

# Adherence to the Mediterranean diet during pregnancy and behavioural problems at 4 years of age

Esther Cendra-Duarte<sup>1,2</sup>  | Josefa Canals<sup>1,3,4</sup>  | Lucía Iglesias-Vázquez<sup>1,3</sup>  |  
Cristina Jordi<sup>1,3</sup> | Francisco Martín-Luján<sup>2,3,5</sup>  | Victoria Arija<sup>1,2,3,5</sup> 

<sup>1</sup>Universitat Rovira i Virgili, Nutrition and Mental Health (NUTRISAM) Research Group, Reus, Spain

<sup>2</sup>Collaborative Group on Lifestyles, Nutrition, and Tobacco (CENIT), Institut d'Investigació en Atenció Primària IDIAP Jordi Gol. Institut Català de la Salut (ICS), Reus, Spain

<sup>3</sup>Institut d'Investigació Sanitària Pere Virgili (IISPV), Tarragona, Spain

<sup>4</sup>Universitat Rovira i Virgili, Department of Psychology, Centre de Recerca en Avaluació i Mesura de la Conducta (CRAMC), Tarragona, Spain

<sup>5</sup>Institut d'Investigació en Atenció Primària IDIAP Jordi Gol. Institut Català de la Salut (ICS), Barcelona, Spain

## Correspondence

Victoria Arija, Nutrition and Mental Health (NUTRISAM) Research Group, Universitat Rovira i Virgili, C/Sant Llorenç 21, 43201 Reus, Spain.  
Email: [victoria.arija@urv.cat](mailto:victoria.arija@urv.cat)

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## Abstract

There is an increasing prevalence of psychological issues in childhood. Lifestyle factors during pregnancy, including maternal nutrition, have been linked to children's behavioural development. This study aims to assess the impact of adherence to the Mediterranean diet during pregnancy on the behavioural problems of children at the age of 4. A total of 231 mother-child pairs were assessed. Maternal adherence to the Mediterranean diet during pregnancy was estimated using a relative Mediterranean Diet Score (rMED). Behavioural outcomes were evaluated through the Child Behaviour Checklist 1½–5, Teacher's Report Form 1½–5, and Behaviour Rating Inventory of Executive Function—Preschool Version questionnaires. The results indicated that a higher rMED score during pregnancy was associated with a reduced probability of obtaining a clinical score for total problems (OR = 0.42; 95% IC from 0.21 to 0.85), including externalising (OR = 0.29; 95% IC from 0.14 to 0.62), attention problems (OR = 0.32; 95% IC from 0.15 to 0.70), attention-deficit/hyperactivity problems (OR = 0.36; 95% IC from 0.15 to 0.87), oppositional defiant problems (OR = 0.06; 95% IC from 0.06 to 0.75), and depressive problems (OR = 0.38; 95% IC from 0.15 to 0.96). This study highlights the importance of maternal diet, especially Mediterranean diet, during gestation for proper child development.

## KEYWORDS

behavioural problem, child, child development, diet, Mediterranean diet, pregnancy, prenatal nutrition

## 1 | INTRODUCTION

During childhood, emotional and behavioural problems constitute a significant proportion of children's long-term difficulties (National Collaborating Centre for Mental Health UK, S. C. I. for E. UK, 2013). These problems, when manifesting in early childhood, frequently

persist into later stages of life, heightening the susceptibility to lower educational achievement, school dropout, substance abuse, engagement in criminal activities, and emotional instability (Frick & Kemp, 2021). In Europe, a comprehensive study involving 7,682 children aged 6–11 across European countries found that 12.8% of children have a mental health disorder (Kovess-Masfety et al., 2016).

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A recent international meta-analysis focusing on children younger than 7 years reported a pooled prevalence of mental disorders at 20.1% (Vasileva et al., 2021). In Catalonia (Spain), and similarly in other countries, prevalent disorders in clinical and community child populations include behavioural disorders, attention-deficit hyperactivity disorder, and anxiety disorders (Kusters et al., 2023; Okwori, 2022; Vasileva et al., 2021).

The prenatal period is a critical phase for brain maturation and future neurodevelopment (Stiles & Jernigan, 2010). Several environmental factors, including the use of toxic substances such as tobacco and alcohol (Olives et al., 2020), psychological distress (Betts et al., 2015), and obesity (Mina et al., 2017), have been the focus of research due to their implication and influence on this developmental process (Reynolds et al., 2019). Besides, evidence indicates that maternal dietary factors exert an important influence on offspring's neurodevelopment, as alterations in the prenatal nutritional environment may predispose children to long-term pathological conditions, both in physical (Jain et al., 2022) and mental development (Cortés-Albornoz et al., 2021). This phenomenon, known as foetal programming, refers to adaptations or changes in growth and development resulting from the impact of adverse environmental factors (Reynolds et al., 2019).

