




RESEARCH ARTICLE

Associations between maternal circulating 25-hydroxyvitamin D concentration and birth outcomes—Mode of delivery and episiotomy rate: A prospective cohort study

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Abstract

Aim: The objective of this study was to evaluate associations between maternal concentrations of 25-hydroxyvitamin D (25(OHD)) and birth outcomes: mode of delivery and episiotomy rate.

Design and Methods: One hundred and seventeen pregnant women were enrolled in an observational, longitudinal, prospective cohort study. Multivariable linear regression analyses were performed to assess relationships between maternal 25(OHD) concentrations and mode of delivery. To account for systematic temporal variation in 25(OHD), a cosinor model to the data was fitted.

Results: No significant statistical associations were found between adjusted maternal 25(OHD) concentrations and risk of eutocic vaginal delivery, instrumented delivery (OR 1.05 [95% CI: 0.97–1.13]), primary Caesarean section (OR 0.99 [95% CI: 0.88–1.11]) or Caesarean section for any other causes (OR 1.04 [95% CI: 0.95–1.14]). High 25(OHD) levels tended to show a protective effect on performance of episiotomy, without reaching statistical significance (OR 0.36 [95% CI: 0.09, 1.37]).

KEYWORDS

25-hydroxyvitamin D, caesarean section, episiotomy, instrumented delivery, pregnancy

1 | INTRODUCTION

Many studies support the importance of vitamin D in several physiological functions beyond bone and muscle health (Joergensen et al., 2014), influencing a significant number of physiological activities. In particular, during pregnancy, vitamin D is involved in many embryogenesis pathways, especially in skeletal development and

calcium homeostasis of the foetus (Hollis et al., 2011). In fact, associations between vitamin D deficiency in pregnancy and higher prevalence of many adverse maternal and foetal outcomes, such as gestational diabetes mellitus (Rajput et al., 2019), preeclampsia (Serrano-Díaz et al., 2018), small-for-gestational age newborns (Bi et al., 2018) and preterm birth (Kassai et al., 2018), among others (Agarwal et al., 2018; Palaniswamy et al., 2015), have been reported.

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2 | BACKGROUND

The vitamin D receptor has been identified in smooth (Vienonen et al., 2004) and skeletal muscle tissue (Bischoff et al., 2001), and many studies have demonstrated the importance of vitamin D in muscle function (Dror et al., 2012; Gernand et al., 2013; Simpson et al., 1985). In this sense, vitamin D seems to regulate contractile proteins of uterine myometrial cells (Loy et al., 2015). Besides, its deficiency could decrease the strength of muscle contractility during labour, causing prolonged labour or foetal malposition, increasing the need for Caesarean section (Tian et al., 2015). There are many studies evaluating the influence of vitamin D on foetal outcomes. However, only a few ones have assessed associations between serum vitamin D levels and the end of labour, showing contradictory results (Table 1).

Regarding mode of delivery, the association between maternal vitamin D levels and the Caesarean section rate has been the main investigated issue. It has been reported that levels of vitamin D above 30 ng/ml decreased the risk of Caesarean section by obstructed labour, as reported by the Spanish cohort INMA (Rodriguez et al., 2015) and other authors as well (Scholl et al., 2012). However, other studies did not support this finding, reporting no association between maternal vitamin D status and Caesarean section rate (Loy et al., 2015; Savvidou et al., 2012; Yuan et al., 2017). In contrast, another relevant aspect, such as the relationship between vitamin D and instrumental delivery, has only been investigated in one study in the United States of America (Gernand et al., 2015), showing that maternal vitamin D status at ≤ 26 weeks was not associated with the risk of prolonged labour or operative delivery. Therefore, nowadays there are inconclusive results in the literature about the relationship between insufficient maternal levels of vitamin D and the rate of obstructed labour, either ending in Caesarean section or ending in instrumental delivery. It is also unknown whether there is a potential association between vitamin D levels and the risk of performance of an episiotomy.

