BMC Ophthalmology

SYSTEMATIC REVIEW

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The association between macronutrients intake and myopia risk: a systematic review and meta-analysis

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Abstract

Background Dietary factors have been suggested as potential risk factors for myopia, but research findings on this relationship are inconclusive. The potential predisposing or protective role of macronutrient (carbohydrate, protein, fat) intake in the development of myopia was systematically reviewed, followed by data synthesis by meta-analysis.

Methods A systematic search was conducted in PubMed, Web of Science, Scopus, and Google Scholar up to the end of June 2023 to identify all relevant studies. All observational studies that assessed the relationship between macronutrient intake with myopia, axial length (AL) of eyes and spherical equivalent refractive error (SE) on individuals younger than 18 years old were included.

Results After removing duplicates and screening studies, four studies were included in the systematic review and meta-analysis. Pooled odds ratios regarding the association between myopia development and nutritional intake were 1.01 (95% CI: 0.94, 1.08), 0.97 (95% CI: 0.86, 1.08), and 0.99 (95% CI: 0.83, 1.18) for carbohydrates, proteins, and fats, respectively, indicating no significant associations. Intake of carbohydrates, proteins, and fats was not significantly associated with either SE or AL.

Conclusions Intake of carbohydrates, fats, or proteins did not influence the risk of myopia. The relationship between the intake of other macronutrients and myopia is suggested to be scrutinized in future studies.

Registration The systematic review protocol was registered on PROSPERO (registration number: CRD42024541369).

Keywords Myopia, Diet, Axial length, Nutrients, Dietary intake, Spherical equivalent

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Introduction

Myopia is an increasing public health concern. The burden of myopia globally, differs in regions. An estimated 22.9% of the global population have myopia and an additional 2.7% are estimated to have high myopia; it is a major cause of suffering worldwide. These values are expected to rise to 49.8% and 9.8% for myopia and high myopia, respectively, by 2050 [1]. This disease is more prevalent among the young population, specifically in East Asia demographics [2]. Uncorrected myopia can negatively affect academic performance, global productivity losses, increased risk of road traffic accidents, impact on well-being and lead to optic disk changes, retinal detachment, glaucoma, maculopathy, and cataract [3, 4]. Axial length (AL) is the combination of anterior chamber depth, lens thickness and vitreous chamber depth. Spherical Equivalent (SE) is an estimate of refractive error of eyes that is calculated for each eye independently. It is calculated by merging the spherical (nearsightedness or farsightedness) and cylindrical (astigmatism) components of refractive error. The measurement of AL and SE are widely used in studies on refractive error and they are the most significant contributor to refractive error [5, 6].

Myopia results from an interplay between environmental factors, genetic predisposition, parental myopia and ethnic differences. It is widely recognized that environmental factors, such as near-work tasks, outdoor light exposure, and time spent outdoors, have a considerable impact on the prevalence of myopia. Prolonged reading sessions (exceeding 30 min) and close reading distances (less than 30 centimeters) can increase myopia risk in children [7]. Engaging in outdoor activities can have beneficial impact on eye health through heightened exposure to natural light, the release of dopamine, the synthesis of vitamin D, and the potential enhancement of visual acuity [8]. Studies show that greater light exposure above 3000 lx can slow axial elongation and lower the risk of myopia [9]. In addition, well-structured and connected green spaces with larger areas, reduced fragmentation and shorter distances between patches are linked to slower progression of myopia [10]. A systematic review found that the COVID-19 pandemic has had a negative impact on myopia progression in children. This was mainly due to reduced outdoor time and increased screen usage [11].

Although the relationship between dietary factors and other ocular diseases, such as night-blindness, cataracts, age-related macular degeneration, and diabetic retinopathy, has been well-established [12, 13], the existence of such a link with myopia is not certain [14, 15]. The intake of carbohydrates, energy, proteins, fats, and cholesterol has been suggested to be associated with myopia [16, 17]. Carbohydrates have been shown to predispose to myopia by promoting hyperinsulinemia and elongating the axial eyeball [18, 19]. Overall, research findings in this field are inconclusive, partly due to variabilities in study populations and sample sizes, as well as the methods used for diet assessment. However, there is not any systematic review related to myopia and macronutrients. Thus, the primary objective of the present systematic review and meta-analysis was to assess the relationship between the dietary intake of macronutrients and the development of myopia in observational studies and among individuals under 18 years old.

