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Level of adherence to vitamin D supplementation guidelines in an antenatal centre in Birmingham, UK, and its effect on biochemical and obstetrical outcomes: a single-centre cross-sectional study

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ABSTRACT

Objectives A third of pregnant women in the UK are vitamin D deficient, which may confer deleterious consequences, including an increased risk of pre-eclampsia, gestational diabetes mellitus and intrauterine growth restriction. This study aims to determine the proportion of women that met National Institute for Health and Care Excellence (NICE) standards for vitamin D supplementation in pregnancy and compare biochemical and obstetrical outcomes according to supplementation status.

Design and setting This is a single-centre cross-sectional study in an antenatal centre in Birmingham, UK. Participants received a questionnaire regarding their experiences with vitamin D supplementation during their pregnancy with their general practitioner. Serum 25-hydroxyvitamin D and bone profile results were obtained during the same appointment and obstetrical outcomes were collected retrospectively once participants had delivered.

Results 41.8% of participants (n=61) received written and/or verbal advice about supplementation, (NICE standards=100%). 72.6% (n=106) had one or more risk factors for vitamin D deficiency, of which 38.7% (n=41, NICE standards=100%) were asked about supplementation. Among those asked, 85.4% (n=41, NICE standards=100%) received the correct dosage. Compared with the supplementation group, the non-supplementation group had offspring that were 1.40 cm (95% CI 0.01 to 2.80, p=0.04) longer at birth; which was significant after adjusting for confounding factors. No significant differences in any biochemical parameters were observed between supplementation categories (p>0.05).

Conclusions Adherence to NICE standards was suboptimal. This may be attributed to insufficient training for general practitioners on the importance of supplementation, causing them to underestimate the consequences of gestational vitamin D deficiency. Recommendations include implementing a mandatory screening tool to identify 'at-risk' women and providing more clinician training to ensure that supplementation during pregnancy is standard of care.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study used a sample from a diverse ethnic population, allowing robust analysis of the effect of vitamin D supplementation on biochemical and obstetrical outcomes with a sample that was representative of the ethnically diverse UK population.
⇒ This study also has some important limitations, including the small sample size compared with other studies that have investigated the effect of vitamin D supplementation on biochemical and obstetrical outcomes, potentially causing our data to be unrepresentative of the general population.
⇒ The sample was also obtained from one geographical location in the UK, causing further issues relating to the relevance of our data to the rest of the population.

INTRODUCTION

In epidemiological studies, vitamin D deficiency and insufficiency has been consistently observed in pregnant and breastfeeding women globally.[1] According to the WHO, vitamin D deficiency and insufficiency is defined as serum 25-hydroxyvitamin D (25(OH)D) levels below 10 and 20 ng/mL (or 25 and 50 nmol/L), respectively.[2] In the UK, 31% of pregnant women were found to have vitamin D insufficiency, posing considerable public health concerns.[3]

Vitamin D deficiency during pregnancy has shown to have deleterious consequences for both the mother and fetus. One meta-analysis demonstrated a negative correlation between serum 25(OH)D levels in the mother and the risk of pre-eclampsia, often associated with maternal and fetal morbidity and mortality.[4] Obstetrical and maternal complications associated with vitamin D deficiency include an increased risk of gestational diabetes mellitus,

which mediates an increased risk of macrosomia and the need for a caesarean section, as well as maternal osteomalacia, myopathy and neonatal vitamin D deficiency.[5–7] In terms of the effects of maternal vitamin D deficiency on the fetus and neonate, several studies and a meta-analysis have observed an increased risk of preterm birth when maternal serum 25(OH)D levels are lower than 50 nmol/L.[8–11] In addition, the risk of delivering small-for-gestational age neonate was shown to be significantly increased in two meta-analyses if mothers were deficient in vitamin D during pregnancy.[8 9]

Due to the apparent harmful effects of maternal vitamin D deficiency in pregnancy, a Cochrane study investigated the potential benefits of vitamin D supplementation in pregnant women.[12] In several trials, authors concluded that women who were administered vitamin D supplementation had a significantly lower risk of developing pre-eclampsia compared with pregnant women administered placebo.[12] Another study, demonstrated that vitamin D supplementation (4000 IU for 6 months) in pregnancy led to a reduced risk of complications such as caesarean sections and hypertensive disorders.[13]

