DOI: 10.1111/1471-0528.13280
www.bjog.org

Systematic review

Vegan–vegetarian diets in pregnancy: danger or panacea? A systematic narrative review

GB Piccoli,[a] R Clari,[a] FN Vigotti,[a] F Leone,[b] R Attini,[b] G Cabiddu,[c,d] G Mauro,[e] N Castelluccia,[e] N Colombi,[e] I Capizzi,[a] A Pani,[c] T Todros,[b] P Avagnina[f]

[a] SS Nephrology, Department of Biological and Clinical Sciences, University of Torino, Torino, Italy [b] Maternal–Fetal Unit, Department of Surgery, University of Torino, Torino, Italy [c] Nephrology, Brotzu Hospital, Cagliari, Italy [d] Study group on kidney and pregnancy of the Italian Society of Nephrology, Rome, Italy [e] Library of the departments of Biological and Clinical Sciences and Oncology, University of Torino, Torino, Italy [f] Struttura Semplice Dipartimentale Clinical Nutrition, Department of Biological and Clinical Sciences, University of Torino, Torino, Italy
Correspondence: Dr GB Piccoli, Struttura Semplice Nephrology, Department of Clinical and Biological Sciences, University of Torino, Regione Gonzole 10, 10043 Orbassano, Torino, Italy. Email giorgina.piccoli@unito.it

Accepted 19 November 2014. Published Online 20 January 2015.

Background Although vegan–vegetarian diets are increasingly popular, no recent systematic reviews on vegan–vegetarian diets in pregnancy exist.

Objectives To review the literature on vegan–vegetarian diets and pregnancy outcomes.

Search strategy PubMed, Embase, and the Cochrane library were searched from inception to September 2013 for pregnancy and vegan or vegetarian Medical Subject Headings (MeSH) and free-text terms.

Selection criteria Vegan or vegetarian diets in healthy pregnant women. We excluded case reports and papers analysing vegan–vegetarian diets in poverty and malnutrition. Searching, paper selection, and data extraction were performed in duplicate.

Data collection and analysis The high heterogeneity of the studies led to a narrative review.

Main results We obtained 262 full texts from 2329 references; 22 selected papers reporting maternal–fetal outcomes (13) and dietary deficiencies (nine) met the inclusion criteria. None of the studies reported an increase in severe adverse outcomes or in major malformations, except one report of increased hypospadias in infants of vegetarian mothers. Five studies reported vegetarian mothers had lower birthweight babies, yet two studies reported higher birthweights. The duration of pregnancy was available in six studies and was similar between vegan–vegetarians and omnivores. The nine heterogeneous studies on microelements and vitamins suggest vegan–vegetarian women may be at risk of vitamin B12 and iron deficiencies.

Author's conclusions The evidence on vegan–vegetarian diets in pregnancy is heterogeneous and scant. The lack of randomised studies prevents us from distinguishing the effects of diet from confounding factors. Within these limits, vegan–vegetarian diets may be considered safe in pregnancy, provided that attention is paid to vitamin and trace element requirements.

Keywords Birthweight, maternal–fetal outcomes, pregnancy, vegan diet, vegetarian diet.

Please cite this paper as: Piccoli GB, Clari R, Vigotti FN, Leone F, Attini R, Cabiddu G, Mauro G, Castelluccia N, Colombi N, Capizzi I, Pani A, Todros T, Avagnina P. Vegan–vegetarian diets in pregnancy: danger or panacea? A systematic narrative review. BJOG 2015;122:623–633.

Introduction

Since Hippocrates, whose famous aphorism declared 'Let food be thy medicine and medicine be thy food', diet has been key for health. In the last few decades, the 'ideal' diet has switched from one at low risk of nutritional deficits to a diet that protects one from diseases induced or enhanced by overeating.[1–3]

In this context, the rediscovery of Mediterranean diets and of vegan–vegetarian diets has gained growing interest, mainly because they provide protection from cardiovascular diseases, metabolic syndrome, and cancer.[4–7] With regard to vegan–vegetarian diets, in 2009, the American Dietetic Association (ADA) stated that 'appropriately planned vegetarian diets, including total vegetarian or vegan diets, are healthful, nutritionally adequate, and may provide health benefits in the prevention and treatment of certain diseases'.[8]

Vegan–vegetarian diets have different connotations in richer and poorer countries, being associated with a higher educational level and income in rich countries, and with poverty in poor countries.[9–16] Furthermore, especially in industrialised countries, the association with particular lifestyles makes it difficult to disentangle their effects from other factors, such as smoking, exercise, or overeating.[17–20]

Pregnancy is a unique situation, as diet affects not only the health of the mother but also that of the newborn, which, in turn, is an important determinant of adult health.[21,22] According to the ADA, 'well-planned vegetarian diets are appropriate during all stages of the life cycle, including pregnancy…'; a similar statement is shared by the Canadian Dietary Association.[23]

Despite the great interest, to the best of our knowledge no systematic reviews have specifically focused on vegan–vegetarian diets and pregnancy, except for a short review on the ADA website that discusses seven papers with various outcomes and contrasting results.[24]

There are at least two good reasons for taking into consideration the advantages and disadvantages of vegan–vegetarian diets in pregnancy. The spreading popularity of vegan–vegetarian diets in healthy, well-resourced populations highlights the need to gather more data on how safe they are during pregnancy. Moreover, we must also determine whether women with various health conditions should continue these diets in pregnancy or not.[25] This is especially important in chronic kidney diseases, which affect about 3% of women of childbearing age, who often follow vegan–vegetarian diets.[26–29]

The aim of the study was to systematically review the literature on chosen vegan–vegetarian diets in pregnancy in an effort to clarify the risks and the benefits of these dietary choices.

Methods

Definitions

Vegan diets are defined as diets without animal or animal-derived food. Vegetarian diets include animal-derived food: eggs, honey, milk, and dairy products.

The maternal–fetal adverse events and the nutritional deficits reported in women on vegan–vegetarian diets were considered 'risks', whereas any decrease in risks, as compared with the control population with different dietary patterns, were considered to be 'benefits'.

Study selection criteria

Study population

Studies of women who choose to follow a vegan–vegetarian diet in pregnancy were included. To separate the effects of the diet as a choice from those of 'forced' vegetarian diets arising from poverty, populations for whom vegan diets were associated with low socio-economic status and/or were associated with the need for caloric or protein supplementation were excluded. We further limited the study to 'normal' physiological pregnancies.

