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Socio-economic status and vitamin D deficiency among women at childbearing age: a population-based case-control study in rural northern China

Shiqi Lin[1,#], Yuan Zhang[1#], Jiajia Li[1#], Gong Chen[1], Lifang Jiang[2], Jian Chai[2], Xinming Song[1*], Lijun Pei[1*]

[1]Institute of Population Research/China Center on Population Health and development, Peking University, Beijing,100871, China.
[2] National Health Commission Key Laboratory of Birth Defects Prevention， Henan Key Laboratory of Population Defects Prevention, Zhengzhou, 450002, China.

[#] Shiqi Lin, Yuan Zhang and Jiajia Li contributed equally to this work and should be considered co-first authors.

[*] Address correspondence to:

Lijun Pei, pei_lj@pku.edu.cn. Xinming Song, Xmsong@pku.edu.cn.

Institute of Population Research, Peking University, No.5 Yiheyuan Road, Haidian District, Beijing 100871, China. +86 010-62751974

Emails of all authors:
Shiqi Lin: linshiqi@pku.edu.cn;
Yuan Zhang: zyzyzhangyuan@pku.edu.cn;
Jiajia Li: lijiajia95@pku.edu.cn;
Gong Chen: chengong@pku.edu.cn
Lifang Jiang: jiangzz66@163.com
Jian Chai: stopdo@163.com
Xinming Song, Xmsong@pku.edu.cn
Lijun Pei: pei_lj@pku.edu.cn.

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Abstract

Objective: To explore the association between socio-economic status (SES) and vitamin D deficiency/insufficiency of women at childbearing age in rural northern China.

Design: A population-based case-control study was conducted.

Setting: Four counties of Henan Province, China from 2009 to 2016.

Participants: 1151 non-pregnant healthy women between 18-40 years old were recruited.

Primary and secondary outcome measures: Serum 25-hydroxyvitamin D (25(OH)D) levels were measured using High-performance Liquid Chromatography-Tandem Mass Spectrometry. Vitamin D deficiency was defined as serum 25(OH)D <20 ng/mL; vitamin D insufficiency was defined as serum 25(OH)D of 20~30 ng/mL. SES was measured separately by women's and their husbands' education levels and occupations, household income and expenditure, as well as aggregately by SES index constructed with principal components analysis.

Results: The median serum 25(OH)D level was 20.90 (13.60-34.60) ng/ml and the prevalence of vitamin D insufficiency and deficiency was 20.16% and 47.80%. After adjusting for confounding and possible mediating factors including diet, lifestyles and health service utilization, household annual income <10000 Yuan was still associated with an increased risk of vitamin D insufficiency (aOR:2.11, 95%CI:1.43-3.12); inadequate household income for expenditure was associated with an elevated risk of vitamin D insufficiency (aOR:1.64, 95%CI:1.10-2.46). Household annual income <10000 Yuan and inadequate household income for expenditure were also associated with elevated risks of vitamin D deficiency (aOR:1.66, 95%CI:1.18-2.34; aOR: 1.92, 95%CI:1.37-2.68). Low SES index was associated with elevated risks of vitamin D insufficiency (aOR: 2.46; 95%CI: 1.57-3.88), while both middle and low SES index were associated with increased risks of vitamin D deficiency (aOR: 1.43, 95%CI: 1.35-2.91; aOR: 1.98, 95%CI: 1.35-2.91).

Conclusions: Low SES was associated with higher risks of vitamin D deficiency/insufficiency of women at childbearing age in rural northern China. More efforts should be devoted to explore potential mechanisms and to narrow down SES inequalities in vitamin D status.

Key words: socio-economic status, vitamin D insufficiency and deficiency, women at

childbearing age, rural northern China

Article summary

Strengths and limitations of the study:

The data was a population-based and representative one of large sample size with the information on the main exposures and blood sample obtained at the same time to minimize recall bias.

Both separate dimensions and aggregate index of SES were taken to thoroughly examine the association between SES and vitamin D status.

It's one of the few studies to target women at childbearing age in rural northern China who were in great need of enough vitamin D both for themselves and for their offspring but were found to be deficient in vitamin D.

The level of serum 25(OH)D might be underestimated because the blood sample of this study was collected in winter when daylight and temperature was lower than that in summer.

The measurement of diet was based on eating frequencies of different kinds of food, which might reduce the measurement accuracies and probably leading to misclassification errors.

Introduction

Vitamin D deficiency/insufficiency could cause many health problems to all ages, recognized as important risk factors for growth retardation, skeletal deformities and osteoporotic diseases[1], and is lined to occurrences of a variety of chronic diseases and thus premature mortality worldwide[2], including China[3]. Since inadequate sunlight exposure and absorption of vitamin D are among the major causes of vitamin D deficiency/insufficiency[1], a series of studies have indicated vitamin D deficiency/insufficiency follows a gradient of socio-economic status (SES)[4-8], a crucial factor determining one's lifestyles. Even though SES may not be itself a direct causal factor for health problems, exploring social inequalities of vitamin D deficiency/insufficiency can help to provide clues to the actual mechanisms involved[9]. However, prior studies concerning this topic were most descriptive ones, based mainly on findings from western and West Asian countries where distribution of lifestyles in different SES was very distinct from that in other countries like China. Moreover, previous researches on the association between SES and vitamin D deficiency/insufficiency often focused on elderly and children, seldom on women at childbearing age. Yet the fact that sufficient vitamin D is vital to those women as well as their offspring underscores the need for performing studies in regions like northern rural China where prevalence of vitamin D deficiency/insufficiency was found to be quite higher than that in regions of lower latitude and more developed economy[3]. The aim of our study is to explore the association between SES and vitamin D deficiency/insufficiency among women at childbearing age in rural northern China.

Materials and methods

Study design and population

The study was a population-based case-control one. The data was from the Study on Population-based Birth Defects Monitoring and Comprehensive Intervention. The Study was a prospective cohort of women at childbearing age from December 2009 to February 2010 in 4 counties of Henan Province, China to explore exposure risk factors for adverse pregnancy outcomes before and in pregnancy. Women between 18-40 years old who intended to become pregnant, lived in the research counties with permanent

residency and didn't have severe heart, liver, kidney, blood or other system diseases or cancers, were recruited. A total of 1151 women at childbearing age participated in our research.

Data collection

Trained healthcare workers conducted face-to-face interviews with participants and their families at baseline to collect information on the women's and their husbands' demographic and social economic characteristics, women's history of diseases and treatment, eating habits and the frequency of dietary and nutrient intake, behavioral exposure factors and the utilization of public health services.

For each participant, a fasting venous blood sample was also collected at baseline by 8 ml. The sample was prepared by centrifugation and stored at -80℃ until analysis..

The study protocol was reviewed and approved by Institutional Review Board of Peking University Health Science Center, and written informed consent was obtained from all subjects before completing the questionnaire and collection of blood samples at the time of the baseline survey.

Definitions of vitamin D insufficiency and deficiency

Serum 25-hydroxyvitamin D (25(OH)D) levels of the 1151 women's blood samples were measured using High-performance Liquid Chromatography-Tandem Mass Spectrometry (HPLC-MS/ MS, Ultimate3000 - API 3200 Q TRAP). Vitamin D deficiency was defined as serum 25(OH)D <20 ng/mL, vitamin D insufficiency as serum 25(OH)D 20~30 ng/mL [10].

Definitions of socio-economic status

In our study, SES was measured by both separate and aggregate indicators. There were six separate dimensions of SES: women's education level, their husbands' education level, women's occupation, their husbands' occupation, household annual income and whether their annual income was enough for expenditure. Aggregating over these six dimensions of SES, we further constructed an SES index using principle components analysis. To make the categorical form of data meet the requirement of principle components analysis, all the six categorical variables were coded into binary ones. Since all data have an equal weight, the co-variance matrix was used and the

Bartlett's test of sphericity was statistically significant (P<0.001), indicating it suitable to use principle components analysis here. The first principal component was taken as a measure of SES index[11], accounting for 29% of total variation. This percentage, though seemed not high, was in accordance with previous studies[12], reflecting that correlations between variables were complex and that each variable may have its own determinant other than SES[11],. The SES index was then divided into three groups: high SES (the highest 33.33%), low SES (the lowest 33.33%) and the middle SES (the rest).

Statistical analysis

Univariate analysis was conducted to find the differences of demographic characteristics, SES, history of chronic diseases, frequency of dietary intake and nutritional supplementation, passive smoking and utilization of public health services between vitamin D sufficiency and insufficiency group, and between sufficiency and deficiency group.