Methods

Search methods

Following the instructions provided in the (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) PRISMA guideline, which is employed by researchers to validate strategies and methods used for conducting meta-analyses. The protocol was registered on PROSPERO (ID: CRD42024541369). We conducted a comprehensive literature search in Medline (PubMed), Web of Science, Scopus, and Google Scholar. All relevant studies published up to August 2023 were assessed. The search strategy was formed using the following operators and terms:

((Myopia OR myopi* OR "short-sightedness" OR "near-sightedness" OR "short sight" OR "short-sighted" OR "near-sight" OR "near-sighted" OR "refractive errors") AND (diet OR "dietary intake" OR "food intake" OR "macronutrient" OR "Micronutrient intake" OR "dietary proteins" OR "dietary carbohydrates" OR "dietary fat" OR "food frequency questionnaire" OR carbohydrates OR proteins OR fats)) and ((Myopia OR myop* OR short sighted* OR nearsighted* OR "refractive errors") AND (diet OR "dietary intake" OR "food intake" OR "macronutrient" OR "Micronutrient intake" OR "dietary proteins" OR "dietary carbohydrates" OR "dietary fat" OR "food frequency questionnaire" OR carbohydrates OR proteins OR fats)) .

Inclusion and exclusion criteria

Inclusion criteria was all observational studies (cohort, case-control, or cross-sectional) that was published in English and conducted on individuals younger than 18 years old. Included studies were conducted on subjects that only had myopia problem without any chronic disorders.

Exclusion criteria was studies on individuals over 18 years old, duplicated articles, grey literature (e.g., conference proceedings, theses) and studies reporting insufficient data.

If the full text of an article was not available, an email was sent to the corresponding author. Articles that authors did not respond to the email and did not send the full texes were excluded. All the records were imported

