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Article *in* Nutrition and health (Berkhamsted, Hertfordshire) · October 2018

DOI: 10.1177/0260106018802968

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Prevalence of vitamin D deficiency in Iran: A systematic review and meta-analysis

Salam Vatandost[1], Marzieh Jahani[1], Ali Afshari[1], Mohammad Reza Amiri[2], Rashid Heidarimoghadam[3] and Younes Mohammadi[4,5]

Abstract

Background: The prevalence of vitamin D deficiency in the Iranian community is very high. Women and older people are at the higher risk of vitamin D deficiency. **Aim:** This study aimed to estimate the prevalence of vitamin D deficiency in Iran by combining the results of various studies. **Methods:** This was a systematic review and meta-analysis. Separate strategies were developed for search in national databases (Irandoc, Magiran, SID) and international databases (Web of Science, PubMed, and Scopus) using the keywords of "vitamin D deficiency," "Iran," and "prevalence." The titles and abstracts of the articles were screened and related full texts were appraised. Those articles that met inclusion criteria were selected for meta-analysis. The heterogeneity of the articles was assessed via the Chi-square test. They were combined using the random-effect approach. In addition, the groups were categorized and analyzed in terms of age and gender. **Results:** Of 639 articles, 30 articles with a sample size of 26,042 people were included for data analysis. The overall prevalence of vitamin D deficiency was reported as 0.56. Subgroup analysis showed that 0.64 of women and 0.44 of men were suffering from vitamin D deficiency. The prevalence of vitamin D deficiency in the age groups under 20, 20–50, and over 50 years was 0.56.4, 0.72.4, and 0.59.8, respectively. **Conclusions:** The Iranian Ministry of Health is expected to design strategies to improve the status of vitamin D at the national level.

Keywords

Prevalence, vitamin D, Iran, meta-analysis, vitamin D deficiency

Introduction

Vitamin D is a secosteroid hormone that helps maintain bone health through absorbing calcium and phosphorus from the intestine and suppressing the release of parathyroid hormone (Holick, 2005). There are two natural forms of vitamin D, these being ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3). Vitamin D2 is available in limited amounts from plant sources and in some supplements, whereas vitamin D3 is found in dietary sources such as fish oil, calf liver, cheese, and egg yolk (Hajiabbasi et al., 2015; Holick, 2005). However, the major source of vitamin D3, contributing 90% of vitamin D intake, is obtained via a photosynthetic reaction in the dermis of the skin that occurs when sufficient exposure to ultraviolet B (UVB) radiation is achieved. Both vitamin D2 and D3 undergo hydroxylation in the liver catalyzed by 25-hydroxylase to form 25-hydroxyvitamin D (25(OH)D) and further hydroxylation in the kidneys or target tissues expressing the enzyme 1-α-hydroxylase to form the biologically active form of vitamin D, 1,25-dihydroxyvitamin D3 (Alshahrani and Aljohani, 2013; Chen et al., 2007; Hajiabbasi et al., 2015). When assessing vitamin D status, however, it is the product of the first hydroxylation step, vitamin D that is the measurement of choice because hepatic 25-hydroxylase is regulated only by vitamin D concentration and no other stimuli such as parathyroid hormone (PTH), which stimulates renal production of 1α-vitamin D when vitamin D concentrations are low.

[1] Student Research Committee, Hamadan University of Medical Sciences, Iran
[2] Department of Library and Information Science, Hamadan University of Medical Sciences, Iran
[3] Research Center for Health Sciences, Hamadan University of Medical Sciences, Iran
[4] Modeling of Noncommunicable Diseases Research Center, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran
[5] Department of Epidemiology, Hamadan University of Medical Sciences, Iran

Corresponding author:
Younes Mohammadi, Modeling of Noncommunicable Diseases Research Center, School of Public Health, Hamadan University of Medical Sciences, Fahmide St., Hamadan 6517838736, Iran.
Email: u.mohammadi@umsha.ac.ir

Table 1. Keywords and search strategies in this study.

Databases	Search strategy
Web of Science	• (TS= ("Vitamin D3 Deficiency") AND TS= (IRAN) AND TS= (prevalence)) OR (TI= ("Vitamin D3 Deficiency") AND TI= (IRAN) AND TI= (prevalence)) • (TS= (Vitamin D3) AND TS= (IRAN) AND TS= (prevalence)) OR (TI= (Vitamin D3) AND TI= (IRAN) AND TI= (prevalence))
PubMed	• ("Vitamin D3 Deficiency"[Mesh]) AND "Iran"[Mesh] AND prevalence [mesh] • ("Vitamin D3 Deficiency"[Mesh]) AND "Iran"[Mesh] • ("Vitamin D3 Deficiency/epidemiology"[Mesh]) AND "Iran"[Mesh] • ("Vitamin D3 Deficiency"[Mesh] AND "Iran"[Mesh] AND prevalence [mesh]) OR ("Vitamin D3 Deficiency" [tiab] AND Iran [tiab] AND prevalence [tiab])
Scopus	• (INDEXTERMS("Vitamin D3 Deficiency") AND INDEXTERMS(IRAN) AND INDEXTERMS(prevalence)) OR (TITLE-ABS-KEY("Vitamin D3 Deficiency") AND TITLE-ABS-KEY(IRAN) AND TITLE-ABS-KEY(prevalence))
Persian (SID, Irandoc, Magiran)	• Vitamin D3 deficiency, Iran, prevalence, vitamin D3 (in advance search with Farsi keywords)

Furthermore, concentration and half-life of vitamin D is higher than PTH (Kumar and Thompson, 2011).

