Meta-Analysis of Zinc Deficiency and Its Influence Factors in Children Under 14-year-old in China

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Abstract

Background: In recent years, zinc deficiency in children has attracted global attention. There are some differences in zinc deficiency in different countries and regions. However, there are few multi-center and large-sample studies on zinc deficiency in children in mainland China.

Objective: To evaluate the status of zinc deficiency and its influence factors in children under 14-year-old in mainland China, and to provide evidence-based evidence for the strategy of prevention and treatment of zinc deficiency in children.

Methods: PubMed, Embase, CNKI and other databases were searched about the cross-sectional survey literature on zinc deficiency and its influencing factors of under 14-year-old children in mainland China from 2005 to 2021. Stata 14.0 statistical software was used for Meta-analysis. Two independent reviewers identified eligible studies.

Results: We identified 55 studies with 292,877 healthy children and adolescents in the Meta-analysis. The overall zinc deficiency rate was 27.0% (95% CI 22.8%-31.3%). From coastal areas of China showed that the zinc deficiency rate was 21.7% (95% CI 16.2%-27.1%) as 29.6% (95% CI 24.9%-34.4%) from inland area of China. The zinc deficiency rate in the male group was greater than that in the female group, and the difference was statistically significant [OR=1.052, 95% CI (1.019, 1.087), p=0.002]. The zinc deficiency rate in infant group was higher than that in toddler group [OR=1.38, 95% CI (1.16, 1.64), p=0.000], preschool group [OR=1.475, 95% CI (1.163, 1.870), p=0.001], and school-age group [OR=1.746, 95% CI (1.257, 2.426), p=0.001], with statistical significance. There was no significant difference in zinc deficiency rate between the toddler group and the preschool group [OR=1.059, 95% CI (0.918, 1.222), p=0.429], the toddler group and the school-age group [OR=1.136, 95% CI (0.848, 1.523), p=0.394], and the preschool group and the school-age group [OR=0.986, 95% CI (0.754, 1.291), p=0.919]. There was no statistically significant difference in zinc deficiency rate between the groups of well-educated and the poor-educated dietary provider. (OR=1.095, 95% CI (0.867, 1.383), p=0.446), and no statistical significance in zinc deficiency rate between urban group and rural group [OR=1.192, 95% CI (0.810, 1.637), p=0.432].

Conclusions: At present, zinc deficiency in children and adolescents in mainland China is still serious, especially in infants. The zinc deficiency rate in male children was more serious than that of female children. The zinc deficiency rate of children in inland areas was higher than that in coastal areas. Factors such as different educational level of food providers and different areas from urban or rural were not the major influencing factors of zinc deficiency.

Keywords: Zinc; Zinc deficiency; Factors; Children; Meta-Analysis

Background

Zinc is an essential micronutrient distributed throughout the body, which is involved in a variety of metabolic processes in the body. Zinc deficiency will affect a variety of body functions, including growth and development, immune function, reproductive function and neurobehavioral development, which will bring serious harm to the health of the body. In 1963, Prasad et al. [1] reported on cases of adolescent hypogonadism and dwarfism caused by zinc deficiency [2]. Thus, uncovering the important impact of zinc deficiency on human health for the first time. In 1974, Moynahan [3] described that Acrodermatitis Enteropathica (AE) is associated with severe zinc deficiency, which is an autosomal recessive genetic disease related to zinc metabolism defects, further confirming zinc Importance to human health. It is reported that approximately 116,000 child death in 2011 was related to zinc deficiency, mainly due to the prevalence and severity of infectious diseases such as diarrhea [4]. Walker et al. [5] showed that the prevalence of zinc deficiency is more serious in three regions of the world (Africa, Asia and Latin America). There are different in the status of zinc deficiency in different countries. At
present, there are few multi-center studies on zinc deficiency in China. The main purpose of this study is to conduct systematic reviews and meta-analysis by collecting relevant studies to explore the overall zinc deficiency status of children aged 0-14 years in mainland China in the past 15 years and some related influencing factors, in order to provide evidence-based basis and data support for the comprehensive prevention and treatment of zinc deficiency in children in China. The research results are reported as follows.