Outcome measures

We selected only papers in which information was available on maternal and/or fetal outcomes, including birthweight, gestational age, small for gestational age, pre-eclampsia, all other maternal and fetal complications, or nutritional parameters or deficits.

Study design

We considered randomised controlled trials, observational cohorts, and case series.

We did not include case reports and only included articles reporting on studies with at least five cases.[30]

Search strategy

The search strategy was deliberately broad in order to increase sensitivity, following the guidelines of the Cochrane Collaboration. Database-specific search strategies were applied to PubMed (September 2013), Embase (September 2013), and the Cochrane Central Register of Controlled Trials (September 2013). Reference lists of selected papers were checked for other relevant papers.

Search terms were used as free terms, and as Medical Subject Headings (MeSH) or Emtree terms (indexed on Pubmed or Embase). Terms referring to pregnancy were combined with 'OR', terms referring to the diet were combined with 'OR', and terms referring to both were combined with 'AND'. The following free terms were used on all databases: 'pregnancy', 'vegan' and 'vegetarian'. The following MeSH terms were used: pregnancy, pregnancy complications, pregnancy trimester, pregnancy outcome, pregnancy high-risk, and diet vegan–vegetarian. The following Emtree terms were used: pregnancy, pregnancy outcome, vegan, vegan diet, vegetarian, and vegetarian diet. An additional manual search was carried out on reviewed studies to allow us to identify references that might have been missed in previous searches. No limits were placed on the search, which was performed in duplicate by RC and GBP (working independently and matching their results).

The abstracts and titles were screened by RC and GBP, and any disagreement were resolved by discussion. We tried to contact the authors when the abstract alone was available. The final selection of the articles was agreed upon and the data were extracted in duplicate.

Data collection and analysis

The following data were extracted in duplicate. Baseline data: title, author, objective, year, journal, study period (as stated in the paper), multicentre or single centre, country, type of study, number of cases, control group, maternal age, subcategories, parity, type of diet(s). Maternal and fetal outcomes: maternal weight gain, hypertension, pre-eclampsia, proteinuria, gestational age at delivery, birthweight, preterm delivery, malformations, stillbirth/neonatal death, small for gestational age (SGA), admission to neonatal intensive care unit, other neonatal complications (whenever reported), and maternal and fetal follow-up. Nutritional deficits: any kind of nutritional deficit in the mother or in the newborn, as assessed during pregnancy, at birth, or in the first weeks after parturition. All available data regarding diet patterns and supplementations were also extracted. Statistical significance was reported when available in the papers.

The papers were divided into two major categories: reporting on the maternal and/or fetal outcomes mentioned above; reporting on nutritional deficits.

The choice of whether to perform a narrative review or a meta-analysis depended on the analysis of the type and quality of the retrieved evidence. As we were expecting to deal with high heterogeneity and a lack of randomised trials, a descriptive narrative review was planned: the pooling of data was intended when the same outcomes, with the same measures, were available in two or more papers.

Results

We retrieved and screened 2329 titles and abstracts; 262 papers were then assessed in full and two papers were identified from reference lists, leading to a final selection of 13 studies reporting on maternal and/or fetal outcomes, and of nine studies on dietary deficiencies (Figure 1).

As expected by the nature of the topic, no randomised trials were found, and all the studies were observational (11 prospective, five retrospective, and five cross-sectional). For one study it was not possible to define the design, as it was only available as an abstract.[31] The main characteristics of the studies are reported in Tables S1 and S2.

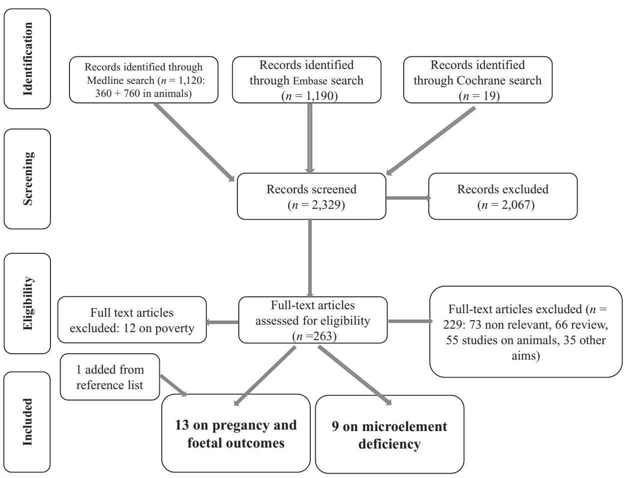

Figure 1. Flow chart reporting on the selection process of the papers considered for the present review.

The geographical origins of the studies were widespread: four were from North America, 14 were from Europe, and four were from Asia (all from India). The studies dated from 1977 to 2013, and varied in the number of cases. The two largest studies involved an entire Seventh-Day Adventist community (7285 people, with the number of women unspecified) and 7928 children born of vegan–vegetarian and non-vegetarian mothers, investigating the role of maternal nutrition in the pathogenesis of hypospadias (Tables S1 and S2).[31–52]

Most of the studies on maternal–fetal outcomes were single-centre studies and the main outcomes that were measured included maternal outcomes (body mass index, gestational weight gain, and incidence of pre-eclampsia/eclampsia or other complications during pregnancy) and fetal outcomes (birthweight, number of SGA babies, birth length, head circumference, gestational age, stillbirths/miscarriages, and fetal malformations) (Tables 1 and 2).[31–43] Two studies reported maternal outcomes alone, six studies reported fetal outcomes alone, and five studies reported on both.