To better identify the relationship between SES and vitamin D status, we examined associations between vitamin D status and separate dimensions of SES, as well as associations between vitamin D status and SES index. We conducted four multivariate logistic regression models in this study to explore: (1) the association between vitamin D insufficiency and separate dimensions of SES, i.e., women's and their husbands' education and occupation and household annual income and enough annual income for expenditure; (2) the association between vitamin D insufficiency and SES index; (3) the association between vitamin D deficiency and separate dimensions of SES; and (4) the association between vitamin D deficiency and SES index. In all four models, vitamin D sufficiency were taken as a reference group and all other variables which were statistically significant in univariate analyses were controlled.

Patients and public involvement

No patients were involved in the development of the research question, study design or interpretation of the data. There are no plans to disseminate the results of the research to study participants or the relevant patient community.

Results

Participant characteristics and univariate analysis results

The median serum 25(OH)D level of the 1151 women at childbearing age was 20.90 (13.60-34.60) ng/ml. The prevalence of vitamin D insufficiency and deficiency was 20.16% and 47.80%, respectively. (Table 1).

Table 2 shows the results of univariate analysis. There were significant differences between vitamin D sufficiency and insufficiency group in women's age, women's and their husbands' education level, household annual income, enough household income for expenditure, SES index, gravidity, nutritional supplement, eggs intake, fresh meat intake, milk intake, picky eating habits and accepting physical examination during the past year. While the sufficiency and insufficiency group were similar with regard to women's and their husbands' occupation. Between vitamin D sufficiency and vitamin D deficiency group, there were significant differences in women's age, women's and their husbands' education level and their husbands' occupation, household annual income, enough household income for expenditure, SES index, gravidity, passive smoking, nutritional supplement, eggs intake, milk intake, vegetable and fruit intake, picky eating habits, doing physical exercise regularly, accepting eugenic publicity and accepting physical examination during the past year. The sufficiency and deficiency group were similar with regard to women's occupation.

Multivariate Logistic regression analysis

The aforementioned statistically significant variables were included in multivariate logistic regression models to examine the association between SES and vitamin D insufficiency and deficiency (Table 3). After adjusting for women's age, gravidity, nutritional supplement, eggs intake, fresh meat intake, milk intake and picky eating habits, compared with household annual income≥10000 Yuan, household annual income <10000 Yuan was associated with an increased risk of vitamin D insufficiency (OR:2.11, 95%CI:1.43-3.12); inadequate household income for expenditure was associated with an elevated risk of vitamin D insufficiency (aOR:1.64, 95%CI:1.10-2.46). And after adjusting for women's age, gravidity, nutritional supplement, eggs intake, milk intake, vegetables and fruits intake, picky eating habits, passive smoking and physical exercise, household annual income <10000 Yuan and inadequate

household income for expenditure were also associated with an elevated risk of vitamin D deficiency (aOR: 1.66, 95%CI:1.18-2.34; aOR: 1.92, 95%CI:1.37-2.68) , respectively. While accepting eugenic publicity was associated with a decreased risk of vitamin D deficiency (aOR:0.43, 95% CI:0.31-0.60). Women's education, husband's education and husband's occupation were neither associated with Vitamin D insufficiency nor with Vitamin D deficiency.

In table 4, multivariate logistic regression models were performed to further explore the associations between SES index and vitamin D insufficiency or deficiency. After adjusting for women's age, gravidity, nutritional supplement, eggs intake, fresh meat intake, milk intake and picky eating habits and accepting physical examination during the past year, low SES index was independently associated with an elevated risk of vitamin D insufficiency (aOR: 2.46, 95%CI: 1.57-3.88). While after adjusting for women's age, gravidity, passive smoking, nutritional supplement, eggs intake, milk intake, vegetable and fruit intake, picky eating habits, passive smoking and physical exercise, accepting eugenic publicity and accepting physical examination during the past year, both middle and low SES index were associated with increased risks of vitamin D deficiency (aOR: 1.43, 95%CI: 1.35-2.91; aOR: 1.98, 95%CI: 1.35-2.91). Accepting physical examination during the past year was associated with a reduced risk of vitamin D deficiency (aOR: 0.42, 95%CI: 0.31-0.58), suggesting it a protective factor for vitamin D deficiency.

Discussion

Our study found that the prevalence of vitamin D insufficiency and deficiency among non-pregnant women at childbearing age in 4 counties of Henan Province, China, was 20.16% and 47.80%, respectively. Compared with countries with similar latitude like US and some other Asian countries in lower latitude like Cambodia, the insufficiency prevalence in our study was lower (US, 36%[13]; Cambodia, 35.6%[14]), yet the deficiency prevalence was higher (US, 42%[13]; Cambodia, 29%[14]). Albeit the sufficiency prevalence in our setting was much higher than the average vitamin D sufficiency in northern rural China (20.3%)[15], the medium serum 25(OH)D level was similar (20.9ng/ml vs 22.0ng/ml[15]), suggesting a higher rate of severely low serum

25(OH)D level in our study. In fact, the prevalence of severe vitamin D deficiency (<10ng/ml) in our study was 15.99% with a medium of 5.63ng/ml. The condition of vitamin D deficiency among women at childbearing age in our setting is an alarming phenomena and worth attention.

After taking into consideration of lifestyles and health service utilization, we examined how separate dimension of SES, namely, education, occupation and income and expenditure related to vitamin D status and found that only low income and inadequate income for expenditure were significantly associated with vitamin D insufficiency and deficiency. Although these dimensions of SES are interrelated, it has been proposed that each provides somewhat different resources and thus displays different relations with health outcomes. Income reflects better nutrition, housing, schooling, and recreation; occupation manifests prestige, responsibility, physical activity, and work exposures; and education indicates better access to information and resources to promote health[16]. In the case of vitamin D status, it was found out that adult women with lower education level in Europe were less prone to take vitamin D supplement[17-19] and education was the primary contributor to inequalities in the prenatal health service utilization in rural western China[20], partly confirmed by our result that after adjusting for nutrition supplement and health service utilization, education was no longer a significant risk factor. Yet until now, there were limited studies concerning other possible ways through which other dimensions (like income and occupation) of SES could affect vitamin D status. Different from cardiovascular diseases to which education was the most significant indicator[16], our findings implied that income and expenditure were the most significant SES indicators of vitamin D status, meaning that there might exist a distinctive pathways between low SES and vitamin D deficiency/insufficiency.

In multivariate models of the SES index, we found that low SES index was independently associated with an elevated risk of vitamin D insufficiency, while middle and low SES index were both associated with increased risks of vitamin D deficiency. Several pathways could explain this result. Different tendencies to sunlight exposure could be one[21], knowledge and access to healthy diet and behavioral habits could be

another[22]. It's worth noting that physical examination during the past year was associated with a reduced risk of vitamin D deficiency, a pathway of SES to vitamin D status that was hardly noticed before. Although previous studies also indicated an association between SES and vitamin D status[14 23-26], our result further pointed out that for women at childbearing age in rural northern China, a considerable association still existed even after controlling for potential mediators, namely in our study, diet and nutrional supplement, health service utilization, physical exercise and passive smoking. Considering SES couldn't be a direct factor for vitamin D deficiency/insufficiency, there could be other mediators of SES in influencing vitamin D status needed to be detected; and given the complexity in analying whether SES was an independent risk factor for health issues[27], the potential mediators analyzed in our study also need more exploration. In a word, the mechanisms underlying the association between SES and vitamin D status needs further study.

The associations between SES and health issues are pervasive across ages and regions, and reflect effects of inequalities of diet qualities, lifestyles and access to health care resources[28]. Our findings suggested that there also existed health inequalities in vitamin D status among women at childbearing age. Maternal vitamin D deficiency/insufficiency not only has adverse health effects on mothers themselves, but also means their fetuses will develop in a low vitamin D state[29]. It's still inconclusive whether this influence on fetuses acts at later pregnancy or throughout the whole gestational process, but it's very likely that maternal vitamin D begins its vital role in fetal development in early pregnancy because 1,25(OH)2D induces decidualization which is key to implantation[29] and the early pregnancy is a stage when the growth trajectory is set and bone development starts[30]. Some studies did find the association between maternal vitamin D status in early pregnancy and fetal and neonatal growth[30]. Nevertheless, the vitamin D deficiency/insufficiency in women at childbearing age is quite universal and vitamin D level is found to be lower in early pregnancy than in later pregnancy, and in non-pregnant women than in pregnant ones[13]. Initiating vitamin D supplementation before pregnancy could help guarantee a sufficient serum 25(OH)D level at early pregnancy. Our findings call for public and the government to pay more

attention to narrowing down social inequalities and to providing support for women with low SES, who were often found to be less educated, poorer, more obese, more likely to currently smoke, more physically inactive and less likely to frequently drink milk[13]. In addition, though middle SES was only associated with vitamin D deficiency, middle SES subgroups should not be considered exempt from concerns about serum 25(OH)D concentrations on account of the vitamin D insufficiency-to-deficiency transition.