Pregnant women who are at a greater risk of vitamin D deficiency (ie, those of South Asian, African, Caribbean or Middle Eastern origin, those with limited sunlight exposure, those with a diet low in vitamin D and those with a pre-pregnancy body mass index above 30 kg/m^2) should also be offered supplementation.[14] 'Healthy Start' is a national statutory programme that facilitates nutritional safety for low-income pregnant women. The 'Healthy Start' vitamin contains 700 IU of vitamin A, 20 mg of vitamin C and 300 IU of vitamin D per daily dose. It is available to pregnant women on the National Health Service (NHS) if they receive either child tax credit, employment and support allowance, income support, jobseeker's allowance and pension or universal credit. Due to the apparent benefits of vitamin D supplementation, the National Institute for Health and Care Excellence (NICE), the public body in the UK that provides evidence-based national guidance or health and care in England, have published guidelines regarding vitamin D supplementation during pregnancy.[14] These guidelines state that all pregnant mothers should be given information and advice on the importance of taking vitamin D supplementation, and the 'Healthy Start' vitamin supplementation should be offered to all eligible women by their primary care physician or in the antenatal booking appointment.[14]

Given the importance of an adequate vitamin D status in pregnancy, we undertook a study to evaluate the supplementation status of women attending an antenatal unit of an inner-city hospital in UK hospital, against adherence to NICE clinical standards by primary care physicians.

MATERIAL AND METHODS

Study design

This was a single-centre cross-sectional study investigating vitamin D supplementation status of women attending antenatal clinics at City Hospital, Birmingham, UK. Birmingham is a major urban city in the West Midlands region of the UK (latitude 52.4862° N) with an ethnic distribution of 50% British white, 20% Asian and 6% black British/Caribbean.[15]

Study protocol

The inclusion criteria included women who attended antenatal clinics irrespective of gestational age, ethnicity, gravidity, parity and body mass index (BMI); who planned to receive ongoing antenatal care and agreed to provide written consent to participate in the study. Women were consented at their antenatal clinical appointments, at the same time as they completed the study questionnaire regarding their experience of vitamin D supplementation during their current pregnancy (online supplemental data 1). Blood samples were taken for serum urea and creatinine, electrolytes and bone profile (25(OH)D, parathyroid hormone (PTH), adjusted calcium and phosphate levels). These biochemical indices were measured as vitamin D supplementation in pregnancy has been consistently shown to have direct effects on the bone profile in pregnant women, which in turn has known influences on the serum electrolyte homoeostasis.[16 17] Obstetrical outcomes were collected retrospectively after delivery. BMI was calculated at the women's' 'booking' appointment (ie, the first antenatal appointment that occurs at 8–12 weeks' gestation). Vitamin D intake was only assessed through the mothers' supplementation status and did not include assessment of the mothers' diets.

The primary objective was to evaluate the adherence to the NICE standards for supplementation of vitamin D in pregnancy. Secondary objectives were to identify any relationship between maternal vitamin D status and feto-maternal outcomes—neonatal anthropometric data (fetal birth weight, length and head circumference) after adjusting for confounders. Exploratory analyses were undertaken on the biochemical measurements during pregnancy in relation to vitamin D status of the mother.

Completion of questionnaires

Data were collected between 01 September 2017 and 31 December 2017. Following verbal and written consent, a questionnaire regarding their age, gravidity and parity, gestational age, BMI, ethnicity, sunlight exposure levels and amount of vitamin D in their diet was completed (online supplemental data 1). Participants were asked whether they were given verbal or written advice about vitamin D supplementation and the dosage prescribed by their general practitioners, their eligibility for the 'Healthy Start' vitamin and the dosage that they were taking, if any, at the time of questionnaire completion.

Blood sampling and analytical methods

Non-fasting peripheral venous maternal blood samples were taken for analysis of serum total 25(OH)D, 25(OH)D_2, 25(OH)D_3, phosphate, albumin, adjusted calcium, alkaline phosphatase, potassium, sodium, urea, creatinine and PTH. All biochemical analyses, with the exception of PTH and 25(OH)D, were performed on the Abbott Architect. Adjusted calcium (Ca) was calculated using an equation derived from local population data for the Abbott Architect method (adjusted Ca (mmol/L)=measured Ca (mmol/L)+(0.0134×(41–albumin (g/L)))). Concentrations of serum intact PTH were determined using the Roche Cobas sandwich immunoassay kit with electrochemiluminescent detection on the Roche Cobas E411 platform. Total 25(OH)D was the sum of 25(OH)D_2 and 25(OH)D_3 concentrations, measured by liquid chromatography tandem mass spectrometry on a Waters Acquity UPLC—TQD Mass Spectrometer, following liquid–liquid extraction of the serum. Intermediate precision for this assay is: 25(OH)D_3, 6.6% at 18.9 nmol/L, 7.5% at 38.6 nmol/L and 5.5% at 107.2 nmol/L; 25(OH)D_2, 10.8% at 3.6 nmol/L, 6.5% at 37.5 nmol/L and 6.3% at 108.4 nmol/L. The results were used to identify differences in biochemical parameters between those who were taking the correct dosage of vitamin D supplementation (as outlined by NICE), and those who were not.

