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Relationship between *Chlamydia Trachomatis* infection, infertility, and serum 25-hydroxyvitamin D: a cross-sectional study from NHANES 2013–2016

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Abstract

Background *Chlamydia trachomatis* is a common sexually transmitted disease that is associated with considerable morbidity and harmful sequelae, including pelvic inflammatory disease and infertility. Strategies for prevention and treatment of infertility in women with *C. trachomatis* infection require further investigation. There is evidence suggesting that vitamin D could be a potential treatment. This study aimed to investigate the relationship between serum 25-hydroxyvitamin D [25(OH)D] levels, chlamydia seropositivity, and the risk of infertility in women.

Methods We conducted this cross-sectional study using 2013–2016 National Health and Nutrition Examination Survey data. Women aged 18–39 years with complete serum 25(OH)D and chlamydia Pgp3Ab multiplex bead/enzyme-linked immunosorbent assay data available were included. The correlation between 25(OH)D level, chlamydia seropositivity, and infertility was evaluated using the weighted chi-squared test and the *t*-test with multivariate logistic regression and moderation effect models.

Results Among the 1424 women who met our eligibility criteria, the weighted chlamydia seropositivity rate was 36.8%. The 25(OH)D level was significantly lower in the seropositive group compared with seronegative control. ($P=0.009$). After adjusting for ethnicity, the effect of 25(OH)D was no longer significant ($P=0.693$). Further analysis in the chlamydia-seropositive subset revealed that the vitamin D level was lower in the infertile group ($P=0.024$). In an interaction model, 25(OH)D was found to antagonizes the positive relationship between chlamydia and infertility (OR = 0.985, 95% CI: 0.971–0.999, $P=0.040$).

Conclusion The serum vitamin D level may be more related to the prognosis in terms of infertility than to the risk of chlamydia infection. This finding may reveal a possible treatment strategy for chlamydia infection.

Keywords ***Chlamydia trachomatis***, 25-hydroxyvitamin D, Infertility, NHANES

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Background

Chlamydia trachomatis is a common sexually transmitted disease and a threat to public health worldwide. According to a World Health Organization report, in 2020, an estimated 128.5 million new *C. trachomatis* infections occurred worldwide among adults aged 15–49 years [1]. In the US, 1.6 million chlamydia infections were reported in 2021 [2]. Chlamydia infections may cause symptoms including change in vaginal discharge, pain or discomfort in the lower abdomen, and burning sensation when urinating. However, it has been reported that only 6–17% of infections in women are symptomatic [3]. Transmission is facilitated by the large proportion of asymptomatic chlamydia infections in women, which means that many women are unaware that they have this harmful condition. The sequelae of chlamydia include pelvic inflammatory disease, an increased risk of becoming infected with human immunodeficiency virus, and ectopic pregnancy, which is potentially fatal [4]. Furthermore, chlamydia infection can cause infertility through multiple mechanisms. For example, occlusion of the fallopian tubes by scarring leads to salpingitis and tubal factor infertility [5]. Evidence from an *in vitro/in vivo* study showed that chlamydia infection causes an elevated myeloid cell-associated inflammatory response [6], underscoring the important role of inflammatory damage in development of infertility among women with *C. trachomatis* infection [7].

Infertility has emerged as a significant public health concern worldwide. The emotional, psychological, and social implications of infertility are profound. It is important that researchers identify strategies for prevention of infertility, especially for women who already have known risk factors, for example, chlamydia infection [8]. Research focusing on intervention and treatment for chlamydia has identified a potential preventative role of vitamin D [9]. There is also a broad consensus that vitamin D has a pleiotropic role in the immune system. Vitamin D deficiency is known to lead to a higher prevalence of several infectious diseases and worse outcomes [10].

Therefore, we performed this population-based, cross-sectional study to determine whether vitamin D affects the risk of chlamydia infection and the development of infertility after infection using a cohort that participated in two cycles (2013–2016) of the National Health and Nutrition Examination Survey (NHANES) [11]. Our hope was that we would be able to shed light on the potential role of vitamin D in prevention and treatment of chlamydia and avoidance of its sequelae.

Methods

Study design and population

The NHANES is conducted by the National Center for Health Statistics and provides information on the health and nutrition status of the noninstitutionalized civilian population in the US. All NHANES protocols are approved by the CDC's National Center for Health Statistics Ethics Review Board, and all survey respondents provide written informed consent.