Current research highlights the significance of a healthy maternal diet, characterised by high consumption of fruits and vegetables, plenty of vitamins, minerals, and antioxidants. Such dietary habits play a crucial role in promoting optimal neurological function and preventing behavioural issues in offspring, specifically hyperactivity-related problems (Miyake et al., 2020b). The Mediterranean diet stands out as a healthful dietary pattern based on high consumption of unprocessed foods, vegetables, fruits, whole grains, legumes, fish, nuts, and olive oil, a low-to-moderate intake of dairy products (mostly in the form of cheese or yogurt), and a low intake of red meat, animal fats, and sugars (Trichopoulou et al., 2014). This dietary pattern is, therefore, rich in monounsaturated fatty acids (MUFA), omega-3 and omega-6 polyunsaturated fatty acids (PUFA), and antioxidants, all of which have been demonstrated to be important for the proper neurological and behavioural development of children (Miyake et al., 2020b; Schuchardt et al., 2010). Adherence to the Mediterranean diet during pregnancy has been associated with several benefits for both the mother and the foetus (Amati et al., 2019; Biagi et al., 2019; Crovetto et al., 2021; Zaragoza-Martí et al., 2022), including neurodevelopment (Crovetto et al., 2023). Recognising this, recent nutritional research has focused on exploring the relationship between prenatal adherence to the Mediterranean diet and offspring's behavioural outcomes. In this sense, children born to mothers with low adherence to this dietary pattern were found to be more susceptible to developing externalising problems and more prone to experiencing depression, anxiety, and autistic traits compared to those born to mothers with high adherence (House et al., 2018; Steenweg-de Graaff et al., 2014).

Considerable efforts have been devoted to investigating child development with a focus on various dietary constituents, including nutrients, specific food items, supplements, and the distinction

### Key messages

- Maternal nutrition during pregnancy has a significant impact on children's development.
- Previous studies showed that prenatal adherence to the Mediterranean diet is associated with beneficial outcomes for both mother and foetus and in children's development outcomes.
- Adhering to a Mediterranean diet during pregnancy is related to lower behavioural problems, especially externalising and attention-deficit hyperactivity disorder, and psychological problems such as depression, in children at 4 years of age.
- Attention should be directed towards maternal nutrition during the prenatal period to ensure proper child neurodevelopment, encouraging mothers to follow healthy nutritional habits.

between healthful and less healthful dietary patterns (Collet et al., 2021; Mesirow et al., 2017; Miyake et al., 2020b; Ocansey et al., 2019). However, limited research has explored the potential influence of the maternal Mediterranean diet and its impact on the behavioural development of children.

The primary objective of this study was to assess how adherence to the Mediterranean diet during pregnancy influences the behavioural outcomes of children at the age of 4 within a cohort of healthy women from the Spanish Mediterranean region.

## 2 | MATERIAL AND METHODS

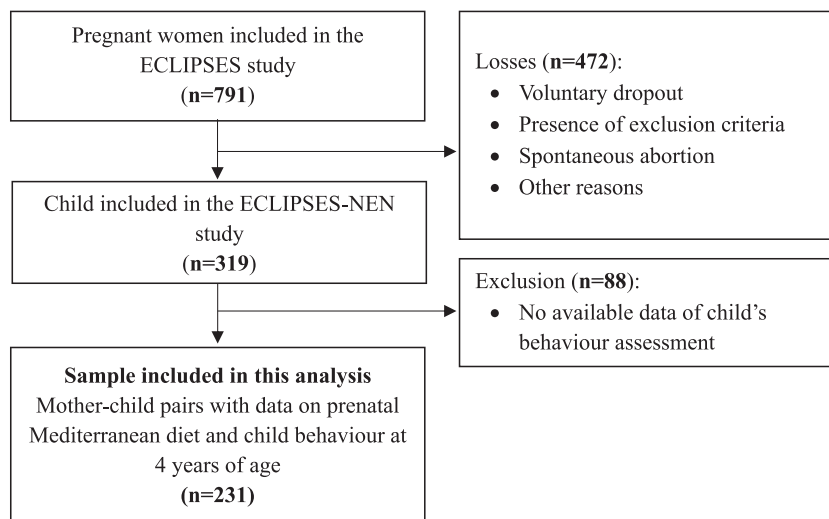
### 2.1 | Study population

The present study draws upon the ECLIPSES study, a community-based research initiative conducted among pregnant women in the province of Tarragona (Catalonia, Spain), which evaluates the enduring effects of dietary, psychological, and environmental factors during pregnancy on offspring outcomes (Arija et al., 2014).

Participants' recruitment was conducted during their initial routine visit with midwives at primary care centres. Inclusion criteria encompassed age over 18, gestation of less than 12 weeks, absence of anaemia, proficiency in understanding the local languages (Catalan or Spanish) and grasping the study's characteristics. The research progression led to the ECLIPSES-NEN study, a subsequent phase involving a follow-up of the women's children up to the age of 4 to comprehensively assess their neurocognitive and behavioural development.

The analyses were conducted based on data from 231 mother-child pairs, comprising information on adherence to the Mediterranean diet during pregnancy and the behavioural assessment of children at 4 years of age (Figure 1). Drop-out was due to voluntary abandonment (such as moving or transfer to other obstetric services),

**FIGURE 1** Flowchart of the ECLIPSES and ECLIPSES-NEN study.



the presence of exclusion criteria (such as maternal or foetal complications during pregnancy), spontaneous abortion, or other reasons.