There are some strengths of our study. The data based was a representative one of large sample size, high measurement accuracy and good quality control. The information on the main exposures and blood sample was obtained at the same time to minimize recall bias. In addition, separate dimensions of SES and the SES index were both taken to comprehensively explore the associations between SES and vitamin D status and the potential underlying mechanisms. The SES index was constructed using principle components analysis to aggregate over education and occupation of women's and their husbands, household income and expenditure, avoiding the potential bias that might be brought about by single indicator, and thus improving the test power and the reliability. What's more, compared with previous studies which were mainly descriptive ones, our study adopted multivariate logistic regression analyses to adjust for many potential confounding and mediating factors including diet and nutrition, physical exercise, passive smoking and public health service utilization, helping better identify how SES was associated with vitamin D status.

However, limitations also existed. The level of serum 25(OH)D might be underestimated because the blood sample of this study was collected in winter when daylight and temperature was lower than that in summer. Fortunately, it might not affect the estimation of associations between SES and vitamin D status since the collections of blood samples and interviews about exposure factors were conducted at the same time and thus the season could not be a confounding factor. Due to limited data, family assets and living conditions, which were also usual indicators of SES, were not included in our analysis. But considering family income and expenditure are thought to be a more reliable measure of SES[12] and can largely reflect family wealth, and because income,

education, and occupation and employment are most widely used indicators of SES in epidemiological studies[27] than assets and living conditions, this limitation wouldn't change our conclusion. Also, our measurement of diet was based on eating frequencies of different kinds of food which might reduce the measurement accuracies and probably lead to misclassification errors. Future studies can avoid this by adopting tables of dietary nutrition.

In conclusion, vitamin D insufficiency or deficiency was quite common among women at childbearing age in rural northern China. SES was remarkably associated with vitamin D insufficiency and deficiency. The underlying mechanisms could be nutritional and behavioral factors and utilization of public services, but there might be other pathways needed to be detected. It's suggested that more efforts should be paid on improving nutritional status, health education of women at childbearing age and equalities of health care services to change their current state of vitamin D insufficiency and deficiency.

Author statement: Ms. Shiqi Lin, Dr. Yuan Zhang, and Mr. Jiajia Li conducted the analysis and writing of the article and reviewed and revised it. Dr Lijun Pei and Dr Xinming Song conceptualized and designed the study and the project where the data came from, coordinated and supervised data collection, and critically reviewed and revised the manuscript for important intellectual content. Dr. Gong Chen, Dr. Lifang Jiang, and Dr. Jian Chai designed the data collection instruments, acquired data, and revised the paper critically for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved.

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Ethics approval: The study was approved by the Institutional Review Board of Peking University Health Science Center (IRB00001052-08083).

Patient consent: Written informed consent was obtained from all subjects/patients.

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Table 1 Serum 25(OH)D distribution among women at childbearing age

Serum 25(OH)D（ng/ml）*	n	%	Medium（25%-75%）
Sufficient	369	32.06	40.20（35.10-47.50）
Insufficient	232	20.16	24.35（22.03-26.88）
Deficient	550	47.80	13.30（7.75-16.60）
Total	1151	100	20.90（13.60-34.60）

Serum 25(OH)D: Serum 25-hydroxyvitamin D.* Sufficient (≥30 ng/ml); Insufficient (20–30 ng/ml); Deficient (<20 ng/ml)

Table 2 Demographic, socio-economic and other exposure characteristics by vitamin D status

Vitamin D status	Sufficient (n=369)	insufficient (n=232)		deficient (n=550)	
Exposure variables	**N(%)**	**N(%)**	**P**	**N(%)**	**P**
Demographic variables					
Age					
＜28	222(60.20)	113(48.71)		260(47.27)	
28-	147(39.80)	119(51.29)	0.006	290(52.73)	<0.001
BMI					
＜24	244(66.12)	147(63.36)		352(64.00)	
24-	92(24.93)	58(25.00)		129(23.45)	
28-	33(8.94)	27(11.64)	0.548	69(12.55)	0.230
Gravidity					
0	119(32.25)	53(22.94)		129(23.50)	
1	159(43.09)	97(41.99)		193(35.15)	

⩾2	91(24.66)	81(35.06)	0.008	227(41.35)	<0.001
History of chronic diseases					
No	42(11.38)	26(11.21)		62(11.27)	
Yes	327(88.62)	206(88.79)	0.95	488(88.73)	0.96
Socio-economic status					
Women's education					
High school or above	126(34.24)	51(21.98)		133(24.23)	
Junior high or below	242(65.76)	181(78.02)	0.001	416(75.77)	0.001
Husband's education					
High school or above	128(34.69)	58(25.00)		154(28.00)	
Junior high or below	241(65.31)	174(75.00)	0.012	396(72.00)	0.031
Women's occupation					
Others	79(21.41)	45(19.40)		119(21.64)	
Unemployed or famers	290(78.59)	187(80.60)	0.553	431(78.36)	0.935
Husband's occupation					
Others	210(57.22)	143(62.17)		368(67.15)	
Unemployed or famers	157(42.78)	87(37.83)	0.231	180(32.85)	0.002
Household annual income					
⩾10000 (YUAN)	278(75.34)	122(52.59)		309(56.39)	
< 10000 (YUAN)	91(24.66)	110(47.41)	<0.001	239(43.61)	<0.001
Household income for expenditure					
Surplus	189(51.22)	65(28.02)		165(30.05)	
Inadequate or deficit	180(48.78)	167(71.98)	<0.001	384(69.95)	<0.001
SES index					
High	161(43.99)	57(24.78)		154(28.21)	
Middle	124(33.88)	71(30.87)		188(34.43)	
Low	81(22.13)	102(44.35)	<0.001	204(22.13)	<0.001
Nutritional factors					
Nutritional supplement					
No	231(62.60)	179(77.16)		437(79.45)	
Yes	138(37.40)	53(22.84)	<0.001	113(20.55)	<0.001
Meat intake					
⩾4 time per week	56(15.18)	12(5.17)		68(12.39)	
1-3 times per month	164(44.44)	118(50.86)		229(41.71)	
< once per month	149(40.38)	102(43.97)	0.001	252(45.90)	0.202
Fish intake					
⩾1 time per week	29(7.86)	13(5.60)		37(6.74)	
1-3 times per month	62(16.80)	26(11.21)		68(12.39)	
< once per month	278(75.34)	193(83.19)	0.074	444(80.87)	0.117
Eggs intake					
Everyday	143(38.75)	60(25.86)		151(27.50)	
4-6 times per week	101(27.37)	71(30.60)		109(19.85)	
⩽ 3 times per week	125(33.88)	101(43.53)	0.004	289(52.64)	<0.001
Milk or dairy products intake					

⩾ 4 times per week	89(24.12)	26(11.21)		92(16.76)	
<4 times per week but at least once per month	96(26.02)	73(31.47)		177(32.24)	
Almost never	184(49.86)	133(57.33)	<0.001	280(51.00)	0.011
Beans and soy products intake					
Everyday	103(27.91)	57(24.57)		130(23.68)	
4-6 times per week	76(20.60)	66(28.45)		88(16.03)	
1-3 times per week	92(24.93)	61(26.29)		149(27.14)	
< once per week	98(26.56)	48(20.69)	0.092	182(33.15)	0.053
Vegetables and fruits intake					
Everyday	256(69.38)	159(68.53)		424(77.23)	
4-6 times per week	81(21.95)	56(24.14)		68(12.39)	
⩽ 3 times per week	32(8.67)	17(7.33)	0.730	57(10.38)	0.001
Picky eating habits					
No	323(87.53)	221(95.26)		510(92.90)	
Yes	46(12.47)	11(4.74)	0,002	39(7.10)	0.006
Passive smoking					
No	171(46.34)	90(38.79)		186(33.82)	
Yes	198(53.66)	142(61.21)	0.069	364(66.18)	<0.001
Physical exercise					
No	298(80.76)	200(86.21)		490(89.42)	
Yes	71(19.24)	32(13.79)	0.084	58(10.58)	<0.001
Accept eugenic publicity					
No	156(42.74)	115(45.70)		325(59.41)	
Yes	209(57.26)	113(49.56)	0.067	222(40.59)	<0.001
Accept physical examination during the past year					
No	176(47.83)	135(58.44)		295(72.61)	
Yes	192(52.17)	96(41.56)	0.011	149(27.39)	<0.001