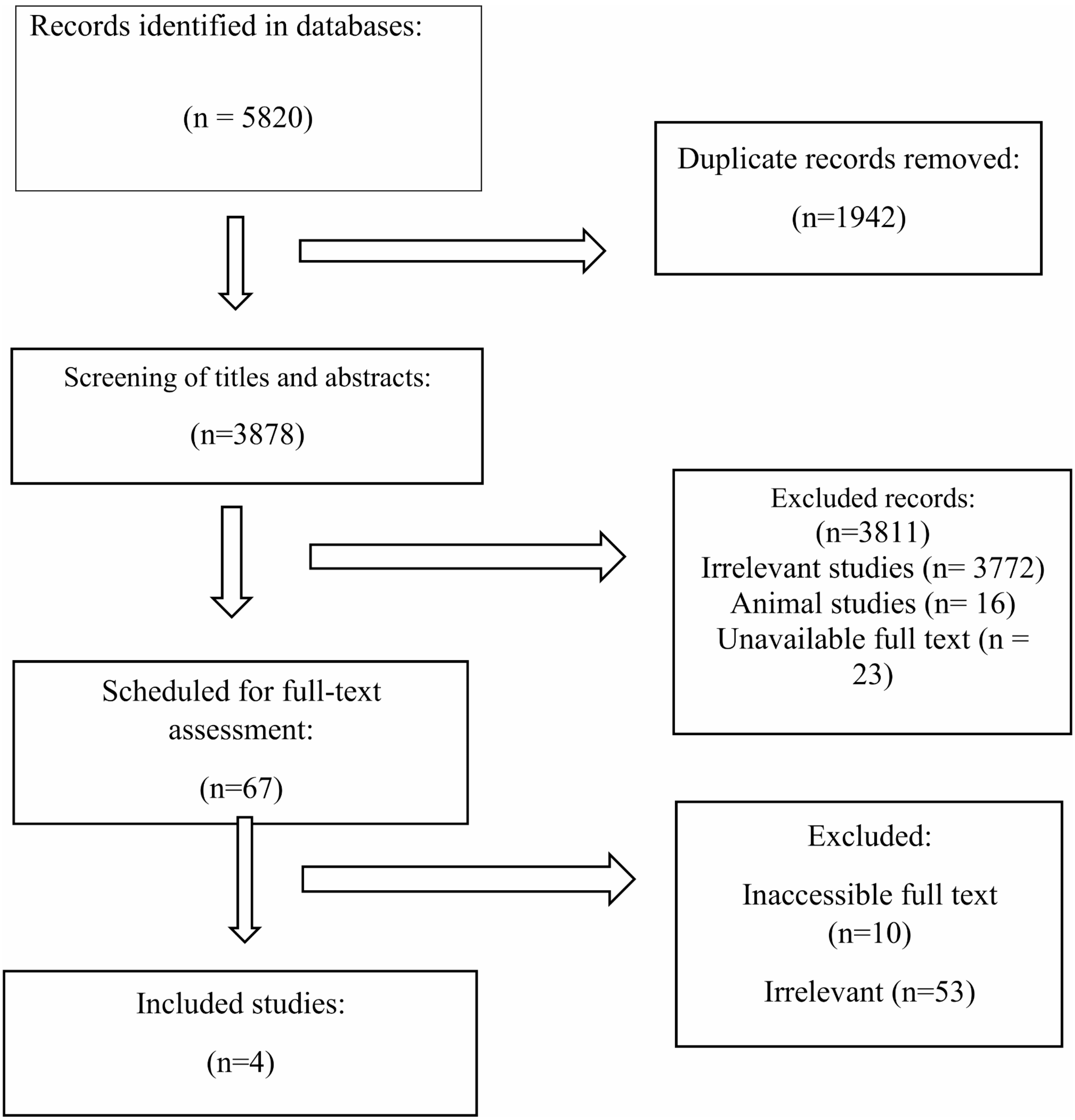

Fig. 1 The PRISMA flow diagram of study selection

into a reference manager tool (EndNote 9) and screened based on the title and abstract after the removal of duplicates. Discrepancies were resolved by either a thorough discussion between the two reviewers who independently conducted the literature search. If the bilateral discussion was futile to reach an agreement, a third reviewer was included to reach a consensus. Additionally, the bibliographies of the included articles were manually screened. The references of related review articles were checked to find undetected appropriate studies.

Data extraction and quality assessment

The first author's name, time of publication, location and design of the study, the size of the population studied, age of participants, macronutrients assessed, and main outcomes (i.e., OR of myopia, spherical equivalent (SE), and axial length (AL)) were gathered. Quality appraisal was conducted by two independent reviewers (SM, MHB) using a tool developed by the National Institute of Health (NIH). Third reviewer (RK) resolved any discrepancy. Agreement between reviewers for quality assessment was measured by kappa statistic that was in acceptable range of 0.66 to 0.97 for different items.

Statistical analysis

Odds ratio (OR) with a 95%CI was used for the dichotomous main outcome (i.e., myopia). Regression coefficients obtained from fully adjusted models with 95% CIs were pooled for continuous outcomes (i.e., AL and SE). The expected methodological and clinical heterogeneity between studies (based on Cochran's Q and I^2 statistics) was addressed by using random-effects models. We conducted meta-analysis in different subgroups of lipids. Since four studies were included in meta-analysis, publication bias was not assessed [20]. STATA 17.0 software (Stata Corporation, College Station, TX) was used to conduct analyses at a two-tailed $P<0.05$ threshold for statistically significant observations.

Results

Studies' characteristics

After removing duplicates ($n=1942$), the titles and abstracts of a total of 5,820 articles were reviewed for eligibility criteria, according to which 3,811 papers were removed at this phase due to irrelevant studies, animal studies and unavailable full text. Sixty-seven studies were chosen for full-text reviewing, which led to the exclusion of 55 irrelevant studies and 7 studies whose full texts were unavailable. Ultimately, four studies encompassing 1721 patients were included (Fig. 1). Table 1 summarizes the characteristics of these studies, two of which were cross-sectional and the other two were cohort studies evaluating the risk of both SE and AL for 3 to 4 years. As mentioned, the tool developed by the National Institutes of Health (NIH) was used for qualifying the studies. The risk of bias was assessed in individual studies (Table 2).

