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ORIGINAL ARTICLE

# Vitamin D levels in pregnant women and their newborns

## Niveles de vitamina D en mujeres embarazadas y sus recién nacidos

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**What do we know about the subject matter of this study?**

The physiology and pathophysiology of vitamin D have been extensively studied. Measuring this vitamin in pregnant women provides useful information for deciding whether to supplement this group. The scientific literature shows a high correlation between maternal and newborn levels. In most studies worldwide, vitamin D levels in mother-child dyads are low. This deficiency/insufficiency is associated with morbidity in both the pregnant mother and the newborn.

**What does this study contribute to what is already known?**

A national population is explored, representative of a region in south-central Chile (36º 46' 22" south latitude). It confirms a high percentage of vitamin D deficiency and insufficiency in pregnant women and their newborns, with a significant correlation between the two.

## Abstract

Vitamin D is crucial for biological functions and bone metabolism, being important in pregnant women (PW) and newborns (NB). **Objective:** To determine the levels of 25 OH Vitamin D (25 (OH) D) in pregnant women and their newborns, and to explore the relationship in the dyad. **Patients and Method:** Observational and descriptive study. 25(OH)D levels were measured in PW before delivery and in NB after birth. Anthropometric variables of PW and their NB were recorded, as well as nutritional classification according to gestational age of the NB. **Results:** 172 PW and their NB were evaluated. The mean ± SD age of the mothers was 30.4 ± 5.9 years. The mean ± SD gestational age and birth weight of the newborns were 38.6 ± 1.1 weeks and 3434 ± 505 grams, respectively. The average 25(OH)D level in PW was 18.4 ng/mL, and in the NB, it was 16.4 ng/mL. 89.5% of the PW and 95.4% of the NB presented deficiency/insufficiency. A significant correlation was observed between the levels of 25(OH)D in the mothers and their newborns. There were no significant differences in

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25(OH)D levels according to the nutritional status of the newborn. **Conclusions:** Our study showed a high percentage of vitamin D deficiency/insufficiency in pregnant women and their newborns. A significant correlation in 25(OH)D levels between PW and newborns was observed. These results highlight a public health problem that must be addressed promptly with modifications in national guidelines for vitamin D supplementation during pregnancy.

## Introduction

Vitamin D is a prohormone that participates in calcium and phosphorus metabolism and in a wide range of additional biological functions1. Its functions are carried out by increasing intestinal absorption of calcium and phosphate, enhancing renal tubular reabsorption of both elements, and providing the mineral necessary for the formation of new bone tissue[2].

In humans, vitamin D3 (cholecalciferol) is naturally obtained through exposure to ultraviolet B (UVB) sunlight in the 290-315 nm range, via a thermodependent isomerization reaction that converts 7-dehydrocholesterol into vitamin D3. The latter then diffuses into the circulation through the capillary bed and enters the bloodstream reversibly bound to vitamin D-binding protein (VDBP). In serum, most vitamin D metabolites bind preferentially to VDBP, but they are also known to associate with serum albumin. Vitamin D3 undergoes its first step of activation in the liver by 25-hydroxylase (CYP27A1). The product of 25-hydroxylation, 25-hydroxyvitamin D3 [25(OH)D3] (calcidiol), is the main circulating form of vitamin D3 and, in humans, is present in plasma in concentrations that vary between populations, depending on latitude, pollution, sun exposure, sex, eating habits, and health regulations. The second step of activation occurs mainly in the kidney by the cytochrome P450 enzyme, 25(OH)D-1α-hydroxylase (CYP27B1). This process leads to the formation of the active metabolite of vitamin D3, 1,25-dihydroxyvitamin D3 [1,25(OH)2D3] (calcitriol)[3,4].

In addition to its classic functions, vitamin D has been attributed with a wide range of additional biological functions, such as cell growth, apoptosis, angiogenesis, differentiation, and immune system regulation, functions referred to as non-classical functions of vitamin D[1,5,6].