SES index, Socio-economic Status index

Table 3 Multivariate logistic analysis of socio-economic status and health service utilization

variables between vitamin D sufficiency and insufficiency or deficiency group

Vitamin D status	Insufficient (n=232)	Deficient (n=550)
Exposure Variables	**aOR(95%CI) ***	**aOR(95%CI) †**
Socio-economic status		
Women's education		
High school or above	1.00	1.00
Junior high or below	1.19(0.77-1.85)	1.07(0.75-1.53)
Husband's education		
High school or above	1.00	1.00
Junior high or below	1.01(0.66-1.55)	1.05(0.74-1.49)
Husband's occupation		
Others	-	1.00
Unemployed or agriculture	-	1.18(0.86-1.62)
Household annual income (YUAN)		
10000-	1.00	1.00
< 10000	2.11(1.43-3.12)	1.66(1.18-2.34)
Household income for expenditure		
Surplus	1.00	1.00
Inadequate or deficit	1.64(1.10-2.46)	1.92(1.37-2.68)
Accept eugenic publicity		
No	-	1.00
Yes	-	0.84(0.61-1.17)
Physical examination during the past year		
No	1.00	1.00
Yes	0.77(0.53-1.11)	0.43(0.31-0.60)

aOR, adjusted odds ratio; * In logistic model for Vitamin D insufficiency, odds ratios were adjusted for women's age, gravidity, nutritional supplement, eggs intake, fresh meat intake, milk intake and picky eating habits. †In logistic model for Vitamin D deficiency, odds ratios were adjusted for women's age, gravidity, passive smoking, nutritional supplement, eggs intake, milk intake, vegetable and fruit intake, picky eating habits, passive smoking and physical exercise.

Table 4 Multivariate logistic analysis of SES index and health service utilization variables between

vitamin D sufficiency and insufficiency or deficiency group

Vitamin D status	Insufficient (n=232)	Deficient (n=550)
Exposure variables	**aOR(95%CI)***	**aOR(95%CI) †**
SES index:		
High	1.00	1.00
Middle	1.30(0.83-2.03)	1.43(1.01-2.04)
Low	2.46(1.57-3.88)	1.98(1.35-2.91)
Accept Eugenic Publicity		
No	-	1.00
Yes	-	0.82(0.59-1.13)
Physical examination during the past year		
No	1.00	1.00
Yes	0.73(0.51-1.05)	0.42(0.31-0.58)

SES index, Socio-economic Status index; aOR, adjusted odds ratio; * In logistic model for Vitamin D insufficiency, odds ratios were adjusted for women's age, gravidity, nutritional supplement, eggs intake, fresh meat intake, milk intake and picky eating habits. † In logistic model for Vitamin D deficiency, odds ratios were adjusted for women's age, gravidity, passive smoking, nutritional supplement, eggs intake, milk intake, vegetable and fruit intake, picky eating habits, passive smoking and physical exercise.

Reporting checklist for case-control study.

Based on the STROBE case-control guidelines.

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Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

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		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	#3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	#4	Present key elements of study design early in the paper	4-5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of	4-5

		recruitment, exposure, follow-up, and data collection	
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls. For matched studies, give matching criteria and the number of controls per case	4-5
Eligibility criteria	#6b	For matched studies, give matching criteria and the number of controls per case	n/a
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for cases and controls.	4-5
Bias	#9	Describe any efforts to address potential sources of bias	11
Study size	#10	Explain how the study size was arrived at	4-5
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	5-6
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	6
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	n/a
Statistical methods	#12c	Explain how missing data were addressed	n/a
Statistical methods	#12d	If applicable, explain how matching of cases and controls was addressed	n/a
Statistical methods	#12e	Describe any sensitivity analyses	n/a
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for cases and controls.	6
Participants	#13b	Give reasons for non-participation at each stage	n/a
Participants	#13c	Consider use of a flow diagram	n/a

Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for cases and controls	6-7
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	n/a
Outcome data	#15	Report numbers in each exposure category, or summary measures of exposure. Give information separately for cases and controls	7-8
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
Main results	#16b	Report category boundaries when continuous variables were categorized	7-8
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	#18	Summarise key results with reference to study objectives	8-10
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	11-12
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	8-10
Generalisability	#21	Discuss the generalisability (external validity) of the study results	n/a
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

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Socio-economic status and vitamin D deficiency among women at childbearing age: a population-based case-control study in rural northern China

Shiqi Lin[1,#], Lifang Jiang[2#],Yuan Zhang[1#], Jian Chai[2], Jiajia Li[1], Xinming Song[1*], Lijun Pei[1*]

[1]Institute of Population Research/China Center on Population Health and development, Peking University, Beijing,100871, China.
[2] National Health Commission Key Laboratory of Birth Defects Prevention， Henan Key Laboratory of Population Defects Prevention, Zhengzhou, 450002, China.

[#] Shiqi Lin, Lifang Jiang and Yuan Zhang contributed equally to this work and should be considered co-first authors.

[*] **Address correspondence to:**

Lijun Pei, pei_lj@pku.edu.cn. and Xinming Song, xmsong@pku.edu.cn.

Institute of Population Research, Peking University, No.5 Yiheyuan Road, Haidian District, Beijing 100871, China. +86 010-62751974

Emails of all authors:
Shiqi Lin: linshiqi@pku.edu.cn;
Lifang Jiang: jiangzz66@163.com
Yuan Zhang: zyzyzhangyuan@pku.edu.cn;
Jian Chai: stopdo@163.com
Jiajia Li: lijiajia95@pku.edu.cn;
Xinming Song, xmsong@pku.edu.cn
Lijun Pei: pei_lj@pku.edu.cn.

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Abstract

Objective: To explore the association between socio-economic status (SES) and vitamin D deficiency/insufficiency of women at childbearing age in rural northern China.

Design: A population-based case-control study was conducted.

Setting: Four counties of Henan Province, China from 2009 to 2010.

Participants: 1151 non-pregnant healthy women between 18-40 years old.

Primary and secondary outcome measures: Serum 25-hydroxyvitamin D (25(OH)D) levels were measured using High-performance Liquid Chromatography -Tandem Mass Spectrometry. Vitamin D insufficiency was defined as serum 25(OH)D ≥20 and <30 ng/ml, deficiency as ≥10 and <20 ng/ml and severe deficiency as <10ng/ml. SES was measured separately by women's and their husbands' education levels and occupations, household income and expenditure, as well as aggregately by SES index constructed with principal components analysis.

Results: The median serum 25(OH)D level was 20.90 (13.60-34.60) ng/ml and the prevalence of vitamin D insufficiency, deficiency and severe deficiency was 20.16%, 31.80% and 15.99%, respectively. After being adjusted, household annual income <10000 RMB was associated with increased risks of vitamin D insufficiency (aOR:2.10, 95%CI: 1.41~3.14), deficiency (aOR: 1.58, 95%CI: 1.09~2.29) and severe deficiency (aOR: 2.79, 95%CI: 1.78~4.38); inadequate household income for expenditure was associated with elevated risks of vitamin D insufficiency (aOR:1.66, 95%CI: 1.08~2.54) and deficiency (aOR: 1.81, 95%CI: 1.26~2.62); low SES index was associated with elevated risks of vitamin D insufficiency (aOR: 2.40, 95%CI: 1.52~3.80) and deficiency (aOR: 1.64, 95%CI: 1.08~2.50); both middle and low SES index were associated with increased risks of vitamin D severe deficiency (aOR: 1.70, 95%CI: 1.02~2.84; aOR: 2.45, 95%CI: 1.45~4.14).

Conclusions: Lower SES was associated with higher risks of vitamin D deficiency/insufficiency of women at childbearing age in rural northern China. More should be done to explore potential mechanisms and to narrow down SES inequalities in vitamin D status.

Key words: socio-economic status, vitamin D insufficiency and deficiency, women at childbearing age, rural northern China

Article summary

Strengths and limitations of the study:

The data was a population-based and representative one of larger sample size with the information on main exposures and blood samples obtained at the same time to minimize recall bias.

Both separate dimensions and aggregate index of SES were taken to thoroughly examine the association between SES and vitamin D status.

It's one of the few studies to target women at childbearing age in rural northern China for whom sufficient vitamin D were important both for themselves and for their offspring, but also among whom vitamin D insufficiency/deficiency were found to be prevail.

The level of serum 25(OH)D might be underestimated because the blood sample of this study was collected in winter when daylight and temperature was lower than that in summer.