Levels of 25(OH)D less than 20 ng/mL or less than 50 nmol/L have been recognized as vitamin D deficiency (Holick et al., 2011). In addition to inadequate natural sources of vitamin D, liver failure, nephrotic syndrome, chronic kidney disease, lifestyle diseases such as rickets, and hyperparathyroidism are also some main causes of vitamin D deficiency (Anderson et al., 2010). Vitamin D deficiency can impair bone mineralization, and result in rickets in children, bone softness, osteoporosis, and pathologic fractures in adults and lead to many morbidities (Cantorna et al., 2004). In addition, recent studies have reported a relationship between vitamin D deficiency and cardiovascular diseases (Ghergherechi et al., 2012), immune system diseases (Bischoff-Ferrari et al., 2006; Cantorna et al., 2004), colorectal cancers (Gorham et al., 2005), and type 2 diabetes (Pittas et al., 2014). It is believed that until the occurrence of severe signs such as bone fractures, vitamin D deficiency shows no specific symptoms (Powers et al., 2012, Michael and Holick, 2007). Bone fractures have negative effects on the quality of life and even increase the financial costs and mortality rate (Haq et al., 2016).

Vitamin D deficiency is a common and serious problem. Various studies showed that around one billion people worldwide are suffering from vitamin D deficiency (Fallahi et al., 2016; Michael, 2005; Uriu-Adams et al., 2013). For instance, 40–100% of European and American older men and women in the community and more than 50% of postmenopausal women with osteoporosis had insufficient amounts of this vitamin (Pearson, 2008; Sullivan et al., 2005).

In Iran, vitamin D deficiency is considerd a major health concern. Many studies indicated the high prevalence of vitamin deficiency in the Iranian population (Ghanei et al., 2015; Mirbolouk et al., 2016; Talaei et al., 2011). However, there is no comprehensive and reliable information on the prevalence of vitamin D deficiency in Iran. The limitations of previous studies include differences in geographic domain, age and gender, sampling techninques, sample size, definition of vitamin D deficiency, study design and seasonal differences. Accordingly, the prevalence of vitamin D deificiency in Iran has been reported to range from 0.16 to 0.85 (Kelishadi et al., 2016; Rahnavard et al., 2010; Saiedi et al., 2013).

Given the significant role of vitamin D in health and complications caused by vitamin D deficiency, there is a need to collect data about the current status of the vitamin D deficiency in Iran. Therefore, the present study aimed to estimate the prevalence of vitamin D deficiency in Iran by combining the results of various studies in a systematic review.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was used for conducting this study. The keywords "vitamin D deficiency," "Iran," and "prevalence" were used to search both national and international databases (Table 1).

Search strategies

Both international databases, such as Web of Science, PubMed, and Scopus, and national databases, such as SID, Magiran, and Irandoc, were searched using appropriate search strategies (Table 1). Furthermore, as a manual search, the backtracking of references of selected articles was performed.

Selection process

In this study, the PICO (population/intervention/comparison/outcome) approach, with a focus on P and O due to the descriptive nature of the study, was used. The criteria of article selection were as follows:

- study setting in Iran (P);
- considering a level of less than 20 ng/dL (50 nmol/L) as vitamin D deficiency;
- reporting the point prevalence of vitamin D deficiency in the results of the study (O);

- accessibility of the full text of the article;
- sample size more than 100 cases.

After searching the keywords in the mentioned databases, selected studies were imported to the Endnote reference management software and duplicates were deleted. The title and abstracts of the remaining articles were studied by two researchers separately and those studies that did not meet the mentioned criteria were excluded. Then, full text of the potentially relevant papers were retrieved and read for data extraction, quality assessment, and meta-analysis. In the cases of disagreements between the two researchers on an article, discussions were made to reach agreement. Lack of access to the full text articles led to their exclusion from the study.

Data extraction

An electronic data collection form was designed and developed for data extraction. It included questions about the name of the first author, age, gender, province, prevalence, and sample size.

Risk of Bias

The Newcastle–Ottawa Quality Assessment Scale (adapted for cross-sectional studies) was used to assess the risk of bias in the included studies (Wells et al., 2017). The checklist has three sections (selection, Comparability and outcome) with the related questions.

Summary measures

Prevalence rate with 95% confidence interval was considered as summary measure of interest.

Data synthesis

We synthesized the data from these studies using a statistical approach called meta-analysis. A prevalence rate as summary measures, and sub-group analysis by age and gender, were performed. Heterogeneity was assessed using the Chi-square test.

Results

The process of the study selection is presented in Figure 1. During the initial search, 639 articles were retrieved. Next, 321 articles were deleted as they were duplicates; 208 more articles were excluded after reading titles and abstracts. The full texts of 113 articles were read and 80 articles were deleted as they were irrelevant to the goals of the study. In addition, one article was deleted due to a lack of access to its full text. Finally, 30 articles were chosen for data analysis. The characteristics of these studies are presented in Table 2.