Most studies compared vegetarian and non-vegetarian women during pregnancy: one study compared pregnant and non-pregnant women (all lactovegetarians),[51] and another compared pregnant vegetarians and non-vegetarians with non-pregnant vegetarian women.[52] Two of the studies contained no control subjects.[38,41]

Fetal outcomes

The reported fetal outcomes were heterogeneous (Tables 1 and 2): five studies showed lower birthweight in the children of vegetarian mothers,[31,39,40,42,43] which was significant in one study,[31] and was non-significant in two studies.[40,42] Statistical significance was not reported in two studies.[39,43] Differences range from 20 to about 200 g, but the clinical relevance of these differences is uncertain. Conversely, birthweight and length were higher in children of vegetarian mothers in two studies,[36–38] although not significantly so in one.[36] The second of these studies reported a significantly higher birthweight (mean 99 g above that of non-vegetarians), and involved a community of Seventh-Day Adventists. Neither of the two studies adjusted for gestational age and sex, thus making the meaningful pooling of data almost impossible. Furthermore, in other studies differences in populations are present, as is the case for pregnancies in Hindu mothers, who do not differ with regard to diet, but who are ethnically and culturally different from European mothers.[42]

As for malformations, one large study that enrolled about 8000 children reported an increased risk of hypospa-

Table 1. Main fetal outcomes in the papers analysed

Author (year)	Ref.	All cases (*n* vegans-vegetarian)	Gestational age vegan–vegetarian	Gestational age controls	Birthweight vegan–vegetarian	Birthweight controls	Other fetal outcomes
Wen (2013)	31	852 women (ns)	Not reported		Not reported		Vegetarian diet during second trimester associated with lower fetal [−0.39 (−0.71, −0.08)] and placental weight [−0.40 (−0.79, −0.01)] (abstract)
Robic (2012)*	32	27 women (9)	Not reported		Not reported		No significant differences between groups in pregnancy weight gain and birthweight (abstract)**
Alwan (2011)	33	1257 women (114)	4.5% pregnancies delivered before 37 weeks		Not reported		Vegetarians most likely to take iron supplements (OR 2.9, 95% CI 2.0–4.3, $P < 0.0001$). Positive relationship between iron intake and customised birth centile (adjusted change per 10 mg/day total iron intake = 2.5, 95% CI 0.4–4.6, $P = 0.02$)
North (2000)	35	7928 children (3211)	Not reported		Not reported		Vegetarian aOR 4.99 (95% CI 2.1–11.88) of boy with hypospadias compared with omnivores. Other associations: omnivores with iron supplementation (OR 2.07, 95% CI 1.00–4.32), influenza in first trimester (aOR 3.19, 95% CI 1.50–6.78)
Lakin (1998)	36	19 women (4)	$40^{+5\,\pm\,5}$ weeks	$40^{+1\,\pm\,9}$: omni 40 weeks $50^{+5\,\pm\,5}$: diab. omni	3770 ± 500 g	3673 ± 485 g omni, 3365 ± 302 g diab. omni	(Not statistically significant)
Fonnebo (1994)	38	7285 (most vegetarians)	281.3 days: SDA	281.9 days: non-SDA	3599 g SDA	3500 g non-SDA	(Birthweight $P < 0.001$). Birth length (cm): 50.7 (SDA), 50.4 (non-SDA) (difference 0.3, 95% CI 0.1–0.5). RR of death from 28 weeks of gestation onward: 0.87 (95% CI 0.43–0.75)
Reddy (1994)	39	144 women (48)	38.7 (38.1–39.3) weeks	39.5 (39.1–39.8) weeks	3102 g (2926–3278 g)	3449 g (3343–3554 g)	(Birthweight $P < 0.001$). Head circumference (cm): 33.6 (33.0–34.2) in vegetarians, 34.7 (34.3–35.0) in omnivores ($P < 0.001$). No significant differences in length/APGAR index at 1 and 5 minutes
Ward (1988)	40	73 Gujerat (53) 92 Harrow (59)	Not reported		2885 ± 547 g Gujerat 2905 ± 517 g Harrow	2904 ± 383 g Gujerat 2926 ± 635 g Harrow	(Not statistically significant)
Carter (1987)	41	775 women (775)	Not reported		Not reported		One mother had four SGA babies
Campbell-Brown (1985)	42	144 women (59)	38.6 ± 1.5 weeks: Hindu	38.6 ± 2.2 weeks: Hindu 39.5 ± 1.5 weeks: European	2905 ± 517 g Hindu	2926 ± 635 g Hindu 3349 ± 446 g European	Significant birthweight difference between Hindus and Europeans ($P < 0.001$). Low birthweight: Hindu: 22% vegetarians, 21% omnivores; Europeans 3.8%.** Light-for-dates: Hindu: 34% vegetarians 33% omnivores, 6% Europeans**

Table 1. (Continued)

Author (year)	Ref.	All cases (*n* vegans-vegetarian)	Gestational age vegan–vegetarian	Gestational age controls	Birthweight vegan–vegetarian	Birthweight controls	Other fetal outcomes
Thomas (1977)	43	32 women (14)	Not reported		3.1 ± 0.8 (kg)	3.3 ± 1.2 (kg)	Live births (%): 86 (vegans), 88 (nonvegans). Stillbirths/miscarriages (%): 14 (vegans), 12 (Non-vegans)**

ns, not specified; omni, omnivores; Ref., reference; RR Relative risk; SDA, Seventh-Day Adventist; veg, vegetarians.
North (2000): hypospadias in 1% of children from mothers taking iron tablets in first trimester ($P = 0.041$). Lakin (1998): lower weight of placenta in vegetarian mothers ($P < 0.05$); lower intake of all n-6 and n-3 LCPUFA in vegetarians ($P < 0.01$); lower concentration of DHA ($P < 0.05$) and total n-3 LCPUFA ($P < 0.01$) in vegetarian cord. Reddy (1994): lower DHA levels in cord artery and plasma phospholipids in vegetarians ($P < 0.05$). Ward (1988): no statistically significant differences in maternal plasma concentration of zinc and copper between groups. Campbell-Brown (1985): Hindus had a lower average zinc status than Europeans, but there was no evidence of relation with slower rate of intrauterine growth. Ward (1988): Gujerat and Harrow were ethnic groups living in western Countries, in which vegan habits were linked to a cultural habit and not to lack of resources.
*Abstract.
**Statistical analysis not available.

dias in the children of vegetarian mothers (adjusted odds ratio, aOR 4.99; 95% confidence interval, 95% CI 2.1–11.88). There were, however, other associations with an increased incidence of hypospadias: omnivores with iron supplementation versus those without supplementation (adjusted OR of hypospadias 2.07), and having had influenza in the first trimester (adjusted OR of hypospadias 3.19).

Maternal outcomes

Maternal outcomes were also highly heterogeneous, and pregnancy complications such as pre-eclampsia, eclampsia, or hypertension, with or without proteinuria, were not clearly defined in any of the papers.

