Archives of Gynecology and Obstetrics (2024) 309:2099–2106
https://doi.org/10.1007/s00404-024-07410-8

Do serum vitamin D levels affect assisted reproductive outcomes and perinatal outcomes in young non-PCOS patients? A retrospective study

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Received: 9 November 2023 / Accepted: 1 February 2024 / Published online: 1 March 2024

Abstract

Purpose This study aimed to determine the influence of serum vitamin D levels on assisted reproductive and perinatal outcomes in young non-polycystic ovary syndrome (PCOS) patients.

Methods A total of 3397 non-PCOS women under 35 years who underwent their first IVF/ICSI cycle at the Reproductive Medicine Center of the Third Affiliated Hospital of Zhengzhou University, from 2018 to 2019, were included. The women were categorized into two groups based on their serum 25(OH)D concentrations: deficient group [25(OH)D < 50 nmol/L] and non-deficient group [25(OH)D ≥ 50 nmol/L]. Ovulation induction results, clinical pregnancy rate, cumulative live birth rate (CLBR), and perinatal outcomes of both groups were compared.

Results A total of 1113 non-PCOS women had successful pregnancies in their first completed IVF cycle. Comparison of laboratory results between the two groups revealed a significantly higher number of oocytes retrieved in the vitamin D-non-deficient group (15.2 ± 6.8 vs. 14.5 ± 6.7, $p = 0.015$). After controlling for confounding factors, there was no significant difference in the CLBR between the vitamin D-deficient group and the non-deficient group (71.0%, 1,973/2,778 vs. 69.0%, 427/619, $p = 0.314$, unadjusted). The prevalence of gestational diabetes mellitus (GDM) was higher in the vitamin D-deficient group than in the vitamin D-non-deficient group in both fresh-cycle singleton live births (3.8% vs. 1.2%) and twin live births (2.3% vs. 1.5%).

Conclusion This study demonstrated that vitamin D-deficient group had a lower number of oocytes retrieved than the non-deficient group and a higher prevalence of GDM, suggesting that vitamin D deficiency impacts assisted pregnancies and perinatal outcomes in infertile non-PCOS women. However, further studies are required to confirm these findings.

Keywords Vitamin D · Assisted reproductive treatments · Non-PCOS women · Pregnancy outcomes · Perinatal outcomes

What does this study add to the clinical work

This single-center retrospective cohort study suggests that maternal serum vitamin D deficiency reduces the number of oocytes retrieved after ART to some extent and increases the risk of GDM. This provides a certain reference for clinicians to judge whether patients need to supplement vitamin D and guide patients how to supplement serum vitamin D, so that patients can obtain better clinical outcomes.

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Introduction

Vitamin D, a fat-soluble steroid hormone, is synthesized endogenously from 7-dehydrocholesterol in the skin in response to ultraviolet beta rays. Approximately 80% of vitamin D in the human body is produced in the skin, while only 20% comes from the diet [1]. Vitamin D plays an integral role in the human body by binding to vitamin D receptors (VDRs) in different organs. VDRs are present in various tissues and organs and have specific functions in each of them [2], including reproductive tissues such as the testes, placenta, uterus, and ovaries, suggesting that vitamin D may be involved in reproductive processes [3]. Vitamin D deficiency has been implicated in infertility issues such as reduced fertility, reduced mating success, increased pregnancy complications, gonadal insufficiency, hypogonadism, uterine hypoplasia, and follicular dysgenesis. Several studies have supported the role of vitamin D in the transport of calcium ions through the placenta, placental steroidogenesis, and endometrial metaphase [4–6].

However, the mechanism by which vitamin D affects the outcome of assisted reproductive technologies (ART) remains unclear. Some studies [7, 8] have reported no relationship between serum vitamin D concentrations and in vitro fertilization (IVF) success, while others [9, 10] have found a negative association between vitamin D insufficiency or deficiency and embryo quality, clinical pregnancy rates, and sustained pregnancy rates after IVF. Several meta-analyses [11–13] have reported a lower live birth rate in women with vitamin D deficiency undergoing IVF than in those with normal serum vitamin D concentrations.

