



Original/Síndrome metabólico

# Correlation of serum vitamin D level with type 1 diabetes mellitus in children: a meta-analysis

Changwei Liu<sup>1</sup>, Mi Lu<sup>2</sup>, Xiaona Xia<sup>1</sup>, Jingwen Wang<sup>1</sup>, Yuanyuan Wan<sup>1</sup>, Lianping He<sup>3</sup> and Mei Li<sup>1</sup>

<sup>1</sup>Nanjing Children's Hospital Affiliated to Nanjing Medical University (Nanjing), Jiangsu. <sup>2</sup>School of Medical Imaging and laboratory, Wannan Medical College (Wuhu), Anhui. <sup>3</sup>School of Public Health, Wannan Medical College (Wuhu), Anhui. China.

## Abstract

**Objective:** to assess the relationship between serum vitamin D level and type 1 diabetes mellitus (T1DM) in children.

**Methods:** the following electronic databases were searched until Sep 2014 to identify relevant studies that assessed the relationship between serum vitamin D with T1DM: PubMed\EMbase\Medline\Central Register of Controlled Trials\CBM\Chinese National Knowledge Infrastructure (CNKI)\wangfang; The NOS scale was used to evaluate the quality of studies, and the statistical tests were performed by Stata 11.0 software.

**Result:** a total of 10 studies were included in this study. Our results showed that serum vitamin D was significantly lower in children with T1DM than in healthy controls (MD = -0.60,  $P < 0.05$ ). No evidence support publication bias in present study.

**Conclusion:** the meta-analysis suggests that serum vitamin D level is associated with T1DM in children.

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Key words: Serum vitamin D. T1DM. Meta-analysis.

## CORRELACIÓN DE LOS NIVELES DE VITAMINA D EN SUERO Y LA DIABETES MELLITUS TIPO 1: UN METAANÁLISIS

### Resumen

**Objetivo:** evaluar la relación entre sueros de vitamina D y la diabetes mellitus tipo 1 (T1DM) en niños.

**Métodos:** fueron utilizadas las siguientes bases de datos electrónicas hasta septiembre de 2014 para identificar los estudios que evaluaron la relación entre la vitamina D y la T1DM: PubMed, EMBASE, MEDLINE, Central Register of Controlled Trials, CBM, China National Knowledge Infrastructure (CNKI), wangfang; las enfermedades a la escala se utilizan para evaluar la calidad de los estudios, y los ensayos estadísticos fueron realizados mediante el software Stata 11.0.

**Resultado:** fueron incluidos un total de 10 estudios. Nuestros resultados mostraron que los niveles séricos de vitamina D fueron significativamente menores en los niños con T1DM que en los controles sanos (MD = -0,60,  $P < 0,05$ ). No hay evidencia de sesgo de publicación en el presente estudio.

**Conclusión:** el metaanálisis sugiere que la vitamina D está asociada con la T1DM en niños.

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Palabras clave: Serum de vitamina D. T1DM. Metaanálisis.

### Introduction

Diabetes mellitus is a group of metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both<sup>1</sup>. The most common classifications include type 1 diabetes mellitus, type 2 diabetes mellitus, and gestational diabetes<sup>2</sup>. Of those, autoimmune destruction of the  $\beta$ -cells of the pancreas which lead to absolute insulin deficiency was defined as type 1 diabetes mellitus (T1DM)<sup>3</sup>. In Finland, the incidence of T1DM among children has an increasing trend with age and is highest among 14 years or under in the world<sup>4</sup>. The National Pediatric Diabetes Audit reported that 26 867 children and the

**Correspondence:** Mei Li.  
Nanjing Children's Hospital Affiliated to Nanjing Medical University.  
Nanjing (Jiangsu), 210008, China.  
E-mail: limeilimei6868@126.com

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youth (aged 0-25 years) suffered from diabetes, and most (95%) of them were T1DM<sup>5</sup>. Diabetic ketoacidosis (DKA) is an acute potentially life-threatening complication of diabetes, which remains the leading cause of hospitalization, morbidity and death in children with T1DM. Therefore, taking into account the incidence rate and fatality rate of T1DM and DKA among children, it is essential to prevent the complication of diabetes.