The total sample size was 26,042. The age range of the studies participants was from 7 to over 80 years. Moreover, the studies were conducted in 30 out of 31 provinces and geographic regions of Iran, indicating that the studies properly represented the overall status of Iran. Vitamin D status was most commonly reported in Tehran, the capital of Iran, compared with all other provinces (eight of 30 studies). Hence it had the largest share in the current study.

The point prevalence of vitamin D deficiency was reported as 0.57. The lowest prevalence was reported as 0.16 in a study by Shakeri et al. (2014) in Khorasan province and the highest prevalence was reported as 0.85 in a study by Kaykhaei et al. (2011) in Sistan and Baluchistan province (Figure 2).

The result of quality assessment is presented in Table 2. The majority of studies obtained the high score (over 8) and three studies obtained a score less than 8.

Furthermore, a sub-group analysis by age and gender was performed. To determine the prevalence of vitamin D deficiency in individuals with an age less than 20 years old, the results of seven studies with a sample size of 3360 people indicated a prevalence of 0.56 (Figure 3).

In individuals aged 20–50 years old, three studies with a sample size of 3693 showed the prevalence of vitamin D deficiency as 0.72 (Figure 4).

To determine the prevalence of vitamin D deficiency in individuals aged over 50 years old, the results of five studies with a sample size of 5179 showed a prevalence of 0.60. Therefore, vitamin D deficiency was more prevalent in this age group than the age group under 20 years (Figure 5).

A gender-based analysis was performed on 13 studies that reported the number of male participants with a sample size of 6135. The prevalence of the vitamin D deficiency in men was reported as 0.44 (Figure 6).

The gender-based analysis showed that the prevalence of vitamin D deficiency in Iranian women was reported as 0.64 (Figures 6 and 7). The result of the heterogeneity test was statistically significant and moderate ($I^2 = 57\%$, $p < 0.05$). Therefore, it indicates inconsistency in the prevalence of vitamin deficiency.

Discussion

More than half of the Iranian population was reported to suffer from vitamin D deficiency. Therefore, vitamin D deficiency in Iran is a major health concern. The lowest and the highest prevalence rates were reported in Tehran province (0.27) and Sistan and Baluchistan province(0.85), respectively (Azizi et al., 2000; Kaykhaei et al., 2011). Given the prevalence of vitamin D deficiency between age groups, the highest prevalence of vitamin D deficiency was reported in the age group 20–50 years (0.72). Moreover, vitamin D deficiency in women was more common than that in men. The Iranian studies revealed the major factors affecting vitamin D deficiency in Iran. Dressing habits, especially in women, play an important role in the prevalence of vitamin D deficiency in the Middle East. In these countries, women's clothing prevents sun exposure (Haq et al., 2016, Rafraf et al., 2014). Lack of a diet rich in vitamin D, including fish and foods enriched by this vitamin due to economic issues, and the high use of cosmetics

