations between vitamin D status and the incidence of gestational diabetes, preeclampsia, mode of delivery and size of newborns. A relationship between vitamin D deficiency and insufficiency during pregnancy and subsequent incidence of respiratory infections in children (p<0.05) was demonstrated.

CONCLUSIONS: 1. The current model of vitamin D supplementation in pregnant women in Poland is insufficient, particularly in winter. 2. Vitamin D deficiency in pregnant women fosters development of bacterial vaginosis during pregnancy and recurrent respiratory infections in children, suggestive of the role of vitamin D in prevention of infections.
INTRODUCTION

Pregnancy increases the demand for vitamins and microelements, including vitamin D. Adaptation of calcium metabolism to pregnancy involves doubling of calcitriol synthesis that necessitates an adequate supply of vitamin D (Kovacs & Kronenberg 1997). While only less than 10% of vitamin D is derived from dietary sources, skin synthesis, requiring ultraviolet (UV) radiation, remains the main source of vitamin D (Holick 2009). Unfortunately, in Poland UV availability is sufficient only from May to September (Pludowski et al. 2013). On the other hand, UV is regarded as the major environmental, physical hazard to the human skin (Osmola-Mańkowska et al. 2012). Furthermore, the amount of vitamin D in most multivitamin supplements designed for pregnant women is not sufficient, while not all pregnant women declare taking those supplements (Bojar et al. 2012; Skowrońska-Jóźwiak et al. 2014).

Vitamin D takes part in reproduction processes and seems to be significant in therapy of infertility (Grzechocinska et al. 2013). Maternal vitamin D deficiency during pregnancy may be associated with adverse pregnancy outcomes, such as miscarriage, preeclampsia (Bodnar et al. 2007), preterm birth (Møller et al. 2012), gestational diabetes (Senti et al. 2012) and bacterial vaginosis (Bodnar et al. 2009). Vitamin D deficiency during pregnancy may affect child’s health, because maternal circulating 25(OH)D is the most significant regulator of neonatal circulating 25(OH)D concentrations and predominates over genetic factors that determine neonatal circulating vitamin D concentrations (Novakovic et al. 2012). Offspring of vitamin D-deficient mothers are at risk of not only classical bone complications such as rickets, low bone mineral density and the reduced postnatal linear growth (Pawley & Bishop 2004), but also of respiratory infections and asthma (Camargo et al. 2004) later in life. Data available in Poland on the effects of vitamin D deficiency in pregnant women are very scarce.

The aim of this study was to evaluate seasonal variation of vitamin D3 concentrations and a relationship between vitamin D3 status in pregnant women and pregnancy outcomes, health of pregnant women and their children.

PATIENTS AND METHODS

The study included 102 healthy pregnant women, of aged between 21 to 40 years, mean age 30.5±4.9 years, investigated in the third trimester of gestation. The majority of women (64%) declared taking vitamin supplements and most of them were taking 400IU of vitamin D daily. The women were subsequently divided into three groups: those with sufficient serum vitamin D3 – above 30ng/ml (Group I), with vitamin D3 insufficiency, defined as the concentration of 25(OH)D in the range of 20–30ng/ml (Group II) and vitamin D deficiency – less than 20ng/ml (Group III), according to definition based on Endocrine Society’s Practice Guidelines on Vitamin D (Holick et al. 2011). Concentrations of 25(OH)D were determined by electrochemiluminescence assay (Elecys, Roche). Characteristics of investigated subjects is presented in Table 1.

In statistical analysis the standard descriptive statistics were used, including the typical measures of the distribution characteristics of the population – the mean value, standard deviation (SD). Assessment of differences between more than two groups of patients, in which distribution of the most variables did not meet the criteria of normal distribution, was performed with non-parametric Kruskall-Wallis test, followed by the post-hoc analysis for multiple bilateral comparisons in order to identify significant differences between particular groups. The distribution of qualitative variables in particular groups was presented in cross tabulations. Significance of the differences between the distributions of the analysed qualitative variables among particular groups was assessed with Chi-square test. For all the performed tests, the differences were considered significant for p<0.05.

The design of study was approved by the Ethics Committee of Medical University at Lodz.

RESULTS

Complete medical data and questionnaire on the course of pregnancy, mode of delivery, health of pregnant women and their offspring were completed for 69 women. There were 42 physiological labours and 27 caesarean sections. Indications for cesarean delivery included: fetal distress (n=6); maternal disparity (n=2); breech presentation (n=3); previous Cesarean section delivery (i.e. risk of scar dehiscence) (n=3); lack of progress of labour (n=4), while maternal indications (n=9) included severe short-sightedness, perivaginal warts and dehiscence of the pubic symphysis.