Vitamin D is a group of fat-soluble secosteroids and the synthesis of vitamin D begins in the skin, where cholesterol is exposed to ultraviolet B photons<sup>6</sup>. In addition, it can also be obtained from foods or supplements<sup>7</sup>. More and more studies found that the vitamin D not only associates with the level of calcium, phosphorus, but also with the blood glucose metabolism and insulin resistance. Relevant studies had shown an association between low ultraviolet B irradiance and high incidence rates of T1DM in children<sup>8</sup>. In recent years, several studies reported a high prevalence of vitamin D deficiency in patients with T1DM, which suggested that vitamin D deficiency correlated with the severity and frequency of T1DM<sup>9</sup>. However, subsequent studies reported inconsistent results<sup>10</sup>. Thus, the aim of our meta-analysis was to examine the association between serum vitamin D and T1DM in children, then provide a comprehensive reference to prevent T1DM in children.

## Materials and Methods

### Literature search

To identify relevant studies that regarding of the association between serum vitamin D level and T1DM, we searched literatures with the English and Chinese language restriction using terms “vitamin D”, “25(OH) D”, “T1DM” and “childhood” in database of PubMed, EMbase, MEDLINE, CENTRAL, CBM, Chinese National Knowledge Infrastructure (CNKI) and Wangfang until September 2014. Eligible full texts were retrieved from the above data.

### Inclusion and exclusion criteria

Included criteria: (1) The study was case-control study; (2) The papers published on the relationship between serum vitamin D level and T1DM in children; (3) all T1DM subjects met the criteria of diagnosis. Excluded criteria: (1) Did not meet the inclusion criteria; (2) The paper was a review; (3) The data was not extracted.

### Data extraction

According to the inclusion and exclusion criteria, we screened the literature, extracted the data and evaluated the literature quality independently. Data ex-

tracted includes basic information, research design, diagnostic methods, the possible bias, and the features of the objects, results and outcomes.

### Quality Assessment

All studies included and their biases were independently assessed by two reviewers using Newcastle-Ottawa Scale (NOS). The NOS contains eight items, categorized into three dimensions including the selection, the comparability and the outcome or exposure of interest<sup>11</sup>. A ‘star system’ was used to judge data quality: The scores ranged from 0 to 9 stars. Studies with scores of 7 stars or greater were considered to be of high quality<sup>12</sup>. The scores were added up to compare the study quality in a semi-quantitative fashion. Studies with scores of 5 stars or greater can be included in our meta-analysis. Disagreements between the reviewers were resolved by open discussion.

### Statistical analysis

All statistical tests were performed using Stata11.0 software. We choose appropriate indexes according to the data types. Q test was performed in count data. If heterogeneity was existing among studies ( $I^2 \geq 50\%$ ), a random-effects model was applied to estimate the relationship between serums vitamin D level and T1DM; otherwise, a fixed effects model was applied. In addition, we also calculated the value of mean difference (MD) and 95% confidence interval (CI).

## Results

### Results of literature research

A total of 69 relevant publications were systematically identified through the previous listed database. Of them, 59 articles were excluded because they either did not meet the inclusion criteria or failed to provide adequate information to determine. Finally, 10 literatures were included in the meta-analysis which assesses the relationship between serum vitamin D and T1DM<sup>13-22</sup>. Characteristics of the selected studies are presented in table I. Quality of literature to assess the stability by deleting the studies with scores of 6 stars, the samples less than 50 cases and some studies in which the serum vitamin D levels are too low or too high. There was no significantly statistical change after remerging the results.

### The correlation of serum vitamin D with T1DM

A total of 10 literatures were included and heterogeneity testing was carried out in our meta-analysis, due

**Table I**  
General character of studies included

first author	year	n	T1DM	control	NOS score
Bruna Franchi	2014	224	58	166	8
Somia H. Abd-Allah	2014	240	120	120	8
Seham FA Azab	2013	120	80	40	7
Lingfei Wang	2013	95	52	43	6
Ristan M Greer	2012	102	56	46	8
Xiaoyan Huang	2012	50	26	24	6
Yan Zhu	2011	152	52	100	6
Jill H Simmons	2011	57	27	30	7
Bassam S. Bin-Abbas	2011	200	100	100	7
Abdulbari Bener	2008	340	170	170	8
Abdulbari Bener	2008	1580	741	839	8

to  $I^2$  value was 80.1%, a random-effects model was applied for meta-analysis. The serum vitamin D level in T1DM was lower than in the control (Fig. 1). MD (95%CI) = -0.60(-0.70,-0.49),  $z=5.51$ ,  $P<0.05$ .

#### Publication bias

Funnel plots and Egger's test were used to test possible bias among literatures, which showed a better symmetry (Egger's test:  $t=-1.82$ ,  $P=0.107$ ), suggesting a low likelihood of publication bias.

