UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

HOSPITAL DE CLÍNICAS DE PORTO ALEGRE

RESIDÊNCIA MULTIPROFISSIONAL EM SAÚDE

Bianca Fasolo Franceschetto

DIETAS VEGETARIANAS X ONÍVORA E O CRESCIMENTO E DESENVOLVIMENTO NOS PRIMEIROS 1000 DIAS: UMA REVISÃO SISTEMÁTICA

Porto Alegre, 2021

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Trabalho de conclusão da Residência Integrada e Multiprofissional e em Área Profissional da Saúde do Hospital de Clínicas de Porto Alegre como requisito para obtenção do título de nutricionista especialista em Saúde da Criança.

Orientador: Drª. Soraia Poloni

Porto Alegre, 2021

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A comissão examinadora, abaixo assinada, aprova o Trabalho de Conclusão de Residência desenvolvido por Bianca Fasolo Franceschetto, como requisito para obtenção do título de especialista em Saúde da Criança.

Comissão Examinadora:

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Drª. Soraia Poloni – Orientador – HCPA

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Me. Arlene Gonçalves dos Santos Fernandes – HCPA

RESUMO

Introdução: As dietas vegetarianas estão crescendo em diversos lugares do mundo e os primeiros 1000 dias de vida é um período que recebe cada vez mais atenção. Dessa forma, o objetivo deste trabalho foi verificar através de uma revisão sistemática, o impacto das dietas vegetarianas no crescimento e desenvolvimento durante os primeiros mil dias de vida. **Métodos:** Essa revisão foi realizada com o método proposto pela Cochrane Collaboration, as buscas foram realizadas nas seguintes bases de dados: *PubMed*, *Embase* e *Cochrane*, com os desfechos de crescimento e desenvolvimento. A seleção dos artigos foi feita de modo independente por dois pesquisadores, as decisões foram comparadas e um terceiro revisor decidiu sobre a inclusão do estudo. **Resultados:** A partir de 2,058 estudos identificados inicialmente, 19 preencheram os critérios e foram incluídos. Seis subtipos de dietas vegetarianas foram identificados nestes estudos (vegetariana, vegana, macrobiótica, antroposófica, ovo-lacto-vegetariana e a dieta *plant-based*). Dez estudos avaliaram peso ao nascer com dietas vegetarianas, cinco encontraram peso ao nascer menor em crianças vegetarianas em comparação com onívoras (porém, dentro da faixa normal) e dois estudos encontraram um risco aumentado de baixo peso ao nascer em neonatos vegetarianos. Em relação aos demais desfechos de crescimento, 3/7 estudos (todos da década de 80) observaram que a dieta macrobiótica teve desfechos negativos no crescimento e no desenvolvimento, já outros cinco estudos da mesma década (sendo um de 1978) que avaliaram dieta vegetariana e vegana, não apresentaram resultados negativos. Apenas dois estudos avaliaram o desenvolvimento neurológico, um deles constatou que as crianças em dieta macrobiótica tinham atraso no desenvolvimento motor e da linguagem, já o outro observou que o neurodesenvolvimento de crianças com dietas vegetarianas foi normal. **Conclusão:** as dietas vegetarianas parecem estar associadas a um menor peso ao nascer e maior risco de baixo peso ao nascer. Os subgrupos das dietas vegetarianas apresentaram resultados diferentes, sendo a macrobiótica com resultados negativos no crescimento e desenvolvimento durante os primeiros mil dias, enquanto as crianças nas demais dietas vegetarianas parecem crescer e se desenvolver normalmente no período dos 1000 dias.

Palavras-chave: *diet, vegetarian; vegetarians; first 1000 days; growth and development*

SUMÁRIO

1 INTRODUÇÃO

No ano de 2008 começou a ficar evidente a importância da fase inicial da vida, fase de maior desenvolvimento neurológico. Esse período, que inicia na concepção e vai até o segundo ano de vida, ficou conhecido como os primeiros mil dias de vida. Para um desenvolvimento neurológico adequado, é importante que nesse estágio da vida a criança tenha um responsável presente de referência, um ambiente saudável e uma nutrição que atenda a todas as necessidades que esse período mais ativo de neurodesenvolvimento demanda. (VICTORA et al., 2008)(SCHWARZENBERG; GEORGIEFF, 2018).

Em relação à alimentação e nutrição, atualmente acompanha-se um crescimento de pessoas aderindo à dieta vegetariana em todo o mundo. Esses crescentes seguidores citam diversas razões para praticarem esse padrão alimentar, como: benefícios à saúde, questões éticas, temor com impactos ambientais e sociais causados pelo consumo de carne e aflição com o sofrimento de animais (CULLUM-DUGAN; PAWLAK, 2015; LEITZMANN, 2014).

Tendo em vista o aumento da incidência de adeptos às dietas vegetarianas em diversas fases da vida (incluindo gestação, infância e adolescência), uma revisão sistemática de 2017 avaliou essas dietas em crianças de 0 a 18 anos. O objetivo foi verificar o consumo alimentar e o estado nutricional, mas os autores não tiveram conclusões concretas sobre benefícios ou riscos para a saúde das dietas vegetarianas atuais no campo nutricional ou no estado de saúde dessa população (SCHÜRMANN; KERSTING; ALEXY, 2017b).

Assim, a presente revisão restringiu o período de maior vulnerabilidade na questão de desenvolvimento e crescimento, os primeiros mil dias de vida, para avaliar possíveis impactos dessas dietas vegetarianas. Com isso, o trabalho justifica-se pela necessidade de estudar as dietas vegetarianas nos primeiros mil dias de vida e seus possíveis impactos no crescimento e desenvolvimento. A questão norteadora do trabalho foi: existe diferença no crescimento e desenvolvimento durante os primeiros mil dias de vida em indivíduos com dietas vegetarianas versus onívora?

2 REVISÃO BIBLIOGRÁFICA

2.1 Primeiros 1000 dias de vida

Os primeiros 1000 dias de vida correspondem ao período da concepção ao segundo ano de vida. A importância dessa fase foi evidenciada em estudo conduzido por Victora et al., (2008), que fez parte de uma série da revista Lancet sobre maternidade e desnutrição infantil. Nesse estudo, observou-se que danos sofridos no início da vida levam a prejuízos permanentes e também podem afetar as gerações futuras, concluindo que a prevenção desses danos é importante para a saúde em longo prazo, além de trazer benefícios para a educação e a economia (VICTORA et al., 2008).

Durante os primeiros mil dias de vida se formam estruturas e processos primários importantes, como os sistemas sensoriais, o hipocampo, a mielinização e os sistemas neurotransmissores monoamina, sendo esse o período mais ativo de desenvolvimento neurológico. Portanto, ainda que o neurodesenvolvimento continue ao longo da vida de uma pessoa saudável, até os dois anos de vida o cérebro passa por uma grande reestruturação e muitas mudanças de desenvolvimento esperadas nesse período não serão capazes de ocorrer mais tarde na vida (SCHWARZENBERG; GEORGIEFF, 2018).

Para que o neurodesenvolvimento seja saudável e adequado, deve-se dar atenção aos fatores socioeconômicos, interpessoais e nutricionais da criança, considerando que o cérebro progride na existência de um ambiente saudável e de uma dieta adequada (SCHWARZENBERG; GEORGIEFF, 2018). Já existem evidências abordando a relação entre a nutrição na infância e o desenvolvimento de doenças crônicas não transmissíveis na idade adulta, como a obesidade, hipertensão e diabetes. Com isso, influências maternas durante a gestação, amamentação e introdução alimentar apresentam alvos potenciais para intervenções com objetivo de reduzir a incidência das doenças crônicas não transmissíveis, pois esses riscos à saúde podem ser programados pelo estado nutricional durante os primeiros 100 dias de vida (MAMELI; MAZZANTINI; ZUCCOTTI, 2016).

Evidenciando o papel da nutrição no desenvolvimento nesse estágio da vida, um estudo de 2019 avaliou o impacto de um programa de nutrição multissetorial no desenvolvimento motor e de linguagem de crianças de 4 a 41,9 meses. Esse programa compreendeu o fornecimento de alimento (mistura de milho e soja fortificada com micronutrientes e óleo), suporte em saúde (atividades de fortalecimento e promoção de saúde e uso de serviços preventivos e curativos) e cuidados (nutrição, higiene e comunicação sobre

mudanças de comportamento) para gestantes e crianças nos primeiros mil dias de vida. Foram obtidos resultados significativamente positivos no desenvolvimento motor e de linguagem das crianças que participaram do programa, quando comparadas com os integrantes do grupo controle (OLNEY et al., 2019).