The laboratory didn't participate in any vitamin D standardization program or use standardization of 25(OH)D measurements, which might affect comparison between the present study and other studies.

Introduction

Vitamin D deficiency/ insufficiency has been concerned to be of high prevalence in both developing and developed countries and is linked to occurrences of a variety of chronic diseases and premature mortality[1]. In China, it's also reported that vitamin D deficiency/ insufficiency is common in almost all age groups and areas[2] and is pertinent to clinical issues besides skeletal problems, such as metabolic syndrome[3] and its complications[4], dyslipidemia[5] and cardiovascular diseases[6] and even emotional, behavioral and attentional problems[7], depression[8], as well as reduced sperm quality[9] and lower total testosterone[10]. In particular, maternal vitamin D deficiency/insufficiency has been found to be associated not only with adverse gestational and neonatal outcomes like low birth weight, prematurity[11], and gestational

diabetes mellitus[12], but also with offspring vitamin D deficiency[11], impaired intra-uterine growth[13, 14], type I diabetes, nutritional rickets and pneumonia in adulthood[15]. Albeit still inconclusive, maternal vitamin D might begin its vital role in fetal development in early pregnancy[13], thus suggesting the importance of having adequate vitamin D concentration when preparing for pregnancy. In a word, given that sufficient vitamin status is so vital for women themselves and their offspring and that serum 25(OH)D concentrations were low among them[3] and their newborn babies in Chinese populations[2, 16, 17], it's of significance to target the vitamin D status and its influencing factors of women at childbearing age.

Since inadequate sunlight exposure and absorption of vitamin D are among the major causes of vitamin D deficiency/insufficiency[18], a series of studies have indicated vitamin D deficiency/insufficiency follows a gradient of socio-economic status (SES)[19-23], a crucial factor determining one's lifestyles. Even though SES may not be itself a direct causal factor for health problems, exploring social inequalities of vitamin D deficiency/insufficiency can help to provide clues to the actual mechanisms involved[24]. However, prior studies concerning this topic were most descriptive ones, based mainly on findings from western and West Asian countries where distribution of lifestyles in different SES was very distinct from that in other countries like China. Moreover, previous researches on the association between SES and vitamin D deficiency/insufficiency often focused on elderly and children, seldom on women at childbearing age. Therefore, the aim of our study was to explore the association between SES and vitamin D deficiency/insufficiency among women at childbearing age in rural northern China where prevalence of vitamin D deficiency/insufficiency may be higher than that in regions of lower latitude and more developed economy[2].

Materials and methods

Study design and population

This was a population-based case-control study. The data of the present research was based on the Study on Population-based Birth Defects Monitoring and Comprehensive Intervention Project which aimed to establish a prospective cohort of married but unpregnant women at child-bearing age in 2009-2010 in Henan Province,

collect their baseline characteristics including basic demographic and socio-economic characteristics, dietary intake and behavioral factors as well as their blood samples, follow them until their pregnancy results were observed so as to explore the association between pre-pregnancy risk factors and pregnancy results. A multi-stage cluster sampling method was used to obtain a representative sample of targeted population. 1) In the first stage, 4 counties (Hui County, Mengzhou County, Xinmi County and Luanchuan County; the latitudes of which are 35°17′ N, 34°50’ N, 34°32' N and 35°51’ N, respectively) were randomly selected from 158 counties in Henan Province; 2) In the second stage, 40 towns (the next administrative unit below County) were randomly selected from the 4 counties. 3) In the third stage, 5 villages were randomly selected from each town. 4) In the fourth stage, 10 women at child-bearing age and their husbands were randomly selected in each village. The selection criteria was 1) married women with local permanent residency, 2) between 18-40 years old, 3) not pregnancy at present, 4) living in the research counties with local registered permanent residency and 5) without any severe heart, liver, kidney, metabolic diseases, blood or other system diseases or cancers. Finally, 1151 of 2000 women had pregnancy results and were thus included in the project. In our study, cases were defined as women with serum 25(OH)D <30 ng/mL and were further subdivided into three groups: 1) vitamin D insufficiency: serum 25(OH)D ≥ 20–and < 30 ng/ml; 2) deficiency: serum 25(OH)D ≥ 10 and < 20 ng/ml; 3) severe deficiency: serum 25(OH)D < 10ng/ml. Controls were those with serum 25(OH)D ≥ 30 ng/ml. Altogether, there were 369 controls and 782 cases, among whom 232 were of vitamin D insufficiency, 366 of deficiency and 184 of severe deficiency.

Collection of data and blood sample

Trained healthcare workers conducted face-to-face interviews with participants and their families at baseline to collect information on the women’s and their husbands’ demographic and social economic characteristics, history of adverse pregnancy outcomes, women’s history of diseases and treatment, eating habits and the frequency of dietary and nutrient intake, behavioral factors, environmental factors and the utilization of public health services.

For each participant, a fasting venous blood sample (8 ml) was also collected at

baseline by professional healthcare workers. The collection time of blood samples was in December, 2009, and January and February, 2010. The sample was prepared by centrifugation and stored at -80℃ at Peking University until analysis.

The study protocol was reviewed and approved by Institutional Review Board of Peking University Health Science Center, and written informed consent was obtained from all subjects before completing the questionnaire and collection of blood samples at the time of the baseline survey.

Measurement of vitamin D status

Serum 25-hydroxyvitamin D (25(OH)D) concentration is the parameter of choice for the assessment of vitamin D status. The serum 25-hydroxyl vitamin D3 concentrations of the 1,151 women's blood samples were quantitatively determined by High-performance Liquid Chromatography-Tandem Mass Spectrometry (HPLC-MS/ MS, Ultimate3000 - API 3200 Q TRAP) method to overcome inaccuracy problems associated with immunoassays and protein binding assays[25]. Vitamin D severe deficiency was defined as serum 25(OH)D <10 ng/mL, vitamin D deficiency as ≥10 and <20 ng/ml and insufficiency as ≥20 and <30 ng/ml [26].

Definitions of socio-economic status

In our study, SES was measured by both separate and aggregate indicators. There were six separate dimensions of SES: women's education level, their husbands' education level, women's occupation, their husbands' occupation, household annual income and whether their annual income was enough for expenditure. Women's or husbands' educational level was grouped into "high school or above" and "junior high school or below"; Women's and husbands' occupation was grouped into "unemployed or farmers" and "other occupations"; Household annual income was grouped into "≥ 1000 RMB" and "<1000 RMB"; and household income for expenditure was measured by the question "whether your family have enough income for expenditure in your daily life?" and we grouped the answers of "a lot more income than expenditure", "a little more income than expenditure" and "balanced" into "surplus" and "income is not enough for expenditure" and "a lot more expenditure than income" into "inadequate or

deficit".

Aggregating over these six dimensions of SES, we further constructed an SES index using principal components analysis. To make the categorical form of data meet the requirement of principle components analysis, all the six categorical variables were coded into binary ones. Since all data have an equal weight, the co-variance matrix was used and the Bartlett's test of sphericity was statistically significant ($P<0.001$), indicating it suitable to use principal components analysis here. The first principal component was taken as a measure of SES index[27], accounting for 29% of total variation. This percentage, though seemed not high, was in accordance with previous studies[28], reflecting that correlations between variables were complex and that each variable may have its own determinant other than SES[27]. The SES index was then divided into three subgroups, namely, high, middle and low SES subgroup with the 33rd and 66th percentiles as the cut-off points.

Covariates

A number of possible confounding factors were also assessed including demographic variables, nutritional factors, behavioral factors and the utilization of health services.

Demographic variables included age, the body mass index (BMI), gravidity and history of chronic diseases. BMI was calculated by weight/height^2 and was grouped into <24 kg/m^2 as normal weight or underweight, ≥ 24 kg/m^2 to <28 kg/m^2 as overweight and ≥ 28 kg/m^2 as obesity[29]; we defined history of chronic diseases as having been diagnosed of any one of the following diseases: anemia, hypertension, hyperlipemia, heart disease, diabetes, hyperglycemia, thyroid diseases, phenylketonuria, epilepsy, asthma, chronic renal diseases, systematic lupus erythematosus, rheumatic arthritis, deep vein thrombosis, cancer, depression or anxiety and schizophrenia.

Nutritional factors included nutritional supplement, meat intake, fish intake, eggs intake, milk or dietary products, beans and soy product intake and vegetable intake. Nutritional supplement was evaluated by having taken any of the following during the past month: vitamin A, multivitamin B, vitamin B1, vitamin B2, vitamin B6, vitamin

B12, vitamin C, vitamin E, cod-liver oil or vitamin D, iron preparations, calcium tablets and zinc supplements. Food intake was measured by average frequencies of the food intake during the past year. The frequencies included "everyday", "4-6 times per week", "1-3 times per week", "1-3 times per month" and "hardly ever" and were divided into 2-3 groups according to distribution of the answered frequencies of different food.

