Letter to the Editor

Vitamin D deficiency during pregnancy and the risk of preeclampsia

Madam, pregnancy is a state of increased requirement of macro- and micro-nutrients, making the pregnant women susceptible to develop deficiencies of various micronutrients. Pregnant women in several countries have been reported to have low circulating 25-hydroxyvitamin D [25 (OH) D] levels. Vitamin D has now been shown to be of considerable importance not only for bone health, but also for glucose regulation, immune function and good uterine contractility in labour. Vitamin D deficiency correlates with infertility, preeclampsia, gestational diabetes mellitus, bacterial vaginosis and an increased risk for cesarean delivery. The aim of this letter is to summarize the available evidence on the effect of vitamin D deficiency on the risk of preeclampsia and to report any trials of vitamin D supplementation during pregnancy on this outcome, especially if reported from developing countries.

A nested case control study,[1] from the United States of America (USA), showed that vitamin D deficiency was associated with an increased risk of preeclampsia. Midgestation 25(OH) D levels were lower in women who developed severe preeclampsia compared to uncomplicated pregnancies. It was also seen that level of 25(OH)D less than 50 nmol/L were associated with a significant odds of 5-fold increased risk compared with levels of at least 75 nmol/L (adjusted OR = 5.41; 95% CI: 2.02 - 14.52). A second similar study[2] also conducted in USA on nulliparous singleton pregnant women followed women from below 16 weeks gestation to delivery and found that 25(OH) D levels were significantly lower in cases (preeclamptic women) when compared to controls. They also found a monotonic dose-response relation between serum 25(OH) D concentrations at less than 22 weeks and risk of preeclampsia - a 50 nmol/L decline in 25(OH) D doubled the risk of preeclampsia. Similary, lower levels of vitamin D were shown in women with early-onset severe preeclampsia compared to controls.[3] Other studies have, however, failed to report a positive association between vitamin D deficiency and preeclampsia. A prospective cohort study from Canada on pregnant women at high risk of preeclampsia showed no difference in the rates of preeclampsia by 25(OH) D concentration. Another nested case-control study[4] in USA compared first trimester total and free 25(OH)D levels among women who subsequently developed preeclampsia versus normotensive pregnancies, showing the levels to be similar. There was a tendency towards increased risk of preeclampsia with 25(OH) D levels < 15 ng/mL, but the association was non-significant (adjusted OR = 1.35; 95% CI: 0.40 - 4.50).

We found one observational study from Norway on 23,423 nulliparous pregnant women looking at the use of vitamin D supplements during pregnancy,[5] demonstrating that vitamin D supplements reduced the risk of preeclampsia by 27% (OR = 0.73; 95% CI: 0.58 - 0.92). It also showed that a total dietary intake of vitamin D of 15-20 microg/d was associated with a significant 24% reduction compared to less than 5 microg/d. Therefore, overall there is a very strong evidence based on epidemiological studies of a link between

vitamin D deficiency and risk of preeclampsia in pregnant women from developed countries. However, no study on such an association has been reported from developing countries. Therefore, these findings have not been confirmed in other populations, and the role of vitamin D in preeclampsia is as yet unclear. The proposed pathogenesis is that vitamin D levels impair the normal Th1 to Th2 cytokine balance, with higher Th1 cytokine expression impairing the immunological tolerance of embryo implantation. Vitamin D deficiency is common even in countries with abundant sunlight and it is important that studies be conducted in developing countries, including Pakistan, to assess the burden of vitamin D deficiency during pregnancy, particularly during winter. Efforts need to be made to supplement vitamin D deficient women in order to avoid adverse effects to the mother as well as the foetus.

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