#### Discussion

The etiology and natural history of T1DM are still unknown, but both genetics and environmental factors certainly contribute to the development of T1DM<sup>23</sup>. It is confirmed that immune factors play a decisive role in onset of T1DM<sup>24</sup>. T1DM is a T cell-mediated disease that ultimately destroys the capacity of the body to produce and secrete insulin<sup>25</sup> and was characterized by the apoptotic destruction of pancreatic  $\beta$ -cell<sup>26</sup>.

Vitamin D is a fat-soluble secosteroids and plays a central role in the metabolism of calcium and phosphorus. Vitamin D deficiency is a risk factor for type 1 diabetes. Previous studies showed that 1, 25-(OH) 2D3 influences insulin secretion in the pancreatic beta-cell. Indeed, 1,25 D3 prevent human pancreatic islet cells from destruction<sup>27</sup>. evidence based on observational studies revealed that vitamin D supplementation in infancy might be protective against the development of type 1 diabetes<sup>28</sup>. Compared with the normal group, this study showed a significantly statistical difference in serum vitamin D level between a child with T1DM and without, which suggested that children with T1DM have a vitamin D deficiency.

This present research indicates that serum vitamin D is significantly lower in children with T1DM than in healthy. Because only some case-control studies were included in this research, causal association was not sure. In addition, Age, illumination, BMI, dieting and physical activity are important determinants of the level of serum vitamin D. Thus, the relationship between serum vitamin D levels in children with T1DM should be further studied. Moreover, there is heterogeneity between the studies included. The possible reason may be that studies are from different area, diagnostic crite-

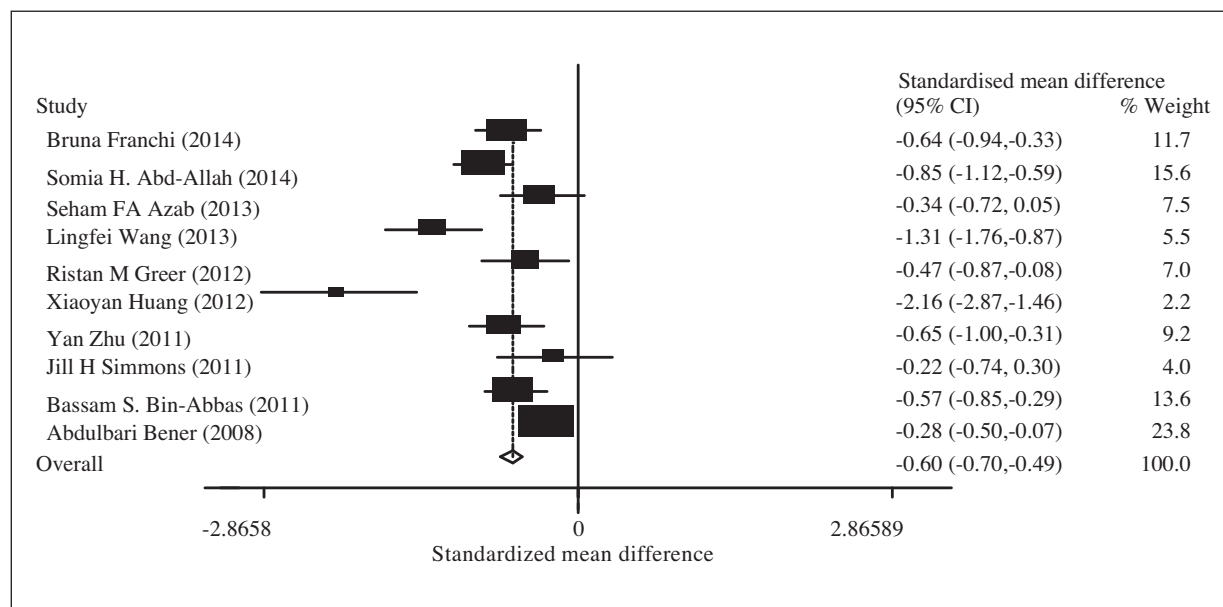


Fig. 1.—forest plot of the correlation of serum vitamin D with T1DM in children.

ria, and sample size. Sensitivity analysis was conducted to assess the stability. There was no significant statistical change in conclusion after deleting relevant factors.

## Conclusion

The meta-analysis suggests that serum vitamin D is associated with T1DM in children. And provide a comprehensive reference to prevent T1DM in children.

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## Conflict of interest

None declared.

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