**Methods**

**Literature and search strategy**

Search Chinese and English databases such as PubMed, Embase, Cochrane Library, Web of Science, China Biomedical Literature Database (CBM) and other Chinese and English databases until February 8, 2021. Search terms are "Zinc", "Zinc deficiency", "Zinc status", "Micronutrient deficiencies", "Micronutrient status", "Micronutrient deficiency", "China/Chinese", and "Child/Children". The search is based on a combination of subject terms and free words. And incorporate unpublished documents including dissertations, conference reports and other unpublished documents through manual retrieval and literature retrospective methods. The search is carried out independently by two reviewers, and when there is a disagreement, through consultation or a third reviewer joins in the analysis and discussion and reaches a consensus.

**Inclusion and exclusion criteria**

**Inclusion criteria:** 1) The subjects of the study were healthy children and adolescents aged 0-14 years in mainland China; 2) The outcome of the study is the plasma (serum) zinc level, and the testing equipment is not limited; 3) The types of studies include published and unrestricted A publicly published cross-sectional study on zinc levels and zinc deficiency in children; 4) The study languages are limited to Chinese and English.

**Exclusion criteria:** 1) The subject is in the period of acute infection and inflammation, such as fever, acute diarrhea and other diseases; 2) The outcome indicator of the study is not plasma (or serum) zinc, such as hair zinc, nail zinc and other detection methods; 3) The research sample size is less than 1000 cases, and the research time is earlier than 2005; 4) The literature for which the research data cannot be extracted; 5) The literature of systematic reviews or reviews, case reports, etc.

**Data extraction and quality evaluation**

Data extraction was conducted after literature screening, including the first author, publication year, research area, research sample size, zinc level and zinc deficiency rate, and related influencing factors. According to the cross-sectional study quality evaluation checklist recommended by the Agency for Healthcare Research Quality (AHRQ) [6], two researchers independently evaluated the quality of the final included studies. When there is a disagreement, discuss with the third researcher and reach an agreement. The evaluation list includes 11 items. For each item, the answer is "yes", "no" or "do not know". The total score is 11 points, of which the answer to "yes" is 1 point, and the answer to "no" or "do not know" The score is 0. The higher the total score, the better the quality of the research. 0 to 3 are classified as low-quality studies, 4 to 7 are classified as medium-quality studies, and 8 to 11 are classified as high-quality studies.

**Statistical analysis**

Stata14.0 software (version 11) was used for statistical analysis. Q test and I2 value were used to quantitatively evaluate the heterogeneity among the included studies. If there is no significant heterogeneity among the included studies or the heterogeneity is small (P≥0.10 and/or I2 value ≤50%), the fixed effects model is used for Meta-analysis; if the heterogeneity is large [P<0.10 and (or) I2 value >50%), then use subgroup analysis, Meta regression or one-by-one elimination of sensitivity analysis to further analyze the source of heterogeneity. If there is still heterogeneity after treatment, then use random effects model for Meta-analysis, the analysis result is P<0.05 indicating that the difference is statistically significant. The outcome indicators of zinc deficiency rate were expressed by odds ratio (OR value) and its 95% confidence intervals (CI); the funnel chart method was used and the Egger test was used to quantitatively identify publication bias.

**Results**

**Literature search results**

Preliminary search was used to obtain 5835 documents, Endnote document management software was used to eliminate duplicate documents, and 278 documents were obtained by browsing document titles and abstracts to enter the full-text reading screening, and finally 55 documents [7-61] were included in the Meta-analysis and evaluation of this article. The sample size was 292,877 cases. The literature screening process is shown in Figure 1, and the basic information of the included literature is shown in Table 1.

**Literature quality evaluation results**

Literature quality evaluation results showed that the 55 included literatures were scored 3-9 points according to the AHRQ cross-sectional study evaluation scale. Among them, 3 literatures scored more than 7 points, which were high-quality literature, and 37 literatures scored 4-7 points. They are medium-quality documents, 15 documents are scored 3 points, and they are low-quality documents.

**Meta-analysis results**

In this study, the overall zinc deficiency rate of children aged 0-14, the rate of zinc deficiency in different genders, different age groups, and the influencing factors of zinc deficiency were analyzed by Meta-
The results of the analysis of the overall zinc deficiency rate in children: A heterogeneity test was carried out on 55 included literatures, and the results showed that $I^2=99.9\%$, $p=0.000$, there is obvious heterogeneity. The sensitivity analysis method was eliminated one by one, and it was found that the heterogeneity did not change significantly, so the random effects model was used for the meta-analysis. Meta-analysis results show that the zinc deficiency rate of children in mainland China is 27.0% (95% CI: 22.8% to 31.3%) (Figure 2).