Association between macronutrient intake and myopia

Carbohydrate (CHO) intake was investigated in all studies [15, 17, 21, 22], and protein (PRO) and fat intake was analyzed in 3 studies [15, 17, 22]. Dietary data were collected by a 3-day food diary and food frequency questionnaires. Among these papers, only one study stratified the results by gender [21]. The relationship between carbohydrate intake and myopia was statistically significant in just one study [21]. Others failed to detect any significant link between protein intake and myopia, SE, or AL [15, 17, 22]. Only one study reported that a higher intake of saturated fats and cholesterol could predict longer AL [22](Fig. 2).

None of the studies showed a significant association between the intake of macronutrients and myopia except for Berticat et al., who observed that a higher intake of carbohydrates was linked to a lower risk of myopia in females.

Table 1 Characteristics of the studies included in meta-analysis

First author	Year	Country	Study Design	Number of participants	Mean. age of participants	Macronutrients assessed	comparator groups	dietary assessment	definition of myopia	Outcomes	Results
Li, M	2021	Singapore	Cohort	467	9 years	Carbohydrates, Fat, Protein	daily intake of nutrients	semi-quantitative FFQ	SE ≤ −0.50 D	Myopia SE, AL	Findings showed no significant association between macronutrient intake and risk of myopia, SE, or AL
Berticat, C	2020	French	Cross-sectional	86	9.5 years	carbohydrates	Amount of carbohydrates intake in myopic and Non-myopic groups	FFQ	SE ≤ −0.50 D	Myopia	Refined carbohydrates consumption could be associated with childhood myopia, with a higher probability in girls and an unexpected lower probability in boys
Chua, SYL	2018	Singapore	Cohort	317	36.5 months	Carbohydrates, Fat, Protein	First tertile of nutrients intake compare with third tertile	A three-day food diary	SE ≤ −0.50 D	Myopia SE, AL	There was no significant association between the intake of proteins, fats, or carbohydrates and SE, AL, or myopia
Lim, LS	2010	Singapore	Cross-sectional	851	12.81 years	Carbohydrates, Fat, Protein	First quartile of nutrients intake compare with fourth quartile	Semi-quantitative FFQ	SE ≤ −0.50 D	Myopia SE, AL	Higher intake of saturated fats and cholesterol was associated with longer AL. The intake of other nutrients had no association with SE, AL or myopia.

FFQ: food frequency questionnaire, SE: spherical equivalent

Table 2 Quality assessment of the cohort and cross-sectional studies included using the National Institute of Health (NIH) quality assessment tool

Author, year	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Quality rating
Li, M et al., 2021	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	No	Yes	NA	NA	Yes	Good
Berticat, C et al., 2020	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	No	Yes	NA	NA	Yes	Good
Chua, SYL et al., 2018	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	No	Yes	NA	NA	Yes	Good
Lim, LS et al., 2010	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	No	Yes	NA	NA	Yes	Good

NA: not applicable, NR: not reported

Pooled ORs regarding the association of the intake of CHO (OR=1.01, 95% CI: 0.94, 1.08), PRO (OR=0.97, 95% CI: 0.86, 1.08), and fat (OR=0.99, 95% CI: 0.83, 1.18) were not statistically significant. In most of the cases, heterogeneity between studies was not considerable.

Figure 3 depicts the forest plot representing the association between SE and macronutrient intake. Regression coefficients (Beta) in fully adjusted models were considered as effect sizes. There was no significant association between the intake of CHO, PRO, or Fat and SE. Also, there was no significant association between CHO, PRO, and Fat intake and AL (Fig. 4).

Discussion

As far as we know, the association between myopia and macronutrient intake has not been previously investigated through systematic review and meta-analysis. The results of the present meta-analysis, based on the data obtained from observational studies, showed no significant relationship between macronutrient intake and risk of myopia. Based on the latest reports, non-genetic factors may be the main culprits to be blamed for the considerable rise observed in myopia frequency in less than 2 to 3 generations [23, 24]. One of these non-genetic factors is believed to be diet, but the results of the latest studies investigating the association between diet and myopia have been inconclusive, especially in children of school age [19, 25].