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age. It is a multisystem disorder characterized by oligo or anovulation, and consequently oligo or amenorrhea, and the development of hyperandrogenism, resulting from circulating luteinizing hormone (LH) levels and the altered ratio of LH to follicle stimulating hormone (FSH) [14]. PCOS is also associated with hyperinsulinemia, impaired glucose tolerance, and sometimes even type 2 diabetes mellitus (T2DM). Evidence has suggested a correlation between IR pathogenesis and vitamin D (VD) deficiency, placing hypovitaminosis as a causal factor for the metabolic syndrome in PCOS women [15]. However, it is unclear whether assisted reproductive outcomes in patients with non-PCOS are affected by serum vitamin D levels. Therefore, this study aimed to assess whether serum vitamin D levels influence assisted reproductive outcomes and perinatal outcomes in young non-PCOS patients.

Methods

Patients

This single-center, retrospective, observational cohort study was conducted at the Reproductive Medicine Center of the Third Affiliated Hospital of Zhengzhou University. Ethical approval was obtained from the Ethics Committee of the Third Affiliated Hospital of Zhengzhou University. IVF/ICSI cycles performed from 2018 to 2019 were included in the study. A total of 3397 non-PCOS women were included for analysis, of which 1113 had pregnancy outcomes available. After screening based on the inclusion and exclusion criteria given below, the serum 25-hydroxyvitamin D[25(OH)D] concentrations of all patients were measured by electrochemiluminescence prior to ovarian stimulation. The patients were grouped according to their serum 25(OH)D concentrations: < 50 nmol/L as the deficient group, and ≥ 50 nmol/L as the non-deficient group.

Inclusion and exclusion criteria

The inclusion criteria were: (1) age < 35 years; (2) ovulation induction using the early follicular phase long protocol or the mid-luteal phase long protocol; and (3) first fresh cycle of egg retrieval. The exclusion criteria were: (1) patients with PCOS and/or insulin resistance; (2) uterine anomalies, fibroids, endometriosis, adenomyosis; (3) cycles with incomplete data; (4) preimplantation genetic testing cycles; (5) chromosomal abnormalities in either spouse; and (6) intake of vitamin D supplements in the 6 months prior to assisted conception or during pregnancy.

Controlled ovarian hyperstimulation protocols

Deregulation process

a. Long protocol: long-acting GnRH-a (treprostinil acetate) 3.75 mg was injected intramuscularly on 2–4 days of the menstrual cycle. Thirty days after pituitary downregulation, follicle size was monitored by ultrasound, and the blood luteinizing hormone (LH), follicle stimulating hormone (FSH), estradiol (E2), progesterone (P), and human chorionic gonadotropin (β-hCG) concentrations were measured in the fasting state, and gonadotropin (Gn) was administered to initiate ovulation after meeting the criteria for down regulation. If pituitary downregulation was too deep, Gn initiation was delayed for 3–4 days depending on the situation.
b. Mid-luteal long-acting GnRH-a long protocol: Blood E2 and P concentrations were tested in the fasting state

5–7 days after ovulation to confirm ovulation. If the E2 concentration was 100–300 ng/L (367–1101 pmol/L) and the P concentration was ≥ 5 μg/L (15.9 nmol/L), 1.3–1.875 mg of treprostinil acetate was administered intramuscularly.

Ovulation process

The Gn step-up regimen was used to initiate the ovulation process. The Gn initiation dose was determined based on the patient's age, body mass index (BMI) and weight, anti-Müllerian hormone (AMH) concentration, antral follicle count, and basal FSH concentration. (a) Gn 87.5–150 IU/day was initiated in patients aged < 30 years, with a minimum initiation dose of 75–100 IU in highly responsive patients; (b) Gn 150–225 IU/day was initiated in patients aged 30–35 years. Three to four days after Gn initiation, follicle development and blood E2 concentrations were monitored by ultrasound. If follicles had started developing and the E2 concentration was 100–300 ng/L (1101 pmol/L), the original Gn dose was maintained; if the E2 concentration was ≥ 500 ng/L (1835 pmol/L), Gn dose was reduced in small increments; if the E2 concentration was < 50 ng/L, Gn dose was increased in small increments. To promote ovulation, the Gn dosage was adjusted according to the number of follicles, follicle size, and serum hormone levels in real time.