According to the different regions of the study, different detection equipment of serum zinc and the quality of the research literature, the subgroup analysis was carried out, and the results were found to be significantly heterogeneous. The random effects model was used to merge the effect size (Table 2).

### Table 1: Characteristics of studies included in the meta-analysis.

| Information of the Research | Number of Studies | Sample Size | Research Serial Number |
|-----------------------------|-------------------|-------------|------------------------|
| Publication time (2006~2020) | -                 | -           | -                      |
| Research age group (0~14Y)   | -                 | -           | -                      |
| Research areas (43 cities and towns in mainland China) | -                 | -           | -                      |
| Male                         | -                 | 47162       | -                      |
| Female                       | -                 | 36790       | -                      |
| Education level of food providers group | -                 | 7406       | (7,42,53,61)       |
| Well-educated                | -                 | 4112        | -                      |
| Poor-educated                | -                 | 3294        | -                      |
| Research area group          | -                 | 10497       | (7,32,36,42,50) |
| Urban                        | -                 | 6875        | -                      |
| Rural                        | -                 | 3622        | -                      |

According to the different regions of the study, different detection equipment of serum zinc and the quality of the research literature, the subgroup analysis was carried out, and the results were found to be significantly heterogeneous. The random effects model was used to merge the effect size (Table 2).
Subgroup analysis according to different testing instruments: There were 35 studies with a total of 164,768 cases using Beijing Bohui (BH) series type number testing equipment, 6 studies with a total of 16,274 cases using Beijing Puxi (MB-5) type testing equipment, and 14 studies with a total of 111,835 cases using other brand testing equipment for children undergoing serum zinc examination. The results of meta-analysis indicated that the zinc deficiency rates of the three subgroups were: 28.4% of children in the BH group, and children in the MB-5 group. The rate was 22.1%, and the zinc deficiency rate of children in other groups was 25.7%; further meta-regression analysis showed that the BH group t=0.44, p=0.658, other groups t=-0.14, p=0.890, the difference was not statistically significant, indicating that the current research data is not enough to prove that factors of different detection instrument are the source of heterogeneity in this meta-analysis.

Subgroup analysis according to the quality of different research literature: There are 3 research documents with high AHRQ score included totaling 6890 cases, 37 research documents with medium scores included totaling 222,018 cases, and 15 research documents with low scores included totaling 63,969 cases. The meta-analysis results show that the zinc deficiency rates of children in the three subgroups are as follows: The zinc deficiency rate of children in the high scores group was 34.3%, the rate of zinc deficiency in children in the middle scores group was 28.1%, and the rate of zinc deficiency in children in the low scores group was 22.9%; further meta-regression analysis showed that the medium scores group t=-0.92, p=0.363, the low scores group t=-0.49, p=0.623, the difference was not statistically significant, suggesting the current research quality factors are not a source of heterogeneity in this meta-analysis.

Comparison of zinc deficiency rates among children of different genders: There are 21 literatures reported on the zinc deficiency rates in the male and female groups. A total of 83,952 children were included, of which 47,162 were in the male group and 36,790 were in the female group. Meta-analysis was performed. The results are as following (Figure 3).

The result of heterogeneity test showed that p=0.078, I^2=32.2%, there is a certain degree of heterogeneity, using fixed-effects model analysis, Meta-analysis results show that the male group zinc deficiency rate is higher than the female group, the difference is statistically significant [OR=1.052, 95% CI (1.019, 1.087), p=0.002]. Using one-by-one elimination sensitivity analysis, in which Zhao Feng [28] and Wang Lian-bing [61] were eliminated, the results of the heterogeneity test decreased (P value and I^2 were: 0.188/22.0%; 0.210/20.1%, respectively). After excluding two studies of Zhao Feng [28] and Wang Lian-bing [61] at the same time, it was found that the heterogeneity decreased significantly (p=0.543, I^2=0). Consider these two studies as the main source of heterogeneity, but through intensive reading literature analysis still cannot confirm the exact reasons for the heterogeneity.

Comparison of zinc deficiency rates among children of different age groups: This study is divided into infant group (0~1 years old), toddler group (1~3 years old), preschool group (3~7 years old), and school-age children and adolescent group (7~14 years old) according to different ages. Meta-analysis of zinc deficiency rates in age groups (Table 3).