Behavioral factors included picky eating habits, passive smoking and physical exercises. Picky eating habits were measured by the question "do you have picking eating habits, i.e., having preferences to some special food such as fruit and vegetables and keeping eating them every day while rejecting other kinds of food such as meat?"; having passive smoking was defined as "being passively inhaled cigarette smoke by smokers around you for more than 15 minutes every day"; taking physical exercises meant taking any one of the following indoor or outdoor exercises at least once a week for more than 30 minutes per time: walking, running, ball games, Tai Chi or other health-promotion physical exercises, swimming and other sports.

Utilization of health services included accepting eugenic publicity and accepting physical examination during the past year. Having accepted eugenic publicity was defined as having received materials (like brochures) from health service institutions during the past year about knowledge of eugenics such as how to prepare for pregnancy; having accepted physical examination during the past year was defined as having received systematic inspections of the body for signs and symptoms of disease or abnormality during the past year.

Statistical analysis

Univariate analysis was conducted to test the differences of vitamin D status across different demographic characteristics, SES, nutritional variables and utilization of public health services through χ^2 test.

To better identify the relationship between SES and vitamin D status, we examined associations between vitamin D status and separate dimensions of SES, as well as associations between vitamin D status and SES index. Six multivariate logistic regression models were performed in this study to explore: (1) the association between

vitamin D insufficiency and separate dimensions of SES, i.e., women's and their husbands' education and occupation and household annual income and enough annual income for expenditure; (2) the association between vitamin D insufficiency and SES index; (3) the association between vitamin D deficiency and separate dimensions of SES; (4) the association between vitamin D deficiency and SES index; (5) the association between vitamin D severe deficiency and separate dimensions of SES; and (6) the association between vitamin D severe deficiency and SES index. In all the models, vitamin D sufficiency were taken as a reference group and the potential confounding factors were adjusted.

Patients and public involvement

No patients (participants) involved.

Results

Participant characteristics

The median serum 25(OH)D level of the 1,151 women at childbearing age was 20.90 (13.60-34.60) ng/ml. The prevalence of vitamin D insufficiency, deficiency and severe deficiency was 20.16%, 31.80% and 15.99%, respectively. (Table 1).

Table 2 shows vitamin D status by demographic, socio-economic, nutritional supplement and utilization of health services. Overall, 51.69% of the study population were < 28 years old, 64.55% were of normal BMI, 78.89% were unemployed or farmers, 73.02% had junior high school or below educational attainment, 61.71% had household annual income ≥10000 RMB and 63.57% felt their household income were inadequate or deficit for expenditure.

Multivariate Logistic regression analysis

Table 3 displays multivariate logistic analysis of association between socio-economic status and vitamin D level. After adjusting for confounding factors, compared with household annual income ≥10000 RMB, household annual income <10000 RMB was associated with an increased risk of vitamin D insufficiency (aOR:2.10, 95%CI: 1.41~3.14), deficiency (aOR: 1.58, 95%CI: 1.09~2.29) as well as severe deficiency

(aOR: 2.79, 95%CI: 1.78~4.38); inadequate household income for expenditure was associated with an elevated risk of vitamin D insufficiency (aOR:1.66, 95%CI: 1.08~2.54) and deficiency (aOR: 1.81, 95%CI: 1.26~2.62). While accepting physical examination during the past year was associated with a decreased risk of vitamin D deficiency (aOR:0.49, 95% CI: 0.34~0.70) and severe deficiency (aOR: 0.25, 95%CI: 0.15~0.41).

In table 4, multivariate logistic regression models were performed to further explore the association between vitamin D level and SES index or health service utilization. After adjusting for confounding factors, low SES index was associated with an increased risk of vitamin D insufficiency (aOR: 2.40, 95%CI: 1.52~3.80) and deficiency (aOR: 1.64, 95%CI: 1.08~2.50); both middle and low SES index were associated with increased risks of vitamin D severe deficiency (aOR:1.70, 95%CI: 1.02~2.84; aOR: 2.45, 95%CI: 1.45~4.14). Accepting physical examination during the past year was associated with a reduced risk of vitamin D deficiency (aOR: 0.49, 95%CI: 0.35~0.70) and severe deficiency (aOR: 0.24, 95%CI: 0.15~0.39), suggesting it a protective factor for vitamin D deficiency.

Discussion

Our study found that the prevalence of vitamin D insufficiency and deficiency (serum 25(OH)D <20ng/ml) among women at childbearing age who intended to become pregnant in 4 counties of Henan Province, China, was 20.16% and 47.80%, respectively. Compared with countries with similar latitude like US and some other Asian countries in lower latitude like Cambodia, the insufficiency prevalence in our study was lower (US, 36%[30]; Cambodia, 35.6%[31]), yet the deficiency prevalence was higher (US, 42%[30]; Cambodia, 29%[31]). Albeit the sufficiency prevalence in our setting was much higher than the average vitamin D sufficiency in northern rural China (20.3%)[32], the medium serum 25(OH)D level was similar (20.9ng/ml vs 22.0ng/ml[32]), suggesting a higher rate of severely low serum 25(OH)D level in our study. In fact, the prevalence of severe vitamin D deficiency (<10ng/ml) in our study was 15.99% with a medium of 5.63ng/ml. The condition of vitamin D deficiency among women at

childbearing age in our setting is an alarming phenomena and worth attention.

After taking into consideration of lifestyles and health service utilization, we examined how separate dimension and aggregate index of SES related to vitamin D status and found that lower income, inadequate income for expenditure and lower SES index were significantly associated with vitamin D insufficiency and deficiency while education and occupation were not. Several pathways could explain this result. Different tendencies to sunlight exposure could be one[33], knowledge and access to vitamin D supplement and behavioral habits could be another[34]. It's worth noting that in our study, physical examination during the past year was associated with a reduced risk of vitamin D deficiency, a pathway of SES to vitamin D status that was hardly noticed before. Although previous studies also indicated an association between SES and vitamin D status[30, 35-38], our result further pointed out that for women at childbearing age in rural northern China, a considerable association still existed even after controlling for potential mediators, namely in our study, diet and nutrional supplement, health service utilization, physical exercise and passive smoking. Considering SES couldn't be a direct factor for vitamin D deficiency/insufficiency, there could be other mediators of SES in influencing vitamin D status needed to be detected. For example, it was found out that adult women with lower education level in Europe were less prone to take vitamin D supplement[39-41]. Yet until now, there were limited studies exploring possible ways through which different dimensions and composite SES could affect vitamin D status. The mechanisms underlying the association between SES and vitamin D status needs further study.

In this study, the principal component analysis was used to construct SES index. There are different ways of measuring SES in studies of vitamin D status. The most commonly seen is focusing on one dimension of SES by using individual SES indicators such as education attainment, income, expense management, and occupation[36, 38]. Indicators such as "poverty-income ratio", a ratio of family income to poverty threshold used in National Health and Nutrition Examination Survey (NHANES) in US[42], also focuses on one dimension of SES, i.e., family income, but

takes into consideration of local development to create an index[30]. Another way is to develop composite SES indexes with scales given to different indicators or indicator combinations. For example, Kuppuswamy's socioeconomic status, a relatively well-established tool in India, assigns 7 scores to education, 10 for occupation, and 12 for family income and makes 5 groups of SES[43] and SES index for German Health Interview and Examination Survey for Adults (DEGS1), assigns different score to different combination of specific kinds of occupation, income and education[37]. While some others develop a specific questionnaire based on local conditions to get an SES score. For instance, EPICES, a French evaluation of low socio-economic status and inequalities in Health Examination Centers, aggregates a lot more social dimensions such as leisure activities[35]. In our study, we not only evaluated several individual dimensions of SES to examine their separate associations to vitamin D deficiency/insufficiency, but also constructed an SES index. Since there is no well-recognized way of measuring SES in local area and it seems lack of credibility to assign scores to different SES dimensions by arbitrary, the principal components analysis we used was a 'data-driven' one and thus could avoid subjective judgement to some extent. Though hardly seen in analyzing vitamin D status, principal components analysis has proven to be quite validated and robust in constructing SES in other epidemiological studies[27]. By summing effects of individual SES indicators, we could get a better view of the association between SES and vitamin D insufficiency/deficiency and increase the test power.