Trigger timing

When at least one dominant follicle was ≥ 20 mm in diameter or 2–3 follicles were ≥ 18 mm in diameter, Gn was discontinued and 250 μg of recombinant hCG was injected. After 36–38 h, egg retrieval was performed under vaginal ultrasound monitoring, and routine luteal phase support was given.

Embryo transfer

Ultrasound-guided fresh embryo transfer was performed on the third day after oocyte retrieval, and excess viable embryos were cultured to blastocyst stage and cryopreserved for subsequent frozen embryo transfer (FET) cycles. The number of embryos transferred was one or two depending on the number of available embryos. Fresh embryo transfer was cancelled if the embryo and endometrium were not synchronous or women had a high risk of ovarian hyperstimulation syndrome and factors seriously affecting embryo implantation.

Measurement of serum vitamin D concentrations

Before ovulation, discarded serum samples were routinely collected, archived in the laboratory, and stored frozen at – 20 °C. The samples were subjected to electrochemiluminescence assays for the determination of serum 25(OH)D concentrations at our center, which is certified by the National Vitamin D External Quality Assessment Scheme for 25(OH)D and 1,25(OH)2D testing.

Observed indicators

In terms of pregnancy, a transvaginal ultrasound was performed after 4 weeks from the embryo transfer. Clinical pregnancy was confirmed if the fetal heartbeat was observed by transvaginal ultrasound. Live birth was defined as the birth of a neonate.

CLBR: In an IVF/ICSI cycle (one egg retrieval cycle, including fresh embryo transfer and subsequent FET), the CLBR was calculated as the number of cycles with the first live birth (≥ 28 weeks of gestation) divided by the number of all egg retrieval cycles, with the end-of-observation criterion being at least one live birth or exhaustion of all embryos triggered by ovulation induction, over the 2-year observation period [16].

Statistical methods

Statistical analysis was performed using SPSS 22.0 (IBM, Chicago, USA). Binary variables are expressed as rates (%), and normally distributed continuous variables are expressed as the means ± standard deviations. A Chi-square test or Fisher's exact test was used to compare binary variables between two independent samples, and a *t* test was used to analyze normally distributed continuous variables between two independent samples. Univariate logistic regression or linear regression was used to analyze the effects of vitamin D deficiency on clinical and perinatal outcomes, and multivariate logistic regression or linear regression was used to adjust for confounders. The results of binary variables are expressed as odds ratios (ORs) or adjusted ORs and 95% confidence intervals (CIs), and the results of continuous variables are expressed as the mean differences (MDs) or adjusted MDs and their 95% CIs. A P value < 0.05 was considered to indicate significant differences.

Results

A total of 3397 non-PCOS infertile women were included in the analysis, 1113 of whom achieved pregnancy. The median age (interquartile range) of the total cohort was 28 (25–31) years. The prevalence of vitamin D deficiency (serum 25(OH)D concentration < 50 nmol/L) was 81.7% (2778/3397 women), and that of vitamin D non-deficiency

Table 1 Comparison of baseline data between VD-deficient and VD-non-deficient groups