Our meta-analysis demonstrated that carbohydrate consumption had no effect on the likelihood of myopia. The consumption of sugary foods has been noted to be positively associated with the prevalence of myopia in children [26]. In another study, Liu et al. showed that whole grain intake of more than 50% was inversely associated with risk of myopia, especially in 9–12-year-old children [27]. Consumption of refined carbohydrates and saturated fat can predispose to myopia by inducing hyperinsulinemia. In animal models, saturated fats could induce insulin resistance via promoting the proportion of endotoxin-containing bacteria in the gut and consequently increasing plasma endotoxin levels [28, 29]. Similar findings have been observed in human studies [30]. The potential role of insulin has been suggested in modulating cellular proliferation and eye structural formation [31]. Chronic hyperinsulinemia can result in the suppression of insulin-like growth factor binding protein-3 (IGFBP-3) and the induction of insulin-like growth factor-1 (IGF-1) in scleral fibroblasts, leading to axial elongation in the eye, a unique feature of myopia. Also, hyperinsulinemia may facilitate myopia development by increasing the gene expression of ZENK, promoting ZENK-immunoreactive cells in the retina, as well as up-regulating IGF-2 in the retina [32]. Based on the carbohydrate-insulin model, dietary regimens with a

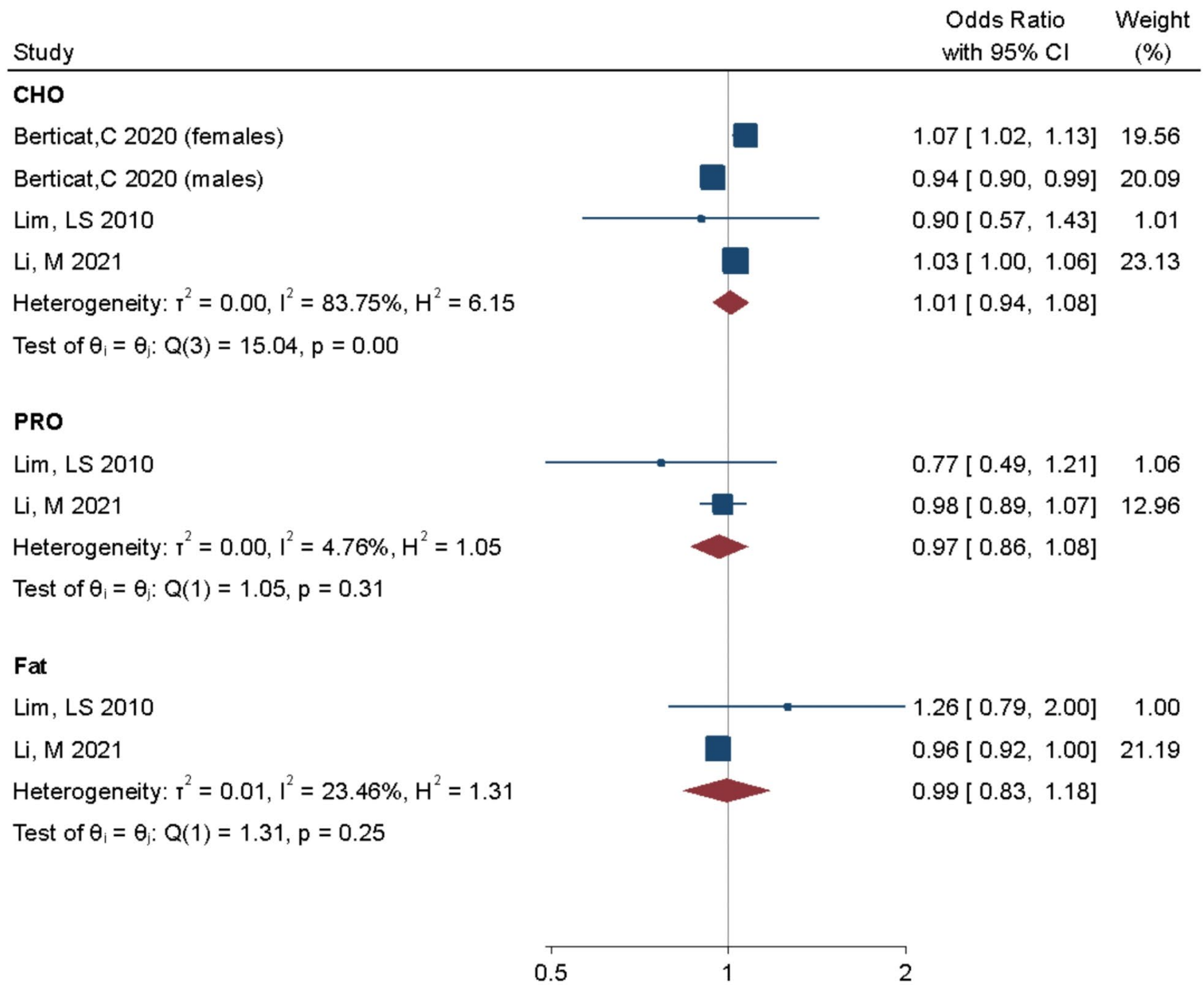

Fig. 2 Forest plot regarding the association between macronutrient intake and risk of myopia