Note: The comparison of zinc levels uses Standardized Mean

| Table 2: Subgroup analysis of zinc deficiency rates in Chinese children. |
|---|
| Subgroup Factors | Number of Research Documents | Sample Size | Heterogeneity Test Results | Meta-analysis Results | Effect Model |
|---|
| Area | | | I (%) | P | Zinc Deficiency Rate (%) | 95%CI | Regression (P) |
| Coastal | 18 | 137,641 | 99.8 | 0.000 | 21.7 | 0.162-0.271 | 0.023 | Random |
| Inland | 37 | 119,022 | 99.9 | 0.000 | 29.6 | 0.249-0.344 | - | Random |
| Instrument | *BH | 35 | 164,768 | 99.9 | 0.000 | 28.4 | 0.234-0.334 | 0.658 | Random |
| MB-5 | 6 | 16,274 | 98.2 | 0.000 | 22.1 | 0.226-0.336 | - | Random |
| *Other | 14 | 111,835 | 99.9 | 0.000 | 25.7 | 0.179-0.335 | 0.89 | Random |
| Research quality score | High | 3 | 6890 | 99.8 | 0.000 | 34.3 | 0.083-0.603 | - | Random |
| Middle | 37 | 222,018 | 99.9 | 0.000 | 28.1 | 0.226-0.336 | 0.363 | Random |
| Low | 15 | 63,969 | 99.7 | 0.000 | 22.9 | 0.171-0.287 | 0.623 | Random |

Note: BH: Include BH2100, BH5100, BH5100plus, BH5300, BH5500, BH5800, BH7100, BH7100s; Others: Include Au5800, ICP-MS, QL8000, AA7001M, AA-7010, ICPQ-1012, PES100, WL-3.

Figure 4: Meta-analysis of zinc deficiency rate in Chinese children forest plot.
Table 3: Meta-analysis for different age groups.

| Comparison of Zinc Deficiency Rates in different Age Groups | Number of Research Documents | Sample Size | Heterogeneity Test Results | Meta-analysis Results | Effect Model |
|-------------------------------------------------------------|-----------------------------|-------------|--------------------------|----------------------|-------------|
| Infants group vs. Toddler group                             | 31                          | 37137/72923 | I²=95.6%, OR=0.999, 95% CI (0.959, 1.040), p=0.311 | Random               |             |
| Infants group vs. Preschool group                           | 30                          | 35411/42795 | I²=95.6%, OR=1.000, 95% CI (0.982, 1.018), p=0.983 | Random               |             |
| Infants group vs. School-age children and adolescents group | 21                          | 28348/42102 | I²=95.6%, OR=1.000, 95% CI (0.959, 1.040), p=0.311 | Random               |             |
| Toddler group vs. Preschool group                           | 33                          | 77581/48741 | I²=95.6%, OR=1.000, 95% CI (0.982, 1.018), p=0.311 | Random               |             |
| Toddler group vs. School-age children and adolescents group | 19                          | 54420/40923 | I²=95.6%, OR=1.000, 95% CI (0.982, 1.018), p=0.311 | Random               |             |
| Preschool group vs. School-age children and adolescents group| 23                          | 38946/45624 | I²=95.6%, OR=1.000, 95% CI (0.982, 1.018), p=0.311 | Random               |             |

Figure 5: Labbe plot of Heterogeneity Evaluation of Different Educational Levels of Dietary Providers.

Comparison of zinc deficiency rates between infant group and toddler group: There are 31 literatures reporting the values of zinc deficiency rates in infant group and infants. Meta-analysis was performed. The results are as follows: Heterogeneity test p=0.000, I²=95.6%, there is a significant heterogeneity, using random-effects model analysis, Meta-analysis showed that the zinc deficiency rate in the infant group was higher than that in the toddler group, and the difference was statistically significant (OR=1.321, 95% CI (0.922, 1.894), p=0.093). The sensitivity analysis was eliminated one by one, and the heterogeneity and analysis results did not change significantly. According to the analysis of subgroups in coastal and inland areas, the results show that in coastal areas, OR=2.278, 95% CI (1.348, 3.849), p=0.002, suggesting that the zinc deficiency rate in the infant group in the coastal area is higher than that in the preschool group, and the difference is statistically significant. Significance: OR=1.228, 95% CI (0.959, 1.574), p=0.104 in the inland area, suggesting that there is no statistically significant difference in the zinc deficiency rate between the infant group in the inland area and the preschool group. Further Meta regression analysis, t=-1.91, p=0.42, the difference was not statistically significant, suggesting that regional factors of the existing research data are not the main source of the heterogeneity.