Parameters	VD deficiency group ($n=2778$)	VD non-deficiency group ($n=619$)	*P* value
Age of the woman (years)	28.5 ± 3.0	28.3 ± 3.3	0.066
Age of male (years)	29.7 ± 4.1	29.4 ± 4.5	0.205
Female BMI (kg/m^2)	22.9 ± 3.2	22.8 ± 3.1	0.867
Duration of infertility (year)	3.3 ± 2.2	3.2 ± 2.3	0.775
≥ 1 time previous pregnancy (%)	41.9 (1165/2778)	48.0 (297/619)	0.006
Antral follicle count	18.2 ± 6.3	18.2 ± 6.0	0.903
Anti-Müllerian hormone (ng/L)	5.1 ± 3.6	5.0 ± 3.4	0.653
Type of infertility			
Primary infertility (%)	58.4 (1622/2778)	51.5 (319/619)	0.002
Secondary infertility (%)	41.6 (1156/2778)	48.5 (300/619)	
Conception method			
In vitro fertilization (%)	71.5 (1985/2778)	70.4 (436/619)	0.613
Intra-cytoplasmic sperm injection (%)	28.5 (793/2778)	29.6 (183/619)	
Main etiology of infertility (%)			
Tubal factor	64.9 (1804/2778)	66.7 (413/619)	0.400
Ovulation disorders	11.6 (321/2778)	10.7 (66/619)	0.527
Male factor	41.5 (1152/2778)	42.0 (260/619)	0.807

Table 2 Comparison of laboratory outcomes in the VD deficient and VD non-deficient groups

Parameters	VD deficiency group ($n=2778$)	VD non-deficiency group ($n=619$)	*P* value
Dosage of Gn used (IU)	2238.5 ± 947.8	2197.3 ± 947.4	0.327
Starting dosage of Gn (IU)	151.6 ± 50.5	149.8 ± 48.9	0.415
Duration of Gn treatment (days)	13.8 ± 2.8	13.7 ± 2.4	0.332
Endometrium thickness on hCG day (mm)	11.1 ± 2.2	11.1 ± 2.3	0.737
Number of retrieved	14.5 ± 6.7	15.2 ± 6.8	0.015
2PN rate (%)	63.2% ± 20.6%	63.4% ± 20.0%	0.830
Available blastocyst formation rate (%)	39.0% ± 29.8%	41.3% ± 28.8%	0.073

(serum 25(OH)D concentration > 50 nmol/L) was 18.3% (619/3397 women) (Table 1).

A comparison of laboratory outcomes between the vitamin D-deficient and -non-deficient groups revealed that the number of oocytes retrieved was significantly higher in the vitamin D-non-deficient group than in the vitamin D-deficient group (15.2 ± 6.8 vs. 14.5 ± 6.7, $p=0.015$). The blastocyst formation rate was also higher in the vitamin D-non-deficient group than in the deficient group, although the difference was not statistically significant (41.3% ± 28.8% vs. 39.0% ± 29.8%, $p=0.073$). No significant differences were observed in the total amount of Gn administered, the Gn initiation dose, Gn administration days, endometrial thickness, or 2PN rate between the two groups (Table 2).

A comparison of the clinical outcomes between the two groups revealed no significant differences in the clinical pregnancy rate, sustained pregnancy rate, miscarriage rate, or CLBR of the first IVF cycle (Table 3).

A comparison of the perinatal outcomes of fresh cycles revealed that the incidence of low-birth-weight infants among singleton live births was significantly higher in the vitamin D-non-deficient group than in the vitamin D-deficient group (8.2% vs. 4.1%, $p=0.021$), while the incidence rates of preterm delivery, overdue delivery, macrosomia, and birth defects were not significantly different between the two groups (Tables 4 and 5). The incidence of gestational diabetes mellitus (GDM) was higher in the vitamin D-deficient group than in the vitamin D-non-deficient group for both fresh-cycle singleton live births (3.8% vs 1.2%) and twin live births (2.3% vs 1.5%), but the differences were not statistically significant. Furthermore, no significant differences were observed in the incidence of other obstetric outcomes, namely, gestational hypertension, placental abruption, placenta previa, and premature rupture of membranes, between the two groups (Tables 4 and 5).

