

Obesity and Vitamin D Deficiency— Current Concepts on their Impact on Pregnancy

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Abstract

Both obesity and vitamin D deficiency are linked to morbidity and ultimately mortality. Vitamin D sufficiency is believed to confer many health benefits; however, with the exception of the classic functions related to bone health these are not yet well understood, especially in relationship to pregnancy and infant health outcomes.¹ Conversely, insufficiency is associated with adverse health outcomes, which are consequently related to public health concerns that arise from these and these need addressing.^{2,3} While the links between health and vitamin D are being considered and researched, there are an increasing number of reports that demonstrate vitamin D deficiency is prevalent particularly among people who are darker skinned, those who live at latitudes above 52°, and are therefore exposed to reduced sunlight especially in the autumn and winter months, those who through lifestyle choices cover their bodies, preventing sunlight exposure, and in obese people.³⁻⁶ Obesity is also of growing concern. Health journalists and academics sometimes dramatically refer to 'obesity epidemics,' which is not surprising as over one-third of Americans are obese.⁷⁻⁹ This problem, if not addressed, will lead to adverse health outcomes for individuals as well as being a long-term burden both to families and society.¹⁰⁻¹¹ It is interesting to note that both vitamin D deficiency and obesity have shared risks for mortality and morbidity including cardiovascular disease, diabetes, respiratory problems, cancer, and musculoskeletal disease. This paper considers current concepts and the links between obesity and vitamin D deficiency in pregnancy seeking to determine whether being vitamin D deficient and obese is simply double trouble, where both are present, or whether there are other factors that need further exploration, reviewing the associated implications for practice.¹²⁻¹⁵

Keywords

Vitamin D, obesity, pregnancy

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Background and Literature Review

Obesity in pregnancy carries risks. Raja et al.¹⁶ carried out a review of deliveries between January 2002 and December 2007. Obese mothers (body mass index [BMI] ≥ 30) were shown to be at significantly higher risk from multiple morbidities ($p < 0.05$), including gestational diabetes; antepartum hemorrhage; preterm delivery before 37 and 33 weeks of gestation; induction of labor; analgesia use (beyond inhalational methods and local infiltration); cesarean sections; massive postpartum hemorrhage; higher birthweights; and a greater need for neonatal care (special care baby unit [SCBU], high-dependency unit [HDU], neonatal intensive care unit [NICU]) compared with mothers with a BMI < 30 . These findings add to the growing consensus that obesity increases the risks involved with pregnancy.¹⁷⁻¹⁸

Furthermore, it has been reported that obese pregnant women have an increased use of healthcare services, especially for BMI < 35 ,¹⁹ increased cesarean section rate,²⁰ and increased risk for infant mortality, both of which may involve cardiometabolic morbidity.²¹ Catalano²² suggests that this may be related to a decrease in insulin sensitivity, and therefore overweight and obese women are at increased risk for metabolic dysregulation in pregnancy, i.e. gestational diabetes, preeclampsia, and fetal overgrowth.

The presence of vitamin D in sufficient quantities is thought to modify the risk for adverse cardiometabolic outcomes,^{23,24} although the association remains unclear.²⁵ Vitamin D is also thought to play an important role in insulin resistance and glucose homeostasis²⁶ and it has been proposed that vitamin D supplementation may be an effective addition to the standard treatment of obesity and its associated insulin resistance.²⁷

A couple of decades ago, four small studies²⁸ suggested that obese subjects have higher 1, 25-dihydroxy vitamin D (1,25-vit D) serum concentrations than nonobese controls. There are also studies that support the theory that 1,25-vit D stimulates lipogenesis.²⁸ In an animal study,²⁹ mice with knocked-off vitamin D receptors had smaller subcutaneous and visceral white adipose tissue depots, furthermore these mice were also resistant to high-fat diet-induced weight gain. Parikh²⁸ tested the hypothesis that obesity is linked to higher levels of circulating 25 (OH) D using a large subject group of healthy individuals. The result was that nonobese participants had almost twice as much circulating 25 (OH) D as the obese subjects. It would seem obese individuals are at a greater risk for vitamin D deficiency because vitamin D is thought to be sequestered by excess adipose tissue not because as originally suggested that they do not like to go out in the sun.³⁰