Comparison of zinc deficiency rates between infant group and school-age children and adolescents: There are 21 literatures reporting the values of the zinc deficiency rate in the infant group and school-age children and adolescents. Meta-analysis was performed. The results are as follows: Heterogeneity test p=0.000, I²=96.9%, there is a large heterogeneity, and the random effects model is used for analysis. The results of Meta-analysis showed that the zinc deficiency rate in the infant group was higher than that in the school-age children and adolescent group, and the difference was statistically significant (OR=1.746, 95% CI (1.257, 2.425), p=0.001). The sensitivity analysis was eliminated one by one, and the heterogeneity and analysis results did not change significantly. According to the analysis of subgroups in coastal and inland areas, the results show that in coastal areas, OR=4.203, 95% CI (2.425, 7.284), p=0.000, suggesting that the zinc deficiency rate of infants in coastal areas is higher than that of school-age children and adolescents, and the difference is statistically significant. Scientific significance: OR=1.321, 95% CI (0.922, 1.894), p=0.104 in the inland area, suggesting that there is no statistically significant difference in the zinc deficiency rate between the infant group in the inland area and the school-age children and adolescents. Further Meta regression analysis, t=-2.42, p=0.026, the difference is statistically significant, suggesting that regional factors may be one of the sources of heterogeneity.

Comparison of zinc deficiency rates between the toddler group
and the preschool group: There are 33 literatures reporting the values of zinc levels and zinc deficiency rates in the toddler group and the preschool group. Meta-analysis was performed. The results are as follows: Heterogeneity test \( p=0.000, I^2=92.7\% \), there is large heterogeneity, random effects are used. Model analysis and Meta-analysis showed that there was no statistically significant difference in the zinc deficiency rate between the infant group and the preschool group \([OR=1.059, 95\% CI (0.918, 1.222), p=0.429]\). The sensitivity analysis was eliminated one by one, and the heterogeneity and analysis results did not change significantly. According to the analysis of subgroups in coastal and inland areas, the results showed that in coastal areas, \( OR=1.341, 95\% CI (1.092, 1.647), p=0.005 \), suggesting that the zinc deficiency rate of children in coastal areas is higher than that in preschool groups, and the difference is statistically significant. The results show that in the inland area: \( OR=0.938, 95\% CI (0.779, 1.129), p=0.496 \), suggesting that there is no statistically significant difference in the zinc deficiency rate between the inland children group and the preschool group. Further Meta regression analysis, \( t=2.11, p=0.043 \), the difference is statistically significant, suggesting that regional factors may be one of the sources of heterogeneity.

Comparison of zinc deficiency rates between the toddler group and school-age children and adolescents: There are 19 literatures reporting the values of zinc levels and zinc deficiency rates in the toddler group and school-age children and adolescents. Meta-analysis was performed. The results are as follows: Heterogeneity test \( p=0.000, I^2=95.9\% \), there is a large heterogeneity, randomized Effect model analysis, the results of Meta-analysis showed that there was no statistically significant difference in the zinc deficiency rate between the infant group and school-age children and adolescents \([OR=1.136, 95\% CI (0.848, 1.523), p=0.394]\). The sensitivity analysis was eliminated one by one, and the heterogeneity and analysis results did not change significantly. According to the analysis of subgroups in coastal and inland areas, the results show that in coastal areas, \( OR=1.364, 95\% CI (1.034, 2.365), p=0.034 \), suggesting that the zinc deficiency rate in the coastal area is higher than that of school-age children and adolescents, and the difference is statistically significant. The results show that in the inland area: \( OR=1.049, 95\% CI (0.715, 1.537), p=0.857 \), suggesting that there is no statistically significant difference in the zinc deficiency rate between the inland children group and the preschool group. Further META regression analysis, \( t=1.42, p=0.174 \), the difference was not statistically significant, suggesting that regional factors are not the main source of heterogeneity.