Nesse sentido, a nutrição adequada é essencial para o desenvolvimento satisfatório do cérebro e para o estado nutricional saudável, e todos os nutrientes são importantes. Entretanto, alguns têm efeito particularmente significativo durante o desenvolvimento inicial. Os nutrientes fundamentais para o desenvolvimento do cérebro são definidos por aqueles cuja deficiência, principalmente em períodos críticos, resulte em disfunção de longo prazo. Os principais macronutrientes e micronutrientes que estimulam o desenvolvimento inicial do cérebro são: proteína, *long chain polyunsaturated fatty acids* (LC-PUFAS), ferro, zinco e iodo. Assim, a ingestão desses nutrientes é importante para garantir um neurodesenvolvimento adequado (CUSICK; GEORGIEFF, 2016).

A nutrição adequada pode ser verificada com a avaliação do crescimento e do desenvolvimento infantil, com medidas antropométricas e escalas. O crescimento é o melhor indicador de saúde da criança, dessa forma, o seu acompanhamento é muito importante. Com esse acompanhamento é possível identificar se a alimentação está atendendo as necessidades nutricionais naquele momento, e possibilita a intervenção caso isso não esteja acontecendo de maneira satisfatória. Por exemplo, crianças desnutridas em fase de recuperação começam a apresentar um crescimento compensatório, em resposta à desaceleração no ritmo de crescimento normal que apresentaram por causa da desnutrição, da falta de nutrientes para promover a continuidade normal do crescimento (BRASIL - MINISTERIO DA SAÚDE, 2002; BRASIL, 2019)

2.2 Dieta vegetariana

A dieta vegetariana é caracterizada pela abstenção do consumo de carne e derivados (carne vermelha, aves, suína, frutos do mar e carnes de qualquer outro animal). Essa dieta é subdividida em: ovolactovegetariana (inclui ovos e laticínios), lactovegetariana (inclui leite e laticínios), ovovegetariana (inclui ovos) e vegetariana estrita ou vegana (exclui todos os produtos de origem animal da alimentação) (CULLUM-DUGAN; PAWLAK, 2015; MARSH et al., 2009). Também há a *plant-based diet* (dieta a base de plantas), que como o nome já diz, faz de sua base alimentos de origem vegetal, mas nem todos que seguem essa dieta são motivados a evitar produtos de origem animal (ROSENFELD; BURROW, 2017).

Os seguidores desse padrão alimentar estão crescendo em diversos países nos últimos anos, e as razões que levam as pessoas a seguirem essas dietas são diversas: benefícios à saúde, questões éticas, preocupação com o sofrimento dos animais e apreensão com impactos ambientais e sociais causados pelo consumo de carne (CULLUM-DUGAN; PAWLAK, 2015; LEITZMANN, 2014). Atualmente os países com maiores percentuais de indivíduos seguindo dietas vegetarianas são: Austrália com 5,5% da população total seguindo uma dieta vegetariana, Irlanda com 6%, Brasil com 8%, Reino Unido com 9%, Alemanha com 9%, Áustria 9%, Itália 10%, Taiwan 12%, Israel 13% e Índia 38% (SAWE, 2019).

As dietas vegetarianas e veganas são nutricionalmente adequadas para todos os ciclos de vida, inclusive para prevenção e tratamento de doenças, desde que adequadamente planejadas (CULLUM-DUGAN; PAWLAK, 2015). Uma meta-análise que compreendeu uma grande quantidade de estudos, tendo uma população total de mais de 130.000 vegetarianos e 15.000 veganos, observou que indivíduos vegetarianos apresentaram uma redução significativa do risco de incidência e mortalidade por doença isquêmica do coração (-25%) e de incidência de câncer (-8%), já a dieta vegana (vegetariana estrita) conferiu uma redução significativa do risco de incidência de câncer (- 15%) (DINU et al., 2017).

2.3 Dieta vegetariana na infância

A Academy of Nutrition and Dietetics (2015) relata que dietas vegetarianas e veganas são nutricionalmente adequadas para todos os ciclos de vida, como citado anteriormente, inclusive na infância, desde que as adequações nutricionais sejam realizadas. Ainda, essa posição afirma que crianças vegetarianas e veganas atingem um crescimento adequado e menor risco de problemas de saúde como obesidade quando comparadas com não vegetarianas. Essa condição pode ser evidenciada devido ao maior consumo de frutas e vegetais e menor consumo de gorduras saturadas por crianças vegetarianas (CULLUM-DUGAN; PAWLAK, 2015).

Quanto às adequações nutricionais, o consumo alimentar de indivíduos vegetarianos inclui maior ingestão de frutas, legumes, grãos integrais, nozes, produtos de soja, fibras e fitoquímicos, e menor ingestão de gordura saturada e colesterol comparado à dieta não vegetariana. Assim, na dieta vegetariana deve-se atentar para o consumo adequado de proteína, já que os vegetais não possuem proteínas contendo todos os aminoácidos essenciais, no entanto, com a combinação adequada daqueles que se complementem em relação aos aminoácidos limitantes (como arroz e feijão, por exemplo), é possível obter um perfil de

aminoácidos de qualidade semelhante a animal. Outros nutrientes que necessitam de atenção nessa dieta, para garantir a ingestão satisfatória, são proteínas, ácidos graxos ômega 3, ferro, zinco, cálcio, vitamina D e vitamina B12 (CRAIG; MENGLS, 2009). Lembrando que proteína, LC-PUFAs, ferro e zinco são nutrientes-chave para o neurodesenvolvimento nos primeiros mil dias de vida (CUSICK; GEORGIEFF, 2016).

Uma revisão sistemática de 2017, sobre dietas vegetarianas em crianças de 0 a 18 anos, relatou que indicadores de crescimento como peso corporal, altura e outras medidas antropométricas de bebês, crianças e adolescentes com dieta vegana ou vegetariana são semelhantes aos do grupo controle com dieta onívora, estando dentro dos valores adequados de referência ou ligeiramente abaixo. Porém, os autores ressaltaram que seus achados não foram concretos quanto à existência de benefícios ou riscos para a saúde das dietas vegetarianas atuais, devido à heterogeneidade dos estudos encontrados, ao número pequeno das amostras e a escassez de estudos recentes. (SCHÜRMANN; KERSTING; ALEXY, 2017)

2. 4 Gestação e dieta vegetariana

Como já mencionado, a Academy of Nutrition and Dietetics (2015) relata que dietas vegetarianas são nutricionalmente adequadas para todos os ciclos de vida, incluindo gravidez e lactação. Essa posição ressalta que mulheres vegetarianas durante a gravidez e lactação devem garantir a ingestão adequada de vitamina B12, ferro, folato e zinco e, se necessário, recomendar suplementação para garantia da ingestão desses nutrientes. Além disso, refere que neonatos nascidos de mães vegetarianas, em países desenvolvidos, apresentam maior peso ao nascer e menor prevalência de baixo peso ao nascer em comparação com mães não vegetarianas (CULLUM-DUGAN; PAWLAK, 2015).

Uma revisão sistemática narrativa de 2015 observou que dietas vegetarianas ou veganas durante a gestação não demonstram risco de eventos adversos graves (como pré-eclâmpsia, síndrome HELPP e defeitos congênitos importantes), desde que os déficits de nutrientes principais, como vitamina B12 e ferro, fossem corrigidos. Ainda, perceberam que quando essas dietas são feitas de livre escolha e não relacionadas ao acesso limitado aos alimentos ou à pobreza, os desfechos da gravidez são semelhantes aos relatados na população onívora e que, com os dados disponíveis, esse padrão alimentar é considerado seguro nesse período, desde que se garanta a ingestão dos nutrientes mencionados acima (PICCOLI et al., 2015).