Although pregnancy does not appear to effect bioavailability of vitamin D,³¹ McAree et al.³ found that obese pregnant women were more likely than nonobese women to have inadequate levels of 25 (OH) D in pregnancy. This has been reported in previous studies and may be related to decreased bioavailability of vitamin D from cutaneous stores or its deposition in body fat.³⁰ Bodnar et al.³² noted that there is a twofold increase in maternal and neonatal vitamin D deficiency as maternal BMI increases from 22 to 34 kg/m². She was able to demonstrate the link between fetal and maternal serum 25 (OH) D, which is significant for the health of infants.

It has been suggested that the presence of nuclear vitamin D receptors and of the vitamin D-activating 1- α -hydroxylase enzyme in the placenta and the decidua means that vitamin D acts as a modulator of fetal-placental development and function³³ and is coupled with pregnancy progression, as well as playing a part in placental insufficiency and its sequela in fetal and maternal wellbeing during pregnancy. Vitamin D deficiency is associated with an increased caesarean section rate,^{34,35} preeclampsia,³⁶ low birthweight,^{1,2} bacterial vaginosis,^{1,2} and in the presence of both obesity and vitamin D deficiency the problem of gestational diabetes is increased.³² This clearly demonstrates the need for pregnant women to be vitamin D replete despite a recent Cochrane review³⁷ that suggests there is not sufficient data or robust enough studies with sufficient power to make absolute conclusions. However, vitamin D deficiency in pregnancy has been recognized as a serious concern for pregnant women especially if they are dark skinned or obese.^{3,4,5,32}

It would seem that, although 25 (OH) D deficiencies and obesity are associated and that vitamin D levels are likely to be lower to the point of being pathologic when an individual is obese, any further mechanisms of cause or association are not yet understood. These are clearly matters that need to be dealt with from both an individual and population perspective.

Implications for Practice

Efforts to tackle the problems highlighted above have been hampered by the lack of high-quality evidence and thus it is difficult for clinicians to undertake any large-scale population or individual deficiency prevention programs.^{5,37,38} The scale of the problem for pregnant women is now becoming clearer, and there are an unacceptable number of women with vitamin D deficiency.³⁸ The report of Bodnar et al.³² of prepregnancy BMI in relation to gestational and cord 25 (OH) D levels suggest that adiposity around conception may predict pregnancy and neonatal vitamin D status. Therefore there are clear markers available to see who are at greatest risk (i.e. those who are obese and those who have darker skin) and advice may be given according to government recommendations (The UK and US have different recommendations). However, details of interventions remain unclear and evidence regarding timing and optimal dosing for supplementation during pregnancy is lacking.^{5,38}

The majority of vitamin D is obtained through exposure of the skin to sunlight (ultraviolet B-[UV-B] light in the range 270–290 nm). At this wavelength, 7-dehydrocholesterol in skin is converted to previtamin D, which isomerizes to vitamin D₃ and is then metabolized by the body to its active and inactive metabolites.³⁹ Although advising pregnant women to expose themselves to the sunlight by going for walks, which would enhance both vitamin D status and general fitness thus tackling obesity, their lifestyle needs to be taken into consideration. For example, some

cover up their whole bodies for religious reasons. Also in the Northern hemisphere the weather is not always amenable to such activity. Also, prolonged exposure to the sun is not without risks as it is associated with eye and skin disease. Furthermore, modern living means people spend more time indoors and engage in activities, such as watching television and computer-based activities,³² thus reducing natural exposure to the sun and reducing its potential to ameliorate vitamin D deficiency.