Statistical analysis

Data were recorded in a database (MS Access version 2019) and statistical analyses were undertaken using Stata/MP V.15 (StataCorp). Categorical data are presented as count (%). Continuous variables are presented as mean (±SD) or median with IQR. Student's t-test was used to compare mean values between groups and Pearson's χ^2 test for categorical variables. All p values are two-sided and a value below 0.05 indicated statistical significance. A multiple regression model was used to determine relationship between fetal birth weight and maternal serum 25(OH)D levels. Serum 25(OH)D concentrations were used both as continuous and categorical variables. In the latter situation, serum 25(OH)D levels were categorised as per NICE guidance, into normal (>50 nmol/L), insufficient (25–50 nmol/L) and deficient (<25 nmol/L).[18]

Patient and public involvement

The research question was first devised and designed following the repeated frustrations expressed in multiple antenatal clinics by mothers who were unable to obtain the 'Healthy Start' supplementation, despite many being eligible. The results of this study will be disseminated to the public in the form of information leaflets and education sessions for laypersons on the importance of enquiring about their supplementation during antenatal care.

RESULTS

Data were collected from 162 women, of which 146 were able to fully complete the questionnaire. Participants ethnicity comprised of 37.9% Asians, 25.5% Afro-Caribbeans, 28.6% Caucasians and 8.1% mixed or other ethnicity which was representative of the demographics of the local population. Maternal BMI, age and proportion of mothers with diabetes (gestational, type 1 and type 2) was higher in the supplemented group, but these differences were non-significant. Maternal baseline characteristics are shown in table 1.

Guideline compliance

Receiving written or verbal advice regarding vitamin D supplementation at their booking appointment (NICE standard=100%) was declared by 41.8% participants. Out of the 70 women that were eligible for 'Healthy Start' supplementation, 75.7% were offered supplementation (NICE standard=100%). Out of the 106 women identified as having one or more risk factors for vitamin D deficiency, 38.7% were asked about supplementation, and of the 48 women taking supplementation, 85.4% were taking the correct 10 µg dosage (NICE standards=100%). Table 2 demonstrates compliance levels observed for each standard.

25-hydroxyvitamin D and biochemical parameters

Compared with non-supplemented women, the mean total 25(OH)D and 25(OH)D_3 concentrations were 8.0 nmol/L (95% CI 1.72 to 17.7, p=0.11) and 8.2 nmol/L (95% CI 1.41 to 17.9, p=0.09) greater in supplemented women, respectively, but this was non-significant. 25(OH)D_2 and adjusted calcium levels were 0.25 nmol/L (95% CI –0.30 to 0.81, p=0.37) and 0.01 mmol/L (95% CI –0.04 to 0.02, p=0.51) greater in supplemented compared with non-supplemented women; however, these differences were non-significant. There were no differences between supplementation groups for other biochemical indices. The proportions of women with vitamin D deficiency or insufficiency did not differ between groups. Table 3 demonstrates differences in biochemical parameters between maternal categories.

Obstetrical outcomes

Compared with supplemented women, the non-supplemented group had offspring that were 1.40 cm (95% CI 0.01 to 2.80, p=0.04) longer at birth, which was significant after adjusting for gestational week at birth and presence of gestational diabetes. There were no significant differences in offspring head circumferences and weights between supplementation groups (p=0.87 and p=0.61, respectively). Supplemented women had gestational periods that were on average 0.34 weeks shorter (95% CI –0.46 to 1.14, p=0.40), but this was non-significant. Apgar scores in the supplemented group were on average 0.15 units (95% CI –0.47 to 0.77, p=0.64) and 0.15 units (95% CI –0.21 to 0.50, p=0.42) lower at 1 and 5 min, respectively, compared with the non-supplemented group, but this was non-significant. There were no significant differences in the rate of neonatal unit admission between maternal categories (p=0.19 and p=0.24,