Mais recente, uma meta-analise de 2019 teve como objetivo estabelecer a associação entre dieta vegetariana durante a gravidez e vários desfechos materno-fetais. Foram incluídos 19 estudos observacionais, e os autores concluíram que mulheres asiáticas que seguiram uma dieta vegetariana durante a gestação apresentam maior risco de darem à luz a bebês com baixo peso ao nascer e que os resultados foram inconclusivos em relação aos riscos de hipospádia, retardo do crescimento intrauterino, anemia materna, e diabetes gestacional para mães vegetarianas devido à alta heterogeneidade dos estudos incluídos encontrados (TAN; ZHAO; WANG, 2019).

3 OBJETIVOS

3. 1 Objetivo geral

- Verificar, por meio de revisão sistemática, o impacto de dietas vegetarianas no crescimento e desenvolvimento durante os primeiros mil dias de vida.

3. 2 Objetivos específicos

a) Descrever peso ao nascer de recém-nascidos de mães vegetarianas versus onívoras;
b) Analisar tendências na curva de crescimento nos primeiros mil dias de vida de crianças com dieta vegetariana e onívora;
c) Verificar e comparar descritivamente a idade de aquisição de marcos de desenvolvimento em crianças com dieta vegetariana e onívora

4 RESULTADOS

Artigo:

DO VEGETARIAN DIETS IMPACT IN GROWTH AND DEVELOPMENT IN THE FIRST 1000 DAYS OF LIFE? A SYSTEMATIC REVIEW

Artigo que será submetido à revista Nutrition Reviews após revisão do inglês por empresa especializada

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Abstract:

Aim: To evaluate whether vegetarian diets impact growth and development in the first thousand days of life. **Methods:** Systematic review performed with the Cochrane Collaboration method, with growth and development outcomes. **Results:** 19 studies were included, six subtypes of vegetarian diets were identified. Eight studies assessed birth weight with vegetarian diets, where five found lower birth weight in vegetarian children (but within the normal range) and three found increased risk of low birth weight in vegetarian neonates. As for postnatal growth and development, negative results appeared only in studies from the 1980s with the macrobiotic diet (three studies), while other five studies from that decade (with vegetarian and vegan diets) did not show negative results. **Conclusion:** vegetarian diets seem to be associated with lower birth weight and higher risk of low birth weight. Macrobiotics appears to negatively impact growth and development during the first thousand days of life, while children on other vegetarian diets seem to grow and develop normally.

Keywords *vegetarian; vegan; first 1000 days; child growth*

INTRODUCTION

In recent years, an increase in the number of adherents of vegetarian diets has been observed worldwide. In 2018 a survey conducted in the USA assessing meat-reducing eating behaviors found that two-thirds of the population studied reduced meat consumption in the past three years [1]. Also, a study that investigated the most popular diets among Google users found that veganism, vegetarianism and the gluten free diet were the ones that attract most public interest globally, being veganism the most searched dietary pattern in 23 countries, followed by vegetarianism [2]

Currently, the countries with the highest percentage of individuals following a vegetarian diet are: India with 38% of the total population, Israel 13%, Taiwan 12%, Italy 10%, Austria 9%, Germany 9%, United Kingdom 9%, Brazil 8%, Ireland 6% and Australia 5.5% [3]. Followers of these dietary patterns cite several reasons to join this dietary pattern, such as: health benefits, ethical issues, fear of environmental and social impacts caused by meat consumption and anxiety about the suffering of animals. [4,5]

The vegetarian diet is characterized by abstaining from the consumption of meat and meat products (red meat, poultry, pork, seafood and meat from any other animal). This diet is subdivided into: ovo-lacto-vegetarian (includes eggs and dairy), lacto-vegetarian (includes milk and dairy products), ovo-vegetarian (includes eggs) and strict vegetarian or vegan (excludes all animal products in the diet) [4,6]. There is also pesco-vegetarian (excludes meat and poultry; includes fish, milk, and eggs) and semi-vegetarian (consuming red meat, poultry, or fish no more than once per week, no red meat, and restricting red meat (≤1 times per wk) and poultry intake (≤5 times per wk)) [7]

The plant-based diet can also be vegetarian, which, as the name implies, consists of plant-based foods mainly, but not everyone who follows this diet is motivated to exclude animal products completely [8]. The macrobiotic diet was another widely found in the articles, this diet is predominantly vegetarian, but with an emphasis on natural food, minimally processed foods, rich in complex carbohydrates and low in fat, largely derived from philosophical principles [9].

Because these diets exclude certain foods, there is concern about adequate nutrient intake, especially during pregnancy and childhood. A 2015 systematic review noted that vegetarian or vegan diets during pregnancy did not demonstrate an increased risk of serious adverse events for both mother and baby (such as pre-eclampsia, HELPP syndrome, and major birth defects) since major nutrient deficits, such as vitamin B12 and iron, were corrected during pregnancy. Also, they realized that when these diets are made by choice, properly planned, and not related to limited access to food or poverty, pregnancy outcomes are similar to those reported in the omnivorous population and, with the available data, this dietary pattern might be considered safe during pregnancy [10]

At the same time that the vegetarian diet is gaining more attention, the importance of the ‘first thousand days of life’ – life period that begins at conception and extends to the second year of life - is well established. This concept was first reported in 2008, through a series in the Lancet magazine that showed that the damage occurring in early life can profoundly impact health in the long term [11].

During the first thousand days of life, important brain structures and processes are developed, such as sensory systems, the hippocampus, myelination, and the monoamine neurotransmitter systems, being the most active period of neurological development. Appropriate neurodevelopment occurs in the existence of a healthy environment, a primary caregiver and healthy eating [12].

In view of the increased incidence of adherents to vegetarian diets at different stages of life, it became important to verify evidence of possible impacts of this dietary pattern, especially in the first thousand days of life, since, as mentioned above, this period is of great opportunity and vulnerability for neurodevelopment. Thus, the guiding question of the study was: is there a difference in growth and development during the first thousand days of life in individuals following a vegetarian versus omnivorous diets?

METHODS

The study protocol was registered on PROSPERO (CRD42021232066). To conduct this review, the report for Systematic Reviews and Meta-Analysis Guidelines (PRISMA) [13] was used. The development of the search strategy and the search for articles were carried out with the support of an experienced librarian.

Eligibility Criteria

The PICOS (population, intervention, comparison, outcome, and study design) criteria for inclusion and exclusion are described in **Table 1**. This review included: studies in humans; studies carried out during the gestation period and vegetarian x omnivorous diet focusing on fetal growth; studies with children from 0 to 2 years of age with a vegetarian x omnivorous diet focusing on growth and development; studies that observe the growth and development (with or without observation of other factors) of children with a vegetarian x omnivorous diet; prospective and retrospective cohort studies; cross-sectional studies; case-control studies and randomized controlled trials. Exclusion criteria were: studies in vitro or in animal model; studies whose age range is different from that established; studies of vegetarian populations due to social / economic imposition; studies with transient omnivorous diet during the study follow-up; reviews; expert opinions; case reports;; guidelines; letter to the editor and position papers.

The search was carried out on March 14, 2021. On that day the list of all articles found in the databases was downloaded and then the selection was made in the two following months. The selection of studies was carried out by two independent reviewers, and disagreements were resolved by a third reviewer. The articles were screened initially by the title and abstract, and then, potentially relevant ones were included considering the research

question. After this stage, the articles were fully read and those fulfilling the eligibility criteria were selected. Afterwards, data extraction was performed.

The data collected were related to the publication (journal, year and country of origin), type of study (design, duration of follow-up), population (number of participants, age, sex), factor under study (type of vegetarian and omnivorous diet , follow-up time, diets) and outcome (gestational age, birth weight, birth length, weight, length, head circumference, skinfolds, developmental milestones, head circumference, weight, height, and z-scores from weight to height or percentiles within reference ranges for age and sex, reaching developmental milestones for age according to the Bayley Child Development Scale). All these data will be filled in a standardized spreadsheet developed by the researchers.