Table 3 Comparison of clinical outcomes between VD-deficient and VD-non-deficient groups

Parameters	VD deficiency group	VD non-deficiency group	Unadjusted		After adjustment[a]	
	($n=1965$)	($n=417$)	MD/OR (95% CI)	*P* value	MD/OR (95% CI)	*P* value
Average number of embryos transferred	1.7 ± 0.5	1.7 ± 0.5	− 0.01(− 0.06, 0.04)	0.732	− 0.01(− 0.06, 0.04)	0.620
Fresh cycle clinical pregnancy rate (%)	65.5 (1288/1965)	64.0 (267/417)	1.07 (0.86, 1.33)	0.554	1.09 (0.87, 1.36)	0.443
Fresh cycle continuous pregnancy rate (%)	58.1 (1141/1965)	58.0 (242/417)	1.00 (0.81, 1.24)	0.990	1.02 (0.82, 1.26)	0.868
Fresh cycle live birth rate (%)	57.8 (1135/1965)	57.8 (241/417)	1.00 (0.81, 1.24)	0.990	1.02 (0.82, 1.26)	0.894
Fresh cycle miscarriage rate (%)	11.4 (147/1288)	9.4 (25/267)	1.25 (0.80, 1.95)	0.332	1.23 (0.79, 1.93)	0.364
Cumulative live birth rate (%)	71.0 (1973/2778)	69.0 (427/619)	1.10 (0.91, 1.33)	0.314	N/A	N/A

[a]Multifactorial regression analysis adjusted for female age, male age, female BMI, pregnancy frequency, and type of infertility

Table 4 Comparison of perinatal outcomes of single live births in the VD-deficient group and the VD-normal group

Parameters	VD deficiency group	VD non-deficiency group	Unadjusted		After adjustment[a]	
	($n=812$)	($n=170$)	MD (95% CI)	*P* value	MD (95% CI)	*P* value
Neonatal outcomes						
Gestational age, week	39.1 ± 1.5	38.9 ± 1.7	0.22 (− 0.04, 0.47)	0.095	0.25 (− 0.01, 0.50)	0.059
Premature birth rate (%)	8.6 (70/812)	11.2 (19/170)	0.75 (0.44, 1.28)	0.293	0.72 (0.42, 1.24)	0.237
Post-term birth rate (%)	0.2 (2/812)	0.6 (1/170)	0.42 (0.04, 4.63)	0.477	0.40 (0.04, 4.53)	0.462
Birth weight (g)	3364.7 ± 508.8	3282.6 ± 513.7	82.11(− 2.25, 166.47)	0.056	80.20(− 3.71, 164.12)	0.061
Low birth weight rate (%)	4.1 (33/812)	8.2 (14/170)	0.47 (0.25, 0.90)	0.023	0.46 (0.24, 0.89)	0.021
Macrosomia rate (%)	11.7 (95/812)	8.8 (15/170)	1.37 (0.77, 2.43)	0.281	1.36 (0.76, 2.43)	0.295
Birth defects rate (%)	0.7 (6/812)	0.6 (1/170)	1.26 (0.15, 10.52)	0.832	1.23 (0.15, 10.44)	0.847
Obstetrical outcomes						
Hypertension in pregnancy (%)	2.8 (23/812)	4.1 (7/170)	0.68 (0.29, 1.61)	0.379	0.66 (0.27, 1.59)	0.354
Gestational diabetes mellitus (%)	3.8 (31/812)	1.2 (2/170)	3.33 (0.79, 14.07)	0.101	3.07 (0.72, 13.00)	0.128
Abruptio placentae (%)	0.5 (4/812)	0.6 (1/170)	0.84 (0.09, 7.53)	0.874	0.78 (0.09, 7.13)	0.827
Anterior placenta (%)	0.6 (5/812)	1.2 (2/170)	0.52 (0.10, 2.71)	0.437	0.47 (0.09, 2.46)	0.370
Premature rupture of fetal membranes (%)	3.1 (25/812)	4.7 (8/170)	0.64 (0.29, 1.45)	0.288	0.63 (0.28, 1.43)	0.269