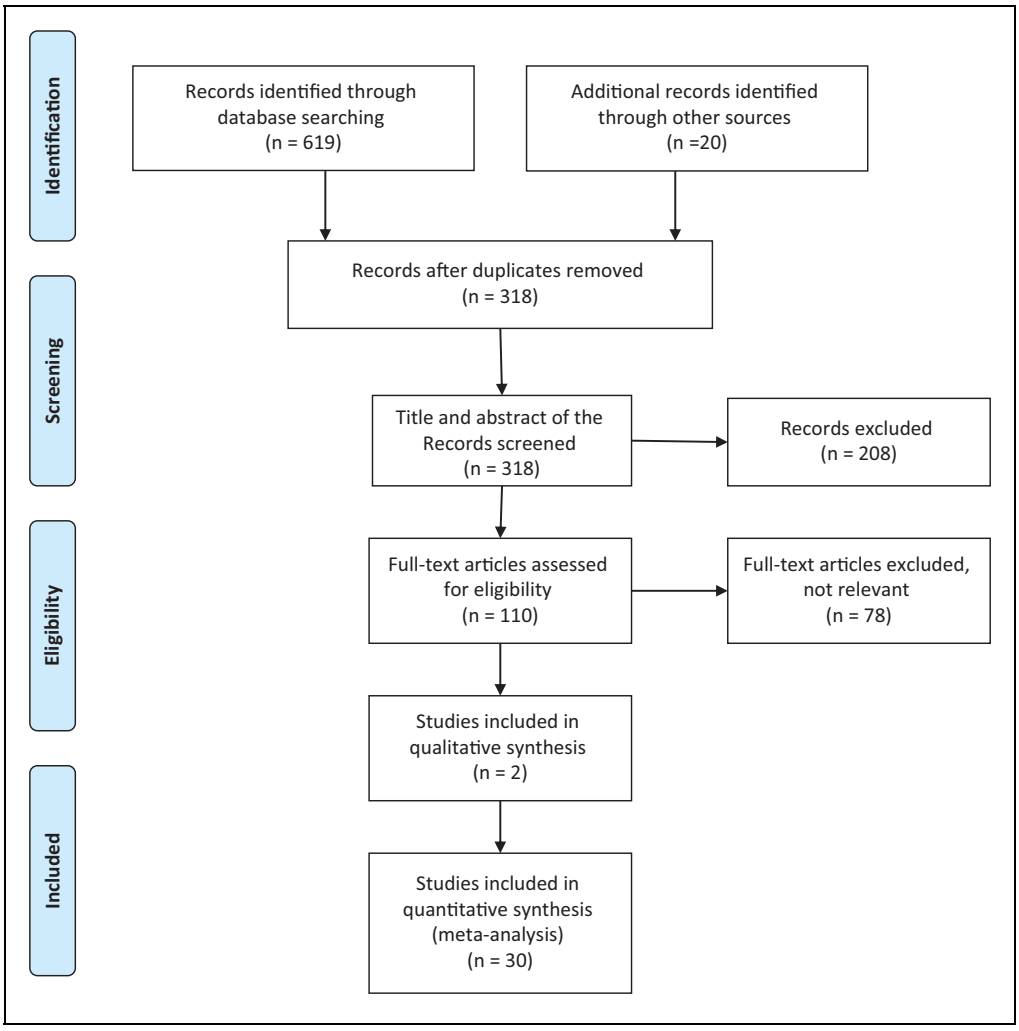

Figure 1. Flow diagram of the different phases of the systematic review.

and sunscreens in Iran are other important factors (Delavari et al., 2009). Moreover, per capita consumption of foods (such as milk, fish, and egg) that provide vitamin D in Iranian population is very low (Delavari et al., 2009).

This study indicated that the prevalence of vitamin D deficiency in Iran was higher than the global level. According to some international studies, such as that by Hilger et al. (2014), the global vitamin D deficiency was reported as 0.37. Comparing the results of our study with those of similar studies indicated that the prevalence of vitamin D deficiency in Iran was about 1.5 times higher than that of the global estimated rate. However, several differences are present between this study and that of the Hilger et al. (2014). For instance, the number of studies included for data analysis was less than our study. In addition, although they did not determine the specific threshold for the definition of vitamin D deficiency, the mean 25(OH)D levels of the participants were less than 20 ng/dL (50 nmol/L). The other difference was the study design, as Hilger et al. (2014) included cohort studies, but we included purely cross-sectional studies.

The study of Haq et al. (2016) was conducted on 136 countries, indicating that the prevalence of vitamin D deficiency was about 0.60, which was close to the results of the present study. However, the regional analysis of this study showed that the prevalence of vitamin D deficiency was 0.66 in the United Arab Emirates (UAE), but the prevalence rate in other countries was reported as 0.53 (Al-Daghri, 2018). vitamin D deficiency was more prevalent in countries in the Middle East than in Europe and America (Al-Alyani et al., 2018; Sullivan et al., 2005). However, the participants of Sullivan et al.'s study were the patients from Abu Dhabi, UAE. Therefore, the results cannot be generalized to the general population. Generally, the reasons for diversity in the prevalence of vitamin D deficiency in the studies arise from differences in the definition of vitamin D deficiency, differences in assays, population (such as age, gender), study design and seasonal variation in levels of 25(OH)D (Haq et al., 2016).

The results indicated that, in the same age groups, there is no significant difference in the prevalence of vitamin D deficiency between Iranian provinces. However, six

Table 2. The characteristics and quality assessment of individual studies with an overall prevalence of vitamin D3 deficiency in meta-analysis.