Comparison of zinc deficiency rates between preschool group and school-age children and adolescents: There are 23 literatures reporting the values of zinc levels and zinc deficiency rates in the infant group and school-age children and adolescents. Meta-analysis was performed. The results are as follows: Heterogeneity test \( p=0.000, I^2=96.1\% \), there is a large heterogeneity, and randomized Effect model analysis, the results of Meta-analysis showed that the preschool group and school-age children and adolescents’ group of zinc deficiency rates were not statistically different \([OR=0.986, 95\% CI (0.754, 1.291), P=0.919]\). The sensitivity analysis was eliminated one by one, and the heterogeneity and analysis results did not change significantly. According to the analysis of subgroups in coastal and inland areas, the results show that in coastal areas, \( OR=0.838, 95\% CI (0.610, 1.151), P=0.275 \), suggesting that there is no difference in the zinc deficiency rate between the preschool group and the school-age children and adolescents in the coastal area. Statistical significance; \( OR=1.067, 95\% CI (0.740, 1.540), p=0.728 \) in the inland area, suggesting that there is no statistically significant difference in the zinc deficiency rate between the preschool group in the inland area and the school-age children and adolescents. Further Meta regression analysis, \( t=1.03, p=0.313 \), the difference was not statistically significant, suggesting that regional factors are not the main source of heterogeneity.

Comparison of zinc deficiency rates among children with different influencing factors: In this study, 4 literatures reported that the zinc deficiency rate of different educational level factors of diet providers totaled 7406 children, of which 4112 were in the high-education group and 3294 were in the low-education group. Another 5 articles reported on urban areas. The influencing factors of zinc deficiency in rural areas totaled 10,497 children, including 6,875 in the urban group and 3,622 in the rural group. Meta-analysis was performed. The results are as follows:

Comparison of zinc deficiency rates among children with different education levels among diet providers: In this study, the educational level of dietary providers (mainly mothers) was divided into high educational level (high school, technical secondary school, college and above) and low educational level (junior high school and below). The heterogeneity test results showed that \( p=0.004, I^2=77.2\% \), there is a large heterogeneity, using random effects model analysis, the meta-analysis results show that there is no statistically significant difference in the zinc deficiency rate between the diet provider’s high-education group and the low-education group \([OR=1.095, 95\% CI (0.867, 1.383), p=0.446]\) (Figure 4).

Using one-by-one elimination sensitivity analysis, the study by Yu Xinpeng [53] was eliminated. The results showed that the heterogeneity test \( P=0.946, I^2=0, \) and the heterogeneity decreased significantly, suggesting that this study may be the main source of heterogeneity. The Labbe test for heterogeneity evaluation was further performed, and the result graph showed that the study deviated from the valid line (Figure 5).

But by reading the literature in detail, the reason for the heterogeneity was not found. Using fixed effects model analysis, the difference was not statistically significant \([OR=0.972, 95\% CI (0.834, 1.136), P=0.448]\) (Figure 4).

| Study | \( OR (95\% CI) \) | Weight |
|-------|------------------|--------|
| Test X (2020) | 0.83 (0.56, 1.22) | 18.72 |
| Da-Ho Ma (2014) | 3.69 (0.73, 1.46) | 19.68 |
| Yang-Ming Yang (2019) | 4.29 (4.08, 4.82) | 20.96 |
| Jing-Ming Lu (2011) | 1.29 (1.12, 1.70) | 20.91 |
| Min-sung Li (2011) | 1.07 (0.63, 1.79) | 21.03 |

Figure 6: Forest plot comparing zinc deficiency rate between urban group and rural group.
significant difference in publication bias (t=1.43, p=0.168). Further analysis, and the results showed that there was no statistically indicating that the publication bias was less likely; the Egger test was in a funnel plot. Funnel plots were roughly symmetrical (Figure 7), the male and female groups was conducted to test the publication bias not change significantly.

1.637), p=0.432] (Figure 6). The sensitivity analysis was eliminated one by one, and the results of heterogeneity and Meta-analysis did not change significantly.

Publication bias: Meta-analysis of the rates of zinc deficiency in the male and female groups was conducted to test the publication bias in a funnel plot. Funnel plots were roughly symmetrical (Figure 7), indicating that the publication bias was less likely; the Egger test was further analysis, and the results showed that there was no statistically significant difference in publication bias (t=1.43, p=0.168).

Discussion

Zinc is a mineral that is very important to human health, and it is an essential trace element distributed throughout the body. According to the concept of type I/II nutrient proposed by M. Golden [62], zinc belongs to type II nutrient, and type II nutrient can be regarded as a “growth nutrient”, that is, a type of nutrient that is essential for growth. In the state, cell growth will stop. Zinc is distributed in all organs, tissues, body fluids and secretions in the human body. Most of the zinc is located in non-fat tissues. Among them, the zinc in skeletal muscle and skeletal tissue accounts for 83% of the total body zinc [63], and more than 95% of zinc is in the cells inside. When zinc-containing foods or drugs are ingested, zinc is released into the intestine in the form of zinc ions, and combines with endogenous secretory ligands or exogenous substances in the intestinal lumen, in the distal duodenum and jejunum. The proximal absorption and transport enter the portal venous system, and then are rapidly absorbed in the liver and released into the systemic circulation for transport to other tissues [64]. Circulating serum zinc only accounts for 0.1% of body zinc, and about 70% of serum zinc is bound to albumin, so any condition that changes the serum albumin concentration will affect the serum zinc level [65]. Zinc excretion in the body is mainly excreted through the intestine, which accounts for about 50%. Other ways include urine, which accounts for about 15% of the total loss of zinc; epithelial cell shedding, sweat, semen, hair and menstrual blood account for about 17% of the total loss of zinc [66].