Table 1 - PICOS criteria for inclusion and exclusion of studies

Parameter	Inclusion criteria	Exclusion criteria
Participants	Pregnant women and children 0-2 years old	Age range is different from that established;
Intervention	Vegetarian diets; subdivided into: ovolactovegetarian (includes eggs and dairy products), lactovegetarian (includes milk and dairy products), ovovegetarian (includes eggs) and strict vegetarian or vegan (excludes all products of animal origin of food) and Plant based diet	Studies of vegetarian populations due to social / economic imposition; studies in which the population alternate vegetarian and omnivorous diet during the study follow-up; pesco or semi-vegetarian diet.
Control/comparator groups	Omnivorous diet: meat and vegetable consumers	-
Outcomes	Growth (within expected z-scores of healthy children growth charts) and development (expected milestones for age)	-
Study design		

	Prospective and retrospective cohort studies, cross-sectional studies, case-control studies and randomized controlled trials.	Reviews, expert opinions, case reports, short communication, guidelines, letter to the editor and position papers.

Source: Produced by the author.

Search Strategy

Searches were conducted in the following databases: PubMed, Embase and Cochrane Collaboration, on March 14, 2021. The search was also complemented with searches at Prospero to identify possible ongoing studies that have not yet been completed.

The search strategies used were consulted with the librarian and adjusted as appropriate for each database. The strategies used in Pubmed / Medline, Embase and Cochrane Collaboration were as follows (in English), respectively:

- (Fetus [mh: noexp] OR Maternal-fetal exchange [mh] OR Pregnancy [mh] OR Baby [mh] OR Fetus * [tw] OR Fetal [tw] OR Baby * [tw] OR Newborn * [tw] OR baby [tw] OR babies [tw] OR unborn [tw] OR Toddler * [tw] OR Pregnant * [tw] OR nursing [tw] OR newborn * [tw]) AND (Diet, Vegetarian [mh]] OR Vegetarian * [tw]] OR Vegan * [tw] OR Macrobiotic diet * [tw] OR Vegetable based diet * [tw] OR Vegetable diet * [tw] OR Vegetable food * [tw] OR Vegetable food * [tw])
- (Fetus / from OR 'fetomaternal transfusion' / exp OR Pregnancy / exp OR Baby / exp OR Fetus *: ti, ab, kw OR Fetal: ti, ab, kw OR Infant *: ti, ab, kw OR Newborn * : ti , ab, kw OR baby: ti, ab, kw OR babies: ti, ab, kw OR Unborn: ti, ab, kw OR Child *: ti, ab, kw OR Pregnant *: ti, ab, kw OR lactating: ti, ab, kw OR Neonat *: ti, ab, kw) AND (vegetarian diet / exp OR Vegetarian *: ti, ab, kw OR Vegan *: ti, ab, kw OR Macrobiotic diet *: ti, ab, kw OR Plant based diet *: ti, ab, kw OR Vegetable diet *: ti, ab, kw OR Vegetable foods *: ti, ab, kw OR Vegetable foods *: ti, ab, kw)
- Fetus * OR fetal OR infant * OR newborn * OR baby OR babies OR unborn OR small child * OR pregnant * OR lactating OR newborn AND Vegetarian * OR Vegan * OR Macrobiotic Diet * OR Vegetable Based Diet * OR Vegetable Diet * OR Vegetable Food * OR Vegetable Food

A pilot was carried out with key terms to analyze the feasibility of the study and the number of articles available. In addition, the presence of a sentinel article (an article already

known with the theme of the review,) was verified, through a search with pre-determined keywords, in order to verify if the chosen keywords did not exclude relevant articles.

Risk of bias

The assessment of the risk of bias and the methodological quality of the studies was carried out using two questionnaires widely employed in systematic reviews. The Newcastle Ottawa Scale was used to assess observational cohort studies. This questionnaire assesses the methodological quality of observational studies through the assessment of selection, group comparability, outcome assessment methods and adequate follow-up. For cross-sectional studies, the Joanna Briggs checklist was used, the purpose of this checklist is to assess the methodological quality of the study and determine the extent to which the same study addressed the possibility of bias in its design, conduct and method of analysis [14,15]

Data synthesis

The writing of the article will be done in accordance with the PRISMA-P guidelines. In this guideline there is a checklist of 17 items so that a systematic review is planned and everything is explicitly documented (table s1) [13]

RESULTS

Selection of studies

Of the 2,058 articles identified in the databases, 19 studies met the inclusion criteria after screening by reading the titles, abstracts and full text, (**Figure 1)**. These studies included 8 cohorts and 11 cross-sectional studies. They were conducted in 11different countries, USA (n=5), Netherlands (n=3), Israel (n=2), England (n=2), Germany (n=1), Canada (n=1), Italy (n=1), Iran (n=1), Nepal (n=1), China (n=1) and Denmark (n=1).

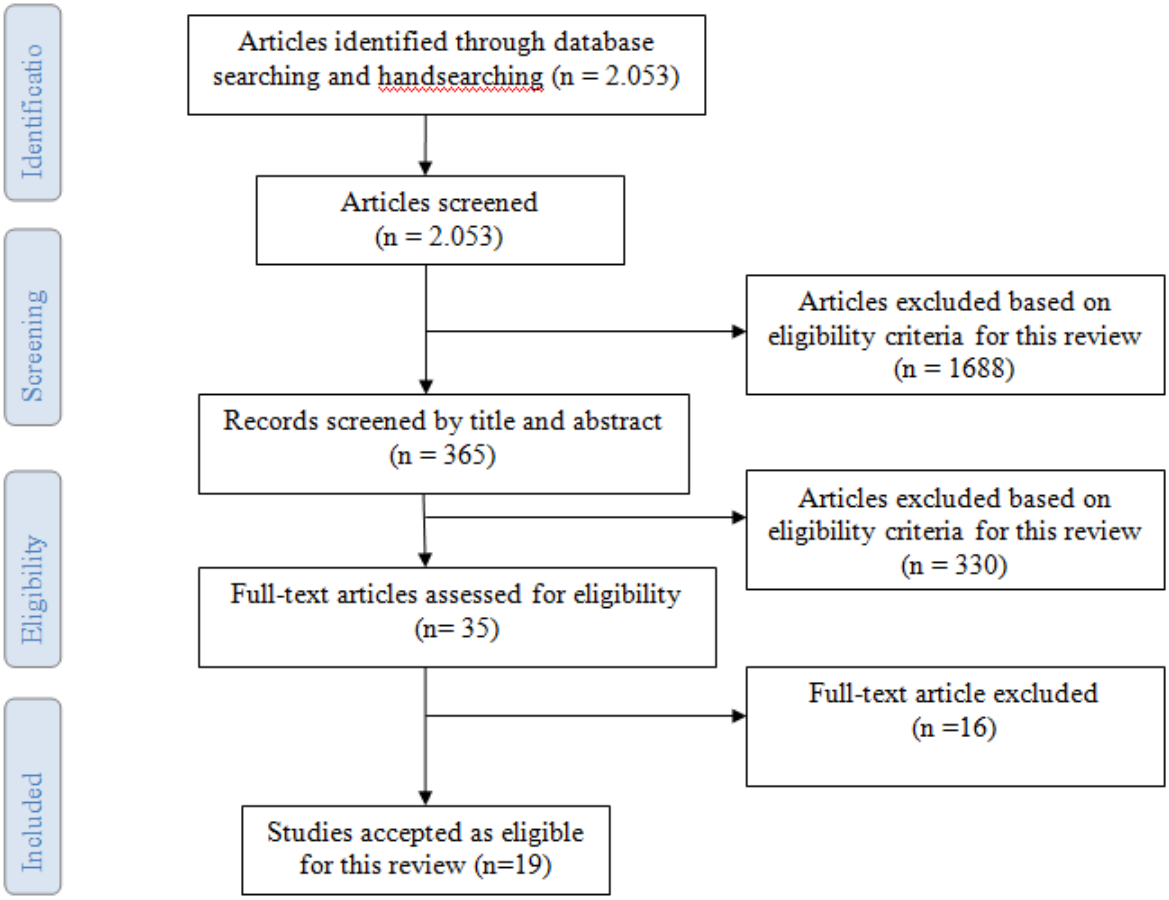

Figure 1 - Flow diagram of literature search and screening process

General characteristics of the studies

The main characteristics of the studies included in this systematic review are described in **Table 2**. At the end of the search, cross-sectional and cohort studies were included, most of which were cross-sectional studies. The sample size ranged from 23 [16] to 5881 [17] participants, and the year of publication from 1978[18] to 2021[19]. As to the types of vegetarian diets, the researched on the vegan and vegetarian diet: four studies evaluated only vegetarian diet without a control group [20] [18] [21], three studies evaluated only vegan diet without a control group [16] [22] [16] and three studies evaluated vegetarian and vegan diets compared to a control group [23] [24] [25]