Author	Journal	Province	Sample size	Event rate	Lower	Upper	Score of the quality: out of 10
Alipour et al. (2014)	Iranian Red Crescent Medical Journal	Tehran	538	0.78	0.74	0.81	10
Rabbani et al. (2008)	Journal of Tropical Pediatrics	Tehran	963	0.35	0.32	0.38	9
Rahnavard et al. (2010)	Iranian Journal of Public Health	Tehran, Tabriz, Mashhad, Shiraz, and Booshehr	2396	0.69	0.68	0.70	9
Mirbolouk et al. (2016)	Nutrition	Rasht	179	0.69	0.62	0.75	9
Shakiba et al. (2009)	Acta Medica Iranica	Yazd	167	0.60	0.52	0.68	9
Heshmat et al. (2008)	Iranian Journal of Public Health	Tehran, Tabriz, Mashhad, Shiraz, and Booshehr	5369	0.45	0.43	0.46	9
Pirdehghan et al. (2016)	Journal of Reproduction and Infertility	Yazd	200	0.78	0.72	0.83	8
Heidari and Mirghassemi (2012)	Caspian Journal of Internal Medicine	Mazandaran	696	0.70	0.65	0.73	9
Rajebi et al. (2016)	Acta Medica Iranica	Tehran	136	0.63	0.54	0.71	8
Saki et al. (2015)	Public Health Nutrition	Fars	477	0.68	0.64	0.72	9
Kazemi et al. (2009)	Journal of Women's Health	Zanjan	68	0.69	0.61	0.77	9
Maghbooli et al. (2007)	BMC Pregnancy and Childbirth	Tehran	522	0.80	0.78	0.77	10
Neyestani et al. (2012)	Public Health Nutrition	Tehran	503	0.64	0.61	0.67	8
Hashemipour et al. (2004)	BMC Public Health	Tehran	1210	0.80	0.78	0.82	7
Ghanei et al. (2015)	Journal of Qazvin University of Medical Sciences	Qazvin	124	0.81	0.73	0.87	8
Rahimi et al. (2005)	Tabriz University of Medical Sciences (Farsi)	Tabriz	252	0.31	0.26	0.37	8
Salek et al. (2007)	Journal of Isfahan Medical School (Farsi)	Esfahan	513	0.40	0.33	0.47	8
Azizi et al. (2000)	Research in Research (Farsi)	Tehran	1172	0.27	0.25	0.30	8
Heydarpour et al. (2006)	Mazandaran University of Medical Sciences	Isfahan	318	0.46	0.41	0.51	8
Talaei et al. (2011)	Indian Journal of Endocrinology and Metabolism	Arak	420	0.84	0.80	0.87	8
Moradzade et al. (2005)	Kurdistan University of Medical Sciences	Tehran, Tabriz, Mashhad, Shiraz, and Booshehr	5329	0.46	0.44	0.48	9
Nikooyeh et al. (2016)	Nutrition Sciences & Food Technology	(West Azerbaijan, Semnan, Lorestan, South Khorasan, Khozestan, and Fars	667	0.47	0.43	0.51	9
Razaghi et al. (2011)	Salmand	Tabriz	140	0.47	0.41	0.53	7
Kaykhaei et al. (2011)	Annals of Nutrition and Metabolism	Zahedan	993	0.85	0.83	0.87	8
Moussavi et al. (2005)	Hormone Research in Paediatrics	Isfahan	318	0.46	0.41	0.51	9
Hovsepian et al. (2011)	Journal of Health, Population and Nutrition	Isfahan	1111	0.28	0.25	0.31	9
Larijani et al. (2016)	Journal of Diabetes & Metabolic Disorders	Tehran	444	0.43	0.39	0.48	7

(continued)

Table 2. (continued)

Author	Journal	Province	Sample size	Event rate	Lower	Upper	Score of the quality: out of 10
Faghih et al. (2014)	International Journal of Preventive Medicine	Shiraz	254	0.23	0.18	0.29	8
Hasannia (2015)	International journal for vitamin and nutrition research	Iran	202	0.62	0.57	0.67	9
Shakeri et al. (2014)	Journal of Pediatric Endocrinology and Metabolism	Khorasan	362	0.16	0.13	0.20	9
Meta-analysis				0.57	0.50	0.63	

