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The concentration of zinc, selenium, and iodine in human mature milk: a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 July 2024 and was last updated on 15 July 2024.

INTRODUCTION

Review question / Objective Our goal was to summarize global concentrations of Zn, Se, and I in human milk, examining differences across study areas, sample years, and analytical methods.

Condition being studied Human milk offers a wealth of both nutritional and non-nutritional compounds crucial for infant development. It is a highly intricate biological fluid, providing optimal nutrition for human infants during the first 6 months of life. It is estimated that approximately 1.4 million child deaths per year and 10% of global burden of childhood diseases are attributable to inadequate breastfeeding, especially within the first 6 months of life. Over the past several decades, a substantial body of research has emerged focusing on the concentration of minerals present in human milk. Several reviews on Zn, I, and Se concentrations in human milk have been published previously. However, many of these studies are dated and lack comprehensive coverage.

Furthermore, it has been widely acknowledged that maternal dietary intake significantly influences the mineral concentration of Zn, I, and Se in human milk. The dietary patterns of individuals vary across different regions and have undergone notable changes in recent decades. However, it remains unclear whether there is a secular trend or geographical variations in the concentration of the three minerals in breast milk. Furthermore, it's important to note that different analytical methods can yield varying results. The extent to which analytical methods influence the levels of the three minerals in human milk remains unknown.

METHODS

Search strategy An electronic search of PubMed, Web of Science, Medline, Scopus, Embase, and the Cochrane Library was conducted for research published in English, and Wanfang and China National Knowledge Infrastructure databases for Chinese language publications up to May 2021. The search terms of “mineral* OR trace element* OR zinc OR iodine OR selenium” and “human milk

OR breastmilk OR breast-milk OR breast milk” were combined with “AND”. The reference lists of relevant studies and review articles were also searched.

Participant or population The review will include studies conducted on healthy mothers.

Intervention No intervention.

Comparator No comparator.

Study designs to be included Research papers of all designs including interventional studies, cross-sectional, case-control, cohort designs and review articles will be included. Articles with no full text available like conference abstracts will be excluded. For multiple reports from the same study, we included the most recent and/or most complete study.

Eligibility criteria Eligible for this meta-analysis included studies that: 1) analysis of mature milk from healthy mothers; 2) data were presented by means or medians, along with standard error of the mean (SEM), standard deviation (SD), range, 95% confidence interval (CI), and/or interquartile range; 3) publication in English or Chinese. Studies were excluded if they: 1) mothers suffered from specific conditions such as gestational diabetes, preeclampsia, or HIV; 2) lactation stage was not identified; 3) pooled samples from multiple mothers or lactation stages. Only the most recent and/or comprehensive study was chosen when multiple reports from the same study were available.

Information sources Mentioned above under search strategy.

Main outcome(s) A total of 183, 47, and 30 studies evaluating the human milk Zn, Se, and I content were included. The summarized means (95% confidence intervals) were 3.02 (2.19, 3.85) mg/L for Zn, 19.1 (14.9, 23.4) ug/L for Se, and 130.0 (110.6, 149.5) ug/L for I. However, there was significant heterogeneity among studies for all three minerals ($I^2 \geq 88.9\%$).

Quality assessment / Risk of bias analysis This systematic review and meta-analysis is conducted to determine whether study areas, sample years, and analytical methods should be considered when analyzing concentrations of Zn, Se, and I of breast milk. Therefore, this review will not assess the effectiveness of the finding or the risk of bias.

Strategy of data synthesis Weighted means and their 95% confidence intervals (CIs) were computed using the inverse-variance weighting method, implemented with the "rma.uni" function from the Metafor package in R Studio. The overall standard deviation (SD) values were calculated using the equations recommended by the Cochrane Handbook, incorporating the SDs from all eligible studies. We presented pooled effect results with 95% CI and SD using forest plots with I^2 and τ^2 parameters to display statistical heterogeneity. Random-effect models were utilized considering high heterogeneity. A multivariate meta-regression model was performed to explore the associations of mineral concentrations with year of sample collection, geographical region, and analytical method.

Subgroup analysis Geographical regions and analytical methods were divided into two groups for analysis purposes.

Sensitivity analysis Not applicable.

Country(ies) involved China.

Keywords Human milk; Zinc, Iodine and Selenium; Breast-feeding; Infants.

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