Another controversial aspect about vitamin D and pregnancy is the potential role of physical activity. Existing investigations show an association between physical activity levels and vitamin D status in older people (Klenk et al., 2015), women (Kluczynski et al., 2011) and adolescent populations (Black et al., 2014). Although studies in pregnant women are scarce, one study conducted in Germany found that physically inactive pregnant women were about 2–7 times more likely to have vitamin D deficiency than those reporting to be physically active (>1 hr/week) after controlling for season and independent risk factors (adjusted OR 2.67 [95% CI: 1.06–6.69] $p = .032$) (Wuertz et al., 2013).

Nurse managers as first-line leaders have a responsibility to encourage changes in the clinical environment (Kodama & Fukahori, 2017). Midwives have an essential role in the screening for adverse pregnancy outcomes and providing prevention care in pregnant women. The role of vitamin D on pregnancy outcomes is an emerging field in obstetrics, and midwives must be involved in the prevention of its deficiency.

TABLE 1 Summary of publications on human studies discussed in the current article

Study design	Country	N	Gestational age at Vitamin D assay (weeks)	Main outcomes	Statistics	Authors	Quality of evidence (GRADE system)
Study cohort	USA (Boston)	253	At delivery	C-section	OR 3.84 (1.71–8.62)	Merewood et al. (2009)	Low
Study cohort	USA	1,153	13	C-section	AOR 1.99 (1.20–3.30)	Scholl et al. (2012)	Moderate
Retrospective cohort study	UK	995	11–13	C-section	$p = .53$	Savvidou et al. (2012)	Moderate
Case-control	India	46–46	At delivery	C-section	OR 2.31 (0.77–6.92)	Tian et al. (2015)	Moderate
Prospective cohort study (INMA cohort)	Spain	2,382	13.5	GDM, PTL, C-section, FGR, SGA, HC, BW	RR = 0.60 (0.37–0.97)	Rodriguez et al. (2015)	High
Cohort study	Singapore	940	26–28	GDM, C-section	OR 1.39 (0.95–2.05)	Loy et al. (2015)	Moderate
Cohort study	USA	2,798	<26	C-section, prolonged labour and vaginal instrumentation	RR 0.78 (0.37–1.64)	Gernand et al. (2015)	Moderate
Cohort study	Turkey	229	13	C-section	$p > .05$	Ates et al. (2016)	Low
Cohort study	China	1924	12–26	C-section	$p > .05$	Yuan et al. (2017)	Moderate
Cross sectional	Iraq	100	37–42	C-section	$p > .05$	Humadi Al-Maini (2019)	Low

Abbreviations: BW, birthweight; C-section, Caesarean section; FGR, foetal growth rate; GDM, gestational diabetes mellitus; HC, head circumference; PTL, preterm labour; SGA, small for gestational age. The p-values that are statistically significant are in bold, that is, when the p-value is less than or equal to 0.005.

Overall, the main objective of this study was to evaluate the association between vitamin D serum levels in pregnant women and fundamental aspects of the end of labour, such as instrumental delivery, Caesarean section, and the rate of episiotomy.

3 | THE STUDY

3.1 | Design and study population

An observational, longitudinal, prospective cohort study was carried out in a tertiary Gynaecology and Obstetrics Service at the 'Virgen de la Arrixaca' University Clinical Hospital. Recruitment was performed from March 2016–September 2019. Participants were Caucasian singleton pregnant women between 11 + 0–13 + 6 weeks of gestation. Inclusion criteria were as follows: ≥ 16 years of age, intention to deliver at the reference hospital, no communication problems and singleton pregnancy. This prospective cohort of pregnant women has been previously published with other primary objectives (Sánchez-Ferrer et al., 2020). For this study, sample size was calculated following clinical criteria from previous publications (Gernand et al., 2015; Loy et al., 2015). It was considered that it would be appropriate to detect a difference of at least 6 ng/ml (with a standard deviation of about 11.12 nmol/L) in 25(OH)D in both groups (episiotomy vs. no-episiotomy). For an alpha error of 0.05 and 80% statistical power to detect differences, a minimum of 58 women would be required in each group.