This study included sexually experienced women of reproductive age (18–39 years) who had 25-hydroxyvitamin D [25(OH)D] and serum chlamydia Pgp3 IgG test results available. Seropositivity for chlamydia was defined as a positive multiplex bead assay or enzyme-linked immunosorbent assay result for Pgp3. We used total serum 25(OH)D (25-hydroxyvitamin D2+D3, nmol/L) tested by ultra high-performance liquid chromatography-tandem mass spectrometry to represent the serum vitamin D level. A response of "yes" to the question: "Have you ever attempted to become pregnant over a period of at least a year without becoming pregnant?" was defined as infertility. Pelvic inflammatory disease was defined as a self-reported history of receiving treatment for the disease.

Covariates

We included several covariates based on previous studies to account for potential confounders [12]. Demographic data, including age, race/ethnicity, educational status, and income level, were collected. Laboratory data indicating metabolism status (plasma glycohemoglobin, cholesterol [mg/dL], direct HDL cholesterol [mg/dL]) and sex steroid hormone levels (testosterone, estrogen, and sex hormone-binding globulin) were also taken into consideration. Questionnaire data related to lifestyle and general health status, including alcohol consumption and smoking history, body mass index (BMI), waist circumference, and other conventional indices were obtained. Seropositivity for other sexually transmitted infections (i.e., herpes simplex virus [HSV1], HSV2, and human papillomavirus) was also recorded to assess for possible correlations. Questionnaire data regarding sexual history were collected, including age at sexual debut and number of male sex partners.

Statistical analysis

The data were analyzed in accordance with the NHANES guidelines for statistical analysis [13]. Continuous variables are shown as the mean±standard deviation for normally distributed data, and as the median with interquartile range for non-normally distributed data, while categorical variables are presented as percentages with 95% confidence intervals (CI). Missing data were imputed using the mice package in R [14], and post-imputation diagnostic tests were performed to ensure the integrity and validity of the imputed data. (Supplementary Fig. 1). NHANES sampling weights were utilized before analyzing the data. Groups were compared using the weighted

chi-squared test and weighted *t*-test. Possible connections were assessed in multivariate logistic regression models. Using the variance inflation factor (VIF) method to test for multicollinearity in the regression models, a VIF of 10 or higher indicates multicollinearity. A moderation effect model was used to assess whether the 25(OH)D level affects the correlation between chlamydia infection and infertility. All statistical analyses were performed using R4.3.0 (64-bit) software (R Foundation for Statistical Computing, Vienna, Austria) and SPSS version 26.0 (IBM Corp., Armonk, NY, USA). A two-sided *P*-value < 0.05 was considered statistically significant.

Results

General characteristics of the study participants

After application of the inclusion and exclusion criteria, we enrolled 1424 survey respondents, 592 of whom were positive for the Pgp3 antibody, indicating previous or recent chlamydia infection (Fig. 1).

The weighted seropositivity rate was 36.8%. The 25(OH)D level was significantly lower in the seropositive group than in the seronegative group ($P=0.009$). There were also significant between-group differences in certain demographic and socioeconomic characteristics, including ethnicity, income status, and education level ($P<0.001$). The average age of participants was similar between the two groups, approximately 28.7 years, showing no significant difference. Seropositive respondents were generally younger at the age of sexual debut than their seronegative counterparts (16.12±2.63 years vs. 17.86±3.34 years, $P<0.001$) and had more male sex partners (7[4,12] vs. 3[1,8], $P<0.001$). In terms of general health indicators, the seropositive group had a higher BMI (29.33±7.72 vs. 28.20±7.74, $P=0.006$), a larger waist circumference (95.62±17.64 cm vs. 93.57±17.64 cm, $P=0.044$), a higher rate of self-reported high blood pressure (12.68% vs. 8.25%, $P<0.001$), and more cases of pelvic inflammatory disease (6.56% vs. 2.19% $P<0.001$). Significant differences in the frequency of human papillomavirus, HSV1, and HSV2 infections were observed between groups. Higher prevalence of human papillomavirus, HSV1, and HSV2 infection in the seropositive group ($P<0.001$) indicated possible co-occurrence of chlamydia and these pathogens. Other variables including blood indexes, hormones and metabolic status revealed no significant between group differences.

