

# Vitamin D deficiency and women infertility in Arab Gulf region: review and meta-analysis

Hassan Raji Jalab

Department of Family Medicine and Community Medicine, College of Medicine, University of Al-Qadisiyah

## Abstract

**Background:** The emergence in the last decade of a substantial amount of data about the high prevalence of vitamin D insufficiency globally and in particular in the Middle East justifies taking this problem seriously and planning to solve health problems associated with vitamin D deficiency. Vitamin D is an essential fat-soluble vitamin which shares major aspects in controlling calcium homeostasis and is crucial for muscle and bone wellbeing in all individuals regardless of their age group. For young ladies, vitamin D insufficiency is a crucial health risk element, especially throughout their childbearing period, when insufficiency can affect the health status of both the mother and the unborn baby.

**The aim of the study:** The aim was to highlight the prevalence of vitamin D deficiency in young Arab women and its association with female fertility.

**Materials and Methods:** This review and meta-analysis included 13 studies, 10 cross-sectional and 3 case-control studies. Collection of data for this study was made by searching the web using google search engine for published articles dealing with vitamin D status in young women in countries in the region of Arab Gulf including Iraq, Kuwait, Kingdom of Saudi Arabia, United Arab Emirates, Oman and the State of Qatar.

**Results:** For the 2424 Arab women at childbearing age, the pooled mean serum vitamin D was 28.04 nmol/ L. Only one study which was from Iraq mentioned that mean serum vitamin D in 35 infertile women was 35.38 nmol/ L. the pooled prevalence rate was of vitamin D insufficiency in infertile women was 83.3 %. On the other hand, the total sample for women who are fertile or otherwise not specified was 3233; the prevalence rates of vitamin D insufficiency in 3233 fertile women ranged from 40.8 % to 100 %, and the pooled prevalence rate was 85.7 %.

**Conclusion:** Vitamin D insufficiency is widely prevalent in women at childbearing age in the region of the Arab Gulf, and it seems that it has minimal if ever effect on fertility in that cohort of women.

**Keywords:** vitamin D deficiency; meta-analysis; Arab Gulf

## INTRODUCTION

The emergence in the last decade of the substantial amount of data about the high prevalence of vitamin D insufficiency globally and in particular in the Middle East justifies taking this problem seriously and planning to solve health problems associated with vitamin D deficiency [1-5]. Vitamin D is an essential fat-soluble vitamin which shares major aspects in controlling calcium homeostasis and is crucial for muscle and bone wellbeing in all individuals regardless of their age group [6]. In summary, the sources of vitamin D to human are of two kinds, either exogenous as a natural component of some foodstuff or endogenous synthesis after skin exposure to solar ultraviolet light. One of the best popular and widely used indexes for vitamin D status in the body is its serum concentration, and accordingly, a serum level of less than 30 nmol / L is considered inadequate in the adult population [7]. The number of observational studies that highlighted the correlation between health status of human being and sufficient vitamin D level is huge and cannot be listed in this review; however, one may see examples of these studies [8-10]. A substantial number of reports correlated sufficient vitamin D with prevention of cardiovascular morbidity [11]. Healthy immune status and prevention of a number of malignant tumors have been linked to normal vitamin D status [12]. In addition, it has been shown that diabetes mellitus prognosis may be better when the status of vitamin D deficiency is corrected and that several mechanisms have been proposed to explain these findings such as enhancement of beta cell function and reducing insulin resistance [13-17]. Moreover, several studies linked vitamin D deficiency to dementia and cognitive impairment [18]. Added to that, several reports linked mental health and depression to vitamin D level [19, 20]. For young ladies, vitamin D insufficiency is a crucial health risk element, especially throughout their childbearing period, when insufficiency can affect the health status of both the mother and the unborn baby [21]. In spite of the potentially dangerous consequences of vitamin D deficiency and even insufficiency, very few studies concerning vitamin D have been directed exclusively toward young women; the bulk of literature in

having studied the problem of vitamin D deficiency in the general population [22].