## 2.2 | Dietary assessment

Maternal dietary habits were evaluated using a Food Frequency Questionnaire (FFQ) validated in our population (Trinidad Rodríguez et al., 2008). Participants self-reported their habitual food consumption during the 12th week, 24th week, and 36th week of pregnancy, as well as at 40 days postpartum.

The questionnaire comprised 45 items, eliciting information on the participants' usual frequency of consumption per week or month. The daily consumption in grams for each item was determined by applying the average consumption ratio usually observed in our population, as derived from prior data obtained from the Food Consumption Estimation study (ECA-REF) (Arija et al., 1996a, 1996b). Additionally, the daily energy intake was also calculated using the REGAL (*Répertoire Général des Aliments*) food composition table (Favier et al., 1995), complemented by data from the Mataix Verdú Spanish food composition table (Mataix et al., 2009).

To evaluate adherence to the Mediterranean diet, we utilised the relative Mediterranean Diet Score (rMED), a modified version of the original Mediterranean Diet Score (Trichopoulou et al., 2003), focusing on the intake of 9 dietary components. For score calculation, each component (excluding alcohol) was expressed as grams per 1000 kcal/day, representing intake as energy density. These values were divided into tertiles, with scores assigned as follows: 0, 1, and 2 points, respectively. Out of the 9 rMED components, 6 were positively scored: fruits (including nuts and seeds but excluding fruit juices), vegetables (including salads), legumes, cereals (including whole grains, refined flours, pasta, rice, bread, and other cereals), fresh fish (including seafood), and olive oil. Two components had inverse scores: total meat (including processed meat) and dairy products (including milk, yogurt, cheese, and creamy desserts).

Alcohol was categorised as 0 points for alcohol consumers and 2 points for non-consumers. The rMED score was calculated for each trimester and then averaged over the three trimesters, resulting in a pregnancy-wide rMED score ranging from 0 points (minimum adherence) to 18 points (maximum adherence). This overall rMED score was divided into tertiles, creating the following categories: 0 to 8 (low adherence), 9 to 10 (moderate adherence), and 11 to 18 points (high adherence).

## 2.3 | Child behaviour assessment

Behavioural problems of children at 4 years of age were assessed by parents using the Behaviour Rating Inventory of Executive Function - Preschool Version (BRIEF-P) (Gioia et al., 2016) and the Child Behaviour Checklist for ages 1.5 to 5 years (CBCL 1½–5) (Achenbach & Rescorla, 2000), and by teachers using the Teacher's Report Form for ages 1.5 to 5 years (TRF 1½–5) (Achenbach & Rescorla, 2000).

The BRIEF-P is a parent-report instrument designed for the behavioural assessment of executive functions of children aged between 2 and 5 years. Comprises 36 items, with responses indicating the frequency of specific behavioural problems (never, sometimes, frequently) over the preceding 6 months. The following test scales and indexes were accounted for in the present study: inhibition, flexibility, emotional control, working memory, plan/organise, behavioural regulation index, flexibility index, meta-cognition index, and the global executive index. T-scores (mean 50, SD 10) were used, where elevated scores suggest a higher degree of behavioural or executive dysfunction, being the clinical range a score of  $\geq 65$  points. We used the Spanish-adapted edition of the BRIEF-P (Gioia et al., 2016) which demonstrated favourable reliability and validity in the data.

The CBCL 1½–5 and the TRF 1½–5 are parent-report and teacher-report tests, respectively, comprised of 99 items with three possible responses (not true, sometimes true, very true) about parental and teacher perception of a child's emotional, behavioural,

and social problems. The assessments provide 6 syndrome scales (emotional reactive, anxious/depressed, somatic complaints, withdrawn, attention problems, and aggressive behaviour), 5 DSM (Diagnostic and Statistical Manual of Mental Disorders)-oriented scales (depressive problems, anxiety problems, autism spectrum problems, attention deficit/hyperactivity problems, and oppositional defiant problems), and 3 broad-band scales formed by the syndrome scales (attention problems and aggressive behaviour constitute the externalising problems, while the remaining ones constitute the internalising problems, and all together form the total problems). T-scores were employed, with scores of 65 or above for both syndrome and DSM-oriented scales considered to be clinical outcomes, and scores of 60 or above for broad-band scales considered to be clinical outcomes.

## 2.4 | Covariates

The baseline information recorded from the participants included the following: age, educational level (primary, secondary, and university studies), and lifestyle habits including smoking (assessed using the Fagerström test (Heatherton et al., 1991)). During pregnancy, anthropometric measurements (weight and height) were collected, from which body mass index (BMI) was calculated and classified according to WHO's criteria (World Health Organisation (World Health Organisation WHO, 2006): underweight ( $<18.5 \text{ kg/m}^2$ ), normal weight ( $18.5\text{--}24.9 \text{ kg/m}^2$ ), overweight ( $25\text{--}29.9 \text{ kg/m}^2$ ), and obesity ( $\geq 30 \text{ kg/m}^2$ ). Maternal anxiety status was also collected during pregnancy, and it was evaluated by the State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1994). The STAI test assessed two distinct concepts of anxiety: "state" and "trait", and in our analyses, we focused on trait anxiety scores. At 4 years of the children, mothers fulfilled the General Health Questionnaire (GHQ) (Goldberg et al., 1997) to provide information on their emotional status (including depression and anxiety symptoms).