Participants were randomly selected from pregnant women who came to the first-trimester ultrasound. A list of all pregnant women enrolled in the first ultrasound of their pregnancy was obtained from the Obstetrics Service of the Hospital, and, by simple random sampling, a sample of 260 women was selected. Among all women invited to participate, 165 (63.5%) were finally enrolled in the study. During the follow-up, there were 31 dropouts, 7 miscarriages and 10 deliveries in another Hospital. Finally, 117 women (71%) were followed until birth and information about mode of delivery was recorded (Figure 1).

3.2 | Data collection

Data were collected during the three trimesters of pregnancy, 1st visit (8–13 weeks of gestation), 2nd visit (16–20 weeks of gestation) and 3rd visit (28–34 weeks of gestation). Data about delivery were obtained during hospitalization, before 48 hr postpartum. Maternal height, weight and blood pressure were measured at recruitment, and BMI was calculated. We recorded maternal age, parity, tobacco and alcohol consumption, previous maternal diseases (hypertension or diabetes), season at blood collection, nutritional supplements consumption and physical activity during pregnancy [quantified by basal metabolic units (METs)/week, through the short version of the IPAQ questionnaire (IPAQ-SF)] (IPAQ Research

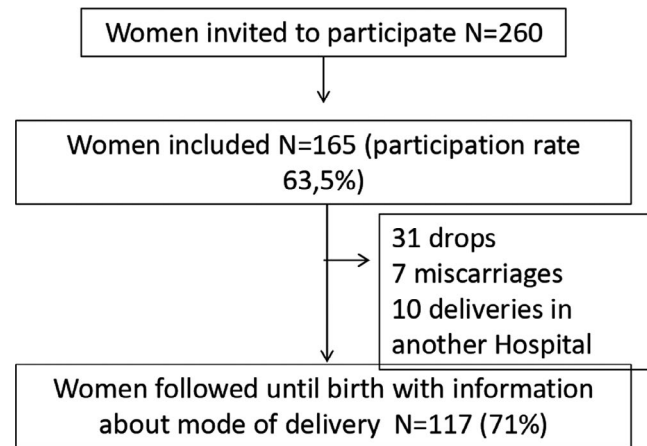


FIGURE 1 Flow diagram of the study

Committee. Guidelines for the Data Processing and Analysis of the International Physical Activity Questionnaire-2005 [Consulted December 2019]. Available at: www.ipaq.ki.se, n.d.). Reliability and concurrent validity of the IPAQ short form among pregnant women have been previously reported by Sanda et al. (2017). These self-reported questionnaires are widely used in large-scale surveys to estimate physical activity level due to their low cost and easy distribution. To calculate the METs/min per week of physical activity performed by each woman, we used the Compendium of Energy Expenditure of the different physical activities from Ainsworth et al. (2000), adopting an average score in METs for each type of activity. The following values were used for the analysis of the IPAQ data: walking: 3.3 METs and intense activities: 8.0 METs. The IPAQ sitting question is an additional indicator variable of time spent in sedentary activity and is reported as median values and interquartile ranges. These data were also recorded at the second and third visits with a survey response rate above 95%. The women who refused to participate argued lack of time for filling out questionnaires.

After delivery, childbirth data were registered: newborns' weight and gender, performance of episiotomy and mode of delivery. Data collection was recorded specifically for the study purposes, including all the necessary obstetric information, which was collected by reviewing woman medical records. About missing data management, we only considered the data from women who were followed during the three trimesters of pregnancy and had information about birth and their mode of delivery.

Birthweight percentiles were calculated using neonatal data by Carrascosa Lezcano et al. (2008). Delivery was classified as eutocic vaginal delivery, instrumental vaginal delivery (including vacuum, forceps or spatulas), primary Caesarean section (we defined primary Caesarean section as delivery by emergency Caesarean for obstructed labour such as non-progression of labour, failed induction and cephalopelvic disproportion) and Caesarean for other causes (such as emergency Caesarean for foetal distress or elective Caesarean sections).