During pregnancy, vitamin D metabolism differs significantly from that in non-pregnant women. In this stage, three main adaptations occur in vitamin D homeostasis: a) increased maternal calcitriol, b) maternal availability of 25(OH)D for optimal neonatal 25(OH) D status, and c) increased maternal concentrations of vitamin D-binding protein. During the first weeks of pregnancy, calcitriol increases 2–3 times, while maternal 25-hydroxyvitamin D crosses the placental barrier and constitutes the main reserve of vitamin D in the fetus[3]. In pregnant women, intestinal absorption of calcium and other minerals doubles. During the last 6 weeks of gestation, the placenta absorbs 5% to 10% of the calcium and phosphate present in the maternal plasma per hour to meet fetal demands. The placenta and fetal kidneys express 1α-hydroxylase, leading to the frequent assumption that they are the sources of the increase in calcitriol in the maternal circulation, but it has been shown that the expression and functional activity of CYP27B1 in the maternal kidneys are substantially upregulated during pregnancy, and that this renal expression is greater than that of the placenta[2].

International reports have shown varying rates of vitamin D deficiency and/or insufficiency in both pregnant women and their newborns[4,7-12].

Vitamin D deficiency during pregnancy has been associated with some adverse neonatal outcomes, as well as an increased risk of complications in the later stages of pregnancy. It has been postulated that vitamin D deficiency could be associated with an increased risk of preeclampsia, gestational diabetes mellitus, and bacterial vaginosis. From a neonatal perspective, research also suggests a possible association between low vitamin D concentrations and an increased risk of premature birth, low birth weight, lower bone mass, and a possible link to the future development of diseases such as bronchiolitis, asthma, type 1 diabetes, multiple sclerosis, and autism[13,14].

The 2016 Chilean National Health Survey, which included 1,591 women of childbearing age between 15 and 49 years old, revealed that 87% of them were vitamin D deficient, of which 16% had a severe deficiency (less than 12 ng/mL)[15]. However, no information is available in our country on vitamin D levels in pregnant women and their newborns. Therefore, it is valuable to obtain local data on vitamin D status in a population in a region of south-central Chile (36º 46' 22" south).

This study hypothesizes that pregnant women and their newborns have a significant percentage of vitamin D deficiency or insufficiency in a region of Chile. The main objective was to determine the levels of 25(OH)D in pregnant women and their newborns and to explore its association in the dyad.

## Patients and Method

Observational, cross-sectional study of a descriptive-exploratory nature. It was conducted on pregnant women hospitalized in the Obstetrics and Gynecology Department of the *Hospital Guillermo Grant Benavente* and their newborns between February 1, 2023, and June 30, 2024. The established inclusion criteria were dyads with informed consent, complete medical records, mothers of legal age (≥ 18 years), and full-term pregnant women (≥ 37 weeks) and their newborns in whom venous puncture could be successfully performed. The exclusion criteria were dyads in which the mother had an oral and/or written language disability; mothers who spoke a language for which no translator was available; pregnant women with severe mental disorder; pregnant women or newborns whose 25(OH)D measurement could not be determined for any reason; and full-term newborns with major malformations and/or chromosomal abnormalities.

Serum 25(OH)D levels were measured in pregnant women during the 48 hours before delivery and in newborns during the 48 hours after birth.

To measure 25(OH)D, 1 mL of blood was collected from the newborn and 3.5 mL of blood from the pregnant woman. It was measured using the chemiluminescence technique on the Siemens Atellica system. The blood sample was collected, stored, transported, and analyzed according to the protocol of the Central Laboratory of the *Hospital Guillermo Grant Benavente*. To determine sufficiency or insufficiency in plasma levels of vitamin D, the standard recommended by the American Association of Clinical Endocrinology[16] was used. Normal plasma concentration was defined as ≥ 30 ng/mL, insufficiency between 20 and 29 ng/mL, and deficiency < 20 ng/mL in the dyad. In newborns, anthropometric variables and nutritional classification according to gestational age were recorded. In pregnant women, data on education, nationality, vitamin D supplementation, and clinical data were obtained through a structured interview and review of the maternal medical record.