Experimental and observational studies suppose that vitamin D plays a crucial role in the complex physiology of reproduction in females. Main data in this regard have emerged from assisted reproductive techniques since these techniques allow the correlation of various fertility parameters such as the size of the ovum, number of fertilized ova and implantation rate to the state of serum vitamin D [23-25]. One of the studies found that implantation rate, the rate of clinical pregnancy and the rate of live birth were significantly and positively correlated to serum vitamin D concentration in women seeking assisted reproduction techniques [26]. Endometrial receptivity and implantation were also proved to be correlated to sufficient serum vitamin D [27]. It has been shown that women endometrium is able to synthesize vitamin D which act through endometrial receptors through modulation of gene expression or immune response regulation [28]. A number of observational studies have found that fertility in women is linked significantly to the sufficient concentration of vitamin D in their sera. For instance, it has been found that the odds ratio for getting pregnant in females with sufficient serum vitamin D was > 2 when compared to women with insufficient vitamin D [24].

The lack of a review about the prevalence of vitamin D deficiency in young women in the region of Arab Gulf and to highlight the link between infertility and vitamin D status justified the planning and conduction of this study.

## MATERIALS AND METHODS

Collection of data for this study was made by searching the web using Google search engine for published articles dealing with vitamin D status in young women in countries in the region of Arab Gulf including Iraq, Kuwait, Kingdom of Saudi Arabia, United Arab Emirates, Oman and the State of Qatar. Phrases such as vitamin D status, vitamin D insufficiency, vitamin D deficiency, young women, women during childbearing age, the prevalence of vitamin D and fertility in addition to Arab Gulf, names of included countries were used in various combinations.

Inclusion criteria included an observational study dealing with vitamin D status in young women with or in relation to fertility provide3d that these studies were carried out in the Arab Gulf region.

Data were collected and transformed into a Microsoft Excel spreadsheet. Summation, multiplication, and division function already built-in in the Excel software were utilized to measure the pooled prevalence rate of vitamin D insufficiency as well as the mean serum vitamin D level.

**Table1: Studies included in this review and meta-analysis**

Study	Country	Author	Year
1	Iraq	Abdul-Rasheed <i>et al.</i> (29)	2015
2	Iraq	Al-Hilali (30)	2016
3	Iraq	Aboud <i>et al.</i> (31)	2017
4	Kuwait	Azizieh <i>et al.</i> (32)	2017
5	Kuwait	Alsejari (33)	2018
6	Oman	Al-kind (34)	2011
7	Oman	Arya and Agarwal (35)	2011
8	Saudi Arabia	Rafique <i>et al.</i> (36)	2018
9	Saudi Arabia	Al-Musharaf <i>et al.</i> (37)	2018
10	Saudi Arabia	Al-Shaikh <i>et al.</i> (38)	2016
11	Saudi Arabia	Al-Jaroudi <i>et al.</i> (39)	2015
12	State of Qatar	Sharif and Rizk (40)	2011
13	United Arab Emirates	Hussein <i>et al.</i> (41)	2016

**Table 2: Type of the study, sample size, and type**

Study	Study design	Sample size and type
1	case-control study	35 primary infertile and 38 fertile
2	cross-sectional study	60 women of childbearing age
3	case-control study	80 healthy control women
4	cross-sectional study	117 healthy adult women
5	cross-sectional study	144 women
6	cross-sectional study	41 apparently healthy women
7	cross-sectional study	20 pregnant women in delivery
8	cross-sectional study	192 infertile women
9	cross-sectional study	578 pregnant ladies
10	cross-sectional study	1000 pregnant lady at delivery
11	case-control study	83 sub-fertile versus 98 controls
12	cross-sectional study	204 health professional females
13	cross-sectional study	1088 pregnant lady

## RESULTS

This review and meta-analysis included 13 studies that are shown in table 1. As observed in table 1, three studies were from Iraq, two studies were from Kuwait, two studies were from Oman, four studies were from Saudi Arabia, one study was from the state of Qatar, and one study was formed the United Arab Emirates. Study number (1) was a case-control study and included 35 primary infertile women and 38 fertile women; study number (2) was a cross sectional study and included 60 women of childbearing age; study number (3) was a case-control study and included 80 healthy control women in addition to anemic