high glycemic index enhance the entry of glucose to cells, resulting in oxidative stress, increased glycation, formation of complicated glycation end products, and glycoxidation [33, 34]. It seems that oxidative stress is a part of the molecular events that play a role in the development of myopia-associated complications [35]. Previous studies have shown the protective effects of whole grains against myopia; however, refined carbohydrates have been noted to have the opposite effect [21, 27]. In this review, the intake of carbohydrates did not show a significant relationship with myopia. This may be due to the fact that the studies analyzed did not segregate the types of carbohydrates consumed.

We found no significant association between protein intake and the likelihood of myopia. A study showed that the dietary intake of animal proteins for one-year decelerated myopia progression in children compared to the control group [36]. In a recent cross-sectional study on 7423 Chinese children, a diet containing plant and animal proteins mitigated the risk of myopia [14]. Compared to carbohydrates, dietary proteins have less prominent effects on the levels of blood sugar and insulin [37]. Therefore, it can be argued that consuming protein-enriched diets reduces the risk of myopia by decreasing IGF-1 and augmenting IGFBP-3 and RXR signaling pathways, and subsequently, suppressing scleral axial growth [18]. In one study, the prevalence of myopia was higher in people with higher protein intake [18]. However, establishing a definite association between protein intake and the risk of myopia needs further investigations.

Our meta-analysis did not show a significant association between fat intake and myopia. Findings showed that a higher intake of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) were associated with lowered risk of high myopia and could inhibit myopia development in young individuals [38]. Also, Lim et al.