### Sample size

The sample size was calculated using a quantitative approach. The first 20 data points were used as a pilot sample to estimate the variability of 25(OH)D levels. With this information, the sample size was determined using simple random sampling, considering an estimated loss of 25%. With a confidence level of 95% and an error of 5%, a final size of 171 dyads was obtained.

### Statistical analysis

A descriptive analysis was performed on all recorded variables. The normality of quantitative variables was assessed in order to apply the Student's t-test or the Mann-Whitney test, as appropriate, to identify differences in anthropometric classifications of 25(OH)D levels by sex. The Mann-Whitney test was also applied to compare 25(OH)D levels according to the seasons of the year and the presence of pathologies in the mother.

In addition, the percentage of small for gestational age (SGA) newborns was calculated in mothers with 25(OH)D levels above and below 20 ng/mL.

The Wilcoxon test was used to compare 25(OH) D levels in pregnant women with and without pathologies, and Pearson's correlation coefficient was used to analyze the relationship between maternal 25(OH) D levels and those of their newborns. The comparison of 25(OH)D levels according to the nutritional status of newborns –large, adequate, or small for gestational age (LGA, AGA, SGA)– was performed using the Kruskal-Wallis test, which was also used to evaluate differences based on birth scenarios.

The data were recorded in an Excel spreadsheet designed for the study and analyzed using Python 3.10 software. A statistical significance level of $p < 0.05$ was considered.

The study was approved by the Scientific Ethics Committee (SEC) of *Hospital Guillermo Grant Benavente* and the Biobío Health Service, and informed consent was obtained from the pregnant women for themselves and their newborns.

## Results

A total of 234 dyads were considered; 62 were excluded due to problems in sampling the pregnant woman or newborn. 172 dyads were enrolled with complete data from both tests.

The mean maternal age ± standard deviation (SD) was 30.4 ± 5.9 years (range 18-44 years). 30% of pregnant women received vitamin D supplementation. Table 1 shows additional information regarding education, sun exposure related to work activity, and pathologies.

The mean gestational age and birth weight ± SD of the newborns were 38.6 ± 1.1 weeks and 3434 ± 504 grams, respectively. 57.6% (n = 99) of the newborns were male. Table 2 shows other anthropometric characteristics of the newborns.

The mean and SD of 25(OH)D levels in pregnant women were 18.4 ± 7.7 ng/mL, and in newborns were 16.4 ± 6.9 ng/mL (Figure 1). Vitamin D deficiency was found in 61.6% (106/172) of pregnant women and 75.6% (130/172) of newborns. 27.9% (48/172) of pregnant women and 19.8% (34/172) of newborns presented insufficiency. 89.5% of pregnant women and 95.4% of newborns presented deficiency or insufficiency of vitamin D. 10.5% (18/172) of pregnant

**Table 1. General characteristics of pregnant women**

| Variables | | N (%) |
|---|---|---|
| Age (years) (30,4 ± 5,9) | ≤ 20 | 11 (6) |
| | 21-39 | 149 (87) |
| | ≥ 40 | 12 (7) |
| Level of Education | Elementary school | 2 (1) |
| | Middle school | 22 (13) |
| | High school | 72 (42) |
| | Superior | 76 (44) |
| Nationality | Chilean | 158 (92) |
| | Venezuelan | 14 (8) |
| Activity | With predominant sun exposure | 7 (4) |
| | Without predominant sun exposure | 165 (96) |
| Vitamin D supplementation | Yes | 52 (30) |
| | No | 120 (70) |
| Pathologies | Obesity | 90 (52) |
| | Gestational Diabetes | 35 (20) |
| | Intrahepatic cholestasis of Pregnancy | 21 (12) |
| | Hypothyroidism | 15 (9) |
| | Chronic Hypertension | 13 (8) |
| | Hypertensive Disorders of Pregnancy | 11 (6) |
| | Type 2 Diabetes Mellitus | 10 (6) |
| | Preeclampsia | 8 (5) |
| | Cholelithiasis | 4 (2) |
| | Insulin Resistance | 4 (2) |
| | Overweight | 4 (2) |
| | Asthma | 3 (2) |
| | Drug Use | 2 (1) |
| | Hyperthyroidism | 2 (1) |
| | Single-kidney | 2 (1) |
| | Syphilis | 2 (1) |
| | Other | 20 (12) |

women and 4.7% (8/172) of newborns had normal levels of 25(OH)D (≥ 30 ng/mL) (Table 3).