Table 2 - Characteristics and findings of studies included in this review (n=19)

Reference; Country	Aim	Study design	Sample features	Anthropometric assessment	Neuropsychomotor development	Main findings
(Yisahak et al., 2021); USA	To comprehensively examine the associations of vegetarianism during pregnancy with maternal and neonatal outcomes.	Prospective cohort study	VG self-defined N = 99 Based on diet: VG N = 32 *Pesco- vegetarian N=7 *Semi-vegetarian N = 301	Gestational age at birth; Birth weight; length at birth; Weight; cephalic perimeter; sum of skinfolds	Not evaluated	Infants in a vegetarian diet were more likely to be small for gestational age [adjusted odds ratio (ORadj) = 2.51, 95% confidence interval: 1.01, 6.21], but not being small for gestational age with postnatal morbidity. Vegetarians increased the odds of inadequate gestational weight gain in the second trimester (ORadj = 2.24, 95% confidence interval: 0.95, 5.27). Authors concluded that vegetarian diets during pregnancy were associated with a constitutionally smaller neonatal size, probably through reduced gestational weight gain of the mothers. Vegetarianism was not associated with small-for-gestational-age morbidities.
(Kesary, Avital, & Hiersch, 2020); Israel	Explore the association of vegetarian-vegan diets and pregnancy outcomes.	Prospective cohort study	VG N = 133 VN N = 234 OM N = 1052	Birth weight centile, small for gestational age (SGA), large for gestational age (LGA) and preterm birth (PTB) incidence	Not evaluated	There was a significant difference in weight gain during pregnancy (P=0.002), birth weight (P<0.001). Maternal vegan diet was a protective factor from excessive weight gain (EWG) but associated with a higher risk for SGA (adjusted odds ratio=1.74; 95% CI 1.05, 2.86) and lower birth weight centile when compared to omnivores (42.6±25.9 vs. 52.5±27.0 P<0.001).

(Avnon et al., 2020); Israel	To determine the effect of a maternal vegan diet on pregnancy outcome	Prospective cohort study	VN N = 60 VG (LOV) N= 64 *Pesco-vegetarian N=37 OM N = 112	Gestational age at birth; Birth weight; low birth weigh; number of small for gestational age (SGA) (Dollberg S, et al., 2005)	Not evaluated	The vegan diet was associated with an increased risk for SGA neonates in comparison to omnivores (RR = 5.9, 95% CI, 1.2–21.8, P= 0.021) and lower mean birthweight neonates, though within the normal range, in comparison to omnivores and LOV (3015 ± 420 g vs. 3285 ± 482 g, P= 0.02). Vegans had lower gestational weight gain in comparison to omnivores (11.6 ± 4.2 kg vs. 14.3 ± 4.6 kg, P<0.001). No difference was found between the four diet groups for the incidence of hypertensive complications, GDM, or preterm birth.
(Daneshzad et al., 2020); Iran	To investigate the association between plant-based maternal diets and infant growth in breastfed infants during the first 4 months of life.	Cross-sectional study	Total N = 290 Iranian mothers and infants. The participants were divided into three categories according to the analysis of food consumption: whole plant diet, healthy plant diet and unhealthy plant diet.	Weight; height; head circumference (WHO, 2006)	Not evaluated	No significant associations between plant-based diet scores and anthropometric indices, including weight, weight status and head circumference (P > 0.05).The results also revealed that greater adherence to unhealthy plant-based diet (containing ultra-processed foods) may be associated with short stature among Iranian children, but healthy plant-based diets were not associated with stunting.

(Yan, Dang, Zhang, & Luo, 2020); China	To examine the type of maternal dietary patterns during pregnancy, the distribution of children's birth weight and the association between dietary patterns and neonatal birth weight in China.	Cross-sectional study	Total N = 15.980 VG N = 5881 “balance pattern” N = 4778 “traditional pattern” N = 4442 “processing pattern” N = 879	Gestational age at birth; Birth weight;	Not evaluated	The dietary pattern considered "balanced" (omnivorous) was a protective factor against the occurrence of low birth weight in the northern region (OR = 0.35, 95% CI: 0.14-0.83). The vegetarian (OR = 1.82, 95%CI: 1.36–3.77), and traditional diet (OR = 1.55, 95% CI: 1.05–3.75) may be positively related to an increased risk of low birth weight, while the "balanced pattern" may keep birth weight within the normal range (OR = 0.35, 95%CI: 0.14–0.83). .
(Ferrara et al., 2019); Italy	To compare the anthropometric birth parameters of three groups of children differentiated according to the dietary pattern followed by their mothers during pregnancy. The second objective was to study the cultural inference of vegetarianism.	Cross-sectional study	VN N = 21 mothers and 21 children VG N = 19 mothers and 21 children OM N = 15 mothers and 21 children	Birth weight; length at birth; (WHO, 2006)	Not evaluated	The birth weight of children of vegan mothers was lower than that of children of omnivorous mothers (P= 0.02). No significant difference regarding birth weight however, has emerged from the comparison between the vegan and the lacto-ovo-/lacto-vegetarian group and between the latter and the omnivorous group. No significant difference when comparing length, head circumference and BMI at birth between the three groups.
(Weder et al., 2019) ; Germany	Evalute energy and macronutrient intake, as well as	Cross-sectional study	VG N = 127 VN N = 139 OM N = 164	Birth weight; weight; height; weight/age; height/age; weight/height	Not evaluated	No significant differences between the three groups were found. The results indicate that VG and VN diet in early childhood can ensure normal

	anthropometry of VG, VN and OM children (1-3 years) in Germany			(WHO, 2006)		growth, as there were no significant differences in proxy-reported anthropometrics compared to OM children of the same age.
(Zulyniak et al., 2018); Canada	Investigate the influence of maternal diet on birth weight.	Prospective cohort study	Total N = 3997 VG: 12,3% European whites: 3.5% / South Asians: 37.1%	Birth weight, small (SGA <10th percentile) or large (LGA ≥90th percentile) for gestational age	Not evaluated	Significant difference in birth weight between European (3432 ±466, P<0.001) and South Asian whites (3265 ± 438, P<0.01) on plant-based diets. Among white Europeans, a plant-based diet was associated with lower birth weight (β=−65.9g per 1-unit increase; P<0.001), reduced odds of an infant born LGA (OR=0.71; 95%CI 0.53 to0.95;P=0.02) and increased odds of SGA (OR=1.46; 95%CI 1.08 to 1.54;P=0.005). Among South Asians living in Canada, a plant-based diet was associated with increased birth weight (β=+40.5g per 1-unit increase; P=0.01).
(Koirala & Bhatta, 2015); Nepal	To assess the proportion of low birth weight and identify the associated factors.	Cross-sectional study	Total N = 255 women. VG N = 25 91.4% of the Hindu religion and non-vegetarian majority (90.2%, 95% CI: 86.3–93.7)	Birth weight	Not evaluated	The results of the multivariate analysis showed that vegetarian mothers were more likely to have low birth weights than non-vegetarian mothers (AOR: 1.47; 95% CI: 0.23–9.36). Low birth weight was also associated with type of delivery, ethnicity, Hindu religion, education, informal work and rest during pregnancy, in addition to eating habits.
(Larsen et al., 2014);	To examine the	Prospective	*Pesco- vegetarian N =	Head circumference.	Age at sitting; Age	Total SDQ (Strengths and Difficulties