Optimal vitamin D concentrations was found only in 31.2% of women, however the results depended on the season, in winter recommended vitamin D concentrations was found only in 16% of women and in summer – in 47%. Severe vitamin D deficiency was shown in 23–58% and hypovitaminosis D in 26–37% of pregnant women depending on the season (Figure 1). The

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<th>Tab. 1. Characteristics of the study group.</th>
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<td>Mean±SD</td>
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<td>Age [years]</td>
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<td>Height [cm]</td>
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<td>Body mass [kg]</td>
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highest concentration of vitamin D was found in IIIrd quarter, the lowest in IVth quarter of the year \( (p=0.018) \) (Figure 2). Monthly fluctuations of vitamin D concentration are presented in Figure 3. Incidence of bacterial vaginosis was significantly higher in women with vitamin D deficiency in comparison to women with optimal vitamin D concentrations \( (p=0.041) \). There was also a significant difference between incidence of bacterial vaginosis in women with vitamin D insufficiency versus those with optimal vitamin D concentrations \( (p=0.002) \). There was, however, no significant difference in the incidence of bacterial vaginosis between women with vitamin D deficiency and insufficiency \( (p=0.517) \) – (Figure 4). There was no relationship between vitamin D levels and the incidence of gestational diabetes and preeclampsia. There was also no statistically significant relationship between maternal vitamin D3 concentrations and the mode of delivery \( (p=0.80) \). Maternal concentration of vitamin D were also unrelated to the size of newborns – Table 2. There was a trend towards higher Apgar score in children of mothers with normal levels of vitamin D (Group I), but this failed to reach statistical significance \( (p=0.2) \). There was, however, a higher incidence of respiratory infections (more than 5 times per year) during the first year of life among children of mothers from Group III. Significant differences in incidence of recurrent infections in children were observed between the group of children born by mothers with vitamin D deficiency and with optimal vitamin D concentrations \( (p=0.003) \), as well as between children of mothers with vitamin D insufficiency and those with optimal vitamin D concentrations \( (p=0.040) \). There was no difference in the incidence of recurrent respiratory infections between children of mothers with vitamin D deficiency (Group II) and insufficiency (Group III) \( (p=0.200) \) – Figure 5.

**DISCUSSION**

Our study demonstrated both insufficiency and seasonal variation of vitamin D levels in pregnant women in Poland. The lowest values were found in the fourth quarter of the year (months October–December), where only 16% of women had optimal levels of vitamin D. Significantly higher values were observed in third quarter, responding to summer – when almost half (47%) subjects had recommended vitamin D levels, i.e. above 30 ng/ml. This dependence is associated with fluctuations in skin synthesis of vitamin D and less exposure to sunlight in autumn and winter in Poland (Pludowski et al. 2013). Similar data on annual fluctuations in vitamin D levels were reported in Poland at the end of eighties XX century, but in that study vitamin D deficiency was even more serious; i.e. in winter mean concentrations of serum 25(OH)D were only 5.5 ng/ml in mothers and even 3.3 ng/ml in their offspring. In summer results were better – 28.8 ng/ml in mothers and 22.1 ng/ml in children (Pluta et al. 1987). However, the seasonal variation of vitamin D concentration is not always observed in Polish women. For instance, in a recent study performed in a group of 150 pregnant women from Warsaw, there was no statisti-
cally significant differences between concentrations of 25(OH)D levels in winter versus summer (Bartoszewicz et al. 2013). Possible explanation for this discrepancies might be related to differences in oral vitamin D supplementation and voluntary avoidance of sun exposure, declared by women in the study (Bartoszewicz et al. 2013). Therefore, we suggest that the presence of a link between season and concentration of 25(OH)D, suggests that in our group the skin synthesis, rather than regularly taken oral supplementation, remains the major source of vitamin D. This is an argument proving inefficiency of vitamin D supplementation in Polish women during pregnancy.