When analyzing vitamin D levels in relation to the seasons of the year, the result yields a p-value of 0.054, which is at the threshold of statistical significance. Therefore, the analysis was complemented with a graphical representation using box-and-whisker plots. This representation shows that the highest vitamin D levels in mothers and newborns were observed in autumn (Figure 2).

A significant correlation of 0.73 was obtained between the 25(OH)D levels of pregnant women and their newborns (Figure 3). No differences were found in 25(OH)D levels between pregnant women who received supplementation (19.8 ng/mL) and those who did not (18.0 ng/mL) ($p = 0.28$). No significant difference was observed in 25(OH)D levels between pregnant women with or without a medical condition ($p = 0.83$). Maternal vitamin D levels were analyzed in relation to different morbidities, showing no statistically significant differences between the groups ($p = 0.083$). This indicates that, when considering each pathology independently, vitamin D levels do not differ significantly.

There were two routes of delivery: vaginal delivery and cesarean section. Cesarean section analyses were subdivided into elective cesarean section and emergency cesarean section; no significant differences were found between the level of 25(OH)D in pregnant women ($p = 0.82$) and in newborns ($p = 0.69$) according to the type of delivery.

The mean ± SD level of 25(OH)D according to nutritional status based on gestational age of the newborn was 17.9 ± 7.5 ng/mL in LGA newborns, 16.1 ± 6.6 ng/mL in AGA newborns, and 14.8 ± 9.3 ng/mL in SGA newborns, with no significant differences ($p = 0.14$). Of the total 172 dyads analyzed, only 11 newborns were classified in the SGA category. Of these, 10/11 newborns had vitamin D levels < 20 ng/mL. As for the mothers, 7/11 also had vitamin D concentrations < 20 ng/mL. Of the 106 mothers who had levels < 20 ng/mL,

**Table 2. Anthropometric Characteristics of the 172 Newborns**

| Variable | Minimum | Q1 | Average | Q3 | Maximum | SD |
|---|---|---|---|---|---|---|
| Gestational Age ( weeks ) | 37 | 38 | 38,6 | 39 | 41 | 1,1 |
| Weight (g) | 2195 | 3103 | 3435 | 3780 | 4710 | 505 |
| Birth length (cm) | 41 | 49 | 50,1 | 51 | 56 | 2,1 |
| Head circumference (cm) | 32 | 34 | 34,8 | 36 | 39 | 1,5 |

**Table 3. 25(OH)D Levels in Pregnant Women and Newborns**

| Vitamin D level | Pregnant Women (n = 172) | Newborns (n = 172) |
|---|---|---|
| < 20 ng/mL | 106 (61.6%) | 130 (75.6%) |
| 20 - 29ng/mL | 48 (27.9%) | 34 (19.8%) |
| ≥ a 30 ng/mL | 18 (10.5%) | 8 (4.7%) |

7 newborns were SGA (6.6%), and of the 66 mothers with levels >20 ng/mL, 4 newborns were SGA (6%). The mean ± SD level of 25(OH)D in female newborns was 16.2 ng/mL ± 6.8 and 16.5 ng/mL ± 7.1 in male newborns, with no significant differences (p = 0.87).