[a]Multifactorial regression analysis adjusted for female age, male age, female BMI, and mode of conception

Discussion

To investigate whether vitamin D has an effect on ART outcomes, we compared the laboratory outcomes of the non-PCOS women infertile vitamin D-non-deficient and deficient groups and found that the number of oocytes retrieved was significantly larger (15.2 ± 6.8 vs. 14.0 ± 6.7, $p=0.015$) and the blastocyst formation rate was higher, albeit not significantly, in the non-deficient group than in the deficient group. Grzeczka et al. [17] found that although vitamin D had a stimulating effect on folliculogenesis, it also had a negative effect on oocyte maturation. In our study, no significant difference was observed in the total amount of Gn administered, the Gn initiation dose, Gn administration days, endometrial thickness, or 2PN rate between the two groups. The reason for this finding may be related to the lack of 25(OH)D measurements in follicular fluid, which is also a limitation of this study.

The literature reports no conclusive evidence on the effect of vitamin D on the pregnancy outcomes of ART. One study [18] found that vitamin D interventions improved ovarian function and egg quality in infertile patients but had no significant effect on pregnancy outcomes in patients who underwent IVF fresh embryo transfer. A large retrospective cohort study by Jiang et al. [19] found that serum vitamin

Table 5 Comparison of perinatal outcomes of twin live births in the VD-deficient group versus the VD-non-deficient group

Parameters	VD deficiency group	VD non-deficiency group	Unadjusted		After adjustment[a]	
	($n=309$)	($n=67$)	MD (95%CI)	*P* value	MD (95%CI)	*P* value
Neonatal outcomes						
Gestational age, week	36.8 ± 1.9	36.6 ± 2.0	0.17 (− 0.34, 0.678)	0.508	0.17 (− 0.34, 0.68)	0.521
Premature birth rate (%)	40.8 (126/309)	38.8 (26/67)	1.09 (0.63, 1.87)	0.766	1.09 (0.63, 1.89)	0.751
Post-term birth rate (%)	0	0	N/A	N/A	N/A	N/A
Birth weight (g)	2633.7 ± 494.6	2581.8 ± 492.0	51.91 (− 79.02, 182.85)	0.436	52.83 (− 78.10, 183.76)	0.428
Low birth weight rate (%)	33.3 (103/309)	38.8 (26/67)	0.79 (0.46, 1.36)	0.393	0.81 (0.47, 1.41)	0.455
Macrosomia rate (%)	0.3 (1/309)	0	N/A	N/A	N/A	N/A
Birth defects rate (%)	1.0 (3/309)	0	N/A	N/A	N/A	N/A
Obstetrical outcomes						
Hypertension in pregnancy (%)	7.8 (24/309)	7.5 (5/67)	1.04 (0.38, 2.84)	0.933	1.08 (0.39, 2.98)	0.890
Gestational diabetes mellitus (%)	2.3 (7/309)	1.5 (1/67)	1.53 (0.19, 12.65)	0.693	1.42 (0.17, 12.00)	0.750
Abruptio placentae (%)	1.9 (6/309)	1.5 (1/67)	1.31 (0.16, 11.04)	0.806	1.56 (0.17, 14.17)	0.694
Anterior placenta (%)	1.6 (5/309)	1.5 (1/67)	1.09 (0.13, 9.45)	0.941	0.88 (0.10, 7.89)	0.906
Premature rupture of fetal membranes (%)	15.5 (48/309)	13.4 (9/67)	1.19 (0.55, 2.55)	0.664	1.13 (0.52, 2.46)	0.754

[a]Multifactorial regression analysis adjusted for female age, male age, female BMI, tubal disease