Table 1 Baseline demographics and clinical variables

Demographic characteristic, mean (SD) or n (%)	Taking vitamin D supplementation* (n=41)	Not taking vitamin D supplementation (n=105)	P value
Age (years)	33.2 (5)	32.1 (4.78)	0.19
Ethnicity, n (%)			0.49
Asian	15 (36.6)	43 (42)	
Afro-Caribbean	11 (26.8)	25 (23.8)	
Caucasian	11 (26.8)	29 (27.6)	
Mixed	1 (2.44)	6 (5.71)	
Others	3 (7.32)	2 (1.90)	
Gravidity	2.85 (1.57)	2.97 (1.59)	0.69
Parity	1.56 (1.43)	1.63 (1.26)	0.79
Body mass index (kg/m^2)	32 (8.95)	29.6 (7.11)	0.09
Smoking status at maternity booking, n (%)			0.50
Current smoker	5 (12.2)	10 (9.52)	
Ex-smoker	1 (2.44)	4 (3.81)	
Never smoked	30 (73.2)	78 (74.3)	
Not specified	8 (9.76)	10 (9.52)	
Diabetes status, n (%)			0.59
Gestational diabetes mellitus	5 (12.2)	7 (6.67)	
Type 1 or 2 diabetes mellitus	3 (7.32)	6 (5.71)	

Results are expressed as mean (SD) or n (%) as appropriate. P values were calculated using the Pearson's χ^2 or Student's t-test.
*Participants were considered if they were taking the correct dosage of vitamin D (10 µg).

respectively). Table 4 demonstrates differences in obstetrical outcomes between maternal categories.

A regression model incorporating the three categories of 25(OH)D status (normal, insufficiency and deficiency), maternal age and BMI, duration of gestation and ethnicity, we found that duration of gestation was the only significant variable (p<0.0001) in accounting for low birth weight in neonates (n=26); this model accounted for 85.8% of variance in low birth weight ($F(9,16)=17.74$, p<0.0001).

DISCUSSION

There is currently a plethora of literature regarding patient-driven difficulties with guideline compliance for antenatal supplementation.[19] This includes simply

Table 2 A table demonstrating the compliance levels for each standard set out by the National Institute for Health and Care Excellence

Clinical standard	Sample size (n)	Compliance n (%)
100% of women should be given written and/or verbal advice about vitamin D supplementation.	146	61 (41.8)
100% of women eligible for the Healthy Start supplementation should be offered vitamin D supplementation.*	70	53 (75.7)
100% of the women with one or more risk factors for vitamin D deficiency should be asked about vitamin D supplementation.†	106	41 (38.7)
If women are taking vitamin D supplementation, 100% should be taking the correct dosage (10 µg).	48	41 (85.4)

*Women are considered eligible if they are at least 10 weeks pregnant or have a child under 4 years old, and their family get income support, and/or income-based jobseeker's allowance, and/or income-related employment and support allowance, and/or child tax credit, and/or universal credit, and/or if the woman in under 18 and pregnant.
†Women are considered to be at risk if they are of South Asia, African, Caribbean or Middle Eastern family origin, and/or have limited exposure to sunlight, and/or eat a diet particularly low in vitamin D, and/or have a pre-pregnancy body mass index or above 30 kg/m^2.

Table 3 A table demonstrating the mean biochemical parameters between women taking vitamin D supplementation during pregnancy, and women who were not taking vitamin D supplementation during pregnancy