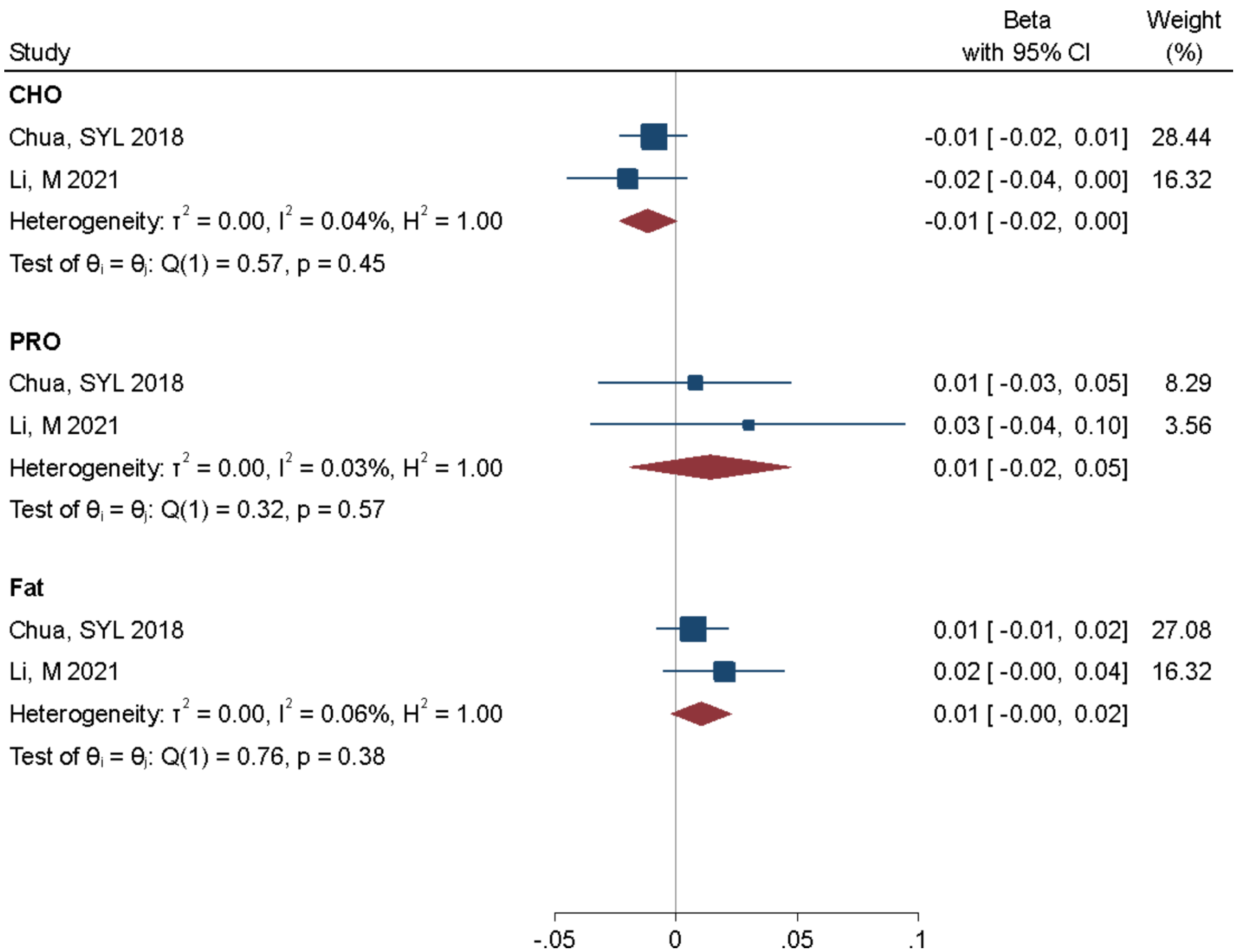

Fig. 3 Forest plot of coefficient regressions regarding the association between macronutrient intake and SE

demonstrated that a higher intake of saturated fats and cholesterol could facilitate the elongation of AL [22]. It is possible that saturated fats may promote hyperinsulinemia and inflammatory responses [39], thereby affecting the elongation of AL and elevation of intraocular pressure [40], and subsequently, increasing susceptibility to myopia. These incongruous results may be justifiable by a number of issues such as the heterogeneity of the studied populations, studies' designs, and different methods used to evaluate food intake. We suggest that type of micronutrients including animal protein, plant protein, saturated fat intake (SFA), monounsaturated fatty acid (MUFA) and polyunsaturated fatty acids (PUFA) intake, refined carbohydrate and whole carbohydrate investigate in the future studies.

This was the first meta-analysis on the relationship between myopia and macronutrients, as the main strength of the study. However, all relevant studies might not have been included in the meta-analysis due to selection only English language, so the effect sizes might have been subjected to bias. The method of quantification of the macronutrients in all studies was not the same and it can lead to heterogeneity. In addition because of limited studies subgroup analyses or sensitivity analyses were not performed. Further systematic review studies can assess studies with different languages and grey literature to mitigate language and publication bias.

Conclusions

In summary, this meta-analysis suggests that the intake of macronutrients may not be associated with myopia. The current data still fails to offer a consistent conclusion on a possible causal link between myopia and intake of macronutrients. More research is needed to verify a definite relationship between the intake of different types of macronutrients and myopia.