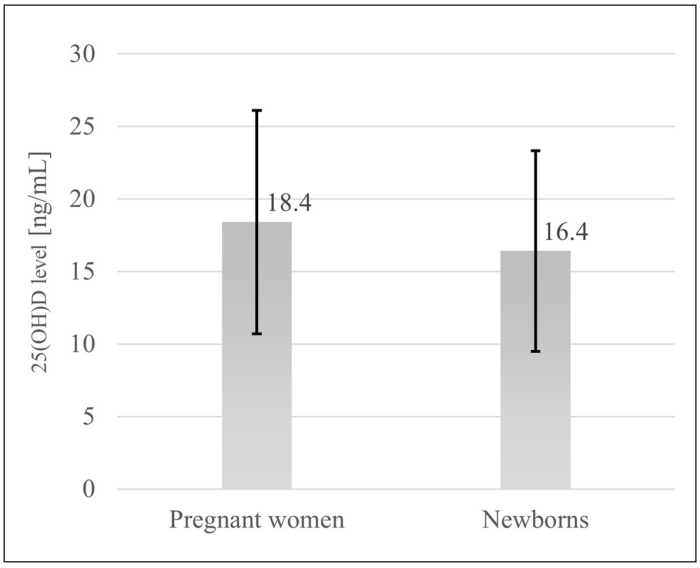


**Figure 1.** Average levels of 25(OH)D in pregnant women and their newborns.

## Discussion

The results obtained are similar to those reported in other dyad studies, revealing that approximately 90% of pregnant women and 95% of newborns have vitamin D deficiency or insufficiency.

Globally, it has been reported that 88% of the general population has plasma concentrations of 25(OH)D < 30 ng/mL, 37% have levels < 20 ng/mL, and up to 7% have levels < 10 ng/mL (5). In Australia, 73% of adults were reported to have plasma levels < 30 ng/mL, and 31% had plasma levels of 25(OH)D < 20 ng/mL[7].

This high percentage of vitamin D deficiency or insufficiency has also been reported in different populations of pregnant women. In some developing countries, a prevalence of vitamin D deficiency ranging from 51.3% to 100% has been documented in pregnant women[4]. Clinical studies in the United States have reported up to 50% vitamin D deficiency in pregnant women, unlike in Europe, where this figure ranges from 10% to 30%[8].

A Chilean study of children aged 8 to 10 years, conducted in Punta Arenas, revealed that 96.3% of them had vitamin D deficiency (< 20 ng/mL) and 3.7% had