Denmark	association between maternal vegetarianism and the risk of impaired neurodevelopment, including more subtle impairments, in children.	cohort study	780 VN N = 19 VG (LOV) N= 193 OM N= 77026		at walking (months) (Goodman, 1997)	Questionnaire) scores: non-vegetarians (95% IC 1,62 to 1,64); pesco-vegetarians (95% IC -0,17 to -0,03); lacto-ovo-vegetarians (95% IC 0,21 to 0,04); vegans (95% IC -0,45 to 0,24). The study findings showed that a large, wealthy population with ample access to healthy foods and dietary supplements does not support the prior clinical impairment of impaired neurodevelopment in children of vegetarian mothers.
(Sanders & Reddy, 1992); England	To report the essential fatty acid status of newborn babies breastfed by vegetarian mothers, in addition, birth weight, head circumference and length were observed.	Cross-sectional study	Hindu VG N = 21 White VG N = 18 VN N = 29 OM N = 32	birth weight; birth length; birth head circumference	Not evaluated	The mean weight of the birth of Hindu babies of vegetarian women was 3.18 kg (3.04 to 3,32 kg; 95% CI) compared to 3.48 (3.35 to 3.62 kg; 95 CI %) for white babies born of omnivores. The mean birth weight of 19 babies born of white and vegan mothers was 3.31 kg (3.08 to 3,35, 95% CI). Babies born of Hindu vegetarian women were lighter, lower and had smaller cephalic perimeter ($p < 0.01$). Significant difference remained after parity adjustments, maternal age, height, duration of gestation and smoking habits.
(Dagnelie, van Staveren, Verschuren, & Hautvast, 1989); Netherlands	To examine whether growth retardation in macrobiotic children observed in one cross-sectional study was	Cohort - mix-longitudinal design	Macrobiotic N = 53 OM N = 57	Birth weight	Sit and support head; locomotion; motor development; speech and language development. (Van	There was a significant difference in birth weight, being macrobiotics with lower birth weight (3290 ± 480 g, P = 0.03) than control infants (3470 ± 420 g, P = 0.03). In psychomotor development, the macrobiotic group was significantly more

	supported by longitudinal data and subsequently whether this had consequences for physical and psychomotor development				Wichen Checklist Schlesinger-was 1982, 1985; Meesters-Timmermans, 1982)	delayed in the development of gross motor skills (sit and support your head: P = 0.04; locomotion: P = 0,01; general: P < 0.001) and had a lower degree of speech/language development (P = 0,03). The difference between the groups in the development of gross motor skills is believed to be due to differences in birth weight and weight gain over the 4 to 8 and 12 months, in the development of speech and language the differences were also attributed to this factor
(O'Connell et al., 1989); USA	Examine the effects of a vegetarian diet on child growth, height and weight	Cross-sectional study	Total VG N = 404 (4 months - 10 years) -collected data up to 2 years	Birth weight; weight; height; weight/age; height/age; weight/height (National Center for Health Statistics Growth Curves for Children, Birth-18 Years, 1977)	Not evaluated	Vegetarian children showed adequate growth, albeit modestly lower than that of the reference population (25^{th} and 75^{th} percentiles). The height-for-age difference between children from the farm and children from the reference population decreased with age (P<0.0001).
(Sanders, 1988); USA	Assess the growth and of children born to vegan mothers and raised on a vegan diet	Prospective cohort study	VG N = 12 (1968) VN N = 27 (1981)	Height; Weight; Cephalic perimeter; (TannerJM, Whithouse RH., 1972)	Not evaluated	Measurements were within the normal range for most children. The girls tended to be below the 50^{th} percentile for weight. The boys, however, tended to be below the 50^{th} percentile for both height and weight. Children raised as vegans can grow and develop normally.
(Dagnelie, van Staveren,	To observe at what age	Cross-sectional	Total N (0-8 years) =	Birth weight; weight/age;	Not evaluated	Macrobiotics had a higher percentage of low birth

van Klaveren, & Burema, 1988); Netherlands	growth in children on macrobiotic diets slows down and whether there is any return to standards later in childhood	study	243 boys 0 to 1: N = 25 / girls 0 to 1: N = 24 / boys 1 to 2: N = 21 / girls 1 to 2: N = 21 all on macrobiotic diet.	height/age; weight/height; arm circumference/age; triceps skinfold/age; subscapular skinfold/age. National survey by Roede, M and van Wieringen, J.C, 1985 and curves by TannerJM, Whithouse RH., 1972 were used as a reference		weight (4.3%) compared to the general Dutch population (2%) (P<0.02). It is concluded that macrobiotic children had a height deficit (P < 0.001) and that this indicates the existence of a chronic nutritional deficiency, which do not allow catch-up growth in height in spite of some catch-up in weight, arm circumference and skinfolds.
(van Staveren, Dhuyvetter, Bons, Zeelen, & Hautvast, 1985); Netherlands	Study the effects of alternative dietary practices on nutrient intake and height/weight status	Cross-sectional study	OM: 50 VG: 33 anthroposophic diet: 26 macrobiotic: 33	weight/age; height/age; weight/height; (Roede, M and van Wieringen, J.C, 1980)	Not evaluated	There was a significant difference in weight for age and height for age between all groups (P ≤ 0.05), but no difference was observed when weight for height was assessed. Vegetarians and anthroposophics were leaner and smaller, but within the normal range. Macrobiotics were clearly smaller and leaner, but also within the normal range.
(Dwyer, Andrew, Berkey, Valadian, & Reed, 1983); USA	Compare the growth curve of vegetarian and non-vegetarian children	Cohort (semilongitudinal)	Total N = 142 Macrobotics N = 77 Other vegetarians N=65	weight; height; weight/age; height/age; weight/height (Hamill PVV, et al., 1979)	Not evaluated	Height was affected more than weight. The curves of macrobiotic vegetarian children were more depressed than those of other vegetarian children (P < 0.05), indicating that there was great heterogeneity in growth among vegetarians, which was associated with food group characteristics.

(Sanders & Purves, 1981); England	Assess the nutritional status of vegan children aged 1 to 5 years.	Cross-sectional study	VN N = 23	Birth weight; weight; height; weight/age; height/age; weight/height (TannerJM, Whithouse RH., 1972)	Not evaluated	The birth weight of vegan children was within the normal range (3^{rd} to 97^{th} centile). Most children grew normally (3^{rd} to 97^{th} centile), but tended to be smaller in stature ($<50^{th}$ centile) and lighter compared to standard.
(Dwyer, Palombo, Valadian, & Reed, 1978); USA	Evaluate the effects of vegetarian diets in early life. Compare anthropometric measurements of these children with the established norms	Cross-sectional study	VG total N = 119 (0 to 5 year) -collected data up to 2 years 0 to 6 months N = 18 6 to 17 months N = 27	weight; height; weight/age; height/age; weight/height; triceps skinfold/age Harvard curves (Stuart, H.C., and Reed R.B., 1959)	Not evaluated	Most children (92%) were below the Harvard 50th percentile for weight than would be expected after 6 months of age, but not earlier, and this was due to their having less fat tissue (evaluated by triceps and subscapular skinfolds). There was an association between vegetarian diets and shorter stature and thinness, being more pronounced in older, non-breastfed children and on a macrobiotic diet.

Abbreviations: OR: Odds Ratio, Adj: adjusted; CI, confidence interval; VG, vegetarian; VN, vegan; LOV, lacto-ovo-vegetarian; OM, omnivorous; SGA, small for gestacional age; LGA, large for gestacional age; PTB, preterm birth; EWG, excessive weight gain.

* Diets that did not meet the inclusion criteria, but appeared in included studies along with diets that met the inclusion criteria (vegetarian)

Risk of bias

The characteristics related to methodological quality are described in **Table 3**. The New Castle Ottawa Scale was used in 8 studies, no study reached the maximum score, but three [26] [27][28] reached 8 points. The JBI Critical Appraisal Checklist for Analytical Cross Sectional Studies was applied to 11 articles, of which 4 [23] [29] [17] [30] reached the maximum score (8 points).