Vitamin D may be obtained from the diet, through the ingestion of oily fish, certain fortified foods, and vitamin D supplements, and ingested vitamin D is metabolized in the same manner as that endogenously produced. Cross-sectional studies suggest that current US/Canadian fortification practices are not effective in preventing hypovitaminosis D, particularly among vulnerable populations during the winter, whereas supplement use shows more promise.⁴⁰

It would appear modern living has precluded, to some degree, people naturally acquiring vitamin D. Wortman et al.³⁰ conducted experiments with full body irradiation and oral vitamin D supplementation. They tested to evaluate the blood concentrations of vitamin D in obese and nonobese subjects in response to UV-B irradiation or an oral dose of vitamin D₂. He also performed studies *in vitro* to determine whether obesity affects the cutaneous production of vitamin D₃. His results showed no difference between nonobese and obese individuals in the capacity of the skin to synthesize D₃. However, the increase in blood vitamin D₃ concentrations was 57 % less in the obese than in the nonobese subjects 24 hours after the exposure. Thus, obesity did not affect the capacity of the skin to produce vitamin D₃, but may have altered the release of vitamin D₃ from the skin into the circulation. These data suggest that the availability of excessive adipose tissue causes a decrease in endogenously synthesized D₃ to be released into circulation. Orally ingested vitamin D was more bioavailable and therefore suggests that vitamin D deficiency in obesity can be corrected by oral supplementation rather than using sunlamps.

The US National Institute for Health and the Endocrine Society⁴¹ recommend that most people will be at optimum levels of vitamin D at 50 nmols/L and that in pregnancy the optimal daily recommended allowance is 600 IU or 15 mcg. In the UK this stands at 400 IU daily. Consideration needs to be given as to how very deplete women, often the obese, will reach adequate levels. One study³¹ involving giving a one-off dose of 70,000 IU reported an increase in 25 (OH) D levels that surged and then returned to normal. It would seem this may act as a boost to 25 (OH) D levels, but a maintenance dose would be required thereafter. Yu et al.⁴² undertook a study of supplementing women from 27 weeks of gestation, but did not achieve 25 (OH) D levels of over 42 nmol/L. Although all women and umbilical cord blood demonstrated a significantly higher level than the no treatment arm, 25 (OH) D levels had not reached sufficiency. Neither of these studies took into consideration women's BMI and how this would influence dosing quantities.

Public and professional education requires further work as repeated studies demonstrate that neither women nor the professionals caring for them have a great awareness of the implications of vitamin D deficiency.³

In many National Health Service guidance documents, managing prepregnancy conditions such as obesity and diabetes are recommended,

but often there is limited provision for such a service. Preconceptual care would help to improve general health and maybe afford some weight loss prior to pregnancy and well as individuals gaining insight and perhaps enthusiasm for a healthier lifestyle. It has been demonstrated in a systematic review⁴³ covering nine randomized controlled trials from 1966 to June 2006 that, although the trials were small and imperfect, they evidenced that vitamin D fortification improved vitamin D status in adults. Therefore in areas such as the UK, where there is limited food fortification, this should be considered as an adjunct to other measures to ensure pregnant women and infants have vitamin D sufficiency.

Conclusion

The discovery of vitamin D and the subsequent near elimination of rickets must rank as one of medicine's great achievements;⁴⁴ however, almost

100 years later, science is still grappling to understand and ascertain the implications of vitamin D deficiency. Therefore, it is difficult to make recommendations for health practitioners to follow when they give advice about supplementation particularly during pregnancy. It is clear from inferences gained from the research to date that pregnant woman who are both obese and vitamin D deficient should not only be concerned about their own health but that of their offspring and that having sufficient vitamin D will improve their long term health outlook.

Interventions in this area, once more clearly understood, will improve intergenerational health and prenatal conditions, which are of vital importance,^{22,45} and surely this will involve further research, preconception care, and a population-wide public health intervention such as universal supplementation of vitamin D during pregnancy. ■

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