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TITLE: VITAMIN D SUPPLEMENTATION IN THE CASE OF MATERNAL VITAMIN D DEFICIENCY WITH COEXISTING LOWER GENITAL TRACT INFECTIONS IMPROVES PERINATAL OUTCOMES

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CONTENT

Background. Implementation of the modern standards of perinatal care in Ukraine has ensured significant drop in main contributors to neonatal and maternal morbidity except intraamniotic infections (IAI), which showed the rise from 4.35% to 5.38%. Lower genital tract infections (LGTI) are very common among otherwise healthy looking pregnant women (40-54%). Untreated LGTI are linked to adverse outcomes. Treatment on the basis of laboratory data alone leads to considerable overuse of antibiotics. No benefit was found in treating women with low- or average-risk pregnancies for asymptomatic bacterial vaginosis. Several host defense mechanisms operate against ascending infection including vaginal acidity, cervical mucus, intact membranes and antibacterial activity of amniotic fluid due to polymorphonuclear leucocytes, lysozyme, β-lysin, transferrin, immunoglobulins and other bacterial inhibitory factors such as polypeptide-zinc complexes in amniotic fluid. Vitamin D is known to regulate innate and adaptive immune processes at the cellular level. Lower maternal vitamin D status may increase risk of infection across gestation. Maternal vitamin D status during pregnancy may modulate fetal immune system development

and infant susceptibility to infections. The implication of maternal deficiency during pregnancy is that the fetus is also affected, with known consequences on fetal growth, dentition, bone density, immune function and risk of infections such as RSV. Infants of women who were deficient throughout pregnancy will maintain or reach a state of deficiency more quickly than an infant whose mother was replete during pregnancy.

Objectives. In order to lower the risk of asymptomatic LGTI for pregnancy outcomes and considering that maternal vitamin D deficiency (MVDD) is associated with increased risk of IAI, all pregnant women who had tested positively for LGTI (namely bacterial vaginosis, colonization with group B streptococcus, C. albicans, U. urealitica, HSV types 1 and 2) underwent evaluation for vitamin D status (25(OH)D by Mann-Whitney U-test, cutoff of MVDD <20 ng/ml). Those who were found deficient then were randomly allotted to the subset with vitamin D supplementation (VDS) either 400 IU/day or 4000 IU/day. During pregnancy the current standard VDS 400 IU/day has a minimal effect on circulating 25(OH)D in the mother and her infant. Daily uptake of 4000 IU/day had been reported to reach the point of 1,25(OH)2D optimization, therefore it was chosen for VDS.

Results. Our study revealed that 89% of women with LGTI had harbored 25(OH)D deficiency (18.9±3.2 ng/ml). VDS in the cohort of women with LGTI showed correlation with fewer adverse pregnancy outcomes comparatively to previous years, especially with regard to maternal preeclampsia, fetal growth, neonatal infectious complications including respiratory distress syndrome, necrotizing enterocolitis, intraventricular hemorrhage, IAI, presumed and confirmed neonatal sepsis, congenital pneumonia. When the data were stratified for patients receiving 400 or 4000 IU/day of VDS, it turned out that this improvement was mostly limited to latter dose with almost threefold decline (2.9) in total number of complication (premature rupture of membranes, preterm delivery, intrauterine growth restriction, stillbirth) and drop of perinatal mortality from 13.3% to 7.8%, better APGAR score and newborn weight (3200 ±200 vs 2850±150).

Conclusion. Because conversion of 25(OH)D to 1,25(OH)2D during pregnancy is unique, by 12 weeks of gestation 1,25(OH)2D level is over 280 ng/ml, that would be toxic due to hypercalcemia to the nonpregnant individual. However, gestational calcium metabolism is uncoupled from

1,25(OH)2D to let it ensure maternal tolerance to the fetal DNA via anti-inflammatory effect in lymphocytes, whereas 1,25(OH)2D consolidates IFN-γ-mediated bactericidal capacity of macrophages reinforcing host defence against ascending of LGTI.
VDS up to 4000 IU/day in the case of MVDD with coexisting LGTI is safe and most effective in achieving 25(OH)D level sufficient for optimal 1,25(OH)2D production, resulting in better perinatal outcomes.