The oldest study showed a high prevalence of 'toxaemia', the old term presumably encompassing all of the hypertensive disorders of pregnancy, in vegetarian and omnivorous mothers (17% in vegetarian mothers, 19.5% in omnivorous),[43] whereas the subsequent study showed a very low risk, as compared with the usual prevalence of about 3–5% reported in the general population (1/775 vegan–vegetarian mothers with pre-eclampsia and four mothers with oedema and/or proteinuria).[41] In the study by Reddy,[39] the prevalence of hypertension with proteinuria was lower (4%) in vegetarians than in omnivores (12%), whereas the risk of eclampsia was higher in vegetarians (2% versus 0%), although the differences were not statistically significant.

Three more recent studies focused on the effect of vegetarian diets on weight gain during pregnancy, and were either favourable, showing lower weight gain,[34] or neutral, showing similar weight gain as compared with omnivores.[31,32]

Nutritional deficits

The nine papers that studied nutritional deficits analysed various variables: magnesium intake,[44] vitamin B12 intake and vitamin B12 deficits,[45,51] anaemia and iron status or intake,[46,48] folate intake,[47] free fatty acids,[49] and trace metals.[50,52] The cohorts are relatively small (23–109 women), with the exception of a large cross-sectional study from India reporting on 1150 women, half of whom were vegetarians (Table 3).

Once more, the heterogeneous outcomes, designs, and measurements prevented us from pooling the data. Within these limits, the studies suggest that pregnant vegan–vegetarian women may be at risk of developing vitamin B12 and iron deficiency.[45,48] Zinc status was reported as being similar to the omnivorous population in one study,[52] and impaired in another.[50] Conversely, folate and magnesium intake was found to be higher in vegan–vegetarians,[44,47] and free fatty acids are reported as being roughly comparable in the two groups.[49]

Table 2. Main maternal outcomes in the papers analysed

Author (year)	Ref.	All cases (*n* vegans–vegetarians)	Maternal age vegan–vegetarians	Maternal age omnivorous	PE vegan–vegetarians	PE omnivorous	Other outcomes
Wen (2013)*	31	852 (ns)	Not reported		Not reported		No association between vegetarian diet during second trimester and maternal weight gain (abstract)**
Robic (2012)*	32	27 (9)	Not reported		Not reported		BMI 32 weeks of gestation: 23.2 ± 1.8 (vegetarians), 24.3 ± 3.2 (non-vegetarians) ($P < 0.05$). No differences in body mass, BMI, body fat percentage, or pregnancy weight gain at birth and 6 weeks after delivery (abstract)**
Stuebe (2009)	34	1388 (31 + 19)	404 mothers ≥35 years		Not reported		Excessive weight gain inversely associated with vegetarian diet in first trimester (OR 0.46; 95% CI 0.28–0.78). No associations between second trimester vegetarian diet and excessive gain (OR 0.70; 95% CI 0.40–1.20)
Drake (1998)	37	114 (31)	25 (ovo-lacto-vegetarians)	29.9 fish 29.8 omni	Not reported		No significant differences in any pregnancy outcomes between groups**
Reddy (1994)	39	144 (48)	29 (27.9–30.3)	28.4 (27.2–29.5) omnivores	Eclampsia 2% Ht + Ptu 4%	Eclampsia 0% Ht + Ptu 12%	Earlier onset of labour: 10.4% (vegetarians), 1.1% (omnivores) ($P < 0.02$). Emergency caesarean deliveries: 10.4% (vegetarians), 2.2% (omnivores) ($P < 0.05$). Anaemia: 19% (vegetarians), 11% (omnivores) (ns). Eclampsia and Ht + Ptu (ns)
Carter (1987)	41	775 (775)	Not reported		1 PE; 4 oedema and/or proteinuria		–
Thomas (1977)	43	32 (14)	Not reported		Toxaemia 17%	Toxaemia 19.5%	Anaemia (%): 12.5 (vegans), 5.5 (non vegans)[2]. Iron Supplements (%): 21 (vegans), 66 (non vegans)**

BMI, body mass index; fish, pescetarians or fish-eaters; Ht + Ptu, hypertension and proteinuria; ns, not significant; omni, omnivorous; PE, preeclampsia and related disorders; Ref., reference; PUFA, polyunsaturated fatty acids.
Wen (2013): maternal weight gain positively associated with energy intake during second trimester [mean difference in weight *z*–score per 500 Kcal/day increment in energy intake, 0.11 (95% CI 0.05, 0.17)], percentage of energy from protein during first trimester [0.15 (0.02, 0.28)] and PUFA during second trimester [0.25 (0.01, 0.49)]; maternal weight gain inversely associated with physical activity during second trimester [−0.29 (−0.43, −0.15)]. Stuebe (2009): excessive weight gain directly associated with total energy intake (OR 1.11), consumption of dairy (OR 1.09), consumption of fried foods (OR 4.24), percentage of energy from protein (OR 1.10), saturated fat (OR 1.33), PUFA (OR 1.32), and trans fat (OR 1.27); gestational age 39.7 weeks (38.7–40.6 weeks) for women with inadequate or adequate gestational weight gain, 40 weeks (39.0–40.9 weeks) for women with excessive gestational weight gain.
*Abstract.
**Statistical analysis not available.

Discussion

Main findings

The main finding of our review regarding vegan–vegetarian diets in pregnancy is that none of the studies reporting maternal–fetal outcomes demonstrated or indirectly suggested a higher risk of severe, adverse pregnancy-related events, such as pre-eclampsia, HELPP syndrome (chracterised by haemolysis, elevated liver enzymes, and low platelet count), or major birth defects (with the

Table 3. Studies dealing with blood or tissue levels of different elements in vegan–vegetarian pregnancies: main results