Regarding information about the children, the following data were recorded at birth: the child's sex and gestational age (calculated from the time since the first day of the last menstruation). At 4 years of age, the months of breastfeeding duration and the children's dietary assessment were recorded. Based on the dietary assessment, a diet quality index was calculated using the Spanish Diet Quality Index (SDQI) (Norte Navarro & Ortiz Moncada, 2011). This index categorises ten food groups based on their nutritional quality: cereals, vegetables, fruits, milk and dairy products, meats (including lean meats, fish, and eggs), legumes, cold meat, sweets (including sweet cereals), sugary beverages, and variety. The index compared real consumption with recommended servings (Sociedad Española de Nutrición Comunitaria SENC, 2004), assigning a score that can range from 0 (does not meet the recommendations) to 10 (meets the recommendations) for each group of food. The sum of the scores allows for a final score ranging from 0 to 100 points.

## 2.5 | Statistical analyses

The results were presented as mean and standard deviation for quantitative variables and percentage for categorical variables. Student's t-test and Chi-square test were used to examine the differences in baseline characteristics among the two categories of rMED adherence (low-moderate and high).

Multivariable analyses were conducted using multiple linear regression models to quantify the association between the exposure and each outcome independently. Logistic regression models were employed to calculate the risk of having a clinical outcome. All models were adjusted for maternal and child covariates based on prior literature as follows: maternal first trimester BMI, maternal smoking during pregnancy, maternal anxiety during pregnancy, maternal anxiety or depression at 4 years, maternal education, gestational age, breastfeeding duration, child's sex, and child's diet quality. For all analyses, statistical significance was set at a  $p$ -value  $< 0.05$ . The analyses were conducted using IBM SPSS Statistics for Windows, version 29.0 (Armonk, NY: IBM Corp).

## 3 | RESULTS

Maternal and child general characteristics are detailed in Table 1 for the total sample and stratified by rMED score categories. Overall, the mother's age mean at enrolment was  $31.75 \pm 4.53$  years and the first trimester BMI mean was  $25.03 \pm 4.48 \text{ kg/m}^2$ . Of the mothers, 46.3% had completed university studies, 14.7% reported tobacco consumption during pregnancy, and 64.3% exhibited symptoms of anxiety or depression at 4-year visit. The trait anxiety during pregnancy means score ( $14.04 \pm 7.92$ ) fell within the average range of this test scores. The overall mean rMED score was  $9.83 \pm 2.07$ . Among the total sample, 62.8% scored for low-moderate adherence to the Mediterranean diet, while 37.2% exhibited high adherence.

Regarding child characteristics (50.2% girls), their mean age was  $4.30 \pm 0.38$  years, with a mean gestational age of  $39.85 \pm 1.23$  months, and an average duration of breastfeeding of  $11.24 \pm 12.56$  months. The mean child's diet quality score was  $61.81 \pm 10.48$ , out of a maximum of 100 points.

The child psychological tests mean scores in the total sample and by rMED categories are presented in Supplementary Table 1. All CBCL  $\frac{1}{2}$ –5, TRF  $\frac{1}{2}$ –5, and BRIEF-P mean scores fell within considered normal ranges. For CBCL  $\frac{1}{2}$ –5, children whose mothers had low-moderate adherence to the Mediterranean diet scored significantly higher for attention problems ( $p$ -value: 0.008) and aggressive behaviour ( $p$ -value: 0.010), both of which constitute the externalising problems, which also resulted in higher scores ( $p$ -value: 0.004), as well as total problems ( $p$ -value: 0.047). At the level of DSM-oriented scales, depressive problems ( $p$ -value: 0.018), attention deficit/hyperactivity problems ( $p$ -value: 0.008), and oppositional defiant problems ( $p$ -value: 0.038) also showed significantly elevated scores compared to children whose mothers had high adherence. In the case of TRF  $\frac{1}{2}$ –5, only externalising problems scored significantly higher ( $p$ -value: 0.025) for children with mothers with low-moderate Mediterranean diet adherence.