Effect of serum 25(OH)D level on the risk of chlamydia infection

In view of the significant between-group differences shown in Table 1, we designed three logistic regression models to assess the possible effects of the serum 25(OH)D level on chlamydia infection and to rule out potential confounders. Model 1 was unadjusted, model 2 was adjusted for ethnicity, and model 3 was adjusted for ethnicity, BMI, income status, education level, and smoking status (Table 2). All the variables included in the multivariate logistic regression models passed

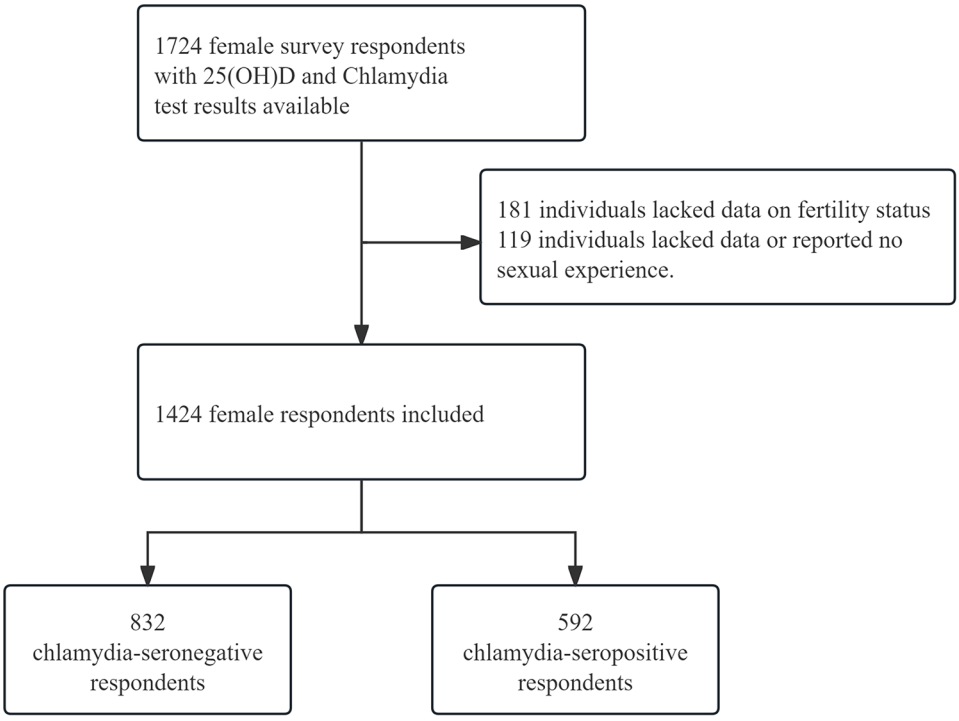

Fig. 1 Participant inclusion flowchart

Table 1 Participant background characteristics according to chlamydia serology status