3.3 | Sampling and vitamin D analysis

At recruitment, during the first trimester of pregnancy, 5 ml of maternal blood was collected. Blood samples were separated by centrifugation at 1,000 g for 5 min, and serum was obtained for vitamin D analysis. The quantitative determination of 25(OH)D in serum was performed by the Liaison 25-OH-Vitamin D total kit of DiaSorin (Stillwater-USA), by chemiluminescent immunoassay technology (CLIA). Studies have shown that CLIA is an effective replacement for high-performance liquid chromatography which is widely used to measure 25-hydroxyvitamin D levels (Kushnir et al., 2010; Pal et al., 2013), and among automated immunoassays, the Liaison kit demonstrated the best performance (Farrell et al., 2012). Detection limit was 4.0 ng/ml with a measuring range between 4.0–150 ng/ml.

The circulating concentration of 25(OH)D in pregnant women was evaluated as a continuous value and also categorized, both in quartiles and using clinically relevant cut-off points: <20 ng/ml (deficiency, reference group), 20–29.99 ng/ml (insufficiency) and >30 ng/ml (sufficient) according to the recommendations of the Institute of Medicine (IOM) (Ross et al., 2011).

According to Barnett and Dobson (2010), to account for systematic temporal variation in 25(OH)D levels—usually following a sinusoidal pattern, a cosinor model for the data was fitted (Barnett & Dobson, 2010). In the cosinor model, the dependent variable [25(OH)D] was modelled as a sine wave characterized by phase shift (location of peak and trough levels on the time axis), height (vertical shift of the sine wave) and amplitude (maximum variation of the sine wave from its mean height) (Mikulich et al., 2003). The predicted annual mean of 25(OH)D concentrations based on month at blood collection for each subject, derived from the sinusoidal model, was then subtracted from the current observed value. Subsequently, the overall mean was added and the resulting deseasonalized 25(OH)D concentrations were used for statistical analyses (Morales et al., 2013).

3.4 | Statistical analyses

Descriptive data are shown as percentages for categorical variables and mean and standard deviation (SD) for continuous variables. Differences in baseline characteristics of participants across quartiles of maternal vitamin D levels were compared using chi-square test for categorical variables and analysis of variance (ANOVA) for continuous variables. Normality of variables was verified using the Shapiro–Wilk test, observing a certain lack of normality in the variables of “less sitting” (physical activity) and weeks of gestation. For this reason, to evaluate the relationship between vitamin D levels (in quartiles) and these variables—in addition to the ANOVA test—the Kruskal–Wallis test was also considered, obtaining the same results in both tests.

Multinomial logistic regressions were fitted to estimate adjusted associations between maternal circulating 25(OH)D (either clinical cut-offs or quartiles) and modes of delivery. Odds ratios (OR) and its corresponding 95% confidence intervals (CI) were calculated.

All tests were two-tailed, and the level of statistical significance was set at 0.05. Statistical analyses were performed with the IBM Statistical Package for the Social Sciences (SPSS) v25 (IBM Corporation, Armonk, NY, USA).

3.5 | Ethics

The study was approved by the Hospital Clinical Research Ethics Committee on April 2017 (No 04/17) and was conducted ethically in accordance with the guidelines of the Declaration of Helsinki. Written informed consents were obtained from all the women at recruitment. The authors adhered to principles of honesty and transparency in reporting the data.

4 | RESULTS

Mean age of participants was 32.6 years (*SD*: 4.7). Thirty-seven per cent of women were primiparous, being the rest multiparous. Only 2.5% of the patients declared isolated consumption of alcohol during pregnancy, while 12.3% were smokers, with an average consumption of 4.7 cigarettes/day. With regard to supplements during pregnancy, only 1% refused to take any type of supplement. Fifty-seven per cent of women received supplements with folic acid and iodine, while 33% reported taking multivitamin-type supplements which included vitamin D (5–10 µg/day). Regarding BMI, 54% of women were in a normal weight range (BMI 18.5–24.9), while 3% were underweight and 29.6% and 13.4% were overweight and obese, respectively. Newborns' gender was 55% females and 45% males. The mean birthweight was 3.280 grams (*SD*: 510).

The maternal mean circulating 25(OH)D at the first trimester of pregnancy was 21.58 ng/ml (*SD*: 7.29). In our study sample, 41% of the women were in a deficiency status with values of vitamin D below 20 ng/ml (5% with a severe deficit with levels below 10 ng/ml) and 47% had insufficient levels (between 20–29 ng/ml). Only 12% of the pregnant women had normal levels of vitamin D, above 30 ng/ml at the beginning of pregnancy according to the recommendations of the Institute of Medicine (Ross et al., 2011). The characteristics of participants according to quartiles of circulating 25(OH)D levels during the first trimester are shown in Table 2.