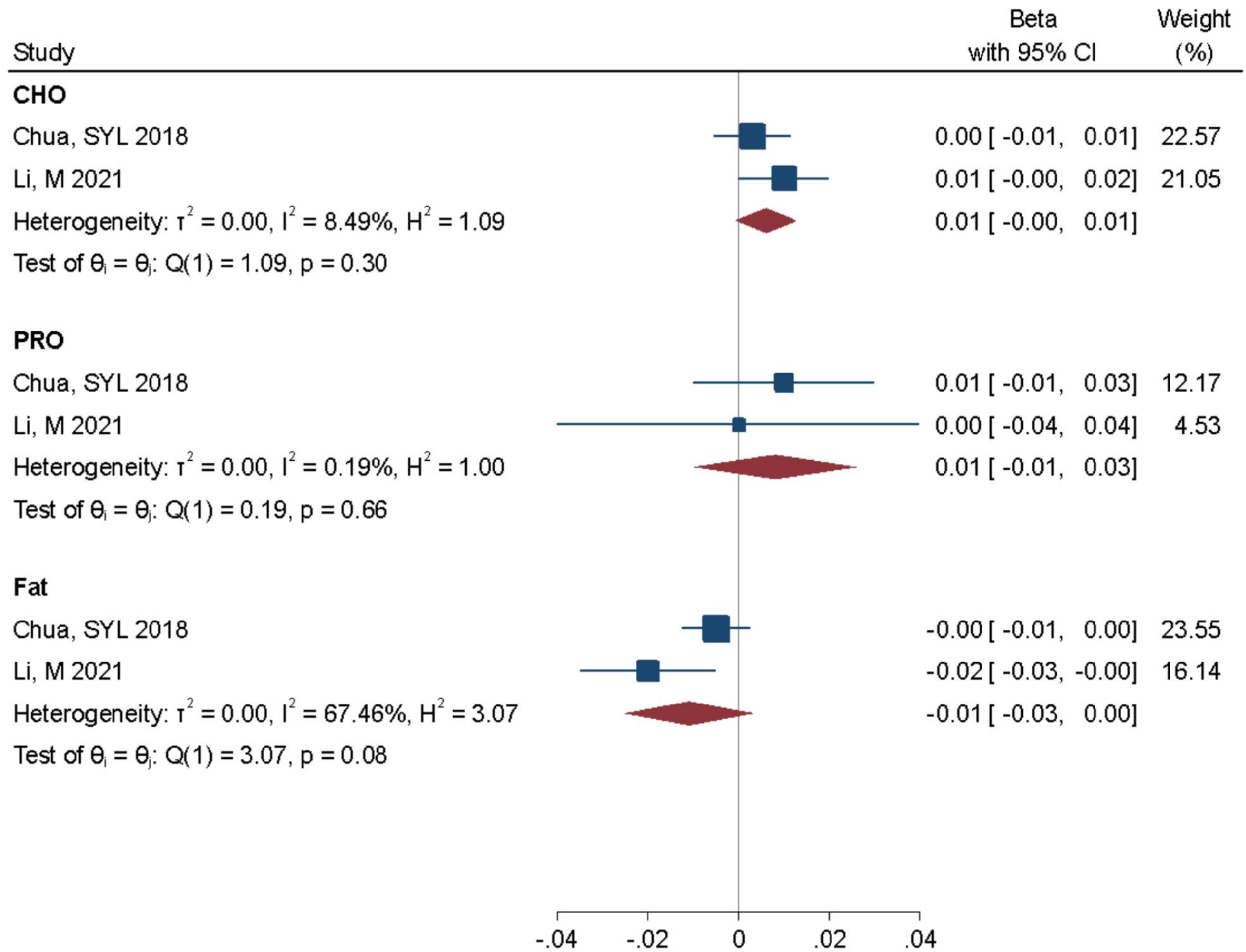

Fig. 4 Forest plot of coefficient regressions regarding the association between macronutrient intake and AL

Acknowledgements
Not applicable.

Author contributions
MHB and RK contributed to the conception and design of the research. SS, FAS and MHB reviewed the literature, and drafted the manuscript. MY contributed to the analysis of data. MHB and RK contributed to the interpretation of the data and revision. MME improved English language of the manuscript. All authors read and approved the final manuscript, and accept its content.

Funding
This study was conducted as the Project number 1400179 and supported by Isfahan University of Medical Sciences.

Data availability
The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of the Isfahan University of Medical Sciences, Isfahan (Research Ethics code: IR.MUI.MED.REC.1400.432).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 9 January 2024 / Accepted: 21 October 2024
Published online: 29 October 2024

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