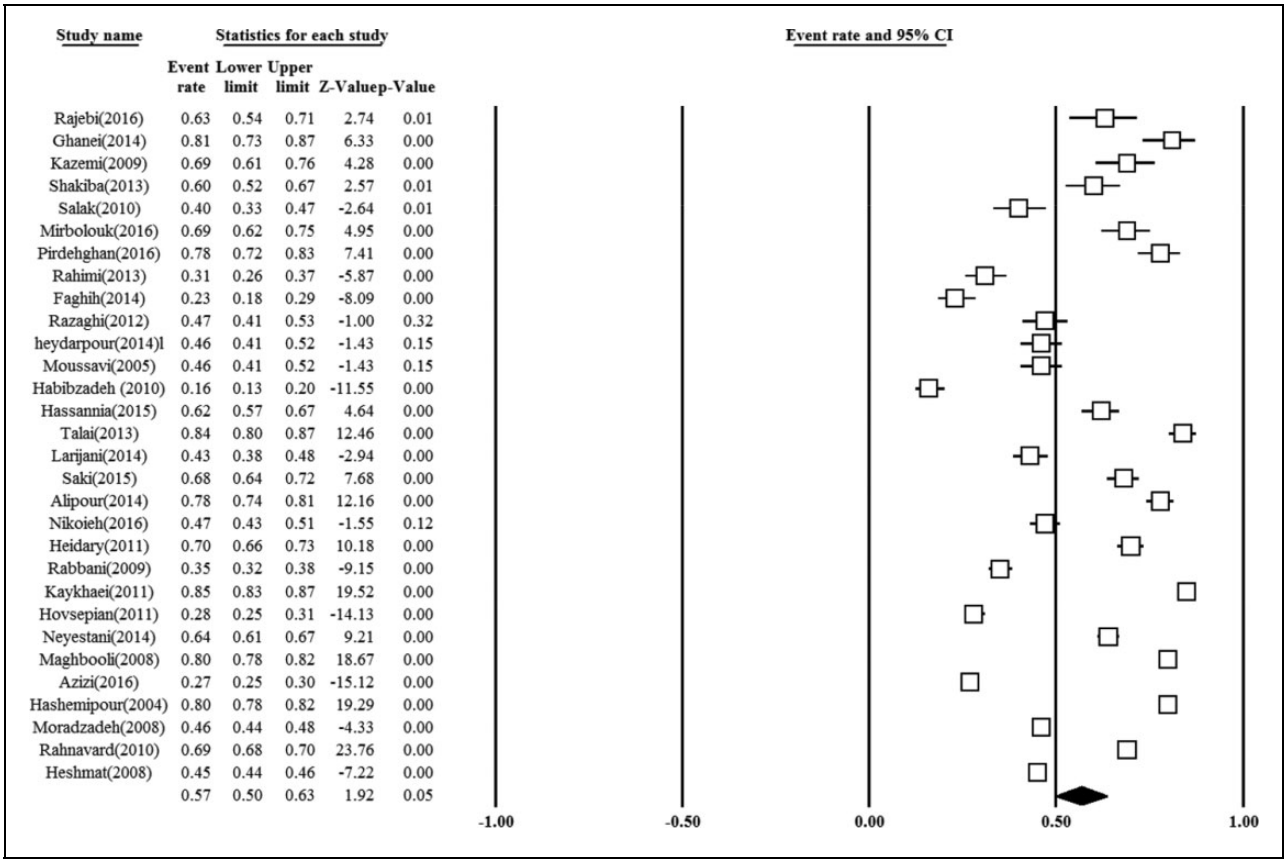

Figure 2. Forest plot for overall prevalence of vitamin D deficiency in Iran.

provinces out of 31 Iranian provinces had prevalence over 0.70 (eight studies). These provinces differ in terms of geographic areas, intensity of sunlight, use of sunscreens, and type of cultural and religious codes of dressing (Mirbolouk et al., 2016). Moreover, the National Profile of Non-Communicable Disease Risk Factors, which reported by the Iranian Ministry of Health and Medical Education, indicated that consuming food sources contain of vitamin D such as milk and cheese, vegetables, egg yolks, orange juice, and fatty fish in Iranian women and the youngest and oldest age group was low (Delavari et al., 2009).

Similar to previous studies, the prevalence of vitamin D deficiency in women was higher than that in men (Asma et al., 2010; Haq et al., 2016; Mithal et al., 2009). However, Hilger et al. (2014) reported no differences in vitamin D deficiency between men and women. Disagreement between Hilger et al.'s study and our study arises from study and methodological differences, and difference in term of study population, number of the searched databases and definition of vitamin deficiency.

The results of the study by Haq et al. (2016) in 136 countries showed that, despite the lack of a difference in the

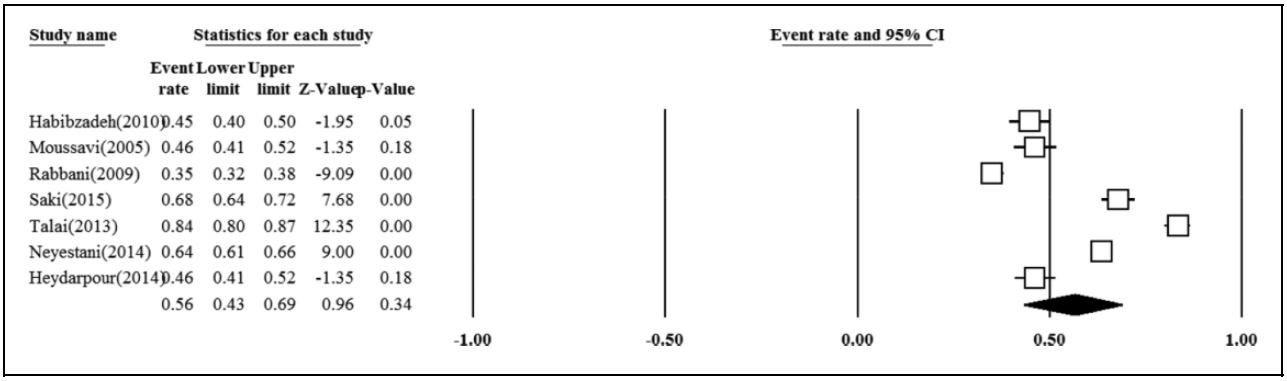

Figure 3. Forest plot for prevalence of vitamin D deficiency in those aged less than 20 years in Iran.

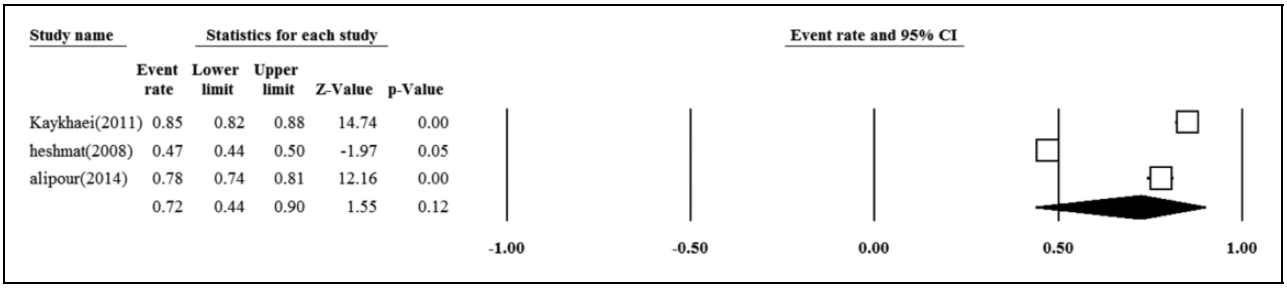

Figure 4. Forest plot for prevalence of vitamin D deficiency at 20–50 years old in Iran.

