A meta-analysis of the relationship between vitamin D deficiency and obesity

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Abstract: Previous epidemiologic studies suggested that vitamin D deficiency may be a risk factor of obesity. However, the result is still controversial. This meta-analysis aims to provide a comprehensive summary on the association between vitamin D deficiency and obesity. We systematically searched Pubmed database, Chinese Wanfang Data Knowledge Service Platform, and Chinese National Knowledge Infrastructure (CNKI), for the literatures on the relationship between vitamin D deficiency and obesity published from 2010 to 2015. The effect sizes of overall odds ratio (OR) and 95% confidence interval (CI) were estimated using Stata 11.0. Heterogeneity was evaluated using random-effects model and forest plots. Fifteen studies were eligible for inclusion in the meta-analysis, which included 3867 subjects with obesity and 9342 health subjects. Meta-analysis results showed that the prevalence of vitamin D deficiency was difference between obesity group and control group, and the pooled OR (95% CI) was 3.43 (2.33-5.06). The prevalence of vitamin D deficiency was associated with obesity in Asians and European-American, OR (95% CI) were 3.70 (1.98-6.90) and 3.09 (1.89-5.04), respectively. No publication bias was found in our study. Vitamin D deficiency may be associated with obesity, irrespective of areas.

Keywords: Vitamin D, obesity, meta-analysis

Introduction

In recent decades, the prevalence of obesity risen steeply worldwide, which has become a major global health problem [1]. Obesity is associated with the development of cardiovascular diseases, hypertension, diabetes mellitus and various cancers, which leads to higher morbidity and mortality rates, reduce the quality of life and cause social discrimination [2, 3]. Obesity is also a complex chronic metabolic disease, which defined by an excessive accumulation of body fat resulting from an imbalance between energy intake and expenditure [4]. In addition, genetic [5], environmental factors [6] and eating behavior [7] play important roles in the development of obesity. There are some studies suggesting that the level of serum 25-hydroxy vitamin D is associated with obesity.

Vitamin D is a lip soluble molecule obtained through exposure to sunlight and intake of foods containing this nutrient naturally. Moreover, vitamin D is responsible for the development and maintenance of bone tissue, as well as for calcium and phosphate homeostasis via coordinate effects on the kidney [8]. Vitamin D must be hydroxylated on carbon 25, forming 25-hydroxyvitamin D [25(OH) D] in the liver, and then on carbon 1, forming 1, 25-dihydroxyvitamin D [1, 25(OH) 2D] in the kidney [9]. Therefore, Serum 25(OH) D level is the most widely accepted biomarker to estimate short-term vitamin D status [10]. The Institute of Medicine (IOM) proposed that serum 25(OH) D levels above 20 ng/mL (>50 nmol/L) are adequate. However, the Endocrinology Society considers that serum 25(OH) D levels over 30 ng/mL (≥75 nmol/L) are optimal [11]. Vitamin D deficiency and insufficiency is high prevalent worldwide, which is a public health concern around the world.

Several studies have shown that vitamin D deficiency is common in children and is associated with increasing age and obesity [12], and low
vitamin D levels increase the risk of obesity in women [13]. However, the impact of vitamin D deficiency on obesity susceptibility is still under debate [14]. Thus, to further investigate the potential role of vitamin D in obesity, we performed the meta-analysis to provide a basis for intervention to obesity.

Materials and methods

Literature retrieval

We requested a literature search for the relation of vitamin D deficiency and obesity, which examined in epidemiologic studies published between 2010 and 2015. An electronic search was undertaken using the Pubmed database, Chinese Wanfang Data Knowledge Service Platform, and Chinese National Knowledge Infrastructure (CNKI). The following medical subject headings (Mesh) were used: (“obesity” OR “body mass index”) AND (“vitamin D” OR “25(OH) D”) in Chinese for Chinese database and in English for Pubmed. All references of the articles selected were also searched manually to identify relevant citations.

Inclusion criteria

The included criteria for the literature were consisted of: a) the paper was published in recent 5 years; b) human subjects; c) adequate data for extracting or calculating; this information may be presented as odds or rate ratios. Exclusion criteria: a) the indicators described in the article were with fewer association or data being incomplete; b) duplicate publication of articles.

Literature screening and quality assessment in process

Two investigators independently reviewed the titles and abstracts of all articles selected in order to assess whether the studies were eligible for inclusion in the meta-analysis, and the consensus were resolved by expert assessment. The following information were recorded for each study: author, year of publication, country, type of study, age and number of participants, method of vitamin D measurement, numbers of obesity and control group with deficient vitamin D status.

Statistical analysis

Meta-analysis was performed using Stata version 11.0. The association between vitamin D deficiency and obesity was evaluated by odds ratio (OR) and 95% confidence interval (CI), heterogeneity test was performed; the random-effect model was applied if heterogeneity exist. publication bias was estimated using funnel plot graphics, Begg's and Egger's test.

Results

Characteristics of the eligible studies

Fifteen studies were eligible for inclusion in the meta-analysis, which included 3867 subjects with obesity and 9342 healthy subjects. Figure 1 shows flow diagram for screening studies. The main characteristics of the studies included in this review are presented in Table 1.