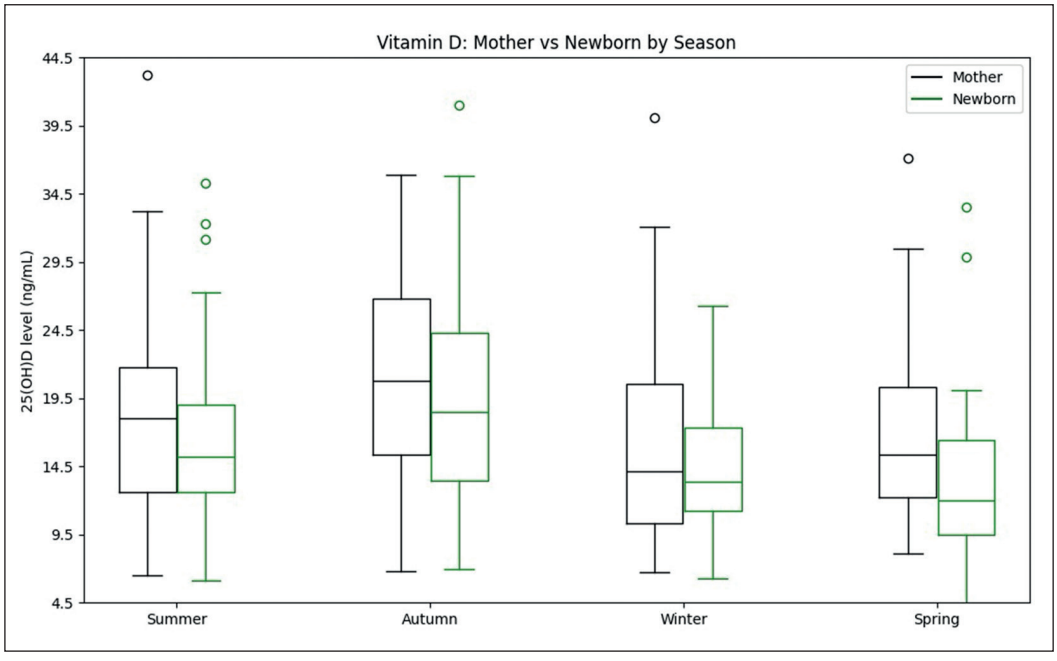


**Figure 2.** 25(OH)D levels in pregnant women and their newborns according to season of the year.

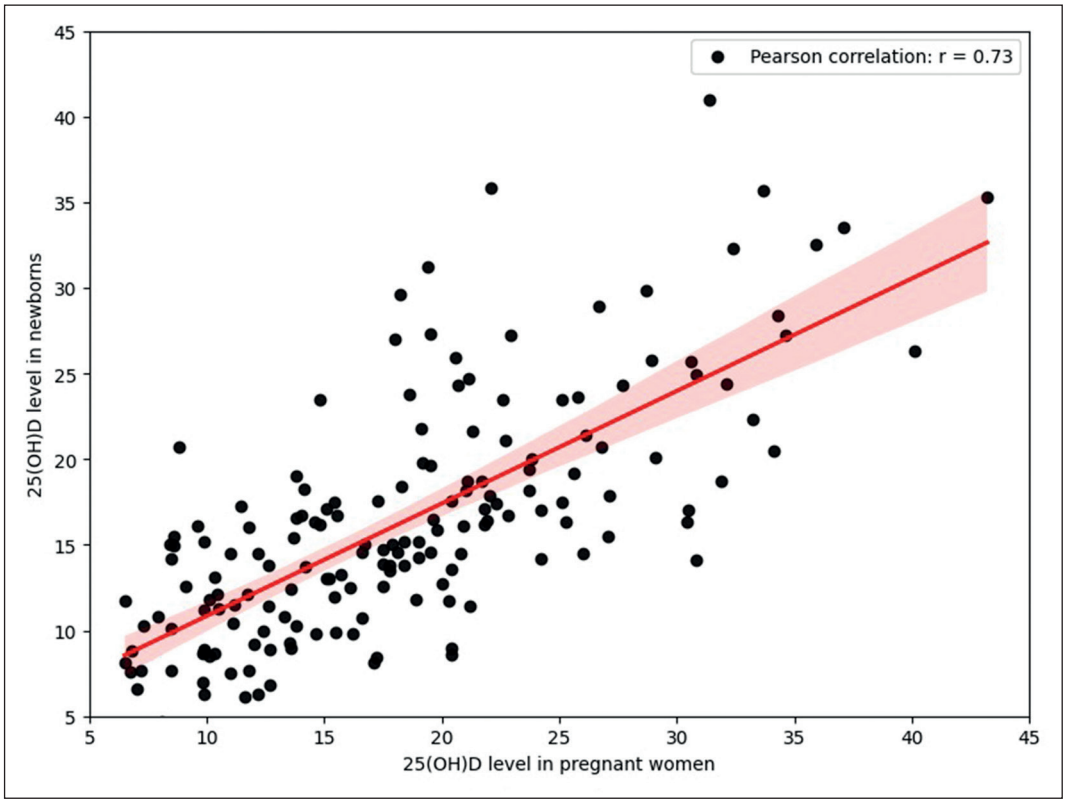


**Figure 3.** Correlation between 25(OH)D Level in Pregnant Women and their Newborns.

insufficiency (20-29 ng/mL) (10). These high percentages of 25(OH)D deficiency in this population may be related to its extreme southern latitude (53° 9' 45" south), with fewer hours of daylight available throughout the year. In a study conducted at our own center (36º 46' 22" south), the results of 90 children hospitalized in the pediatric ICU were analyzed, measuring the serum concentration of 25(OH)D, showing an mean level of 22.8 ng/mL, with a prevalence of vitamin D deficiency of 43.3%[17].

In this study, the mean level of 25(OH)D in the sample of full-term newborns was 16.4 ng/mL, lower than that found in a study of full-term newborns conducted in Colombia, whose mean level was 23.7 ng/mL[11].