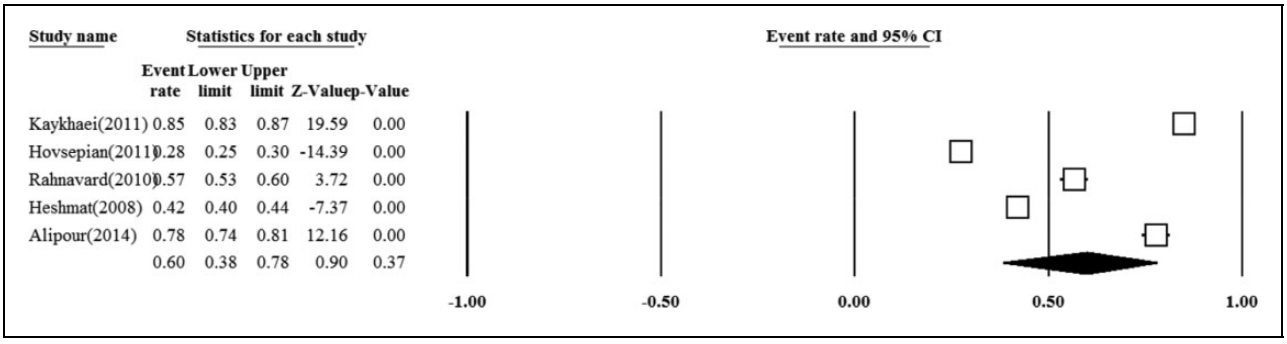

Figure 5. Forest plot for prevalence of vitamin D deficiency at over 50 years old in Iran.

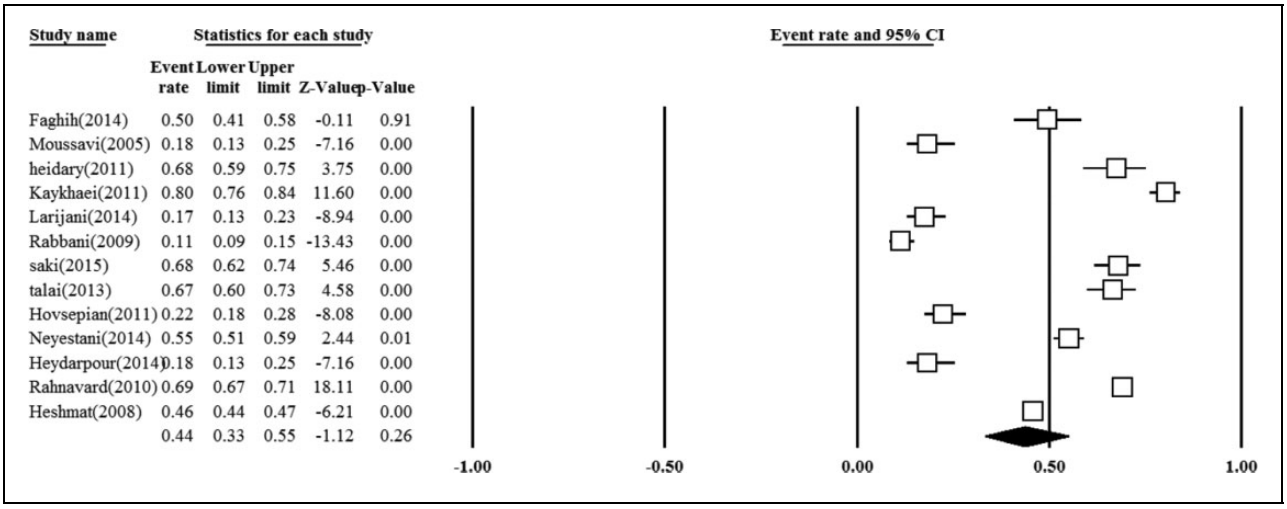

Figure 6. Forest plot for prevalence of vitamin D deficiency in Iranian males.