**TABLE 1** Mother and child baseline characteristics.

| Mother                                              | Total cohort<br>(n = 231) | Adherence to the Mediterranean diet |               |
|-----------------------------------------------------|---------------------------|-------------------------------------|---------------|
|                                                     |                           | Low-moderate<br>(n = 145)           | High (n = 86) |
| Age (years)                                         | 31.75 (4.53)              | 31.20 (4.75)                        | 32.69 (3.97)  |
| First trimester BMI (kg/m <sup>2</sup> )            | 25.03 (4.48)              | 25.17 (4.55)                        | 24.79 (4.39)  |
| Underweight, n (%)                                  | 5 (2.2)                   | 2 (1.4)                             | 3 (3.5)       |
| Normal weight, n (%)                                | 131 (56.7)                | 86 (59.3)                           | 45 (52.3)     |
| Overweight, n (%)                                   | 64 (27.7)                 | 37 (25.5)                           | 27 (31.4)     |
| Obesity, n (%)                                      | 31 (13.4)                 | 20 (13.8)                           | 11 (12.8)     |
| Maternal education level, n (%)                     |                           |                                     |               |
| Primary studies                                     | 44 (19.0)                 | 22 (15.2)                           | 22 (25.6)     |
| Secondary studies                                   | 80 (34.6)                 | 57 (39.3)                           | 23 (26.7)     |
| University studies                                  | 107 (46.3)                | 66 (45.5)                           | 41 (47.7)     |
| rMED adherence (score)                              | 9.83 (2.07)               | 8.60 (1.26)                         | 11.91 (1.39)  |
| Low-moderate, n (%)                                 | 145 (62.8)                |                                     |               |
| High, n (%)                                         | 86 (37.2)                 |                                     |               |
| Smoking during pregnancy (yes), n (%)               | 34 (14.7)                 | 20 (13.8)                           | 14 (16.3)     |
| Anxiety during pregnancy (score)                    | 14.04 (7.92)              | 14.38 (7.44)                        | 13.47 (8.70)  |
| Anxiety/depression at 4 years visit<br>(yes), n (%) | 146 (64.3)                | 97 (68.3)                           | 49 (57.6)     |
| Child                                               |                           |                                     |               |
| Age (years)                                         | 4.30 (0.38)               | 4.31 (0.39)                         | 4.27 (0.37)   |
| Gestational age (months)                            | 39.85 (1.23)              | 39.74 (1.39)                        | 40.05 (0.87)  |
| Sex (girls), n (%)                                  | 116 (50.2)                | 70 (48.3)                           | 46 (53.5)     |
| Breastfeeding (yes), n (%)                          | 185 (80.1)                | 120 (82.8)                          | 65 (75.6)     |
| Diet quality (score)                                | 61.81 (10.48)             | 61.75 (10.82)                       | 61.91 (9.97)  |

Note: Values are expressed as mean (SD, standard deviation) and number (%), according to the type of variable. Cut-off point for Mediterranean diet adherence: Low-moderate: <11 points; High: ≥11 points.

Abbreviations: BMI: body mass index; rMED: relative MEDiterranean diet score.

In the multivariable analyses, a high prenatal adherence to the Mediterranean diet, compared to low-moderate adherence, was associated with lower scores in the following CBCL 1½–5 scales: attention problems ( $\beta = -2.89$ ; 95%CI from  $-4.72$  to  $-1.07$ ), aggressive behaviour ( $\beta = -2.21$ ; 95%CI from  $-4.09$  to  $-0.34$ ), externalising problems ( $\beta = -4.33$ ; 95%CI from  $-7.06$  to  $-1.61$ ), total problems ( $\beta = -3.25$ ; 95%CI from  $-6.29$  to  $-0.21$ ), DSM depressive problems ( $\beta = -2.31$ ; 95%CI from  $-4.21$  to  $-0.40$ ) and DSM attention-deficit/hyperactivity problems ( $\beta = -2.91$ ; 95%CI from  $-4.93$  to  $-0.89$ ) (Table 2). For TRF 1½–5, only the externalising problems showed a statistically significant reduction ( $\beta = -3.07$ ; 95%CI from  $-5.88$  to  $-0.25$ ) with high Mediterranean diet adherence (Table 2).

Similarly, compared to low-moderate adherence to the Mediterranean diet, prenatal high adherence was independently

associated with a reduced likelihood of obtaining clinical scores for attention problems (OR = 0.32; 95%IC from 0.15 to 0.70), and secondary for externalising problems (OR = 0.29; 95%IC from 0.14 to 0.62), and for total problems (OR = 0.42; 95%IC from 0.21 to 0.85) based on parents' information (CBCL 1½–5). Additionally, prenatal high Mediterranean diet adherence was associated with a lower risk of having DSM attention-deficit hyperactivity problems (OR = 0.36; 95%IC from 0.15 to 0.87) and DSM depressive problems (OR = 0.38; 95%IC from 0.15 to 0.96) (Table 3). In the case of TRF 1½–5, only the DSM oppositional defiant problems odds (OR = 0.06; 95%IC from 0.06 to 0.75) had a significantly lower risk of clinical scores (Table 3).

Concerning the BRIEF-P test, no significant associations were identified among the studied variables in any of the multivariable analyses.