The lowest levels of 25(OH)D (below 22 ng/ml) occurred in 56.1% of the samples taken in the spring, compared to the highest levels of 25(OH)D (>37 ng/ml) which happened more frequently (46.3%) in autumn. No other variables analysed in our study sample (parity, smoking, alcohol consumption, pregestational diabetes, maternal age, BMI, physical activity and birthweight percentile) showed differences according to the status of vitamin D at the first trimester of pregnancy. Although in our sample of pregnant women, we did not find a relationship between vitamin D and vigorous physical activity and walking physical activity—using the METS/min per week, women in the lower and upper extreme quartiles of vitamin D (<Q1 and >Q3) tended to have lower vigorous physical activity ($p = .1$).

Regarding the mode of delivery, 73% of the patients had a vaginal delivery, being 51% eutocic and 22% through instrumentation. In these vaginal deliveries, an episiotomy was specifically performed in 33% of them. Twenty-seven per cent of the women underwent a Caesarean section with 7.5% of the patients having a primary Caesarean section.

Pregnant women in the highest quartile of 25(OHD) serum concentrations had an adjusted OR of 2.14 (95% CI: 0.50, 9.17) for instrumental delivery compared with pregnant women in the lowest quartile (p for trend across quartiles = .307). Pregnant women in the highest quartile of 25(OHD) serum concentrations had an adjusted OR of 1.30 (95% CI: 0.21, 8.08) for primary Caesarean section compared with pregnant women in the lowest quartile (p for trend across quartiles = .781). Finally, pregnant women in the highest quartile of 25(OHD) serum concentrations had an adjusted OR of 2.50 (95% CI: 0.41, 15.16) for Caesarean section for other causes compared with pregnant women in the lowest quartile (p for trend across quartiles = .319) (Table 3). All models were adjusted for child's sex, gestational age, parity, age, maternal overweight and total METS.

Finally, the relationship between 25(OHD) levels at the beginning of the pregnancy and the performance of episiotomy during delivery was also assessed. Pregnant women in the highest quartile of 25(OHD) serum concentrations had an adjusted OR of 0.79 (95% CI: 0.24, 2.62) for performance an episiotomy compared with pregnant women in the lowest quartile (p for trend across quartiles = .695) (Table 4). Overall, no significant associations were found in this regard.

5 | DISCUSSION

In this study of singleton pregnant women, we investigated associations between maternal serum vitamin D levels in the first trimester and fundamental aspects of the end of labour. However, we found no statistically significant associations between adjusted vitamin D levels and the risk of finishing labour by eutocic labour, instrumented labour, primary Caesarean section or Caesarean section for any other cause. Besides, no associations between vitamin D levels and the incidence of episiotomy were observed either.

The mean vitamin D levels in maternal blood during the first trimester were 21.58 ± 7.3 ng/ml. Forty-one per cent of women were in a situation of deficit of vitamin D (<20 ng/ml), and 5% had a severe deficit (<10 ng/ml). These results are in agreement with a recent systematic review carried out in pregnant women in which 57% of European pregnant women had values lower than 20 ng/ml and 23% below 10 ng/ml (Saraf et al., 2016). These results confirm a relatively high prevalence of vitamin D deficiency in pregnant women worldwide.

Our findings also show the relationship between vitamin D serum levels and the season in which the analysis was performed. Previous studies have estimated that 25(OHD) levels drop about 20% from late summer to mid-winter (Rosen, 2011). In our results, the lower 25(OHD) levels (less than 22 ng/ml) were more frequently observed

(56.1%) in the spring, after the winter season with lower sun exposure. In order to avoid this bias, crude vitamin D levels were transformed before using them in subsequent analysis. For this purpose, deseasonalized maternal 25(OHD) concentrations derived from a sinusoidal model must be performed on these data. However, only a few studies analysing the relationship between vitamin D status and the mode of delivery have taken into account this methodological issue (Rodriguez et al., 2015). Consequently, this crucial aspect limits the results of those investigations, reducing the validity of their conclusions and making quite difficult the comparability and discussion of the obtained results.