Characteristics	Level	CT seronegative	CT seropositive	*P*
No.		832	592	
Overall		0.632 (0.584–0.68)	0.368 (0.322–0.42)	
25(OH)D (nmol/L)		67.27 (25.86)	62.66 (26.27)	0.009
Age		28.73 (6.18)	28.86(6.14)	0.746
Race/ethnicity	Mexican American	0.1242 (0.084–0.1643)	12.706 (0.0887–0.1652)	< 0.001
	Other Hispanic	0.0761 (0.0547–0.0975)	0.09949 (0.0636–0.1352)	
	Non-Hispanic White	0.6458 (0.58589–0.7058)	0.4742 (0.4033–0.5451)	
	Non-Hispanic Black	0.0503 (0.0315–0.0691)	0.2118 (0.1557–0.2679)	
	Non-Hispanic Asian	0.0611 (0.0422-0.08)	0.0312 (0.0191–0.0432)	
	Other Race -Including multiracial	0.0425 (0.0202–0.0648)	0.0564 (0.0349–0.0779)	
Ratio of family income to poverty		2.66 [1.28,4.67]	1.73[0.94,3.29]	< 0.001
Education level	Less than 9th grade	0.0264 (0.0116–0.0412)	0.0432 (0.0246–0.0618)	< 0.001
	9-11th grade	0.0654 (0.0453–0.0855)	0.118 (0.0943–0.1417)	
	High school graduate	0.1551 (0.123–0.1871)	0.203 (0.1664–0.2397)	
	Some college or AA degree	0.3935 (0.3509–0.436)	0.4323 (0.3907–0.4739)	
	College graduate or above	0.3597 (0.3204–0.3989)	0.2035 (0.1648–0.2422)	
Body Mass Index		28.20 (7.74)	29.33 (7.72)	0.006
Waist		93.57 (17.64)	95.62 (17.64)	0.044
Segmented neutrophils num (1000 cell/uL)		4.82 (2.01)	4.62 (1.74)	0.045
Platelet count (1000 cells/uL)		258.81(58.38)	25449(59,10	0.203
Lymphocyte number (1000 cells/uL)		2.33 (0.67)	2.40 (0.75)	0.161
Infertility	No	0.9005(87.24–92.84)	0.8812 (0.8474–0.9149)	0.477
	Yes	0.0996(0.0716–0.1276)	0.1188 (0.0851–0.1526)	
Pelvic inflammatory diseases	No	0.9781(0.9674–0.9889)	0.93449 (0.9119–0.9569)	0.001
	Yes	0.0219(0.0111–0.0326)	0.0656 (0.0431–0.0881)	
Age at first sex, years		17.86(3.34)	16.12 (2.53)	< 0.001
Lifetime no. of male sex partners		3 [1,8]	7 [4,12]	< 0.001
Smoking status	No	0.7466 (0.7004–0.7929)	0.58509 (0.5321–0.6379)	< 0.001
	Yes	0.2534 (0.2071–0.2996)	0.415 (0.3621–0.4679)	
Alcohol intake	No	0.3009 (0.2409–0.361)	0.2382 (0.1901–0.2863)	0.103
	Yes	0.6991 (0.639–0.7591)	0.7618 (0.7137–0.8099)	
Diabetes	No	0.9512 (0.9329–0.9694)	0.952 (0.9337–0.9704)	0.637
	Yes	0.0376 (0.0229–0.0522)	0.0315 (0.0171–0.0458)	
	Borderline	0.0113 (0.003–0.952)	0.0165 (0.005–0.028)	
Prediabetes	No	0.9457 (0.9287–0.9627)	0.9273 (0.8957–0.9588)	0.258
	Yes	0.0543 (0.0373–0.0713)	0.0727 (0.04129–0.1043)	
Glycohemoglobin (%)		5.21 (0.54)	5.30 (0.66)	0.052
Total Cholesterol(mg/dL)		179.98 (35.41)	176.67 (36.99	0.28
Direct HDL-Cholesterol (mg/dL)		57.76(14.96)	56.76(15.85)	0.265
High blood pressure	No	0.9175 (0.8985–0.9366)	83.52 (0.8071–0.8633)	< 0.001
	Yes	0.0825 (0.0634–0.1015)	0.1648 (0.1367–0.1929)	
Estradiol (pg/mL)		65.79 [30.52,137.00]	67.36[32.01,135.00]	0.551
Sex Hormone Binding Globulin (nmol/L)		67.70 [41.84, 121.06]	65.12 [41.82, 100.57]	0.138
Testosterone, (ng/dL)		25.50 [18.53, 35.32]	26.07 [18.96, 36.40]	0.613
HPV	negative	0.6466 (0.5988–0.6944)	0.4258 (0.369–0.4826)	< 0.001
	positive	0.3534 (0.3056–0.4012)	0.5742 (0.5174–0.631)	
HSV1	negative	0.55599 (0.5253–0.5866)	0.4271 (0.3808–0.4735)	< 0.001
	positive	0.4441 (0.4134–0.4747)	0.5729 (0.5265–0.6192)	
HSV2	negative	0.9372 (0.9191–0.9553)	0.7557 (0.7072–0.8041)	< 0.001
	positive	0.0628 (0.0447–0.0809)	0.2443 (0.1959–0.2928)	

25(OH)D, 25-hydroxyvitamin D; HDL, high-density lipoprotein; HPV, human papillomavirus; HSV, herpes simplex virus

Table 2 Correlation between 25(OH)D and chlamydia in three logistic regression models