Zinc is involved in cell division and growth, intestinal electrolyte absorption, neurotransmission, immune response, enzyme catalysis or stabilization, and functional modification of membrane proteins, gene regulatory proteins and hormone receptors [67–69]. Through these pathways, zinc plays a very important role in the synthesis of DNA and RNA, protein metabolism, and overall growth and development [69]. In view of the various biological functions of zinc, the state of zinc in the body affects various physiological and metabolic functions, such as body growth [70,71], immune function [72,73], reproductive function and neurobehavioral development [74,75]. The clinical manifestations of zinc deficiency in children and adolescents of different ages are different [76,77]. In neonates, infants, toddlers and preschool children, zinc deficiency is mostly manifested as cognitive impairment, behavioral and emotional changes, etc. In severe zinc deficiency, limb or perioral skin lesions can be seen; zinc deficiency in school-age children can be Manifested as growth retardation, blepharon conjunctivitis, hair loss and repeated infections; adolescent zinc deficiency can lead to delayed sexual maturity [78].

PZC is currently recognized as the best available biomarker for the risk of zinc deficiency in the population. When the prevalence of low PZC in children is more than 20%, it is considered that there is an increased risk of zinc deficiency, which requires public health attention.

The main basis for choosing PZC as a biomarker of zinc deficiency in the population is that PZC can reflect the dietary zinc intake; its response to zinc supplementation is consistent, the prevalence of low PZC and the prevalence of insufficient dietary zinc intake. There is agreement between [79], and most age and gender groups have reference data. However, PZC is easily affected by factors such as recent meals, time of day, age, gender, and systemic infection or inflammation. Studies have shown that PZC fluctuates up to 20% a day, mainly due to the amount of meals, usually the highest concentration can be observed before clearing breakfast [80]. Therefore, at the individual level, the correlation between PZC and zinc intake is very poor, and it is currently not recommended to use this indicator to diagnose and treat individuals. In addition, since the collected samples are easily contaminated by the surrounding zinc sources, appropriate precautions must be taken during the collection, processing and analysis of the samples to avoid contamination. At present, the lower limit of plasma (or serum) for children under 10 years of age is set at 65μg/dL (9.9μmol/L) [81,82]. In China, a trace amount of whole blood zinc is more commonly used as a method for detecting zinc content. Because of the small amount of blood taken, it is easier to be accepted by children and parents. In general, except for elements that are not suitable for serum detection, most trace elements have little difference in serum and whole blood, and their absolute values are not the same, but they can all reflect the zinc status of the human body [78].

Zinc deficiency is an important cause of the disease in developing countries, especially infants and young children, but there is little
information about the global prevalence of zinc deficiency. According to reports, nearly one-fifth (17%) of the world’s population is at risk of zinc deficiency, with Asia and Africa having the highest prevalence [83,84]. Hess SY [85] analyzed 20 survey reports in 2017 and concluded that in 13 of 19 surveys, the prevalence of plasma (or serum) zinc levels (PZC) in children below the normal value was greater than 20%, among which the prevalence of low PZC among young children in Cameroon is as high as 83% [86], 68% in Cambodia [87], and the prevalence of low PZC among young children in Kenya, Senegal, South Africa and Vietnam is about 50% [88-91]. The prevalence of low PZC among young children in Latin American countries ranges from 27% to 43% [92-95]. Only Afghanistan, Azerbaijan, Nepal, the Republic of Maldives, Sri Lanka and China have prevalence of low PZC in young children less than 20% [96-100]. The results of 20 countries indicate that zinc deficiency is a public health problem in most of these countries, and zinc intervention strategies should be considered. Due to the vast territory of China, there are obvious differences in the status of zinc deficiency. A survey of 3069 children and adolescents aged 0-17 years from 2016 to 2018 in Zhourshan City, Zhejiang Province from Wang Haiyan et al. [11] showed that the overall zinc deficiency rate was 23.23%; Wang Junwen et al. [16] reported The overall zinc deficiency rate of 14,569 children and adolescents aged 0-17 years in Jiangyou City, Sichuan Province was 11.49% in 2016-2018; Zhao Feng et al. [28] reported that 16683 children and adolescents aged 0-7 years in Fuzhou City, Fujian Province had a total zinc deficiency rate of 11.49% in 2016-2017. The overall zinc deficiency rate was 21.75%.

