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Guest editorial

Vitamin D and the perinatal period in women suffering from schizophrenia

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There is emerging evidence that inadequate levels of vitamin D during the fetal period and early infancy can be a risk-modifying factor for many chronic diseases, including schizophrenia. Offspring of women suffering from schizophrenia have an increased risk of developing the same illness, and these women are often at risk of vitamin D deficiency that can also adversely affect their children during the fetal period and early infancy. In this editorial we discuss the potential advantages and disadvantages of routine screening for vitamin D deficiency for the health of children of women with schizophrenia.

Vitamin D deficiency is prevalent in many northern regions of the world, including industrialised countries. For example, a recent nationwide survey in the UK showed that more than 50% of the adult population have insufficient levels of vitamin D, and that 16% have severe deficiency during winter and spring.[1] With regard to women of childbearing age, a survey from the USA found that 4% of white and 42% of black women of childbearing age have severe vitamin D deficiency.[2]

Risk factors for vitamin D deficiency are pigmented skin (non-white ethnicity), lack of sunlight exposure, atmospheric pollution, skin-concealing garments and strict sunscreen use, exclusively breastfed babies (beyond 6 months), multiple pregnancies at short intervals, obesity, being elderly, being institutionalised, non-fish-containing diet, malabsorption, short bowel, cholestatic liver disease and certain medications (e.g. glucocorticoids, rifampicin, phenytoin, highly active retroviral treatment).[3]

Women with schizophrenia often have a number of the above-mentioned risk factors, such as sedentary lifestyle with limited sunlight exposure, which can be related to symptoms of the illness (e.g. persecutory ideas or negative symptoms of schizophrenia), obesity and non-fish-containing diet. In addition, in countries such as the UK, an increased incidence of schizophrenia has been reported in people of African-Caribbean as well as South Asian origin (although less consistently),[4,5] and thus pigmented skin is another important risk factor for vitamin D deficiency in women with schizophrenia.

If, therefore, many expectant or breastfeeding mothers with schizophrenia are likely to be vitamin D deficient, what effect does this have on their offspring?

Emerging research evidence indicates that vitamin D deficiency may be a risk-modifying factor for schizophrenia and many other chronic illnesses, including osteomalacia, rickets, multiple sclerosis, heart disease, type 1 diabetes and cancer.[6] The mechanism by which vitamin D influences human health has not yet been confirmed, but it has been postulated that it is related to biological mechanisms of 'memorising' the metabolic effects of the early nutritional environment through fetal and neonatal imprinting.[6] Metabolic imprinting is an adaptive process that fine-tunes the expression of specific genes, without directly altering the DNA sequence, to produce a phenotype that is best suited to survive in its predicted environment.[7]

Epidemiological evidence linking vitamin D and schizophrenia is based on studies that have examined the association between winter births and increased incidence of schizophrenia,[8,9] studies that have looked at the increased risk of schizophrenia in migrants to colder climates,[5,10] the reported association between increased sunlight exposure and decreased risk of schizophrenia,[11] and results which showed that vitamin D supplementation in the first

year of life lowered the risk of developing schizophrenia in males.[12]

In-vitro animal and human data provide evidence for a link between vitamin D and brain development.[6] At a tissue level, maternal Vitamin D depletion alters the brain morphology of the developing offspring.[13] Rat pups born to vitamin-D-deprived mothers had enlarged ventricles and longer cortices that were proportionally thinner. As thinning of the neocortex and ventricle overgrowth have been observed in schizophrenia,[15] these results further point towards a possible link between vitamin D deficiency and schizophrenia.[6]

In pregnancy and breastfeeding there is a direct correlation between the vitamin D status of the mother and that of the infant. Suspecting vitamin D deficiency in pregnancy on the basis of clinical signs is difficult, as musculoskeletal pain and weakness, which are the main symptoms of vitamin D deficiency in adults, commonly occur in normal pregnancy. Therefore the only reliable method of diagnosing vitamin D deficiency is measurement of the serum concentration of 25(OH)D, which is used as an indicator of vitamin D levels in the human body. Levels lower than 25 nmol/l are defined as deficiency, levels of 25–50 nmol/l as insufficiency, levels of 50–75 nmol/l as adequate, and levels above 75 nmol/l as optimal.[3]

Taking into consideration first that offspring of mothers with schizophrenia have a higher risk of developing the same illness, secondly that risk factors for vitamin D deficiency are common in women with schizophrenia, and thirdly that epidemiological and *in-vitro* data suggest a link between maternal vitamin D depletion and schizophrenia in children, the question arises as to whether the level of vitamin D should be routinely measured in women with schizophrenia who are at high risk of vitamin D deficiency, as part of preconception counselling and perinatal care.

The potential advantages of such screening are that it could allow early detection and prompt treatment of vitamin D deficiency, and thus could lead to an improved early nutritional environment for the fetus and subsequently the infant, which may lower the risk of schizophrenia and other chronic illnesses linked to vitamin D deficiency.

As the children of women with schizophrenia are at increased risk of developing mental health problems (including schizophrenia), improving the early nutritional environment has obvious value as a potential measure for primary prevention of mental illness. Furthermore, treatment of vitamin D deficiency during the fetal and neonatal period is likely to be important for the future physical health of these children.[6]

In terms of potential disadvantages, there are concerns about possible toxicity and harm caused by the use of high-dose vitamin D supplementation to treat vitamin D deficiency during pregnancy and breastfeeding. The question of what constitutes a safe dose of vitamin D in pregnancy is still the subject of some debate. Lower doses of vitamin D, such as those included in routine antenatal vitamin supplements (400 IU), are often ineffective for treating vitamin D deficiency, which requires higher doses. Another factor that has to be considered is the potential cost of routine screening, particularly given the absence of prospective studies confirming the effect of treatment of vitamin D deficiency in women with schizophrenia in lowering the risk of their children developing schizophrenia.

Based on the evidence currently available, it appears justified to consider screening for vitamin D deficiency, by measuring the serum concentration of 25(OH)D, in those women with schizophrenia who are at high risk of vitamin D deficiency (due to pigmented skin, limited sun exposure, obesity, or a non-fish-containing diet) and who are planning a pregnancy, are pregnant or are breastfeeding.

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CONFLICTS OF INTEREST

None.

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