	Model1		Model2		Model3	
Factors	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
25(OH)D	0.993 (0.988–0.998)	0.010	1.001 (0.996–1.007)	0.693	1.005 (0.998–1.011)	0.129
Mexican American			Reference		Reference	
Other Hispanic			1.265 (0.886–1.806)	0.186	1.34 (0.936–1.917)	0.103
Non-Hispanic White			0.699 (0.503–0.97)	0.034	0.699 (0.451–1.082)	0.102
Non-Hispanic Black			4.143 (2.624–6.54)	< 0.001	4.557 (2.794–7.433)	< 0.001
Non-Hispanic Asian			0.494 (0.329–0.742)	0.002	0.726 (0.446–1.183)	0.184
Other Race -Including Multi-Racial			1.278 (0.537–3.043)	0.565	1.023 (0.409–2.56)	0.959
Body Mass Index					1.006 (0.991–1.022)	0.400
Ratio of family income to poverty					0.906 (0.819–1.002)	0.054
Smoking status (Yes)					2.263 (1.56–3.284)	< 0.001
Less than 9th grade					Reference	
9-11th grade					0.906 (0.517–1.586)	0.713
High school graduate					0.748 (0.396–1.411)	0.348
Some college or AA degree					0.714 (0.433–1.178)	0.174
College graduate or above					0.51 (0.282–0.922)	0.028
intercept	0.913 (0.616–1.355)	0.642	0.564 (0.389–0.817)	0.004	0.523 (0.219–1.251)	0.135

Model1: Unadjusted. Model2: Adjustment of race/ethnicity. Model3: Adjustment of significant sociodemographic variables and health-related variables including educational level, ratio of family income to poverty, body mass index and smoking status. 25(OH)D, 25-hydroxyvitamin D; OR, odds ratio; CI, confidence interval

multicollinearity check (Supplementary Table 1). In model 1, the odds ratio (OR) was 0.993 (95% CI 0.988–0.998, $P=0.010$), indicating a possible protective role of 25(OH)D. However, after adjusting for ethnicity, the effect of 25(OH)D was no longer significant. Hispanic and non-Hispanic black women were at higher risk (OR 4.143, 95% CI 2.624–6.540, $P<0.001$). In model 3, women of black ethnicity remained at a significantly higher risk of chlamydia infection (OR 4.557, 95% CI 2.794–7.433, $P<0.001$), while other racial/ethnic group associations were not significant. Smoking status was a significant predictor. Respondents with smoking history have higher odds of chlamydia seropositivity (OR: 2.263, 95% CI: 1.560–3.284, $P<0.001$). Higher education levels (college graduate or above) were associated with lower odds of chlamydia seropositivity (OR: 0.510, 95% CI: 0.282–0.922, $P=0.028$).

The 25(OH)D level was significantly lower in black women than in women of other ethnicities. ($P<0.001$,Supplementary Table 2) The findings in model 1 might have been confounded by certain demographic characteristics, including ethnicity and education level, to which the vitamin D level was closely related. The evidence did not support a role of 25(OH)D in the prevention of chlamydia infection.

Negative correlation between 25(OH)D and infertility in the chlamydia-seropositive group

Focusing on the chlamydia-seropositive group, we conducted a subset analysis to identify any differences between the chlamydia-seropositive respondents according to fertility status. Significant differences in the 25(OH)D level, age, waist circumference, and HSV2 seropositivity rate were found between the infertile and fertile groups (Supplementary Table 3). The 25(OH)D level was significantly lower in the infertile group than in the fertile group (56.87±21.94nmol/L vs. 63.44±26.72 nmol/L, $P=0.024$). Data revealed no significant between-group difference according to ethnicity ($P=0.576$). Therefore, we estimated that 25(OH)D may have a moderating influence on the relationship between chlamydia infection and infertility, which was confirmed in a moderation effect model adjusted for age, waist circumference, and ethnicity.

We assessed the effect of chlamydia and 25(OH)D levels on infertility status using an interaction model, and found statistically significant interaction effects between chlamydia and the 25(OH)D level (Table 3). Variables included in the model passed multicollinearity check (Supplementary Table 4). The negative β value of the interaction term CT*25(OH)D indicated that 25(OH)D antagonizes the positive relationship between chlamydia and infertility (OR=0.985, 95% CI: 0.971–0.999, $P=0.040$). The moderation effect tested by a single slope showed that the relationship between infertility and chlamydia infection was moderated by the 25(OH)D level (Table 4). A significant positive correlation was observed between chlamydia infection and infertility when the 25(OH)D level was relatively insufficient (average value and one standard deviation below), which disappeared at a higher 25(OH)D level (one standard deviation above the average value).