**TABLE 2** Multiple linear regression between high prenatal adherence to the Mediterranean diet and behavioural problems of the child at 4 years of age.

|                                              | Parent report (CBCL 1½–5 scores)<br>(n = 220) |                |                    | Teacher report (TRF 1½–5 scores)<br>(n = 184) |                |                    |
|----------------------------------------------|-----------------------------------------------|----------------|--------------------|-----------------------------------------------|----------------|--------------------|
|                                              | $\beta$                                       | (95% CI)       | p-Value            | $\beta$                                       | (95% CI)       | p-Value            |
| Syndrome scales                              |                                               |                |                    |                                               |                |                    |
| Emotionally reactive                         | -0.16                                         | (-2.53, 2.19)  | 0.889              | 0.37                                          | (-1.41, 2.16)  | 0.680              |
| Anxious/depressed                            | -0.10                                         | (-2.07, 1.85)  | 0.913              | -0.22                                         | (-1.56, 1.11)  | 0.744              |
| Somatic complaints                           | -1.25                                         | (-3.00, 0.49)  | 0.159              | 1.27                                          | (-0.13, 2.68)  | 0.076              |
| Withdrawn                                    | -0.68                                         | (-2.74, 1.36)  | 0.510              | 0.77                                          | (-0.84, 2.38)  | 0.348              |
| Attention problems                           | -2.89                                         | (-4.72, -1.07) | 0.002 <sup>a</sup> | -1.06                                         | (-2.83, 0.70)  | 0.238              |
| Aggressive behaviour                         | -2.21                                         | (-4.09, -0.34) | 0.020 <sup>a</sup> | -1.32                                         | (-3.11, 0.46)  | 0.145              |
| Broad-band scales                            |                                               |                |                    |                                               |                |                    |
| Internalising problems                       | -1.32                                         | (-4.39, 1.74)  | 0.395              | 0.33                                          | (-2.50, 3.17)  | 0.815              |
| Externalising problems                       | -4.33                                         | (-7.06, -1.61) | 0.002 <sup>a</sup> | -3.07                                         | (-5.88, -0.25) | 0.033 <sup>a</sup> |
| Total problems                               | -3.25                                         | (-6.29, -0.21) | 0.036 <sup>a</sup> | -1.92                                         | (-4.93, 1.08)  | 0.209              |
| DSM-oriented scales                          |                                               |                |                    |                                               |                |                    |
| DSM Depressive problems                      | -2.31                                         | (-4.21, -0.40) | 0.018 <sup>a</sup> | -0.08                                         | (-1.84, 1.67)  | 0.925              |
| DSM Anxiety problems                         | 0.22                                          | (-1.92, 2.38)  | 0.836              | 0.45                                          | (-1.07, 1.97)  | 0.561              |
| DSM Autism spectrum problems                 | -0.28                                         | (-2.24, 1.66)  | 0.770              | 0.72                                          | (-1.06, 2.50)  | 0.425              |
| DSM Attention-deficit/Hyperactivity problems | -2.91                                         | (-4.93, -0.89) | 0.005 <sup>a</sup> | -1.70                                         | (-3.71, 0.30)  | 0.096              |
| DSM Oppositional defiant problems            | -1.33                                         | (-3.13, 0.46)  | 0.146              | -1.13                                         | (-2.59, 0.32)  | 0.126              |

Note: Data shown are linear regression models as  $\beta$  regression coefficient with 95% confidence intervals (CI) and p-value. Models adjusted for: maternal first trimester body mass index, maternal smoking during pregnancy, maternal anxiety during pregnancy, maternal anxiety or depression at 4 years visit, maternal education, gestational age, breastfeeding duration, child's sex and child's diet quality. Adherence to the Mediterranean diet (0: low-moderate, 1: high). Abbreviations: CBCL 1½–5: Child Behaviour Checklist 1½–5; DSM: Diagnostic and Statistical Manual of Mental Disorders; TRF 1½–5: Teacher's Report Form.

<sup>a</sup>p-Value < 0.05.

## 4 | DISCUSSION

The present study investigated the association between maternal adherence to the Mediterranean diet during pregnancy and its influence on the behavioural problems of children at 4 years of age. To the best of our knowledge, this is one of the few studies that has assessed the comprehensive Mediterranean diet pattern during pregnancy in relation to child behavioural problems.

Our findings indicate that higher adherence to the Mediterranean diet during pregnancy was linked to a lower presence of behavioural problems in children at 4 years of age. This association is particularly noteworthy in terms of its impact on externalising problems (which include attention problems, aggressive behaviour, DSM attention-deficit/hyperactivity problems and DSM oppositional defiant problems), as well as depressive problems.

Our results are consistent with previous research reporting an increased risk of externalising problems, but not internalising problems, in children between the ages of 1 and 6 years associated with low adherence to the Mediterranean diet during pregnancy (Steenweg-de Graaff et al., 2014). Similarly, an increasing prenatal Mediterranean diet adherence score has been associated with fewer internalising problems,

anxiety/depression, and autism spectrum disorder in children up to 2 years of age (House et al., 2018). These conflicting results highlight that evidence is still scarce and unclear regarding the prenatal Mediterranean diet and its potential influence on child neurodevelopment. However, when considering the Mediterranean diet as part of a broader, healthy dietary pattern, the evidence becomes more extensive. Several studies support, therefore, our findings by demonstrating a positive effect of high maternal adherence to proper nutrition during pregnancy, characterised by a diet rich in fruits, vegetables, seafood, protein, and in turn healthy fatty acids, minerals (such as calcium and iron), and vitamins (such as folates, vitamin B2, vitamin B6, and vitamin C), on child behaviour. This positive influence is reflected in lower behavioural difficulty (Mahmassani et al., 2022), reduced symptoms of anxiety and depression (Collet et al., 2021), and a decreased risk of low prosocial behaviour, hyperactivity, and emotional problems (Miyake et al. 2020b, 2020a). Conversely, in line with our findings, an unhealthy dietary pattern during pregnancy, characterised by a high intake of processed food, refined cereals, sweet drinks, and confectionery, has been associated with more internalising and externalising problems in 5-year-old children (Jacka et al., 2013). Additionally, this unhealthy dietary pattern has been linked to more