Suggesting a pervasive vitamin D insufficiency/deficiency and health inequalities in vitamin D status among women at childbearing age in rural China, our findings call for attention paid to those population. Maternal vitamin D deficiency/insufficiency not only has adverse health effects on mothers themselves, but also means their fetuses will develop in a low vitamin D state[13]. It's still inconclusive whether this influence on fetuses acts at later pregnancy or throughout the whole gestational process, but it's very likely that maternal vitamin D begins its vital role in fetal development in early pregnancy because 1,25(OH)2D induces decidualization which is key to implantation[13]

and the early pregnancy is a stage when the growth trajectory is set and bone development starts[14]. Some studies did find the association between maternal vitamin D status in early pregnancy and fetal and neonatal growth[14]. Nevertheless, the vitamin D deficiency/insufficiency in women at childbearing age is quite universal and vitamin D level is found to be lower in early pregnancy than in later pregnancy, and in non-pregnant women than in pregnant ones[44]. Initiating vitamin D supplementation before pregnancy could help guarantee a sufficient serum 25(OH)D level at early pregnancy. It's of importance to narrow down social inequalities and to provide support for women with lower SES, who were often found to be less educated, poorer, more obese, more likely to currently smoke, more physically inactive and less likely to frequently drink milk[44].

There are some strengths of our study. The data based was a representative one of large sample size, high measurement accuracy and good quality control. The information on the main exposures and blood sample was obtained at the same time to minimize recall bias. In addition, separate dimensions of SES and the SES index were both taken to comprehensively explore the associations between SES and vitamin D status and the potential underlying mechanisms. The SES index was constructed using principal components analysis to aggregate over education and occupation of women's and their husbands, household income and expenditure, avoiding the potential bias that might be brought about by single indicator, and thus improving the test power and the reliability. What's more, compared with previous studies which were mainly descriptive ones, our study adopted multivariate logistic regression analyses to adjust for many potential confounding and mediating factors including diet and nutrition, physical exercise, passive smoking and public health service utilization, helping better identify how SES was associated with vitamin D status.

However, limitations also existed. The level of serum 25(OH)D might be underestimated because the blood sample of this study was collected in winter (December, January and February) when daylight and temperature was lower than that in summer. Fortunately, it might not affect the estimation of associations between SES

and vitamin D status since the collections of blood samples and interviews about exposure factors were conducted at the same time and thus the season could not be a confounding factor. Due to limited data, family assets and living conditions, which were also usual indicators of SES, were not included in our analysis. But considering family income and expenditure are thought to be a more reliable measure of SES[28] and can largely reflect family wealth, and because income, education, and occupation and employment are most widely used indicators of SES in epidemiological studies[45] than assets and living conditions, this limitation wouldn't change our conclusion. Also for limited data, we didn't get sunlight exposure of every participants, which could be an important mediating factor in our analysis. Furthermore, since there are no general standards of 25(OH)D measurements currently in China, the laboratory didn't participate in any vitamin D standardization program or use standardization of 25(OH)D measurements, which might affect comparison between the present study and other studies.

In conclusion, vitamin D deficiency/insufficiency was quite common among women at childbearing age in rural northern China. Lower SES was remarkably associated with increased risks of vitamin D deficiency/insufficiency. The underlying mechanisms could be nutritional and behavioral factors and utilization of public health services, but there might be other pathways needed to be detected. It's suggested that more efforts should be paid on improving nutritional status, health education of women at childbearing age and equalities of health care services to change their current state of vitamin D deficiency/insufficiency.

Contributors: Dr. Shiqi Lin, Dr. Lifang Jiang and Dr. Yuan Zhang conducted the analysis and interpretation of the data, drafted the work, and reviewed and revised it. Dr Lijun Pei and Dr Xinming Song conceptualized and designed the study and the project where the data came from, coordinated and supervised data collection, and critically reviewed and revised the manuscript for important intellectual content. Dr. Jiajia Li and Dr. Jian Chai designed the data collection instruments, acquired data, and

revised the paper critically for important intellectual content. All authors have approved the final manuscript as submitted and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved.

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Data availability statement: Data are available upon reasonable request. The datasets used and/or analyzed during the current study are available on reasonable request from the corresponding author.

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Table 1 Serum 25(OH)D distribution among women at childbearing age

Serum 25(OH)D*	**n**	**%**	**Medium(25%~75%)(ng/ml)**
Sufficient	369	32.06	40.20(35.10~47.50)
Insufficient	232	20.16	24.35(22.03~26.88)
Deficient	366	31.80	15.40(13.30~17.60)
Severely deficient	184	15.99	5.63(3.24~7.78)
Total	1151	100	20.90(13.60~34.60)

Serum 25(OH)D: Serum 25-hydroxyvitamin D.* Sufficient (≥30 ng/ml); Insufficient (≥20 and <30 ng/ml); Deficient (≥10 and <20 ng/ml); Severely deficient (<10ng/ml)

Table 2 Demographic, socio-economic, nutritional, behavioral and utilization of health service characteristics by vitamin D status

Exposure variables	**25(OH)D level**	**Sufficient (n=369)**	**Insufficient (n=232)**	**Deficient (n=366)**	**Severely deficient (n=184)**
	medium (25%~75%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**
Demographic variables					
Age					
< 28	22.90 (14.40~37.20)	222 (60.20)	113 (48.71)	162 (44.26)	98 (53.26)
28-	19.20 (13.20~31.10)	147 (39.80)	119 (51.29)**	204 (55.74) ***	86 (46.74)
BMI					
< 24	21.20 (13.60~35.30)	244 (66.12)	147 (63.36)	236 (64.48)	116 (63.04)

24-	21.80 (14.40~34.50)	92 (24.93)	58 (25.00)	85 (23.22)	44 (23.91)
28-	19.30 (12.80~31.25)	33 (8.94)	27 (11.64)	45 (12.30)	24 (13.04)
Gravidity					
0	22.90 (14.25~37.80)	119 (32.25)	53 (22.94)	78 (21.37)	51 (27.72)
1	23.20 (14.10~35.70)	159 (43.09)	97 (41.99)	132 (36.16)	61 (33.51)
≥2	18.40 (12.70~28.30)	91 (24.66)	81 (35.06)**	155 (42.47)***	72 (39.13)**
History of chronic diseases					
No	20.80 (13.55~34.65)	327 (88.62)	206 (88.79)	323 (88.25)	165 (89.67)
Yes	21.35 (14.30~34.65)	42 (11.38)	26 (11.21)	43 (11.75)	19 (10.33)
Socio-economic status					
Women's education					
High school or above	24.30 (14.90~38.40)	126 (34.24)	51 (21.98)	93 (25.48)	40 (21.74)
Junior high or below	20.15 (13.20~32.18)	242 (65.76)	181 (78.02)*	272 (74.52)*	144 (78.26)**
Husband's education					
High school or above	22.40 (14.10~37.40)	128 (34.69)	58 (25.00)	103 (28.14)	51 (21.72)
Junior high or below	20.40 (13.33~32.45)	241 (65.31)	174 (75.00)*	263 (71.86)	133 (72.28)
Women's occupation					
Others	20.40 (13.23~36.30)	79 (21.41)	45 (19.40)	74 (20.22)	45 (24.46)
Unemployed or famers	21.10 (13.60~34.20)	290 (78.59)	187 (80.60)	292 (79.78)	139 (75.54)
Husband's occupation					
Others	19.70 (12.70~33.20)	210 (57.22)	143 (62.17)	232 (63.74)	136 (73.91)
Unemployed or famers	23.60 (12.23~32.58)	157 (42.78)	87 (37.83)	132 (36.26)	48 (26.09)***
Household annual income (RMB)					
≥10000	23.00 (14.60~37.70)	278 (75.34)	122 (52.59)	223 (61.26)	86 (46.74)
< 10000	18.50 (11.53~27.38)	91 (24.66)	110 (47.41)***	141 (38.74)***	98 (53.26)***
Household income for expenditure					
Surplus	25.80	189	65	110	55