Table 3 Interaction model for assessment of the effect of chlamydia and the 25(OH)D level on infertility status

Factors	β(95%CI)	SE	OR(95%CI)	*P*
Age	0.065(0.035,0.095)	0.015	1.067 (1.036-1.100)	< 0.001
Mexican American	reference			
Other Hispanic	-0.486(-1.203, 0.230)	0.366	0.615 (0.290–1.231)	0.184
Non-Hispanic White	-0.064(-0.593, 0.464)	0.270	0.938 (0.556–1.603)	0.812
Non-Hispanic Black	-0.087(-0.658, 0.484)	0.291	0.917 (0.517–1.625)	0.765
Non-Hispanic Asian	-0.078 (-0.840, 0.683)	0.388	0.925 (0.417–1.934)	0.840
Other Race -Including multiracial	-0.272(-1.127, 0.582)	0.436	0.762 (0.305–1.719)	0.532
Waist	0.022(0.013, 0.032)	0.005	1.023 (1.013–1.032)	< 0.001
Chlamydia seropositive	0.328(-0.053, 0.709)	0.194	1.389 (0.947–2.032)	0.091
25(OH)D	0.002(-0.006, 0.010)	0.004	1.002 (0.994–1.010)	0.571
Chlamydia seropositive: 25(OH)D	-0.015(-0.030, -0.001)	0.007	0.985 (0.971–0.999)	0.040
Intercept	-2.28(-2.694, -1.867)	0.211	0.102 (0.066–0.152)	< 0.001

25(OH)D, 25-hydroxyvitamin D; OR, odds ratio; CI, confidence interval; SE, standard error

Table 4 Moderating effect of the 25(OH)D level on chlamydia seropositivity and infertility tested by single slope analysis

25(OH)D		Effect	SE	95% CI	*P*
34.316	(- SD)	0.710	0.265	(0.190, 1.230)	0.007
59.607	(Mean)	0.328	0.194	(-0.053, 0.709)	0.091
84.899	(+ SD)	0.054	0.273	(-0.588, 0.480)	0.844

25(OH)D, 25-hydroxyvitamin D; CI, confidence interval; SE, standard error; SD, standard deviation

Discussion

Using nationally representative 2013–2016 NHANES data, we have identified that the chlamydia-seropositive rate is about 36.8% among women of reproductive age in the US, with some variation according to ethnicity. Other factors influencing the risk of chlamydia infection included education level, income status, and sexual behavior. These findings are consistent with those of previous epidemiologic studies [15] The observed disparities in chlamydia infection rates across race/ethnicity and socioeconomic groups highlight the need for policies that promote equitable access to healthcare. Specifically, policies should aim to reduce barriers to STI screening and treatment, improve sexual health education, and ensure that at-risk populations have access to preventive services [16]. Since chlamydia is often asymptomatic, early detection relies heavily on routine screening [17]. Therefore, targeted screening and early treatment programs, particularly for women of reproductive age, are essential to addressing this public health issue within the U.S. healthcare system.

We also found that the 25(OH)D level was significantly lower in the chlamydia-seropositive group. However, after further investigation using logistic models adjusted for ethnicity and other covariates, the evidence was not robust enough to draw a conclusion as to whether the vitamin D level affected the risk of chlamydia infection. Previous studies have confirmed that the vitamin D level varies widely according to ethnicity [18], as does vitamin D metabolism [19]. These disparities complicate the interpretation of vitamin D-related health outcomes in multi-ethnic populations. Therefore, when conducting research on vitamin D in a multi-ethnic population, like those represented in NHANES, it is important to address potential sources of bias.

We focused further on the fertility status in respondents who had tested positive for the serum Pgp3 antibody and found a significant negative correlation between the 25(OH)D level and infertility. The interaction and moderation effect model revealed that higher levels of 25(OH)D may mitigate the effect of chlamydia seropositivity on infertility. When the 25(OH)D level was relatively low, there was a significant relationship between chlamydia infection and infertility, which vanished when the vitamin D level was above an adequate level.