Author year	Ref.	All cases (*N* vegans-vegetarians)	Main results	Conclusions
Koebnick (2005)	44	108 (27)	Dietary magnesium intake (mg/day): 508 ± 14 (OLV), 504 ± 11 (LME), 412 ± 9 (controls) ($P < 0.001$). No significant difference in serum and RBC magnesium between groups. Urinary magnesium excretion higher in OLV ($P = 0.023$) and LME ($P = 0.017$) versus controls. Lower occurrence of calf cramps in OLV ($P = 0.004$) and LME ($P = 0.008$) versus controls	Improved magnesium status and lower frequency of calf cramps during pregnancy in plant-based diets
Koebnick (2004)	45	109 (27)	Vitamin B12 intake during pregnancy (μg/day): 2.5 (1.3–3.8) in OLV, 3.8 (3.0–4.9) in LME, 5.3 (4.3–6.3) in controls ($P < 0.001$). Lower serum vitamin B12 levels in OLV ($P < 0.001$) and LME ($P = 0.05$) versus controls. Higher plasma total homocysteine in OLV ($P = 0.032$) and LME ($P = 0.061$) versus controls	Pregnant women consuming a long-term predominantly vegetarian diet have an increased risk of vitamin B12 deficiency
Sharma (2003)	46	1150 (524)	Anaemia (%): 96.18 (vegetarians), 95.3 (halal meat eaters), 96.2 (jhatka meat eaters) (ns)	Very high prevalence of anaemia during pregnancy, no difference according to diet
Koebnick (2001)	47	109 (27)	Folate deficiency: OR 0.1 (95% CI 0.01–0.56) in OLV, OR 0.52 (95% CI 0.2–1.34) in LME versus WD. RBC folate concentrations in OLV positively related to vitamin B12 intake ($r = 0.51$, $P < 0.0001$)	Long-term high vegetable intake favourably affects plasma and RBC folate concentrations during pregnancy and reduces the risk of folate deficiency with adequate vitamin B12 supply
Sharma (1994)	48	46 (21)	Maternal Hb (g/dl): 9.64 ± 0.46 (vegetarians), 10.16 ± 0.35 (non-vegetarians) ($P < 0.001$). Mothers with Hb <10 g/dl (%): 76.2 (vegetarians), 12 (non-vegetarians). Maternal ferritin (ng/ml): 40.4 ± 18 (vegetarians), 61.6 ± 32.2 (non-vegetarians) ($P < 0.02$)	Higher incidence and risk of anaemia and iron deficiency in strict vegetarian mothers and their newborns
Stammers (1989)	49	47 (28)	Maternal plasma free fatty acid (mmol/l): 1.110 ± 0.157 (vegetarians), 0.964 ± 0.096 (non-vegetarians) (ns). Umbilical cord plasma free fatty acid (mmol/l): 0.523 ± 0.027 (vegetarians), 0.521 ± 0.039 (non-vegetarians) (ns)	No problem with deficiency of arachidonic acid in mothers on vegetarian diet and their offspring
Abraham (1982)	50	60 (20)	Zinc intake (mg/day): 7.35 ± 0.42 (vegetarians), 10.2 ± 0.55 (non-vegetarians), 11.5 ± 0.49 (controls) ($P < 0.001$). copper intake (mg/day): 1.38 ± 0.07 (vegetarians), 1.93 ± 0.25 (non-vegetarians), 1.72 ± 0.20 (controls)*	Lower availability of trace elements in vegetarian diet which could lead to deficiency of zinc and copper
Jathar (1981)	51	60 week (60)	RBC vitamin B12 (ng/l): 157 ± 30.4 (non-pregnant women), 126 ± 12.5 (pregnant women with Hb > 10 g/dl), 81 ± 10.7 (pregnant women with Hb < 10 g/dl) (ns)	In normal pregnancy the fall in erythrocyte vitamin B12 is less marked than the fall in plasma levels of this vitamin
King (1981)	52	23 week (12 + 5)	Zinc intake (mg/day): 12.6 ± 0.9 (pregnant vegetarians), 14.4 ± 0.6 (pregnant non vegetarians) ($P \leq 0.01$). Twenty-one percent lower plasma zinc in non pregnant Women ($P \leq 0.01$)	Zinc status affected by pregnancy more than by ovo-lacto vegetarian dietary habits

cross-sect, cross-sectional; Hb, haemoglobin; LME, low meat eaters; Mg, magnesium; ns, not significant; OLV, ovo-lacto vegetarians; Pro, prospective; RBC, red blood cell; Ref., reference; Ret, retrospective; WD Western diet.
Halal meat and Jhatka meat refer to a particular preparation (slaughter) of animal meat.
*Statistical analysis not available.

exception of a higher incidence of hypospadias reported in one study), provided that the two main potential deficits, i.e. vitamin B12 and iron, were corrected (Tables 1-3).

Data regarding birthweight and duration of gestation are contrasting: five studies showed lower birthweight and two studied showed higher birthweight in the children of vegetarian mothers. Similar observations apply to gestation, reported as a few days shorter in some studies and almost identical in others; the mean duration of pregnancy was within the normal range in all cases. Only one study includes data on preterm delivery (4.5% of all cases).[33] Another report showed that the incidence of emergency caesarean sections was significantly higher in vegan–vegetarian mothers (10.4% versus 1.1%), but the reasons for delivery were not reported.[39] Interpretation of the data is difficult, taking into account the lower incidence of pre-eclampsia and the higher prevalence of anaemia in vegan mothers, thus suggesting the presence of complex confounding factors.[39]

The results reported in a large population of Seventh-Day Adventists raise the issue of the influence of lifestyle. This community have particular lifestyle rules (such as abstention from drugs, alcohol, tobacco, and caffeine-containing beverages), thus making it impossible to distinguish the role of diet alone.[38] This is a crucial issue also reflected in the different social patterns in rich, western countries, in which vegan–vegetarian diets are often chosen in the quest for a healthier lifestyle, compared with low-income countries, in which the nutritional deficits may be linked to forced limitations in the availability of food.[53–64]

Other outcomes provided mixed results. A protective effect on the risk of pre-eclampsia in either one or five cases out of 775 women, depending on the chosen definition, may be inferred from an older study; however, the study lacked a control group. A lower incidence is also reported by an older study, with 'toxaemia' being reported in 17% of vegan–vegetarians, versus 19.5% of omnivores. In this case, however, the incidence is higher than what is usually reported in the literature, raising the issue of the definitions of the study outcomes (Tables S1 and S2).