	(14.70~39.60)	(51.22)	(28.02)	(30.14)	(29.89)
Inadequate or deficit	19.15 (13.05~29.58)	180 (48.78)	167 (71.98)***	255 (69.86)***	129 (70.11)***
SES index					
High	24.50 (14.70~38.70)	161 (43.99)	57 (24.78)	107 (29.56)	47 (25.54)
Middle	20.50 (13.30~35.10)	124 (33.88)	71 (30.87)	124 (34.25)	64 (34.78)
Low	19.90 (12.95~27.90)	81 (22.13)	102 (44.35)***	131 (36.19)***	73 (39.67)***
Nutritional factors					
Nutritional supplement					
No	19.50 (13.10~31.15)	231 (62.60)	179 (77.16)	293 (80.05)	144 (78.26)
Yes	26.30 (14.88~40.33)	138 (37.40)	53 (22.84)***	73 (19.95)***	40 (21.74)***
Meat intake					
≥once per week	21.70 (14.70~36.30)	220 (59.62)	130 (56.30)	213 (58.20)	84 (45.65)
< once per week	19.80 (12.30~32.40)	149 (40.38)	102 (43.97)	153 (41.80)	100 (54.35)**
Fish intake					
≥once per month	23.30 (14.70~36.80)	91 (24.66)	39 (16.81)	81 (22.13)	24 (13.04)
< once per month	20.40 (13.20~34.00)	278 (75.34)	193 (83.19)*	285 (77.87)	160 (86.96)**
Eggs intake					
Everyday	24.15 (14.50~36.60)	143 (38.75)	60 (25.86)	102 (27.95)	49 (26.63)
4-6 times per week	23.70 (16.10~38.18)	101 (27.37)	71 (30.60)	82 (22.47)	27 (14.67)
≤ 3 times per week	17.90 (11.70~29.00)	125 (33.88)	101 (43.53)**	181 (49.59)***	108 (58.70)***
Milk or dairy products intake					
≥ 4 times per week	23.20 (14.70~37.90)	89 (24.12)	26 (11.21)	68 (18.63)	24 (13.04)
<4 times per week but at least once per month	19.35 (12.40~32.30)	96 (26.02)	73 (31.47)	118 (32.33)	59 (32.07)
Almost never	21.15 (13.40~33.63)	184 (49.86)	133 (57.33)***	179 (49.04)	101 (54.89)**
Beans and soy products intake					
Everyday	22.90 (15.10~34.60)	103 (27.91)	57 (24.57)	102 (27.95)	28 (15.22)

4-6 times per week	23.80 (16.60~34.50)	76 (20.60)	66 (28.45)	66 (18.08)	22 (11.96)
1-3 times per week	20.70 (12.48~35.13)	92 (24.93)	61 (26.29)	93 (25.48)	56 (30.43)
< once per week	17.90 (10.20~35.10)	98 (26.56)	48 (20.69)	104 (28.49)	78 (42.39)***
Vegetables and fruits intake					
Everyday	19.70 (12.90~33.30)	256 (69.38)	159 (68.53)	273 (74.59)	152 (82.61)
< once per day	23.90 (15.20~36.30)	113 (30.62)	73 (31.47)	93 (25.41)	32 (17.39)**
Behavioral factors					
Picky eating habits					
No	20.70 (13.63~33.30)	323 (87.53)	221 (95.26)	346 (94.79)	164 (89.13)
Yes	27.10 (11.90~43.20)	46 (12.47)	11 (4.74)**	19 (5.21)**	20 (10.87)
Passive smoking					
No	24.35 (14.75~37.13)	171 (46.34)	90 (38.79)	127 (34.70)	59 (32.07)
Yes	19.30 (12.80~32.30)	198 (53.66)	142 (61.21)	239 (65.30)**	125 (67.93)**
Physical exercise					
No	20.00 (13.30~33.80)	298 (80.76)	200 (86.21)	329 (90.38)	161 (87.50)
Yes	27.65 (16.60~38.48)	71 (19.24)	32 (13.79)	35 (9.62)***	23 (12.50)*
Utilization of health services					
Accept eugenic publicity					
No	18.40 (12.33~30.98)	156 (42.74)	115 (45.70)	216 (59.50)	109 (59.24)
Yes	24.40 (15.00~37.40)	209 (57.26)	113 (49.56)	147 (40.50)***	75 (40.76)***
Accept physical examination during the past year					
No	18.15 (11.78~29.60)	176 (47.83)	135 (58.44)	246 (68.33)	149 (80.98)
Yes	27.20 (17.40~39.20)	192 (52.17)	96 (41.56)*	114 (31.67)***	35 (19.02)***

RMB: the official currency of China; SES index, Socio-economic Status index; * P<0.05; *P<0.01; *P<0.001

Table 3 Multivariate logistic analysis of association of vitamin D status with separate socio-economic status indicators and health service utilization variables

Vitamin D status	Insufficiency aOR(95%CI)*	Deficiency aOR(95%CI) *	Severe deficiency aOR(95%CI) *
Socio-economic status			
Women's education			
High school or above	1.00	1.00	1.00
Junior high or below	1.26(0.79~2.00)	0.99(0.66~1.48)	1.40(0.83~2.36)
Husband's education			
High school or above	1.00	1.00	1.00
Junior high or below	1.08(0.70~1.68)	1.03(0.70~1.51)	1.10(0.67~1.80)
Women's occupation			
Others	1.00	1.00	1.00
Unemployed or farmers	1.58(0.96~2.61)	1.43(0.91~2.24)	1.39(0.81~2.40)
Husband's occupation			
Others	1.00	1.00	1.00
Unemployed or farmers	1.12(0.77~1.65)	1.03(0.73~1.46)	1.53(0.97~2.41)
Household annual income (RMB)			
≥ 10000	1.00	1.00	1.00
< 10000	2.10(1.41~3.14)	1.58(1.09~2.29)	2.79(1.78~4.38)
Household income for expenditure			
Surplus	1.00	1.00	1.00
Inadequate or deficit	1.66(1.08~2.54)	1.81(1.26~2.62)	1.36(0.85~2.16)
Utilization of health services			
Accept eugenic publicity			

No	1.00	1.00	1.00
Yes	1.01(0.67~1.52)	0.82(0.57~1.19)	1.12(0.70~1.77)
Physical examination during the past year			
No	1.00	1.00	1.00
Yes	0.74(0.50~1.09)	0.49(0.34~0.70)	0.25(0.15~0.41)

aOR: adjusted odds ratio; RMB: the official currency of China; *Adjusted for women's age, gravidity, BMI, history of chronic diseases, nutritional supplement, meat intake, eggs intake, fish, milk or intake, vegetable and fruit intake, beans or bean products intake, milk or dairy products intake, picky eating habits, passive smoking and physical exercise.

Table 4 Multivariate logistic analysis of association of vitamin D status with socio-economic status index and health service utilization variables

Vitamin D status	**Insufficiency aOR(95%CI)***	**Deficiency aOR(95%CI)***	**Severe deficiency aOR(95%CI)***
Socio-economic status			
SES index			
High	1.00	1.00	1.00
Middle	1.26(0.80~1.99)	1.23(0.82~1.82)	1.70(1.02~2.84)
Low	2.40(1.52~3.80)	1.64(1.08~2.50)	2.45(1.45~4.14)
Utilization of health services			
Accept eugenic publicity			
No	1.00	1.00	1.00
Yes	0.94(0.64~1.40)	0.77(0.54~1.11)	1.10(0.70~1.72)
Physical examination during the past year			
No	1.00	1.00	1.00
Yes	0.74(0.50~1.09)	0.49(0.35~0.70)	0.24(0.15~0.39)

aOR: adjusted odds ratio; *Adjusted for women's age, gravidity, BMI, history of chronic diseases, nutritional supplement, meat intake, eggs intake, fish, milk or intake, vegetable and fruit intake, beans or bean products intake, milk or dairy products intake, picky eating habits, passive smoking and physical exercise.

Reporting checklist for case-control study.

Based on the STROBE case-control guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE case-controlreporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary	2

		of what was done and what was found	
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	#3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	#4	Present key elements of study design early in the paper	4-6
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls. For matched studies, give matching criteria and the number of controls per case	4-5
Eligibility criteria	#6b	For matched studies, give matching criteria and the number of controls per case	n/a
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one	6-8

		group. Give information separately for cases and controls.	
Bias	#9	Describe any efforts to address potential sources of bias	13
Study size	#10	Explain how the study size was arrived at	4-5
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	6-8
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	8-9
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	n/a
Statistical methods	#12c	Explain how missing data were addressed	n/a
Statistical methods	#12d	If applicable, explain how matching of cases and controls was addressed	n/a
Statistical methods	#12e	Describe any sensitivity analyses	n/a
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for cases and controls.	9
Participants	#13b	Give reasons for non-participation at each stage	n/a

Participants	#13c	Consider use of a flow diagram	n/a
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for cases and controls	9
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	n/a
Outcome data	#15	Report numbers in each exposure category, or summary measures of exposure. Give information separately for cases and controls	9
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-10
Main results	#16b	Report category boundaries when continuous variables were categorized	6-8
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	#18	Summarise key results with reference to study objectives	9-10

Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	13-14
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	10-11
Generalisability	#21	Discuss the generalisability (external validity) of the study results	n/a
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14