The essential role of vitamin D in fertility has been noticed by researchers in recent years. Studies in infertile women have shown a relationship between the vitamin D level and the outcome of assisted reproductive therapy [20] in various etiologies of infertility, including polycystic ovary syndrome [21] and endometriosis [22]. These studies have concluded that vitamin D deficiency could lead to worse clinical outcomes in couples seeking assisted reproductive therapy with different causes of infertility.

A previous study found that chlamydia infection was more severe and prolonged in vitamin D receptor knockout mice than in wild-type mice [9]. The inflammatory response to chlamydia infection was also more prolonged in the vitamin D receptor knockout mice. Studies focusing on chlamydia infection in women had revealed that post-chlamydia tubal factor infertility might be induced by epithelial-mesenchymal transition [23], fibration [24], or inflammation-associated tissue damage and scar formation [25]. Other studies focusing on diseases involving fibrosis [26] and its mechanisms have confirmed that vitamin D regulates the immune response

and inhibits damage caused by inflammation in various tissues, including in the lung and myocardium [27]. An observational study found that an increased serum interleukin-6 level and an inadequate 25(OH)D level were risk factors for tubal factor infertility [28]. The same study also found an interaction between interleukin-6 and 25(OH)D in terms of an increased risk of tubal factor-related infertility. Furthermore, increased levels of interleukin-6 and other proinflammatory factors have been noted in chlamydia infection [29], which could be the mechanism underpinning our finding that 25(OH)D moderated the relationship between chlamydia infection and infertility. We assume that vitamin D acts as a regulator of the immune response and fibrosis in vivo and that a vitamin D deficiency could increase the risk of chlamydia-induced oviduct fibration and scarring.

Evidence from our study, along with previous research, suggests a potential protective role for vitamin D in reproductive health, particularly for women at risk of infertility due to chlamydia infection. Routine screening for vitamin D deficiency could be integrated into reproductive health assessments, and vitamin D supplementation may be potential beneficial for women with both insufficient vitamin D levels and chlamydia infection to improve reproductive outcomes. However, further prospective cohort studies are needed to clarify and strengthen the understanding of the relationship between vitamin D levels and infertility in this population.

A key strength of our study is the use of nationally representative 2013–2016 NHANES data, which enhances the generalizability of our findings to women of reproductive age in the US. Additionally, this is the first study to identify that vitamin D moderates the relationship between chlamydia infection and infertility, highlighting a significant link between lower 25(OH)D levels and increased infertility risk, providing new insights into the protective role of vitamin D in reproductive health. However, our study has some limitations. First, it was based on data from a US population, so the extent to which its findings can be generalized to other countries and regions is unclear. Besides, due to the limitations of the NHANES dataset, the study population is restricted to individuals aged 18–39, so the conclusions may not fully apply to older women within the reproductive age range. Second, it had a cross-sectional design, which means that its results may be confounded by reverse causality and possible bias in that it is difficult to determine the sequence of chlamydia infection and infertility. Furthermore, the pathology of self-reported infertility was unknown, which limited further investigation of the relationship between chlamydia infection and certain types of infertility. A large-scale prospective cohort study that focuses on both the course of chlamydia infection and comprehensive examination of the causes of infertility is now needed.

Conclusion

The results of this study indicate that the serum 25(OH)D level moderates the relationship between chlamydia infection and infertility. When the 25(OH)D level was inadequate or relatively low, there was a significant relationship between chlamydia infection and infertility that disappeared when the vitamin D level was above a certain level. We consider that the 25(OH)D does not influence the risk of chlamydia infection but that it could potentially affects the prognosis in terms of the risk of infertility as a sequela.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41043-024-00681-6.

Supplementary Material 1

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Author contributions

Xu Zhi conducted and designed this work. Statistical analysis and manuscript preparation was performed by Miran Na and Xiya Sun. Lin Zeng contributed to the accuracy of data analysis. Data collection and table preparation was conducted by Yinrou Huang and Mingmei Lin.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This work was based on the public available NHANES data. All NHANES protocols are approved by the CDC's National Center for Health Statistics Ethics Review Board, and all survey respondents provide written informed consent.

Competing interests

The authors declare no competing interests.

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