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Original Article

Relationship between birth weight and total cholesterol concentration in adulthood: A meta-analysis

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Abstract

Background: Although a substantial number of studies have investigated the relationship between birth weight and serum cholesterol later in life, the results vary extensively. The aim of this study was to explore the relationship between birth weight and total cholesterol concentration in adulthood.
Methods: We considered the results of several published observational studies that reported the association between birth weight and total cholesterol concentration in adulthood. The associations were assessed by linear regression coefficients. Summary regression coefficients with 95% confidence intervals (CI) were computed using random-effects models. Subgroup and sensitivity analyses were also conducted to explore possible explanations for heterogeneity among the studies.
Results: A total of 20 studies with 26,122 participants were identified. After adjustment for adult body mass index, the summary regression coefficient for an increment in birth weight of 1 kg was −0.09 mmol/L (95% CI: −0.13, −0.05) for men without heterogeneity ($I^2 = 17.2\%$) and −0.08 mmol/L (95% CI: −0.13, −0.03) for women with low heterogeneity ($I^2 = 34.0\%$). Stratified and sensitivity analyses generally confirmed the robustness of the findings in men. However, subgroup analyses by age indicated that the association of birth weight with total cholesterol was statistically significant only in women aged <50 years. There was no evidence of publication bias in these studies.
Conclusion: Based on our results, lower birth weight was found to be associated with higher concentrations of total cholesterol in men aged >18 years and in women aged <50 years.

Keywords: birth weight; cardiovascular diseases; cholesterol; meta-analysis

1. Introduction

Hypercholesteremia in adulthood is commonly known as an important risk factor for cardiovascular disease. To explore the origin of hypercholesteremia, numerous studies have investigated the effects of birth weight on serum cholesterol in later life, and some meta-analyses have been conducted to explore the association; however, the results are pronouncedly varied. Some studies reported that the association between birth

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weight and total cholesterol only existed in men or women,[1−3] whereas other studies suggested that the association was the same in both the sexes.[4] Additionally, the effect of age on this association should be considered.[5] However, none of the published meta-analyses studies focused on adult serum cholesterol; instead, they assessed the association across various age groups. Additionally, since the last meta-analysis was published, many new studies focusing on adults have been reported.[6−8] Therefore, a new meta-analysis of the relationship between birth weight and total cholesterol in adulthood is justified.

2. Methods

This meta-analysis was reported following the recommendations proposed by the Meta-analysis of Observational Studies in Epidemiology and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) groups.

2.1. Search strategy

We performed a literature search on the electronic databases PubMed (1966 to December 2013), Embase (1966 to December 2013), Web of Science (1972 to December 2013), Scopus (1971 to December 2013), BIOSIS Citation Index (1994 to December 2013), and LWW (Lippincott Williams & Wilkins, 1971 to December 2013). The search strategy consisted of title, abstract words, and subject headings related to birth weight and cholesterol. The search strategy was limited to humans, but not to study design. Additionally, references from relevant articles were reviewed to identify potential relevant studies.

2.2. Study selection

Two independent reviewers, Lianhui Chen (CLH) and Shanshan Chen (CSS), screened papers based on the following inclusion criteria: (1) observational studies; (2) there were no additional manipulations or complications during pregnancy; (3) participants were aged >18 years; (4) birth weight was the exposure of interest; (5) birth weight was not self-reported; and (6) total cholesterol was the outcome of interest. Discrepancies in the selection process were independently resolved by a third reviewer Li Liang (LL). The study selection process is summarized in the PRISMA flow diagram.

2.3. Data extraction and quality assessment

CLH extracted data using a standard form, which was checked by LL and CSS. The following were extracted from each included study: the year of publication, first author's name, study location, sample size, participants' sex, age at examination, regression coefficients between birth weight and total cholesterol, and adjustment for confounders. We thoroughly reviewed those studies without regression coefficients by sex and dispersion measures.[6−14]

We used the Newcastle−Ottawa Scale to quantitatively evaluate the methodological quality of the studies. Two reviewers (CLH and CSS) independently assessed all the eligible studies, and disagreements were resolved by a third reviewer (LL). Those studies with a score ≥7 were included in the final meta-analysis.

2.4. Statistical analyses

All statistical analyses were performed using STATA software (version 12.1; StataCorp, College Station, TX, USA). Heterogeneity among the studies was assessed using Q and I^2 statistics. A p value < 0.1 was considered to be statistically significant for the Q statistic. Heterogeneity was considered low, moderate, and high using I^2 values of 25%, 50%, and 75%, respectively. Linear regression coefficients were derived using random-effects models, because, unlike fixed-effect models, these account for sampling errors and possible heterogeneity between the studies. For studies that did not provide standard errors of regression coefficients, these were estimated from the p value or 95% CI.[3,4,10,15−18]

To explore the potential sources of heterogeneity and the effect of age on the associations, we performed stratified analyses according to participants' age. Additionally, studies were stratified by national income levels according to the World Bank classification. To test the influence of a single study on the summary regression coefficient, sensitivity analyses were performed by omitting each study in turn while pooling results from the remainders. Potential publication bias was examined by Egger's regression asymmetry test.

3. Results

3.1. Study characteristics

The course of the systematic review is illustrated in Fig. 1. In summary, a total of 20 studies were included in the meta-analysis. These studies were published between 1993 and 2013, and included a total of 13,358 male and 12,764 female participants.

Of the 20 studies, 16 were conducted in high-income, two in upper-middle-income, and the remaining studies in lower-middle-income countries. Eight of the studies involved participants aged 50−76 years, and the other studies involved participants aged 18−50 years. The majority of studies included both sexes (85%) and presented a sample size below 1000 participants (65%).

3.2. Quality assessment

After the quality assessment was completed, two studies were considered to be of low methodological quality (scores ≤ 6) and excluded from the final meta-analysis. Since we excluded the studies that had birth weight self-reported in the selection process, most of the studies (82%) received a full score in the selection scale, which was based on the representativeness of subjects and ascertainment of exposure. In the

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