Table 3 - Methodological quality of the included studies

	New-Castle Ottawa Scale				*JBI Checklist for Analytical Cross Sectional Studies*	
Reference; Country	Selection (maximum 04)	Comparability (maximum 02)	Outcome (maximum03)	Final score (maximum 09)	Score for: selection, exposure, standardization of measures, confounding factors and outcomes	Final score (maximum 08)
(Yisahak et al., 2021); USA	03	01	03	07	-	-
(Kesary, Avital, & Hiersch, 2020); Israel	02	02	03	07	-	-
(Avnon et al., 2020); Israel	03	03	01	07	-	-
(Daneshzad et al., 2020); Iran	-	-	-	-	07	07
(Yan, Dang, Zhang, & Luo, 2020); China	-	-	-	-	08	08
(Ferrara et al., 2019); Italy	-	-	-	-	05	05

(Weder et al., 2019) ; Germany	-	-	-	-	08	08
(Zulyniak et al., 2018); Canada	04	01	03	08	-	-
(Koirala & Bhatta, 2015); Nepal	-	-	-	-	07	07
(Larsen et al., 2014); Denmark	04	01	03	08	-	-
(Sanders & Reddy, 1992); England	-	-	-	-	06	06
(Dagnelie, van Staveren, Verschuren, & Hautvast, 1989); Netherlands	03	02	03	08	-	-
(O'Connell et al., 1989); USA	-	-	-	-	08	08

(Sanders, 1988); USA	00	00	02	02	-	-
(Dagnelie, van Staveren, van Klaveren, & Burema, 1988); Netherlands	-	-	-	-	08	08
(van Staveren, Dhuyvetter, Bons, Zeelen, & Hautvast, 1985); Netherlands	-	-	-	-	06	06
(Dwyer, Andrew, Berkey, Valadian, & Reed, 1983); USA	01	00	02	03	-	-
(Sanders & Purves, 1981); England	-	-	-	-	05	05
(Dwyer, Palombo, Valadian, &	-	-	-	-	05	05

Reed, 1978);
USA

Dietary patterns

In the present systematic review, six types of vegetarian diets were identified: vegetarian (without specifications), vegan (strict vegetarian), macrobiotic, anthropophic, ovo-lacto-vegetarian and plant based diet, and the semi-vegetarian and pesco-vegetarian also appeared. In addition, one study [19] classified self-defined vegetarians; vegetarians based on diet (who do not define themselves as vegetarian but follow a vegetarian diet); pesco-vegetarians based on diet and semi-vegetarians based on diet.

Vegetarian diets in the first thousand days of life and anthropometric outcomes

Two studies evaluated vegetarian diets during pregnancy with fetal/newborn outcomes. Kesary, Avital, and Hiersch (2020)[24] found that a vegan diet was associated with a higher risk of small-for-gestational age (SGA), vegan groups had 10.3% SGA and omnivore 6.4%, ($P = 0.036$), and lower birth weight ($P < 0.001$). For Yisahak et al. (2021)[31], vegetarian diets during pregnancy were associated with a constitutionally smaller neonatal size, probably through reduced gestational weight gain in mothers.

Ten studies evaluated the birth weight outcome, with divergent findings. Of these, two found a higher risk of low birth weight with the vegan diet [32] [33], Yisahak et al. (2021), found that babies born of vegan mothers had a significantly lower birth weight than omnivores, although birth was still within the normal range. Avnon et al. (2020)[32] and Sanders & Purves, (1981)[16] observed that the birth weight of vegan children was within the normal range. In a study with vegetarian mothers on Nepal, also had a higher risk of having low birth weight babies, but this study found that this increased risk of low birth weight was associated with other factors such as Hindu religion, ethnicity, education, informal work, rest during pregnancy and eating habits [21]. Zulyniak et al. (2018) [26] had an interesting finding when they observed that there was an ethnicity-dependent difference: while among white Europeans a plant-based diet was associated with lower birth weight, among South Asians living in Canada, a diet based on in vegetables was associated with increased birth weight. Dagnelie, et al (1989)[34] observed a difference in birth weight between macrobiotics and omnivores, being macrobiotics with less weight at birth. Still, for Yan, Dang, Zhang and Luo, (2020)[17] the vegetarian pattern may also be positively related to an increased risk of low birth

weight, while one of the omnivorous diets (called the balanced pattern in the article) can maintain newborn weight within the normal range.

As for height, Dagnelie, Van Staveen, Van Klaveren, & Burema (1988) [29]observed that macrobiotic children had a height deficit and that this indicates the existence of a chronic nutritional deficiency. Van Staven, Dhuyvetter, Good, Zeelen, & Hautvast (1985)[35] found a negative difference in height for age among all omnivorous/vegetarian /anthroposophic/macrobiotic groups, but no difference was observed when weight for height was evaluated and all was within the normal range. For O'Connell et al. (1989)[22] vegetarian children showed adequate growth, although modestly lower than that of the reference population. In the study of Dwyer, Palombo, Valadian, & Reed (1978)[18], most of the children evaluated were below the percentile 50 of Harvard curves for height, an association between vegetarian diets and short stature was found, being more pronounced in older children, not breastfed and on a macrobiotic diet. That is, for Van Staven, Dhuyvetter, Good, Zeelen, & Hautvast, (1985)[35], O'Connell et al., (1989) [22] and Dwyer, Palombo, Valadian, & Reed, (1978)[18] children with vegetarian diets were smaller, but not necessarily outside the normal range. Finally, Dwyer, Andrew, Berkey, Valadian & Reed (1983) [18] observed that the length of the children was affected more than the weight, furthermore, reported that the curves of macrobiotic children were more depressed compared to vegetarian children, indicating that there was a high heterogeneity within vegetarians that were associated with dietary characteristics of the group.

Regarding weight-for-age, van Staveren, Dhuyvetter, Bons, Zeelen, & Hautvast (1985)[35] found that vegetarians, anthroposophics and macrobiotics were leaner and smaller than omnivorous, nevertheless within the normal range, and also, as previously mentioned, there was no difference found when assessing weight for height. In the results of Daneshzad et al. (2020)[36] there was no association between the plant-based diet and anthropometric indices, including weight, and concluded that a healthy plant-based diet was not associated with stunting and that this factor it is likely associated with unhealthy plant-based diets. In the study by Dwyer, Palombo, Valadian, & Reed, (1978)[18] most children were below the Harvard 50th percentile for weight than would be expected after 6 months of age, but not earlier, and this was due to the fact that they had less adipose tissue (measured by triceps and subscapularis skinfolds).

Vegetarian diets in the first thousand days of life and developmental outcomes

Only two studies evaluated neuropsychomotor development. Dagnelie, van Staveren, Verschuren, & Hautvast (1989)[34] assessed through a validated checklist that has 6 to 7 items for each age group in the 5 areas of development: gross motor skills , dynamic motor skills, adaptation, speech/language, and personality (Van Wichen checklist Schlesinger-was 1982, 1985; Meesters-Timmermans, 1982) and found that in psychomotor development, the macrobiotic group was significantly more delayed in the development of gross motor skills and had a lower degree of speech/language development. The discoveries of Larsen et al. (2014)[28] showed that a large and rich population with broad access to healthy foods and dietary supplements do not support prior findings of impaired neurodevelopment in children of vegetarian mothers. In this study, The Strengths and Difficulties Questionnaire was employed[37].

DISCUSSION

Adequate nutrition is a concern in the early stages of life because there are several essential nutrients for brain development, and therefore, nutritional deficiencies in this period will have an impact for life. Children who had adequate nutrition, support, and health care, show improved motor and language development when compared to children who did not have these concerns [38]. Therefore, for neurodevelopment to be healthy and adequate, attention must be paid to the child's socioeconomic, interpersonal and nutritional factors during this period [12].

The Academy of Nutrition and Dietetics (2015) reports that vegetarian and vegan diets are nutritionally adequate for all life cycles, including childhood, as long as nutritional adjustments are made. This position also states that vegetarian and vegan children ensure adequate growth and reduced risk of certain health conditions, such as obesity, when compared to non-vegetarians, likely due to a higher intake of fruits and vegetables and lower consumption of saturated fats by vegetarian children [4].

In this review, a consistent finding across studies was that newborns born to vegetarian mothers had lower birth weight (although still in the normal range) [24 32 33 25 3434] or increased risk of low birth weight than neonates born to omnivorous mothers [17 21 29]. Low birth weight is defined by WHO as birth weight less than 2500g. This condition is caused by intrauterine growth restriction, prematurity or both, therefore, it is a fetal

response to a limited environment that may imply an alteration in the development of organs and tissues [39] [40]. Low birth weight is associated with poor health outcomes such as neonatal mortality and morbidity, chronic non-communicable diseases later in life, and inhibited cognitive growth and development [39].

A Dutch cohort found that the macrobiotics had lower birth weight (3290 ± 480) than control infants (3470±420g; P=0.03) [41]. Another included study noted a very important factor, that the plant-based diet had different results in different locations, concluding that among South Asians living in Canada, a plant-based diet was associated with higher birth weight. Thus, it appears that vegetarian diets carried out with planning, ensuring nutritional balance, do not seem to have negative outcomes in terms of birth weight. For example, a 2014 review looked at dietary patterns and birth weight and found that dietary patterns associated with lower birth weight or increased risk of giving birth to a small for gestational age (SGA) baby were characterized by high intake of meat products processed high in fat, sugar, confectionery, sweets, soft drinks and unspecified or refined grains [42].