In keeping with the presence of factors other than the type of protein in the diet, the data on the deficiency of micro-elements underline that women on a vegan diet are at higher risk of nutritional deficiencies, in particular of iron and vitamin B12. The lack of information on calories and on the overall protein intake prevents us from coming to definitive conclusions, except for the general warning that attention must be paid to all of the dietary deficiencies that have been described in non-pregnant vegetarians.[45–49,51]

Strengths and limitations

The main limitations of this review are related to the high heterogeneity of the data, the lack of homogeneous control groups, and the fact that very few papers supplied the same information in the same form. There is also an intrinsic relationship between dietary patterns and other lifestyle determinants, and none of the studies corrected for the achievement of biochemical goals, such as ferritin or haemoglobin levels, thus making it impossible to conclude whether the differences, when present, result from dietary pattern, lifestyle, or from the lack of attainment of dietary needs. Importantly, information on overall protein and calorie intake is missing in several studies.

Furthermore, the definition of pregnancy-related adverse events were often missing, and are likely to be different in the various settings and to change over time, thus impairing the contextualisation of the results. In such a setting, we felt that a meta-analytic approach was hardly feasible, and might actually even be misleading.

Within these limits, we feel that the main strength of our study is its novelty, which allows for a better understanding of what is already known about vegan–vegetarian pregnancy, suggesting a few hints for counselling, but also pointing out the need for future research.

Interpretation

The overall interpretation of our findings is that when vegan–vegetarian diets are the result of a free choice and are not linked with limited access to food or with poverty, pregnancy outcomes are similar to those reported in the omnivorous population.

These findings are in line with the statements of the American Dietetic Association and the Canadian Dietary Association: 'well-planned vegetarian diets are appropriate during all stages of the life cycle, including pregnancy'.[8,23]

The absence of data regarding potential harm does not mean that there is no risk of harm; however, even taking into account the limits mentioned above, none of the papers we retrieved (which involved hundreds of vegan–vegetarian pregnancies) reported an increased risk of adverse-pregnancy related events, with the possible exception of a higher incidence of hypospadias in children born to vegan mothers.[35]

A second line of interpretation regards the differences that were recorded for some outcomes, such as birthweight, which was higher in some studies and lower in others. It seems reasonable to suppose that the differences are at least partly linked to subtle differences in dietary habits and, in particular in older studies in which less attention was paid to correcting nutritional deficiencies, to the presence of non-described nutritional deficits. The limits related to the available evidence should be taken into consideration in counselling.

Conclusion

Vegetarian–vegan diets are becoming more and more widespread in the overall population in the Western world, where these dietary patterns correlate with healthy lifestyles and higher incomes, unlike other settings in which 'traditional' vegan–vegetarian diets are often associated with lower energy intake and caloric restrictions as a result of lower incomes and educational levels. In the latter cases, several studies have shown that prenatal dietary supplementation (energy, protein, and micro-elements such as iron and vitamins) improved fetal outcomes, especially birthweight.[53–64]

The issue is very complex, as the recent changes in dietary habits towards a 'westernisation' of diets are associated with increased metabolic diseases in several populations.[65,66]

Considering only those who choose vegan–vegetarian diets without financial constraints, and within the limits of highly heterogeneous, often low-quality or old information (when the reporting and research standards were remarkably different), the available data support the safety of vegan–vegetarian diets in pregnancy, provided attention is paid to compensating for the nutritional deficiencies (mainly of vitamin B12 and iron).[45,47]

Counselling hints

Our study should reassure patients and doctors on the feasibility of vegan–vegetarian diets in pregnancy, both as a personal choice and when indicated for the care or the prevention of specific diseases, such as chronic kidney diseases or cardiovascular diseases, but suggests that it is important to pay attention to nutritional deficits (the available evidence identifies iron and vitamin B12 intake as being crucial).

As the available evidence is scant and the number of papers is small, the 'lack of data' suggests extending all the warnings related to vegan–vegetarian diets to pregnant women, including the possibility of vitamin D and calcium deficiencies. The issue of hypospadias, which was reported as being more frequent in one large study, needs further investigation to identify potential confounding factors, and should be mentioned in counselling.[35]

Research recommendations

The limits of the evidence suggest undertaking further research into these important and emerging issues, both with regard to general pregnancy outcomes and for specific diseases, such as kidney or cardiovascular diseases.

On the basis of the current limits of the evidence, we also suggest that each study should include a detailed description of at least the main determinants of the diet, including calories, proteins, and the distribution of macronutrients, iron, calcium, vitamin B12, and vitamin D intake, if possible at least in the first and last trimester of pregnancy.

Contribution to authorship

GBP and RC designed the study; GBP drafted the initial manuscript. GBP, FNV, and RC carried out the reference search, supported by GM, NCa, and NCo, who retrieved the evidence and selected the papers. GBP and RC extracted the data; GC, FL, RA, and IC participated in making the tables and in writing the final version of the manuscript. AP, PA, and TT were assigned to perform a final check of the manuscript, respectively from a nephrologist's, dietician's, and gynaecologist's point of view.

Funding

No financial support was received to develop this study.

Acknowledgements

We thank Frances Perricone, for her careful language assessment. We also thank the library of the ASOU san Luigi for valuable help in retrieving the selected papers.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Studies assessing maternal and/or foetal outcomes in vegan-vegetarian pregnancies.

Table S2. Characteristics of the studies assessing blood or tissue levels of various trace elements and vitamins in vegan-vegetarian pregnancies. ■

References

1 Willett WC. Diet and health: what should we eat? *Science* 1994;264:532–7.

2 Hu FB, Willett WC. Optimal diets for prevention of coronary heart disease. *JAMA* 2002;288:2569–78.

3 Fung TT, Hu FB. Plant-based diets: what should be on the plate? *Am J Clin Nutr* 2003;78:357–8.

4 Zhang C, Ning Y. Effect of dietary and lifestyle factors on the risk of gestational diabetes: review of epidemiologic evidence. *Am J Clin Nutr* 2011;6(Suppl):1975S–9S.

5 Ajala O, English P, Pinkney J. Systematic review and meta-analysis of different dietary approaches to the management of type 2 diabetes. *Am J Clin Nutr* 2013;97:505–16.

6 Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med* 2013;368:1279–90.

7 Yokoyama Y, Nishimura K, Barnard ND, Takegami M, Watanabe M, Sekikawa A, et al. Vegetarian diets and blood pressure: a meta-analysis. *JAMA Intern Med* 2014;174:577–87.