**TABLE 3** Logistic regression between high prenatal adherence to the Mediterranean diet and behavioural problems of the child at 4 years of age.

|                                                              | Parent report (CBCL 1½–5 scores)<br>(n = 220) |              |         | Teacher report (TRF 1½–5 scores)<br>(n = 184) |               |         |
|--------------------------------------------------------------|-----------------------------------------------|--------------|---------|-----------------------------------------------|---------------|---------|
|                                                              | OR                                            | (95% CI)     | p-value | OR                                            | (95% CI)      | p-value |
| <b>Syndrome scales (0: score &lt; 65; 1: score ≥ 65)</b>     |                                               |              |         |                                               |               |         |
| Emotionally reactive                                         | 0.79                                          | (0.35, 1.79) | 0.583   | 0.85                                          | (0.22, 3.22)  | 0.813   |
| Anxious/depressed                                            | 1.01                                          | (0.43, 2.35) | 0.971   | 1.70                                          | (0.30, 9.50)  | 0.541   |
| Somatic complaints                                           | 0.76                                          | (0.32, 1.80) | 0.537   | –                                             | –             | –       |
| Withdrawn                                                    | 0.71                                          | (0.31, 1.63) | 0.424   | 1.83                                          | (0.46, 7.17)  | 0.385   |
| Attention problems                                           | 0.32                                          | (0.15, 0.70) | 0.005*  | 0.23                                          | (0.50, 1.07)  | 0.062   |
| Aggressive behaviour                                         | 0.72                                          | (0.25, 2.05) | 0.545   | 0.14                                          | (0.01, 1.10)  | 0.063   |
| <b>Broad-band scales (0: score &lt; 60; 1: score ≥ 60)</b>   |                                               |              |         |                                               |               |         |
| Internalising problems                                       | 0.78                                          | (0.41, 1.48) | 0.451   | 2.14                                          | (0.74, 6.18)  | 0.160   |
| Externalising problems                                       | 0.29                                          | (0.14, 0.62) | 0.001*  | 0.38                                          | (0.12, 1.17)  | 0.093   |
| Total problems                                               | 0.42                                          | (0.21, 0.85) | 0.016*  | 0.77                                          | (0.31, 1.94)  | 0.590   |
| <b>DSM-Oriented Scales (0: score &lt; 65; 1: score ≥ 65)</b> |                                               |              |         |                                               |               |         |
| DSM Depressive problems                                      | 0.38                                          | (0.15, 0.96) | 0.042*  | 0.97                                          | (0.23, 4.00)  | 0.968   |
| DSM Anxiety problems                                         | 0.92                                          | (0.43, 1.98) | 0.850   | 2.87                                          | (0.45, 18.30) | 0.264   |
| DSM Autism spectrum problems                                 | 1.00                                          | (0.47, 2.14) | 0.985   | 0.82                                          | (0.20, 3.23)  | 0.779   |
| DSM Attention-deficit/Hyperactivity problems                 | 0.36                                          | (0.15, 0.87) | 0.024*  | 0.25                                          | (0.06, 1.01)  | 0.053   |
| DSM Oppositional defiant problems                            | 0.37                                          | (0.12, 1.08) | 0.071   | 0.06                                          | (0.06, 0.75)  | 0.029*  |

Note: Data shown are logistic regression models as odds ratio (OR) with 95% confidence intervals (CI) and p-value. Models adjusted for: maternal first trimester body mass index, maternal smoking during pregnancy, maternal anxiety during pregnancy, maternal anxiety or depression at 4 years, maternal education, gestational age, breastfeeding duration, child's sex, and child's diet quality. Adherence to the Mediterranean diet (0: low-moderate, 1: high). CBCL 1½–5: Child Behaviour Checklist 1½–5; TRF 1½–5: Teacher's Report Form; DSM: Diagnostic and Statistical Manual of Mental Disorders.

(\*) p-value < 0.05. (–) No available cases for one of the two categories of the dependent variables.

attention deficit and hyperactivity problems between the ages of 3 to 8 years (Galera et al., 2018), and higher levels of child emotional-behavioural dysregulation at the age of 7 (Pina-Camacho et al., 2015). Moreover, less fish consumption during pregnancy has been correlated with a higher likelihood of children experiencing emotional difficulties during early adolescence compared to those with higher fish intake (Mesirow et al., 2017).