Biochemistry variable, mean (SD), or n (%)	Reference range	Taking vitamin D supplementation (n=41)	Not taking vitamin D supplementation (n=105)	P value
Total 25(OH)D (nmol/L)	>50	58.8 (26.1)	50.8 (25.3)	0.11
25(OH)D classification				0.45
Adequate (>50)		27 (65.9)	58 (55.2)	
Deficiency (<30)		7 (17.1)	20 (19)	
Insufficiency (30–50)		7 (17.1)	27 (25.7)	
25(OH)D_2 (nmol/L)		3.05 (0.73)	3.31 (1.66)	0.37
25(OH)D_3 (nmol/L)		55.7 (26.1)	47.5 (25.1)	0.09
Adjusted calcium (mmol/L)	2.2–2.6	2.32 (0.08)	2.31 (0.07)	0.51
Phosphate (mmol/L)	0.8–1.5	1.18 (0.19)	1.12 (0.18)	0.10
Albumin (g/L)	35–50	34.7 (2.24)	34.5 (2.58)	0.66
Alkaline phosphatase (U/L)	30–130	105 (59.4)	114 (54.8)	0.39
Parathyroid hormone (pmol/L)	1–6.5	3.21 (1.73)	3.43 (1.51)	0.47
Urea (mmol/L)	2.5–7.8	2.60 (0.79)	2.66 (0.70)	0.68
Sodium (mmol/L)	133–146	136 (1.57)	137 (1.69)	0.08
Potassium (mmol/L)	3.5–5.3	4.16 (0.37)	4.17 (0.37)	0.84
Creatinine (µmol/L)	45–84	53.6 (6.53)	54.3 (6.59)	0.58

Results are expressed as mean (SD) or n (%) as appropriate. P values were calculated using the Pearson's χ^2 or Student's t-test.
25(OH)D, 25-hydroxyvitamin D.

forgetting to take supplementation, concerns regarding taking supplementation during pregnancy and potential side effects. Moreover, compliance is known to be influenced by maternal age, level of education and socioeconomic status.[20] However, there is a dearth of research on physician-driven reasons for poor compliance to antenatal supplementation. From this study, it is evident that there was suboptimal adherence by primary care physicians to the guidelines set out by NICE in our cohort of women attending this particular antenatal clinic, which may be attributed to a number of factors. First, there is currently no formal training for primary care professionals on the importance of supplementation in pregnancy and the feto-maternal consequences of low 25(OH)D levels in mothers. Furthermore, when recording patient details into electronic healthcare records in primary care, there is no alerting system in place that could make healthcare professionals aware of women who are at-risk for (25(OH)D) deficiency. Additionally, the plethora of information available through NHS patient-information leaflets and websites could confuse clinicians as to their reliability, resulting in variable advice offered to mothers. Finally, there is a lack of clarity in the NICE guidelines regarding identification of at-risk women. The guidelines suggest that at-risk women include those that have 'low sunlight exposure' and a 'diet low in Vitamin D', without quantifying an adequate level of sunlight and listing types of diets (eg, vegetarian, vegan) that are low in vitamin

Table 4 A table demonstrating the differences in obstetrical outcomes between women who received vitamin D supplementation during pregnancy and women who did not receive vitamin D supplementation during pregnancy

Obstetrical outcome, mean (SD) or n (%)	Taking vitamin D supplementation (n=41)	Not taking vitamin D supplementation (n=105)	P value
Gestational week at birth	38 (2.77)	38.4 (1.93)	0.40
Late preterm (<37 weeks)	9 (22)	27 (25.7)	0.96
Moderate preterm (<32 weeks)	2 (4.88)	3 (2.86)	0.44
Baby head circumference (cm)	34.1 (2)	34.1 (1.41)	0.87
Baby length (cm)	50 (5.10)	51.4 (2.93)	0.04
Baby weight (g)	3066 (861)	3131 (617)	0.61
Neonatal unit admission	1 (1.89)	8 (7.62)	0.24

Results are expressed as mean (SD) or n (%) as appropriate. P values were calculated using the Pearson's χ^2 or Student's t-test.

D[14]; this lack of clarity may cause general practitioners to misidentify women who require supplementation, as the guidelines do not provide objective risk factors.

Despite low levels of compliance to NICE guidelines, this study demonstrated that supplementation had no significant effect on biochemical parameters between supplementation groups. In a related study, vitamin D supplementation led to a 55% increase in 25(OH)D levels and an 81% reduction in PTH levels at term which was statistically significant; such a difference was however not observed earlier at 27 weeks' gestation.[21] In our study, biochemical parameters were obtained at varying stages of gestation with a mean gestational age of 26.4 weeks. It is possible that if we had measured the biochemical parameters at term, we may have been able to demonstrate a statistically significant difference between the two groups.