women with whom we are not concerned; study number (4) was a cross sectional study and included 117 healthy adult women; study number (5) was a cross sectional study and included 144 women, study number (6) was a cross sectional study and included 41 apparently healthy women; study number (7) was a cross sectional study and included 20 pregnant women in delivery; study number (8) was a cross sectional study and included 192 infertile women; study number (9) was a cross sectional study and included 578 pregnant ladies; study number (10) was a cross sectional study and included 1000 pregnant lady at delivery; study number (11) was a case-control study and included 83 infertile fertile women and 98 fertile women; study number (12) was a cross sectional study and included 204 health professional females, and study number (13) was a cross sectional study and included 1088 pregnant ladies, as shown in table 2. We tried to estimate mean serum vitamin D in women participating in all previously mentioned studies; indeed, the number of fertile or otherwise not specified was large enough to get very good impression about the concentration of vitamin D in Arab women at childbearing age since by summation the number of those women was 2424; pooled mean serum vitamin D was 28.04 nmol/ L, as shown in table 3. Unfortunately, we were unable to estimate the pooled mean serum vitamin D in all infertile women included in previous studies because the majority of these studies did not mention the mean vitamin serum level as they were concerned with the prevalence of vitamin D insufficiency rather than its mean serum concentration. Only one study which was from Iraq mentioned that mean serum vitamin D in 35 infertile women was 35.38 nmol/ L, as shown in table 3. Two studies mentioned the prevalence rate of vitamin D insufficiency in infertile women with a total sample of 275; the prevalence rates in the two studies were 93.8 % and 50.9 %, respectively and the pooled prevalence rate was 83.3 %. On the other hand, the total sample for women who are fertile or otherwise not specified was 3233; the prevalence rates of vitamin D insufficiency in those women ranged from 40.8 % to 100 %, and the pooled prevalence rate was 85.7 %, as shown in table 4.

**Table 3: Mean serum vitamin D**

Study	Mean serum vitamin D (nmol/L) Infertile women	Mean serum vitamin D (nmol/L) fertile or nonspecified women
1	35.38	49.99
2		43.2
3		18.86
4		16
5		
6		27.61
7		
8		
9		
10		30.46
11		
12		
13		26.2
<b>Pooled mean</b>	35.38	28.04

Table 4: Prevalence of vitamin D insufficiency

Study	Infertile women			Fertile women and others		
	Total	Vitamin D insufficiency	Normal vitamin D	Total	Vitamin D insufficiency	Normal vitamin D
1						
2				60	39 (65.0 %)	21 (35.0 %)
3						
4						
5				144	103 (71.5 %)	41 (28.5 %)
6				41	41 (100.0 %)	0 (0.0 %)
7				20	15 (75.0 %)	5 (25.0 %)
8	192	180 (93.8 %)	12 (6.2 %)			
9				578	468 (81.0 %)	110 (19.0 %)
10				1000	864 (86.4 %)	136 (13.6 %)
11	83	49 (59.0 %)	34 (41.0 %)	98	40 (40.8 %)	58 (59.2 %)
12				204	200 (98.0 %)	4 (2.0 %)
13				1088	1000 (91.9 %)	88 (8.1 %)
<b>Pooled prevalence rate</b>	275*	229 (83.3 %)	46 (16.7 %)	3233*	85.70%	14.30%

\*: Sum

#### DISCUSSION

The main findings of the present review and meta-analysis were the highly prevalent state of vitamin D insufficiency in women of the childbearing age in countries comprising the Arab Gulf region, namely Iraq, Kuwait, Kingdom of Saudi Arabia, United Arab Emirates, Oman and the State of Qatar. However, mean serum vitamin D seems to play minimal if ever a role in women infertility since the prevalence rates of vitamin D insufficiency in both fertile and infertile cohorts seems to be nearly similar and that the issue that Arab women may be less fertile due to vitamin D insufficiency needs to be revised.

Infertility is seen in around 60-80 million couples all over the world and is still rising [42- 44]. A demographic observation by the World Health Organization (WHO), accomplished in 2002, in developing countries (except China) showed that 186 million females were sub-fertile [45]. The prevalence rate of infertility in developed and developing countries, referring to a systematic review, was between 3.5 to 16.7% and 6.9 to 9.3% respectively [43]. Another research has indicated the prevalence rate of primary infertility in developed and developing countries at 6.6 to 26.4% and 5 to 25.7% respectively [46]. The prevalence rate of primary infertility has been registered in America 10-15%, in China 9 %, in Australia 19% and in Siberia about 16% [47]. From above data, one can conclude that there is no much difference in the prevalence rate of infertility between Arab countries and various regions of the world and that research work should be directed toward other causes of infertility other than vitamin D insufficiency. So, the claim that sociocultural habits in our region are associated with less exposure of women to the sun with subsequent vitamin D insufficiency should be considered with other forms of disorders such as bone, muscle, and cardiovascular disorders.

#### CONCLUSION

In conclusion, Vitamin D insufficiency is widely prevalent in women at childbearing age in the region of Arab Gulf, and it seems that it has minimal if ever effect on fertility in that cohort of women.

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