Another possible explanation would be weight gain during pregnancy. Kesary, Avital, and Hiersch (2020)[24] showed a significant difference in weight gain during pregnancy between pregnant women with vegan/vegetarian and omnivorous diets. They concluded that a maternal vegan diet is a protective factor against excessive weight gain, but associated with a higher risk for SGA (adjusted odds ratio=1.74; 95% CI 1.05-2.86) and lower birth weight centile when compared to omnivores (42.6±25.9 vs. 52.5±27.0; P<0.001).

Our results also suggest that certain types of vegetarian diets in the first 1000 days of life might be associated with some delay in growth and development postnatally. In particular, these studies with negative outcomes are from the 1980s with the macrobiotic diet, three studies from that decade observed that the macrobiotic diet had negative outcomes on growth and development, while another five studies from the same decade (being one from 1978) found that the vegetarian and vegan diets, did not confirmed those findings. However, the macrobiotic diet seems to have lost strength in recent years. According to Kamiński, Skonieczna-Żydecka, Nowak, & Stachowska (2020)[2] there has been a sharp drop in macrobiotic diet research in recent times, what explains the fact that the studies on macrobiotic diet included in this review are mainly from the 1980s.

On the other hand, recently other vegetarian diet modalities have gained more attention [2]. Studies in different populations of children on vegetarian diets have found that children on vegetarian and vegan diets can grow and develop normally, show adequate growth, although modestly inferior to the reference population in some cases [43] [23] [30] [44] [16]. In addition, Daneshzad et al., (2020)[36] found positive results when evaluating the plant based diet in this age group, concluded that a healthy plant based diet were not associated with short stature and there was no significant association between this diet and anthropometric indices including weight status and head circumference. Furthermore, it was noticed that when there is broad access to healthy foods in these diets, children do not present neurological impairment [28].

Regarding growth, a Dutch macrobiotic child population aged 0-8 years (n = 243), found that macrobiotic diets found that there was no satisfactory growth in height in macrobiotic children and this indicates the existence of a chronic nutritional deficiency [29]. At the same time, other studies [44] [23], [30], [35], did not find a stature deficit in children on vegetarian diets and this result is in line with the results in adults described by Rosell, Appleby, & Key (2005)[45], in a cross-sectional study that assessed whether lifetime adherence to a vegetarian diet is associated with height, age at menarche, adult body weight, and body mass index (BMI). The authors concluded that, compared to people who become vegetarian as adults, lifelong vegetarians do not differ in height, weight, BMI or age at menarche in the case of adult women. Also, the study by O'Connell et al. (1989)[22]concluded that the difference in height for age found between children on a vegetarian diet and children from the reference population decreased with increasing age.

Our systematic review found that weight-for-age of vegetarian children tends to be lower when compared to omnivorous children [35] or below the 50th percentile of the weight-for-age curves [18]. However, this difference was not maintained when weight is compared to height, showing that these children were proportional. Moreover, weight tends to be below the 50th percentile, but still within the normal range [35] [18].

With regard to neuropsychomotor development, in the study by Dagnelie, van Staveren, Verschuren, & Hautvast (1989)[34] the macrobiotic group evaluated had impaired neurodevelopment (especially gross motor skills and speech/language development). On the other hand, in the study of Larsen et al. (2014)[28], a vegetarian population with wide access to healthy foods and dietary supplements did not show any impaired in child neurodevelopment. These results corroborate those described by

Crozier et al. (2019)[46], which noted that after controlling for confounding factors, a vegetarian diet during pregnancy was not associated with poorer neurocognitive development in children aged between 6 and 7 years.

Looking for possible explanations why certain vegetarian diets in the first 1000 days of life may be associated with some delay in growth and development, we observed that in the 1985 Dutch birth cohort included here, macrobiotic infants were the least supplemented with vitamin A, vitamin D and iron (less than 5%)[35]. Additionally, their major source of energy and protein were cereals and pulses, foods with low fat content and rich in non-digestible carbohydrates. However, the authors highlighted that all evaluated groups (vegetarian, anthroposophic and macrobiotics) had energy intake within daily recommendations, except for vitamin D, calcium and riboflavin that were lower in the macrobiotic group. [35]. Another micronutrient that may be related to negative developmental outcomes of the macrobiotic diet is vitamin B12. One study found that the concentration of vitamin B12 in the plasma of macrobiotic infants was low enough to have physiological consequences, which also raised concerns about the neurological aspect of development in these infants [34]

In the end, the present study included articles found in the literature that had different scores in terms of methodological quality. Most articles had median to good results in this analysis, being considered adequate methodological quality and, therefore, making our results in this systematic review more solid. However, one of the studies had a low methodological score regarding quality [30] . However, there is a paucity of studies assessing the outcomes evaluated in vegetarians, with most of the ones included here being from the 1980s. Many things have changed in the past three decades, including eating patterns, growth charts references and living standards, so there is an urgent need to reappraise the outcomes studied in contemporary vegetarian populations.

In conclusion, vegetarian diets appear to be associated with a lower birth weight, but whitin the normal range in most cases. The different subtypes of the vegetarian diet appear to impact growth and development differently on the first 1000 days of life, with macrobiotic diet showing poorer growth and developmental outcomes. In general, more recent studies show that children on vegetarian diets grow and develop as expected for their age or within normal limits in the first 1000 days of life. We further emphasize that there are few robust studies evaluating each subtype of vegetarian diet in the outcomes studied.

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CONCLUSÕES

Em conclusão, os estudos incluídos na revisão apresentaram, em sua maioria, moderada a boa qualidade metodológica e alguns de baixa qualidade metodológica. Os estudos variaram dos anos de 1978 até o ano atual (2021) e tiveram uma variedade de dietas vegetarianas estudadas, foram seis subtipos da dieta encontrados: vegetariana, vegana, macrobiótica, antroposófica, ovo-lacto-vegetariana e a dieta à base de plantas, ainda, apareceram a dieta semi-vegetariana e a pesco-vegetariana.

O peso ao nascer foi a medida mais avaliada nos estudos incluídos nessa revisão (8 dos 19 estudos incluídos). Conclui-se que neonatos de mães vegetarianas apresentam menor peso ao nascer em comparação com o peso ao nascer de neonatos de mães onívoras, mas dentro da normalidade (acima de 2500g). Porém, com base em outros três estudos, dessa revisão, que avaliaram o risco de baixo peso ao nascer, constatou-se que bebês de mães vegetarianas apresentam maior risco de baixo peso ao nascer.

Verificou-se que a tendência de crescimento, avaliadas pelas curvas, nos primeiros mil dias de vida de crianças com alguma dieta vegetariana, tende a ser ligeiramente abaixo da curva de crescimento da população geral ou do Percentil 50th, mas dentro da faixa de normalidade. Houve ainda tendência de menor estatura para idade e peso para idade no grupo vegetariano, mas quando avaliado o peso em relação à estatura, percebeu-se que as crianças eram proporcionais, apresentavam um peso adequado para a estatura.

Quanto ao desenvolvimento, as conclusões foram mais limitadas devido ao baixo número de estudos que avaliaram esse desfecho nos primeiros mil dias de vida com dietas vegetarianas. Apenas dois estudos incluídos avaliaram desenvolvimento, um deles concluiu atraso no desenvolvimento motor e de linguagem de crianças com dieta macrobiótica, já outro não constatou prejuízo no desenvolvimento de crianças vegetarianas.

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6 APENDICE

Tabela S1. Lista de verificação que será utilizada para planejar e documentar a revisão sistemática (PRISMA-P 2015 checklist) (MOHER et al., 2015).

Section/topic	Item #	Checklist item
ADMINISTRATIVE INFORMATION		
Title		
Identification	1ª	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number
Authors		
Contact	3ª	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments

Support		
Sources	5[a]	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records		
Data management	11[a]	Describe the mechanism(s) that will be used to manage records and data throughout the review

Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data		
Synthesis	15[a]	Describe criteria under which study data will be quantitatively synthesized
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2, Kendall's tau)
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)