Comparison with existing literature

In the Maternal Vitamin D Osteoporosis Study (MAVIDOS), a significantly higher proportion of women randomised to receive cholecalciferol during pregnancy were found to be vitamin D replete (>50 nmol/L) at 34 weeks' gestation compared with the placebo group.[22] This differs from our study, where no differences in vitamin D repletion status were seen between the women who were taking supplementation and those who did not. It is worth noting however, that the vitamin D dosage used in MAVIDOS was 1000 IU, contrasting to the 300 IU found in Healthy Start supplementation. In MAVIDOS, treatment and placebo groups were assessed for compliance by asking participants to bring any remaining medication to each assessment. Participants with poor compliance were excluded from analysis. This study also demonstrated that compliance was a significant determinant of maternal 25(OH)D response to supplementation. In our study, if participants stated that they were taking the correct dosage in the questionnaire, we assumed good compliance on the basis of their self-certification. If pill counting was undertaken as is customary in randomised controlled trials, we may have noticed a different outcome; this was however not part of the study design which was intended to make an assessment of adherence to NICE guidance. We may expect that this outcome would have regional variation within the UK.

The Healthy Start supplementation contains 300 IU (7.5 mcg) of vitamin D, which is considered 'low-dose'. It has been previously observed that while vitamin D status was higher in pregnant women who took multivitamin supplements containing low-dose (<10 mcg) vitamin D, serum 25(OH)D insufficiency was still evident after low-dose supplementation use in those with levels below 50 nmol/L.[23] Further studies are required to ascertain whether the Healthy Start supplementations should have various dosage formulations with higher dosages of vitamin D offered to women with insufficiency or deficiency.

We observed that after adjustment, the offspring of supplemented mothers were shorter in length compared with non-supplemented mothers. Offspring length was the only neonatal outcome that demonstrated significant differences between supplementation groups. A literature review reveals that gestational vitamin D status produces varying results for neonatal length. A meta-analysis showed that, neonates of supplemented mothers were significantly longer, while other studies have not found differences in neonatal length between supplementation groups.[24–26] It is worthwhile noting that differences in neonatal length in our study and the aforementioned meta-analysis[26] is minimal (1.6 vs 0.3 cm, respectively), therefore these differences may have negligible long-term consequences. However, since studies have shown that vitamin D supplementation indirectly contributes to skeletal mineralisation and fetal cell mass,[27] this is a plausible explanation for the significant differences in neonatal length. Nevertheless, fetal growth is influenced by a multitude of factors, including placental development, maternal nutrition, genetics and trophoblastic implantation.[28–30] Therefore, vitamin D status is unlikely to play a significant role in fetal length after adjustment for other factors. A more effective method to assess fetal growth would be to use standardised growth assessment (ie, serial ultrasound measurements), such as those used in the INTERGROWTH-21st Project (The International Fetal and Newborn Growth Consortium for the 21st Century), which can adjust for factors affecting fetal growth.[31] In this study, supplementation failed to demonstrate an influence on other neonatal outcomes. In three randomised controlled trials, maternal supplementation did not influence birth weight, nor the risk of having a low birth weight (<2500 g).[21 32 33]

Strength and limitations

The main strength in this study lies in the fact that it used a sample from a diverse ethnic population, allowing robust analysis of the effect of supplementation on biochemical and obstetrical outcomes with a sample that was representative of the diverse UK population. This study also has important limitations, including the small sample size compared with other studies that have investigated the effect of supplementation on biochemical and obstetrical outcomes, and in that respect was inadequately powered. The sample was also obtained from one geographical location in the UK, and hence the results may be different if an ethnically different population was studied elsewhere in the UK. Blood sampling was also carried out in women across a range of gestations in our study. A recent study has demonstrated a significant increase in serum 25(OH)D across trimesters, independent of vitamin D intake from supplements.[34] Therefore, maternal gestational age may have been a confounding factor in biochemical outcomes. Finally, our outcomes were not adjusted for skin colour. This is significant as previous studies have shown pregnant women with darker skin colour on the

Fitzpatrick Scale were significantly more often vitamin D deficient compared with women with lighter skin colour.[35]

Implications for research and practice

Although adherence to NICE standards in this region regarding vitamin D supplementation is suboptimal, this may not have significant clinical consequences. Adequately powered randomised controlled trials are required to examine the clinical effectiveness of antenatal supplementation on feto-maternal outcomes, including pre-eclampsia and neonatal respiratory outcomes. If future trials are able to demonstrate the benefits of vitamin D supplementation, strategies should be implemented to ameliorate adherence to NICE guidelines, including improving the clarity of guidelines and formulating a single reliable source of information for physicians and pregnant women. The aforementioned limitations of this study could be resolved through a multicentre population study of supplementation. In this respect our study and the inherent methodology could be conceived as a forerunner for future studies.

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