The results of this study showed that the overall zinc deficiency rate of children aged 0-14 were 27.0% (95% CI 22.8%-31.3%). It can be seen that overall zinc deficiency among children aged 0-14 years in mainland China is still relatively common. According to the analysis of different subgroups in the coastal and inland areas, the results show that the zinc deficiency rate in the coastal area group is lower than that in the inland area group. This may be related to more seafood food components in the coastal area’s diet and the higher zinc content in seafood foods. The comparison of the zinc nutritional status of children of different genders showed that there was no statistical difference in the total blood zinc levels of children in the male group and the female group, while the zinc deficiency rate in the male group was higher than that in the female group, and the difference was statistically significant [OR=1.052, 95% CI (1.019, 1.087), p=0.002], the reason may be related to the differences between different regions. The comparison of zinc nutrition status among different age groups showed that the trace levels of whole blood zinc in the infant group, toddler group, and preschool group increased in turn. It can be seen that blood zinc levels gradually increase with age. The possible reasons are with age, the diet becomes more diverse and exposure to foods with high zinc content is more abundant. In contrast to the zinc deficiency rate, the infant group has the highest zinc deficiency rate. The possible reason is that the infant’s diet is mainly breast milk, and exclusively breastfed infants can meet their zinc requirements for the first 5-6 months after birth [101], experimental evidence. This is well supported [102-105]. However, after about 6 months of age, breast milk alone cannot provide enough zinc to meet the needs of infants [101,106]. Therefore, if the time of supplementing breastfeeding infants with food is postponed until after six months of age, or if the supplementary food contains insufficient absorbable zinc, the risk of zinc deficiency in infants will be greatly increased.

The results of this meta-analysis showed that there was no statistical difference in the impact of dietary providers on zinc deficiency in children [OR=1.095, 95% CI (0.867, 1.383), p=0.446], but the sample size included in the study was small. Jianghong Liu et al. [42] reported that the children of mothers with higher education are at a lower risk of zinc deficiency compared with those of mothers with lower education levels; Yu Xiping et al. [53] reported that the dietary providers are highly educated. Parents may pay more attention to children’s health, can seek more scientific knowledge of parenting, and can arrange children’s meals reasonably, which is conducive to reducing the prevalence of children’s zinc deficiency. The impact of different factors in urban and rural areas on children’s zinc deficiency, the results of Meta-analysis showed that the difference was not statistically significant [OR=1.152, 95% CI (0.810, 1.637), p=0.432]. Jianghong Liu et al. [42] reported that the serum zinc level of rural preschool children was lower than that of urban children; and Ma Defu et al. [32] reported that the detection rate of zinc deficiency in first-tier cities and second-tier cities was significantly higher than that in plain towns and mountainous towns. Different from previous reports, the study found that this may be related to the more common zinc nutritional supplement intake in plain towns and mountain towns in the region. The results of this meta-analysis also did not show the differences in the rates of zinc deficiency among children in different urban and rural areas, and more studies are still needed for further analysis.

**Conclusion**

At present, the zinc deficiency of children aged 0-14 in mainland China is still severe, especially in infancy; the zinc deficiency rate of male children is higher than that of female children; the zinc deficiency rate of children in inland areas is higher than that in coastal areas; diet provider culture Factors such as different levels and different urban and rural areas are not the main influencing factors of zinc deficiency. These have certain reference significance for assessing the status of zinc deficiency in mainland China and how to improve zinc nutrition.

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**Authors' Contributions**

Yan CJ involved in study design, selection of articles, data extraction, summarizing and synthesizing findings, and manuscript writing. Similarly, Su JY and Lin GX involved in study design, selection of articles, data extraction, summarizing and synthesizing findings, and manuscript writing. All authors read, revised and approved the final draft of the manuscript.

**Availability of Data and Materials**

All data regarding this meta-analysis are contained and presented.
in this meta-analysis document.

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