8 Craig WJ, Mangels AR. Position of the American Dietetic Association: vegetarian diets. *J Am Diet Assoc* 2009;109: 1266–82.
9 Craig WJ. Health effects of vegan diets. *Am J Clin Nutr* 2009;89:1627S–33S.
10 Sommer C, Sletner L, Jenum AK, Mørkrid K, Andersen LF, Birkeland KI, et al. Ethnic differences in maternal dietary patterns are largely explained by socio-economic score and integration score: a population-based study. *Food Nutr Res* 2013;8:57.
11 De Irala-Estevez J, Groth M, Johansson L, Oltersdorf U, Prattala R, Martinez-Gonzalez M. A systematic review of socioeconomic differences in food habits in Europe: consumption of fruit and vegetables. *Eur J Clin Nutr* 2000;54:706–14.
12 Dynesen AW, Haraldsdottir J, Holm L, Astrup A. Socio-demographic differences in dietary habits described by food frequency questions —results from Denmark. *Eur J Clin Nutr* 2003;57:1586–97.
13 Gex-Fabry M, Raymond L, Jeanneret O. Multivariate analysis of dietary patterns in 939 Swiss adults: sociodemographic parameters and alcohol consumption profiles. *Int J Epidemiol* 1988; 17:548–55.
14 Northstone K, Emmett P, Rogers I. Dietary patterns in pregnancy and associations with socio-demographic and lifestyle factors. *Eur J Clin Nutr* 2008;62:471–9.
15 Cuco G, Fernandez-Ballart BJ, Sala J, Viladrich C, Iranzo R, Vila J, et al. Dietary patterns and associated lifestyles in preconception, pregnancy and postpartum. *Eur J Clin Nutr* 2006;60:364–71.
16 Dyett PA, Sabaté J, Haddad E, Rajaram S, Shavlik D. Vegan lifestyle behaviors: an exploration of congruence with health-related beliefs and assessed health indices. *Appetite* 2013;67:119–24.
17 Key TJ, Appleby PN, Rosell MS. Health effects of vegetarian and vegan diets. *Proc Nutr Soc* 2006;65:35–41.
18 Cade JE, Burley VJ, Greenwood DC; UK Women's Cohort Study Steering Group. The UK Women's Cohort Study: comparison of vegetarians, fish-eaters and meat-eaters. *Public Health Nutr* 2004;7:871–8.
19 Chiu TH, Huang HY, Chiu YF, Pan WH, Kao HY, Chiu JP, et al. Taiwanese vegetarians and omnivores: dietary composition, prevalence of diabetes and IFG. *PLoS ONE* 2014;9:e88547.
20 Gilsing AM, Weijenberg MP, Goldbohm RA, Dagnelie PC, van den Brandt PA, Schouten LJ. The Netherlands Cohort Study-Meat Investigation Cohort; a population-based cohort over-represented with vegetarians, pescetarians and low meat consumers. *Nutr J* 2013;12:156.
21 Nyaradi A, Li J, Hickling S, Foster J, Oddy WH. The role of nutrition in children's neurocognitive development, from pregnancy through childhood. *Front Hum Neurosci* 2013;7:97.
22 Zeisel SH. Is maternal diet supplementation beneficial? Optimal development of infant depends on mother's diet. *Am J Clin Nutr* 2009;89:685S–7S.
23 American Dietetic Association; Dietitians of Canada. Position of the American Dietetic Association and Dietitians of Canada: vegetarian diets. *J Am Diet Assoc* 2003;103:748–65.
24 International Confederation of Dietetic Associations. [www.internationaldietetics.org]. Accessed 15 October 2014.
25 Plotnikoff GA. Nutritional assessment in vegetarians and vegans: questions clinicians should ask. *Minn Med* 2012;95:36–8.
26 Williams D, Davison J. Chronic kidney disease in pregnancy. *BMJ* 2008;336:211–5.
27 Piccoli GB, Ferraresi M, Deagostini MC, Vigotti FN, Consiglio V, Scognamiglio S, et al. Vegetarian low-protein diets supplemented with keto analogues: a niche for the few or an option for many? *Nephrol Dial Transplant* 2013;28:2295–305.
28 Piccoli GB, Leone F, Attini R, Parisi S, Fassio F, Deagostini MC, et al. Association of low-protein supplemented diets with fetal growth in pregnant women with CKD. *Clin J Am Soc Nephrol* 2014;9:864–73.
29 Piccoli GB, Attini R, Vasario E, Gaglioti P, Piccoli E, Consiglio V, et al. Vegetarian supplemented low-protein diets. A safe option for pregnant CKD patients: report of 12 pregnancies in 11 patients. *Nephrol Dial Transplant* 2011;26:196–205.
30 Nissen T, Wynn R. The clinical case report: a review of its merits and limitations. *BMC Res Notes* 2014;7:264.
31 Wen X, Justicia-Linde F, Kong K, Zhang C, Chen W, Epstein L, et al. Associations of diet and physical activity with the three components of gestational weight gain. *Am J Epidemiol* 2013;11(Suppl):S1–181. (abstract).
32 Robic T, Benedik E, Bratanic B, Fidler Mis N, Rogelj I, Golja P. Body composition in (NON) vegetarian pregnant women and their neonates. *Clin Nutr Suppl* 2012;7:108.
33 Alwan NA, Greenwood DC, Simpson NAB, McArdle HJ, Godfrey KM, Cade JE. Dietary iron intake during early pregnancy and birth outcomes in a cohort of British women. *Hum Reprod* 2011;26:911–9.
34 Stuebe AM, Oken E, Gillman MW. Associations of diet and physical activity during pregnancy with risk for excessive gestational weight gain. *Am J Obstet Gynecol* 2009;201:58.e1–8.
35 North K, Golding J, The Alspac Study Team. A maternal vegetarian diet in pregnancy is associated with hypospadias. *BJU Int* 2000;85:107–13.
36 Lakin V, Haggarty P, Abramovich DR, Ashton J, Moffat CF, McNeill G, et al. Dietary intake and tissue concentration of fatty acids in omnivore, vegetarian and diabetic pregnancy. *Prostaglandins Leukot Essent Fatty Acids* 1998;59:209–20.
37 Drake R, Reddy S, Davies J. Nutrient intake during pregnancy and pregnancy outcome of lacto-ovo-vegetarians, fish-eaters and non-vegetarians. *Veg Nutr* 1998;2:45–52.
38 Fonnebo V. The healthy Seventh-day Adventist lifestyle: what is the Norwegian experience? *Am J Clin Nutr* 1994;59(Suppl):1124S–9S.
39 Reddy S, Sanders TAB, Obeid O. The influence of maternal vegetarian diet on essential fatty acid status of the newborn. *Eur J Clin Nutr* 1994;48:358–68.
40 Ward R, Abraham R, McFadyen IR, Haines AD, North WRS, Patel M, et al. Assessment of trace metal intake and status in a Gujerati pregnant Asian population and their influence on the outcome of pregnancy. *Br J Obstet Gynaecol* 1988;95:676–82.
41 Carter JP, Furman T, Hutcheson HR. Preeclampsia and reproductive performance in a community of vegans. *South Med J* 1987;80:692–7.
42 Campbell-Brown M, Ward RJ, Haines AP, North WRS, Abraham R, McFadyen IR, et al. Zinc and copper in Asian pregnancies-is there evidence for a nutritional deficiency? *Br J Obstet Gynaecol* 1985;92:875–85.
43 Thomas J, Ellis FR. The health of vegans during pregnancy. Abstract. *Proc Nutr Soc* 1977;36:46A.
44 Koebnick C, Leitzmann R, Garcia AL, Heins UA, Heuer T, Golf S, et al. Long-term effect of a plant-based diet on magnesium status during pregnancy. *Eur J Clin Nutr* 2005;59:219–25.
45 Koebnick C, Hoffmann I, Dagnelie PC, Heins UA, Wickramasinghe SN, Ratnayaka ID, et al. Long-term ovo-lacto vegetarian diet impairs vitamin B-12 status in pregnant women. *J Nutr* 2004;134: 3319–26.
46 Sharma JB, Soni D, Murthy NS, Malhotra M. Effect of dietary habits on prevalence of anemia in pregnant women of Delhi. *J Obstet Gynaecol Res* 2003;29:73–8.