D concentrations in couples were not associated with the clinical pregnancy rates of ART. Liu et al. [20] found that a lower serum vitamin D concentration resulted in a lower IVF rate, but it was not significantly associated with the clinical pregnancy rate, embryo implantation rate, or miscarriage rate. In contrast, several studies [21, 22] have found that vitamin D deficiency is widespread in patients with infertility and that decreased pregnancy rates in patients who have undergone IVF embryo transfer may be related to vitamin D deficiency. Similarly, Hasan et al. [22] showed that pre-conception 25(OH)D sufficiency (≥ 50 nmol/L) was associated with successful pregnancy outcomes after IVF treatment. In contrast, the present study found no significant differences between the vitamin D-deficient and -non-deficient groups in terms of the clinical pregnancy rate in fresh cycles, live birth rate, miscarriage rate, or CLBR, thus indicating that the effect of serum vitamin D concentrations on the pregnancy outcomes of ART is still unclear and more studies are needed for further clarification.

In this study, we compared the perinatal outcomes of fresh cycles and found that the incidence of low-birth-weight infants in singleton live births was significantly higher in the vitamin D-non-deficient group than in the vitamin D-deficient group (8.2% vs. 4.1%, $p=0.021$), which contradicts the findings of Nobles et al. [23], who found that compared with the vitamin D non-deficient group, the neonatal weight of infants in the vitamin D inadequate and -deficient groups was lower by 139.74 g ($p=0.045$) and 175.52 g ($p=0.051$), respectively. Another study [24] found different correlations between maternal vitamin D deficiency and neonatal length, weight, and skinfold thickness among pregnant women with different BMI and different gestational age. The present study also found that the incidence of GDM was higher in the vitamin D-deficient group than in the non-deficient group in both singleton live births (3.8% vs. 1.2%) and twin live births (2.3% vs. 1.5%), but the differences between the two groups were not statistically significant ($p>0.05$). In addition, the incidence rates of gestational hypertension, placental abruption, placenta previa, and premature rupture of membranes were not significantly different between the two groups. This suggests that vitamin D deficiency may increase the incidence of GDM but is not significantly correlated with the incidence of gestational hypertension, placental abruption, placenta previa, and premature rupture of membranes. This finding is similar to that of Milajerdi et al. [25], who found a significant association between vitamin D deficiency and an increased risk of GDM, with the lowest risk of GDM found in patients with serum vitamin D concentrations between 40 and 90 nmol/L. These findings were further confirmed by the study by Rizzo et al. [26], but the exact underlying mechanism needs further investigation.

Conclusion

This single-center retrospective cohort study suggests that maternal serum vitamin D deficiency reduces the number of oocytes retrieved after ART to some extent and increases the risk of GDM. However, further studies are needed to provide evidence on whether vitamin D deficiency is associated with the incidence of low-birth-weight infants. The retrospective nature of this study influenced a large number of factors and may thus have led to some bias in the findings;; therefore, further studies involving multiple centers and including large samples are needed to confirm the relationship.

Acknowledgements We acknowledge the patients who participated in the study. The authors are also grateful to physicians and coordinators who enrolled patients and collected data from all women who participated in this study.

Author contributions Jiaheng Li, Mengnuo Li contributed to the conception and design of the study and drafted the manuscript. Yijiang Li, Xianling Zhao, Yichun Guan, Wenjuan Zhang, Meng Zhang, Seling Wu were involved in the acquisition of data collection. Mengnuo Li, Wei Zheng, Yuchao Zhang analyzed data. All authors revised the article and gave their final approval of the submitted version.

Funding Funding was provided by the Medical Science and Technology Research Project of Henan Province (Joint Construction) [LHGJ20190365], the Key Scientific Research Project of Colleges and Universities in Henan Province [20B320044] and the National Key R&D Program "Fertility Health and Health Security for Women and Children": Clinical Cohort and Intervention Study on Genetic Problems in Assisted Reproduction Offspring (2021YFC2700602).

Data availability Data transparency.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Ethics approval was obtained from the ethical committee of the third affiliated hospital of Zhengzhou University (2021-WZ-003).This study followed the basic principles of the declaration of Helsinki.

Consent to participate and publication Verbal informed consent was obtained from all patients for being included in the study.

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