Although there is some evidence regarding the association between vitamin D levels and muscle capacity (Bischoff et al., 2001; Dzik & Kaczor, 2019; Hazell et al., 2012; Mithal et al., 2013; Moran et al., 2013; Simpson et al., 1985; Viononen et al., 2004), we found no statistically significant associations between adjusted vitamin D levels and the mode of delivery. Regarding Caesarean section rates, previous investigations examined its relationship with the women's vitamin D status in different populations (China, UK, USA and Singapore), without finding a significant association between maternal vitamin D levels and the increased or decreased rate of Caesarean sections (Gernand et al., 2015; Loy et al., 2015; Savvidou et al., 2012; Tian et al., 2015; Yuan et al., 2017). However, these studies cannot be easily compared, as the gestational timing for 25(OH)D serum level assessment was different. Moreover, associations between genetic variation in cytochrome P450, vitamin D binding protein (Robien et al., 2013) or vitamin D receptor (Levin et al., 2012) and 25(OH)D concentrations could also affect vitamin D metabolism and disease susceptibility.

On the other hand, opposite findings have also been published suggesting a link between maternal vitamin D levels and the risk of having a Caesarean section in different populations. Merewood et al., (2009) and Scholl et al., (2012) reported a fourfold and twofold increased risk, respectively, of having a Caesarean section by obstructed delivery in women with lower vitamin D levels. The study by Rodriguez et al., (2015) also showed that 25(OHD) levels ≥ 30 ng/ml decreased the risk of Caesarean section for obstructed delivery (RR = 0.60, 95% CI: 0.37–0.97). These contradictory results in different studies show the need for further studies in larger cohorts. Moreover, a better and more homogeneous definition of the criteria for primary Caesarean section (due to obstructed delivery) and Caesarean sections for other reasons may also help to define the role of vitamin D levels during delivery.

Regarding the role of vitamin D supplementation in the mode of delivery, overall, no sufficient evidence has been found to support this recommendation in recent meta-analysis (De-Regil et al., 2016; Harvey et al., 2014; Roth et al., 2017).

In relation to the end of the delivery by instrumental vaginal delivery and its relationship with maternal vitamin D status, to the best of our knowledge, our results are the first ones reported in Europe and are in agreement with the study conducted in United States by Gernand et al., (2015) in 2,798 pregnant women. They found no associations between maternal vitamin D status and the risk of

TABLE 2 Characteristics of participants according to quartiles of maternal circulating 25(OH)D concentration in pregnancy

	N: 117	<Q1	Q1-Q2	Q2-Q3	>Q3	p-value
Vitamin D (ng/ml)	21.58 (7.29)	≤22	22–29	29–37	>37	
Age (years)	32.6 (4.7)	31.9 (5.0)	32.5 (5.1)	33.1 (4.6)	32.7 (4.4)	0.734
BMI at 12 weeks (kg/m ²)		26.3 (5.5)	24.8 (4.3)	24.2 (4.3)	23.9 (3.7)	0.075
Underweight: BMI <18.5	3					
Normal weight: BMI 18.5–25	54					
Overweight: BMI 25–30	29.6					
Obese: BMI >30	13.4					
Parity (1 or more)	63	43.9	48.6	31.7	43.6	0.475
Smoking during pregnancy	12.3	25.0	5.0	7.0	10.0	
Alcohol consumption	2.5	0	7	0	0	
Pregestational diabetes mellitus	1	25.0		0.5	0	
Season at blood extraction						
Winter		24.4	24.3	20.9	7.3	0.004
Spring		56.1	29.7	34.9	29.3	
Summer		14.6	21.6	11.6	17.1	
Autumn		4.9	24.3	32.6	46.3	
Total vigorous MET-min/week		84.3 (358.7)	435.4 (1193.6)	200.9 (630.5)	76.1 (388.6)	0.110
Total walking MET-min/week		733.4 (813.7)	950.8 (1161.3)	917.7 (1193.5)	914.7 (1202.2)	0.829
TOTAL, METS/min/week		1073.9 (1564.7)	1977.1 (3050.4)	1255.6 (1927.3)	1053.6 (1577.1)	0.227
Sitting total min/week		2727.4 (1349.8)	2.240 (1302.7)	2375.9 (1415.8)	2147.3 (1030.4)	0.218
Mode of delivery						
Eutocic delivery	51					
Instrumental delivery	22					
Caesarean delivery	27					
Primary Caesarean section	7.5					
Newborn gender (females)		63.2	51.4	47.6	51.3	0.542
Gestational age at birth		39.0 (1.7)	38.8 (2.9)	39.0 (1.6)	39.2 (1.6)	0.838
Birthweight percentile		52.4 (27.4)	53 (25.6)	54.5 (25.7)	59.4 (25.9)	0.663