Optimal foetal neurodevelopment relies on various factors that influence foetal growth, a critical period for brain formation (Cusick & Georgieff, 2016). Alterations during this period have the potential to affect offspring outcomes (Emmett et al., 2015; Reynolds et al., 2019). Maternal nutritional status plays an important role in foetal development, as the quality of the prenatal diet contributes to a favourable intrauterine environment (Borge et al., 2019). While all nutrients are essential for neuronal cell growth and development, certain ones exhibit more significant effects during foetal periods: protein, iron, B vitamins such as folate, and long-chain polyunsaturated fatty acid (Georgieff, 2007). These nutrients are necessary for optimal neuronal processes such as myelination, synapse formation, neurotransmitter production (Georgieff, 2007; Miyake et al., 2020a), membrane fluidity, and gene expression regulation (Schuchardt et al., 2010). Suboptimal levels of these nutrients contribute to intrauterine growth retardation,

a lower neuronal number of cells, and reduced oxidative metabolism, which could potentially lead to increased disease risk in children (Georgieff, 2007). Similarly, prenatal malnutrition (involving inadequate nutrient supply and over or under-nutrition) affects hormones and immune factors in the foetus, which has profound effects on foetal growth and programming (Marques et al., 2015). Moreover, exposure to an unhealthy dietary pattern like a high-fat diet during pregnancy increases the levels of inflammatory mediators that can disrupt the balance of growth factors or neurotransmitters and elevate oxidative stress. This alteration in the foetal brain development trajectory raises the risk of behavioural abnormalities in children (Bolton & Bilbo, 2014). On this note, the Mediterranean diet pattern has demonstrated its advantages owing to its well-balanced nutrient content, beneficial fatty acids, and antioxidant vitamins. These components can positively influence neuronal structural development, promote brain health, reduce inflammation, and mitigate oxidative stress (House et al., 2018; Miyake et al., 2020b).

Prenatal nutrition emerges as a significant factor in the behavioural development and psychopathology of offspring. Therefore, heightened consideration of prenatal nutrition not only holds implications for preventing behavioural problems and disorders in children but also for their future personal and academic performance.

Primary prevention programmes targeted at the prenatal period should deliver comprehensive nutritional guidance to pregnant women, encouraging them to enhance their adherence to the Mediterranean diet or similar dietary patterns.

This study has several strengths that are worth mentioning. Firstly, it leverages a representative cohort of mothers and children, derived from a study with a large sample size and a relatively extended follow-up duration. Secondly, the extensive data collection allows for the incorporation of multiple potentially important adjustment variables. Thirdly, the assessment of both child behaviour and maternal Mediterranean diet adherence were conducted through internationally recognised and widely used tools. However, the results should be interpreted considering some limitations: a significant number of participants voluntarily dropped out from the study's outset, a common occurrence in long-term follow-up intervention studies, which could potentially impact the statistical power of the analyses; some unmeasured or unknown risk factors, such as family environment or parenting style, may have introduced residual confounding, as parental warmth and autonomy granting predicted fewer externalising problems, whereas harsh and psychological control predicted an increase in these problems (Pinquart, 2017), but other studies similar to ours were also unable to control for these variables (Pina-Camacho et al., 2015; Steenweg-de Graaff et al., 2014).

## 5 | CONCLUSION

A high adherence to a Mediterranean diet during pregnancy is associated with a reduction in behavioural problems in children at 4 years old, specifically attention-deficit hyperactivity disorder, externalising, and depressive problems. These findings emphasise the importance of prenatal maternal nutrition for proper child development in terms of lifelong mental health and highlight the benefits of the Mediterranean diet.

## AUTHOR CONTRIBUTIONS

Esther Cendra-Duarte conducted the investigation, performed the data analysis and visualisation, wrote the original draft, and reviewed and edited the manuscript. Josefa Canals conducted the conceptualisation, the methodology, and the investigation and reviewed and edited the manuscript. Lucía Iglesias-Vázquez conducted the investigation, and reviewed and edited the manuscript. Cristina Jardí conducted the data curation, investigation and reviewed and edited the manuscript. Francisco Martín-Luján reviewed and edited the manuscript. Victoria Arija designed and conducted the research, was the guarantor of the study, supervised and performed the data curation, and reviewed and edited the manuscript. All authors have read and approved the final manuscript.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

## DATA AVAILABILITY STATEMENT

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

## ETHICS STATEMENT

The study was designed in agreement with the Declaration of Helsinki and the Tokyo update. Approval for all procedures was obtained from the Clinical Research Ethics Committee of the Jordi Gol University Institute for Primary Care Research [Institut d'Investigació en Atenció Primària; IDIAPJGol], the Pere Virgili Health Research Institute [Institut d'Investigació Sanitària Pere Virgili; IISPV] and of the Spanish Agency for Medicines and Medical Devices [Agencia Española del Medicamento y Productos Sanitarios; AEMPS]. Signed informed consent was obtained from all participating women in the study.

## ORCID

Esther Cendra-Duarte  <http://orcid.org/0000-0001-8593-9401>

Josefa Canals  <https://orcid.org/0000-0002-6209-9558>

Lucía Iglesias-Vázquez  <https://orcid.org/0000-0001-7131-4144>

Francisco Martín-Luján  <https://orcid.org/0000-0003-0359-3588>

Victoria Arija  <http://orcid.org/0000-0002-1758-0975>

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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