We have also shown significantly higher incidence of bacterial vaginosis in women with vitamin D deficiency. Bacterial vaginosis involves replacement of physiological vaginal microflora by anaerobic bacteria. Such condition may promote development of pregnancy-related complications, including amniotic fluid infections, preterm birth, and infections in newborns (Koumans et al. 2007). Previously reported linear inverse dose-dependent relationship between vitamin D levels in pregnant women and bacterial vaginosis was also confirmed (Bodnar et al. 2009). The mechanism of action of vitamin D in terms of a contribution towards development of this complication remains unclear. One can speculate, however, that calcitriol influences both the innate and adaptive functions of the immune system (Gunville et al. 2013). Vitamin D modulates the expression of peptides, such as cathelicidin, displays an

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<th>Tab. 2. Duration of pregnancy, mode of delivery and status of newborns, stratified according to maternal vitamin D concentrations (mean±SD).</th>
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<td>% of women</td>
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<td>% of women with gestational diabetes</td>
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<td>% of women with hypertension</td>
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<td>Duration of pregnancy [weeks]</td>
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<td>Apgar score</td>
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<td>Length of newborn [cm]</td>
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<td>% of cesarean section</td>
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<td>% of physiological delivery</td>
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NS – not significant

**Fig 4.** Incidence of bacterial vaginosis depending on vitamin D status.

a – significant difference in bacterial vaginosis incidence between the group of women with vitamin D deficiency and with optimal vitamin D concentrations (p=0.041);
b – significant differences in bacterial vaginosis incidence between women with vitamin D insufficiency and with optimal vitamin D concentrations (p=0.002).

Differences in bacterial vaginosis incidence between women with vitamin D deficiency and insufficiency did not reach the border of statistical significance (p=0.517) – Chi-square test.

**Fig 5.** Incidence of recurrent respiratory infections in children, depending on vitamin D status in mother during pregnancy.

a – significant differences in incidence of recurrent infections in children were observed between the group of children born from mothers with vitamin D deficiency and with optimal vitamin D concentrations (p=0.003);
b – significant differences in incidence of recurrent infections between children of mothers with vitamin D insufficiency and with optimal vitamin D concentrations (p=0.040).

There was no difference between children of mothers with vitamin D deficiency and insufficiency (p=0.200) – Chi-square test.
activity against viruses and bacteria, and thus helps to reduce the severity of infections and intensity of viral replication (Gunville et al. 2013). Moreover vitamin D influences the inflammatory cascade via NFκB and regulates adaptive capacities of immune system, particularly T cells (Gunville et al. 2013). In our study bacterial vaginosis seems to be the most important consequence of hypovitaminosis D for health of pregnant women; however we did not observe higher incidence of other disorders previously described in medical literature, including gestational diabetes or preeclampsia (Bodnar et al. 2007; Møller et al. 2012; Senti et al. 2012). This might be a consequence of overall low incidence of these complications in the studied subjects. There were also no significant differences in the mode of delivery, regardless of supply of vitamin D. However, other authors suggest an increased number of cesarean sections in women with vitamin D deficiency, as a consequence of calcium deficiency on muscles (Scholl et al. 2012).

We observed a trend towards higher Apgar scores in children of mothers with normal levels of vitamin but this failed to reach statistical significance. Farther, results of the present study do not permit us to confirm the hypothesis of possible link between the supply of vitamin D in pregnancy on the parameters employed in order to assess size of a newborn. Both body length and birth weight did not differ between the groups of women with normal and reduced levels of vitamin D. In turn, in literature there appeared an observation about differences in sizes of children born in different seasons of the year; and so children born from October to April were larger and heavier than children born from May to September, whereas the authors interpreted this phenomenon as a consequence of variable supply of vitamin D in different seasons (Krenz-Niedbala et al. 2011).

In current work the possible effect of vitamin D deficiency on the health of the child was reflected in reduced incidence of respiratory infections in children of mothers with normal supply of vitamin D during pregnancy versus those whose mothers had been vitamin D deficient/insufficient. The above mentioned lower incidence of infections in children, whose mothers had been vitamin D sufficient can be interpreted as a result of immunomodulatory actions of vitamin D (Gunville et al. 2013), as in the case of an impact of vitamin D status on development of bacterial vaginosis during pregnancy, and subsequent respiratory infections in children, thus suggestive of a role of vitamin D in prevention of certain infections.

CONCLUSIONS
1. The current model of vitamin D supplementation in pregnant women in Poland is insufficient, particularly in winter months. 2. Vitamin D deficiency in pregnant women fosters development of bacterial vaginosis during pregnancy, and subsequent respiratory infections in children, thus suggestive of a role of vitamin D in prevention of certain infections.

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