Note: Values are percentages for categorical variables and mean (SD) for continuous variables. The p-values that are statistically significant are in bold, that is, when the p-value is less than or equal to 0.005.

prolonged first or second stage of labour, Caesarean delivery or indicated instrumental delivery. Our findings confirm the lack of evidence to establish a relationship between maternal vitamin D levels and the end of labour by vaginal instrumented delivery.

With regard to the association between physical activity and vitamin D, we did not find a relationship between vitamin D status and the mode of delivery after accounting for physical exercise. Moreover, in our study sample, no associations between vitamin D and vigorous or walking physical activity were found. While the available data in women of childbearing age are scarce, one study conducted in Germany found that physical inactivity was a significant risk factor for maternal vitamin D deficiency after controlling for season, vitamin D supplementation and time spent outdoors (Wuertz et al., 2013). Furthermore, a Cochrane review of 14 trials, involving 1,014 pregnant women, evaluated the role of physical exercise and mode of delivery. Overall results showed that pregnant women who were engaged in

vigorous exercise at least two to three times per week have no differences in mode of delivery (Kramer & McDonald, 2009).

Finally, we evaluated maternal vitamin D levels and their relationship with the greater or lower incidence of episiotomy, without finding any statistical significant association between both variables. There are currently no studies on this topic, and our findings are the first approach in this regard.

There is growing consensus among public health professionals that midwifery care has an essential contribution to improve quality of maternal and newborn care. Our results provide novel information about important factors related to potential adverse pregnancy outcomes: low maternal vitamin D levels, Caesarean section rate, instrumental deliveries and performance of episiotomy. Involvement of midwives on many of the topics discussed in this article is of great importance in order to prevent vitamin D deficiency and promote healthy lifestyles among pregnant women (Renfrew et al., 2014).

TABLE 3 Adjusted associations of maternal 25(OH)D concentration^a in pregnancy (ng/ml) with end of delivery

25(OH)D (ng/ml)	N (%)	Instrumental		Caesarean (primary cause)		Caesarean (other causes)		
		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	
As continuous	117	1.05 [0.97, 1.13]	0.236	0.99 [0.88, 1.11]	0.835	1.04 [0.95, 1.14]	0.358	
Quartiles								
Q1: ≤22		Ref	-	Ref	-	Ref	-	
Q2: 22–29		1.63 [0.34, 7.73]	0.541	0.68 [0.08, 5.80]	0.725	2.67 [0.35, 20.54]	0.345	
Q3: 29–37		1.16 [0.29, 4.63]	0.829	0.25 [0.02, 2.77]	0.257	1.15 [0.18, 7.27]	0.882	
Q4: >37		2.14 [0.50, 9.17]	0.307	1.30 [0.21, 8.08]	0.781	2.50 [0.41, 15.16]	0.319	
Clinical cut-offs								
Deficiency	<20	48 (41.0)	Ref	-	Ref	-	Ref	-
Insufficiency	20–29	55 (47.0)	0.99 [0.33, 2.94]	0.980	0.54 [0.12, 2.48]	0.428	1.00 [0.24, 4.07]	0.995
Sufficiency	≥30	14 (12.0)	2.54 [0.53, 12.16]	0.244	0.49 [0.03, 7.69]	0.609	2.34 [0.34, 16.05]	0.387

Note: Abbreviations: CI, confidence interval; OR, odds ratio.