Meta-analysis

Heterogeneity was found in our study ($X^2=4.51$, $P=0.000$, $I^2=81.2\%$). Thus, the random-effects model was used for meta-analysis, and the results showed a pooled OR (95% CI) for the association between vitamin D deficiency and obesity was 3.43 (2.33-5.06), as is shown by the forest plots (Figure 2). The prevalence of vitamin D deficiency was associated with
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<table>
<thead>
<tr>
<th>First author</th>
<th>Year</th>
<th>Country</th>
<th>Design</th>
<th>Age range mean (DP)</th>
<th>n</th>
<th>Method for assessing serum 25(OH) D</th>
<th>Vitamin D deficiency (nmol/l)</th>
<th>Obesity</th>
<th>VitD (+)</th>
<th>N</th>
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<th>N</th>
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<tr>
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<td>Immunoassay</td>
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<td>348</td>
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<td>86</td>
<td>Enzyme immunoassay</td>
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<td>44</td>
<td>50</td>
<td>11</td>
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<td>Ling Feng [23]</td>
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<td>4–14</td>
<td>183</td>
<td>ELISA</td>
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<td>52</td>
<td>78</td>
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<td>64</td>
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<td>39</td>
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<td>Yulian Xiao [29]</td>
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<td>Mexico</td>
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<td>6–12</td>
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<td>27</td>
<td>99</td>
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ELISA, enzyme-linked immunosorbent assay; RIA, radioimmunoassay; HPLC, high performance liquid chromatography; CLIA, chemiluminescent immunoassay.
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Figure 2. Forest plot for association between vitamin D deficiency and obesity.

Figure 3. Forest plot for association between vitamin D deficiency and obesity in Asians.
Relationship between vitamin D deficiency and obesity

**Discussion**

Obesity is caused by combined effect of many factors. Although the diet, gene or other life styles are thought to play an important role in the development of obesity, the role of vitamin can’t be ignored. It is a subject of controversy whether the vitamin D deficiency is a consequence of or a factor predisposing to obesity. Therefore, to further investigate if vitamin D deficiency is associated with changes in BMI, we conducted a meta-analysis from different populations. The results of present meta-analysis were based on 15 articles, which indicated that the prevalence of vitamin D deficiency was associated with obesity and the pooled

**Publication bias**

Begg’s and Egger’s test was used to evaluate publication bias with the funnel plot. A little publication bias was identified according to the

funnel plot (Figure 5) and Egger’s test (P=0.031). We performed a sensitivity analysis by excluding this study from our analysis, and the pooled estimate of OR did not change drastically (Figure 6).

Figure 4. Forest plot for association between vitamin D deficiency and obesity in European-American.

Figure 5. Funnel plot for association between vitamin D deficiency and obesity.

obesity in Asians and European-American, OR (95% CI) were 3.70 (1.98-6.90) and 3.09 (1.89-5.04), respectively (Figures 3, 4).
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OR (95% CI was 3.43 (2.33-5.06). The results from meta-analysis indicated that obese subjects in different subgroups have higher prevalence of vitamin D deficiency.

However, the mechanisms that link excess body weight and vitamin D are not fully elucidated. The possible explanation maybe that certain vitamin D receptor (VDR) polymorphisms are associated with obesity, expression of human VDR in mature mice adiposities lead to expression of VDR in preadipocyte cell lines, thereby inhibited adiposity differentiation and increased adipose mass [15]. Alternatively, some experimental data have suggested that vitamin D deficiency can cause greater adiposity by promoting parathyroid hormone levels and overflow of calcium into adipocytes, thereby increasing lipogenesis [16]. On the other hand, leptin plays a very important role in the occurrence and development of obesity, and vitamin D is an essential factor of generating this leptin, which can cause obstacles of leptin synthesis. Thus, depletion of vitamin D can increase appetite and lead to obesity [17]. Additionally, outdoor activity, food intake and exercise levels can influence 25(OH) D levels [18].

A recent meta-analysis study reported the vitamin D deficiency was associated with obesity irrespective of age, latitude, cut-offs to define vitamin D deficiency and the Human Development Index of the study location [19]. However, Saneei P [20] et al. included 34 studies in the meta-analysis, and their results support a significant inverse weak correlation between serum 25(OH) D levels and BMI in adult population. Our study showed that there are now consistent evidences of an association between the vitamin D deficiency and high risk of obesity incidence, irrespective of areas. These results suggest taking some proper measures to control obesity.

Limitations
Nonetheless, the current study had some limitations. We had limited data on physical activity and sedentary lifestyles, and these may be indirect measures of sunshine exposure. Finally, it must be kept in mind that several confounding factors have not been taken into account in this meta-analysis.

Conclusion
In conclusion, our results indicate positive association between vitamin D deficiency and obesity was found. The concept of maintaining an increased vitamin D status for decreasing adiposity also warrants further evaluation.

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Disclosure of conflict of interest
None.
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