47 Koebnick C, Heins UA, Hoffmann I, Dagnelie PC, Leitzmann C. Folate status during pregnancy in women is improved by long-term high vegetable intake compared with the average western diet. *J Nutr* 2001;131:733–9.

48 Sharma DC, Kiran R, Ramnath V, Khushiani K, Singh PP. Iron deficiency and anemia in vegetarian mothers and their newborns. Indian. *J Clin Biochem* 1994;9:100–2.

49 Stammers JP, Hull D, Abraham R, McFadyen IR. High arachidonic acid levels in the cord blood of infants of mothers on vegetarian diets. *Br J Nutr* 1989;61:89–97.

50 Abraham R. Trace element intake by Asians during pregnancy. *Proc Nutr Soc* 1982;41:261–5.

51 Jathar VS, Inamdar-Deshmukh AB. Erythrocyte vitamin B12 activity in lactovegetarian pregnant Indian women. *Acta Haematol* 1981;65:153–6.

52 King JC, Stein T, Doyle M. Effect of vegetarianism on the zinc status of pregnant women. *Am J Clin Nutr* 1981;34:1049–55.

53 Tofail F, Persson LA, El Arifeen S, Hamadani JD, Mehrin F, Ridout D, et al. Effects of prenatal food and micronutrient supplementation on infant development: a randomized trial from the Maternal and Infant Nutrition Interventions, Matlab (MINIMat) study. *Am J Clin Nutr* 2008;87:704–11.

54 Ganpule A, Yajnik CS, Fall CHD, Rao S, Fisher DJ, Kanade A, et al. Bone mass in Indian children-relationships to maternal nutritional status and diet during pregnancy: the Pune Maternal Nutrition Study. *J Clin Endocrinol Metab* 2006;91:2994–3001.

55 Hui AL, Ludwig SM, Gardiner P, Sevenhuysen G, Murray R, Morris M, et al. Community-based exercise and dietary intervention during pregnancy: a pilot study. *Can J Diabetes* 2006;30:169–75.

56 Widga AC, Lewis NM. Defined, in-home, prenatal nutrition intervention for low-income women. *J Am Diet Assoc* 1999;99:1058–62.

57 Ceesay SM, Prentice AM, Cole TJ, Foord F, Weaver LT, Poskitt EME, et al. Effects on birth weight and perinatal mortality of maternal dietary supplements in rural Gambia: 5 year randomized controlled trial. *BMJ* 1997;315:786–90.

58 Abitbol MM, Taylor-Randall UB, Barton PT, Thompson E. Effect of modern obstetrics on mothers from Third-World Countries. *J Matern Fetal Neonatal Med* 1997;6:276–80.

59 Fikree FF, Midhet F, Souza RMD, Hussain R, Berendes HW. Risk factors for intrauterine growth retardation: results of a community-based study from Karachi. *J Pak Med Assoc* 1994;44:30–4.

60 Sharma DC, Pendse V, Sahay K, Soni BL. The changing pattern of maternal and neonatal anemia at Udaipur during 2 decades in relation to poverty, parity, prematurity and vegetarianism. *Asia Oceania J Obstet Gynaecol* 1991;17:13–7.

61 Mardones-Santander F, Rosso P, Stekel A, Ahumada E, Llaguno S, Pizarro F, et al. Effect of a milk-based supplement on maternal nutritional status and fetal growth in underweight Chilean women. *Am J Clin Nutr* 1998;47:413–9.

62 Ross SM, Nel E, Naeye RL. Differing effects of low and high bulk maternal dietary supplements during pregnancy. *Early Hum Dev* 1985;10:295–302.

63 Viegas OAC, Scott PH, Cole TJ, Eaton P, Needham PG, Wharton BA. Dietary protein energy supplementation of pregnant Asian mothers at Sorrento, Birmingham. II: selective during third trimester only. *BMJ* 1982;285:592–5.

64 McDonald EC, Pollitt E, Mueller W, Hsueh AM, Sherwin R. The Bacon Chow study: maternal nutritional supplementation and birth weight of offspring. *Am J Clin Nutr* 1981;34:2133–44.

65 Singh PN, Arthur KN, Orlich M, James W, Purty A, Job JS, et al. Global epidemiology of obesity, vegetarian dietary patterns, and noncommunicable disease in Asian Indians. *Am J Clin Nutr* 2014;100(Suppl 1):S359–64.

66 Bourne LT, Lambert EV, Steyn K. Where does the black population of South Africa stand on the nutrition transition? *Public Health Nutr* 2002;5:157–62.