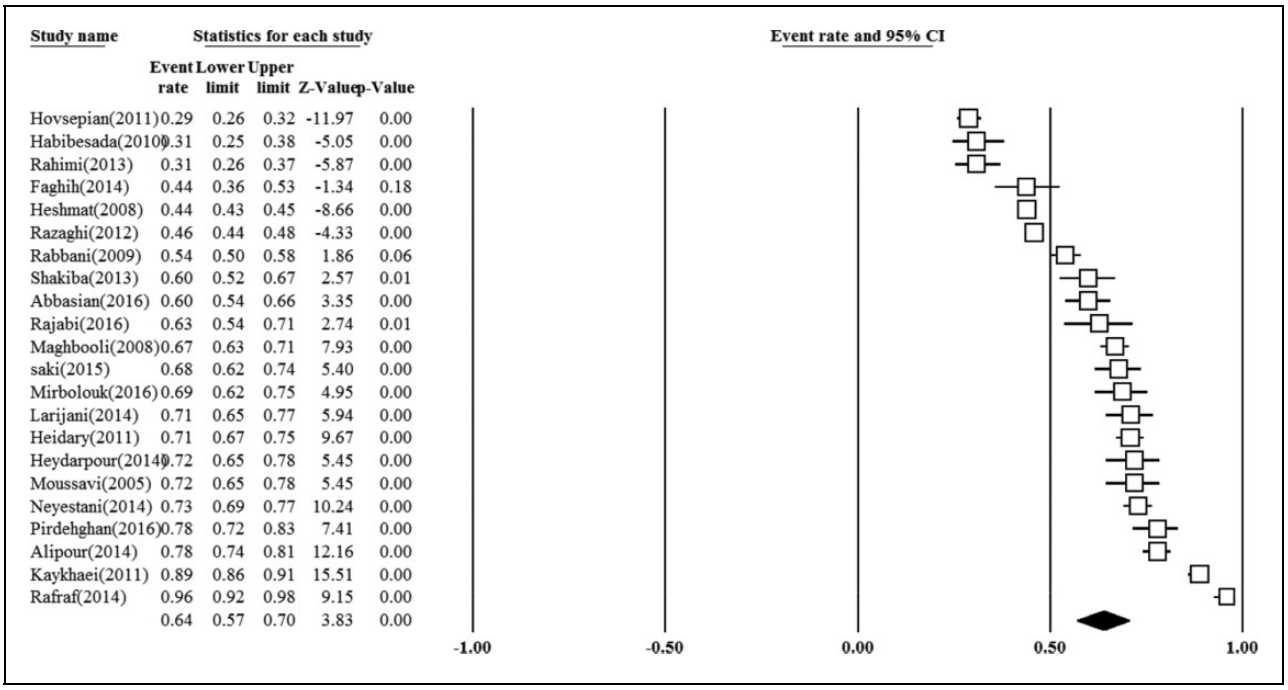

Figure 7. Forest plot for prevalence of vitamin D deficiency in Iranian females.

overall prevalence of vitamin D deficiency among the two genders, the results of regional analysis indicated that the prevalence rates of vitamin D deficiency in Saudi Arabia and the UAE were significantly higher in women than in men (Haq et al., 2016). As a whole, the Islamic codes of dressing for women as it prevents direct exposure of skin to sunlight is an important factor affecting the prevalence of vitamin D deficiency in Muslim countries. According to some articles, the prevalence of vitamin D deficiency in women is 0.78 and even higher (Shakiba et al., 2009). Women are usually more inclined to use sunscreens more frequently and they usually work at home or in an office, which reduces their chance to be exposed to sunlight. These are some other probable reasons for the findings of this study (Shakiba et al., 2009, Mirbolouk et al., 2016).

Vitamin D deficiency in children and adolescents is a common problem all over the world (Ganji et al., 2012; González-Gross et al., 2012). Similarly, our study showed that it had also a high prevalence (0.56) in Iran. Adolescents spend a lot of time watching television and playing computer games (Saki et al., 2015). Therefore, they might be exposed to sunlight for a shorter period of time and might suffer from obesity, which were some factors leading to vitamin D deficiency (Ghergherechi et al., 2012; Valtuena et al., 2013).

Previous studies reported higher prevalence of vitamin D deficiency in children and older people as compared with young people (Hagenau et al., 2009; Hilger et al., 2014). However, results of current study showed that the individuals in the age group 20–50 years old were more likely to suffer from vitamin D deficiency. However, a small number of articles (only three articles) presented data in this age group. Therefore, the results of this study cannot be generalized to this age group in Iran.

A limitation of this study is that the prevalence of vitamin deficiency was reported and not the mean level of vitamin D. Also, those articles without access to their full text were excluded. The results cannot be generalized to other countries, but we believe that they more likely may be applied to Middle East countries, especially Islamic countries. Furthermore, the papers without information on prevalence rate were excluded.

Given the number of articles, number of studied provinces, and the overall sample size, the results of this study can be generalized to the Iranian population. This study indicated that a vitamin D deficiency in the Iranian population is a major health concern. Since vitamin D deficiency is positively associated with bone health (Lips, 2007), cardiovascular diseases (Bischoff-Ferrari et al., 2006), autoimmune diseases (Cantorna et al., 2004), some cancers (Bischoff-Ferrari et al., 2006), diabetes (Pittas et al., 2014), and other diseases, more research is needed to identify related risk factors and taking measures to reduce the prevalence of vitamin D deficiency.

Conclusion

Prevalence of vitamin D deficiency in the Iranian population is very high. Women and older people are at higher risk of vitamin deficiency. Identification and elimination of risk factors to deal with this health concern is crucial. Therefore, the Iranian Ministry of Health must design strategies to improve the vitamin D status of Iranians at the national level.

Acknowledgements

This article was one part of a research project approved by Hamadan University of Medical Sciences (with No. 9603231775). The authors would like to express their gratitude to the student research committee of the university, which financially sponsored this research project.

Ethical Statement

The study has been approved by the Ethics Committee of Hamadan University of Medical Sciences.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/ or publication of this article: This work was supported by the Vice-Chancellor for Research and Technology affiliated with Hamadan University of Medical Sciences, Iran.

ORCID iD

Younes Mohammadi http://orcid.org/0000-0001-7521-4909

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