In a publication from our center, which measured 25(OH)D levels in very low birth weight (< 1500 g) preterm newborns in 2019, a mean level of 19.7 ± 6.7 ng/mL was reported[18], which is comparable to the scientific literature available for this group[19,20]. It should be noted that this value is somewhat higher than the mean observed in full-term newborns in the current study.

Regarding the association between the level of 25(OH)D in the mother and her newborn, this report shows results similar to those published in other dyad studies[11,12,18,21]. A prospective study conducted in Boston with 40 pregnant women with a mean intake of 600 IU revealed that 76% of them and 81% of their newborns presented vitamin D deficiency[12]. In Saudi Arabia, 59% of pregnant women and 70% of their newborns presented a deficiency in vitamin D[21]. In Colombia, a prevalence of hypovitaminosis D was observed in 66% of pregnant women, 83% of umbilical cord samples, and 100% of neonatal peripheral venous samples[11].

Most studies that have evaluated 25(OH)D levels in pregnant women and their newborns have shown a significant correlation between the two[11,22,23]. In a study in Pakistan, there was also a strong positive association (r = 0.66) between maternal and newborn 25(OH)D levels[23]. The study conducted in Colombia also showed a positive correlation (r = 0.67; p = 0.001)[11]. Similarly, in Mexico, a study involving 60 pregnant women and 62 newborns demonstrated a significant association, with a correlation coefficient of 0.78[23]. This positive association was also observed in our study, in which the correlation index between the 25(OH)D levels of pregnant women and their newborns was 0.73, a figure similar to that reported in the abovementioned studies.

In our study, when comparing 25(OH)D levels according to the nutritional status of the newborn (LGA, AGA, SGA), we did not observe a significant difference

between them. However, 25(OH)D levels in AGA and LGA newborns were higher. Similarly, a higher incidence of SGA newborns was observed in mothers whose 25(OH)D levels were < 20 ng/ml, a finding similar to that described in the literature[24].

A significant association has been documented between vitamin D deficiency and adverse maternal and/or neonatal health outcomes, such as premature birth, emergency cesarean delivery, SGA, growth retardation, etc.[25]. It has been reported that body size was significantly greater in newborns whose mothers had normal vitamin D levels, compared to those whose mothers had insufficient or deficient levels at the time of delivery[26]. In a province in Spain, in a cohort of 100 dyads, no significant difference was observed between maternal 25(OH)D serum concentrations and the length and head circumference of newborns. However, a statistically significant difference was observed between birth weight and vitamin D levels in the mother ($p < 0.05$)[27]. It should be noted that other studies have not demonstrated this association[28].

Some studies have analyzed bone mineral density in newborns in relation to 25(OH)D levels and have found an association with lower levels in those newborns whose mothers had deficient 25(OH)D levels. In the study by Boghossian et al.[29], it was observed that in males, weight and lean mass were lower[29].

To our knowledge, this is the first study in Chile and the second in South America to evaluate 25(OH)D levels in pregnant women and their newborns.

Among the possible limitations of the study, we can mention a certain percentage of loss of dyads, due to different factors that meant the enrollment period was extended to complete the required number of dyads. Newborns with vitamin D deficiency in the neonatal period were not followed up for the possible development of morbidity, as this was not one of the objectives of the study.

Among the strengths of this report are the significant number of dyads and the collection of valuable local data, as a first step toward care and interventions aimed at meeting the specific needs of pregnant women in our health center.

## Conclusions

A high percentage of vitamin D deficiency was demonstrated in a group of pregnant women and their newborns. A positive correlation was observed between 25(OH)D levels in both groups.

The evidence provided by our study reveals an important public health problem in our country that must be addressed as soon as possible, proposing specific interventions, such as standardized vitamin D supplementation during pregnancy and the implementation of public policies to promote the fortification of foods with vitamin D, which is currently under development following the enactment of Decree No. 48, amending the Health Regulations, published on July 5, 2022[30].

## Ethical Responsibilities

**Human Beings and animals protection:** Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

**Data confidentiality:** The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

**Rights to privacy and informed consent:** The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

## Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

## Financial Disclosure

Authors state that no economic support has been associated with the present study.

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