Reference: Eutocic delivery (excluding instrumental)

All models adjusted for child's sex, gestational age, parity, age at delivery, maternal overweight and TOTAL METS.

^aDeseasonalized maternal 25(OH)D concentration based on month of blood collection for each subject derived from the sinusoidal model.

TABLE 4 Adjusted association of maternal concentration of 25-hydroxyvitamin D (ng/ml)^a in pregnancy with the incidence of episiotomy

25(OH)D (ng/ml)	N (%)	Episiotomy		
		OR (95% CI)	p-value	
As continuous	117	1.01 [0.95, 1.08]	.680	
Quartiles				
Q1: ≤22	29 (24.8)	Ref	-	
Q2: 22–29	26 (22.2)	0.88 [0.26, 2.96]	.833	
Q3: 29–37	34 (29.1)	0.72 [0.18, 2.93]	.646	
Q4: >37	28 (23.9)	0.79 [0.24, 2.62]	.695	
Clinical cut-offs				
Deficiency	<20	48 (41.0)	Ref	-
Insufficiency	20–29	55 (47.0)	0.42 [0.11, 1.63]	.211
Sufficiency	≥30	14 (12.0)	0.36 [0.09, 1.37]	.133

Abbreviations: CI, confidence interval; OR, odds ratio.

^aDeseasonalized maternal 25(OH)D concentration based on month of blood collection for each subject derived from the sinusoidal model.

5.1 | Strengths and limitations

As a strong point of this study, the measurement of circulating maternal serum concentration of 25(OH)D is appropriate and convenient, since it is the best measure of vitamin D status in humans we currently have. The use of the estimated average annual concentration of 25(OH)D circulating from a single measurement is also noteworthy, in order to take into account seasonal variation and reduce the erroneous classification of exposure ("seasonality"). In addition,

a multivariate analysis adjusted for a wide range of possible confounders has been performed.

Participants were randomly selected from pregnant women who came to the first-trimester ultrasound. This ultrasound is centralized in the Obstetrics Service of the Hospital in which the study was performed, so our study sample may be quite representative of the source population and therefore generalizability of our findings may take place. On the other hand, our results could not be extrapolated to women not attending the first-trimester screening. As with all

observational studies, causal inference is restricted and therefore prevents causal interpretations. Adjustment for known and potential confounders and covariates was also carried out. However, there is always the possibility of residual or unmeasured confounding. Moreover, it cannot be precluded that type II error might explain the negative results observed in our study.

Furthermore, in our study a single blood serum sample was taken for vitamin D analysis in the entire pregnancy, which was carried out in the first trimester. For this reason, it cannot be ruled out that some changes in the levels of vitamin D could happen during pregnancy, leading to higher or lower levels over the pregnancy. Self-reported exercise activity and tobacco/alcohol consumption have to be recognized as a potential study limitation since social desirability bias, over-reporting good routines or under-reporting undesirable behaviours could have occurred.

6 | CONCLUSION

No associations between adjusted maternal vitamin D levels and the risk of eutocic delivery, instrumented delivery, primary Caesarean section or Caesarean section for any other causes were found. Furthermore, no relationships between vitamin D levels and the incidence of episiotomy were shown either. However, our findings provide novel information on the relationship between vitamin D and instrumented delivery, and the association between vitamin D and the incidence of episiotomy, which had not been previously evaluated. From the published literature, it is clear that vitamin D plays an important role at the muscular level, but the current evidence and our results show an uncertain association between maternal vitamin D status and mode of delivery. Therefore, further studies will be warranted to elucidate the evaluated associations.

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CONFLICT OF INTEREST

The authors have no competing interests to declare.

AUTHOR CONTRIBUTIONS

AMT-C, JM and MLS-F: Study conception and design. EA-M, IG-C, MAI, MTP-S and MLS-F: Study execution and acquisition of data. JJA-G, MLS-F, MTP-S, JM and AMT-C: Data analysis and interpretation. MLS-F, JJA-G, MTP-S, EA-M, IG-C, MAI, JM and AMT-C: Drafting the manuscript. All authors provided substantial intellectual contributions and approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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