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Maternal seafood intake and the risk of small for gestational age newborns: a case–control study in Spanish women

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ABSTRACT

Objective To investigate the relationship between seafood consumption during pregnancy and the risk of delivering a small for gestational age (SGA) newborn.

Design This case–control study included women with SGA newborns and controls matched 1:1 for maternal age (±2 years) and hospital.

Setting Five hospitals in Eastern Andalusia, Spain.

Participants 518 pairs of pregnant Spanish women. The SGA group included women who delivered SGA newborns: SGA was defined as a birth weight below the 10th percentile of infants at a given gestational age. Controls were women who delivered newborns with adequate birth weights.

Interventions We collected data on demographic characteristics, socioeconomic status, toxic habits and diet. Midwives administered a 137-item Food Frequency Questionnaire.

Outcome measures We calculated quintiles of seafood intake and applied conditional logistic regression to estimate ORs and 95% CIs.

Results Shellfish intake more than once/week yielded a significant protective effect against an SGA newborn (OR 0.25, 95% CI 0.08 to 0.76, after adjusting for energy, educational level, smoking, prepregnancy body mass index, weight and a history of preterm or low birthweight newborn). The risk of an SGA newborn was lower among women who consumed >29 g/day fish compared with women who consumed ≤8 g (adjusted OR 0.63, 95% CI 0.41 to 0.98; p=0.025 for a trend). Similarly, the risk of an SGA newborn was lower among women who consumed >1 g/day of marine n-3 polyunsaturated fatty acids compared with those who consumed ≤0.4 g/day (adjusted OR 0.58, 95% CI 0.38 to 0.90; p=0.025 for a trend).

Conclusion An average seafood intake of at least 29 g/day during pregnancy, equivalent to 2–3 servings/week, reduced the risk of an SGA newborn, compared with an average seafood intake of less than 8 g/day.

Strengths and limitations of this study

► The sample was representative of a reference population of healthy pregnant women with uncomplicated gestation periods who attended several Andalusian public hospitals.

► The case–control design allowed inclusion of a large number of small for gestational age (SGA) cases.

► We used previously established Spanish fetal growth curves to define the average size for gestational age, and we measured seafood consumption with a Food Frequency Questionnaire previously validated in the Spanish population.

► Spanish pregnant women had a relatively high fish intake (and shellfish intake) compared with pregnant women in other European countries.

► The control group was selected, based on 'density sampling', from the same hospitals that served the women with SGA newborns.

INTRODUCTION

Seafood is an important source of nutrients. It contains proteins, vitamin D, minerals (iodine and selenium), and essential n-3 long-chain polyunsaturated fatty acids (n-3 LCPUFAs). There are three categories of seafood: lean fish, fatty fish and shellfish (molluscs, crustaceans and cephalopods).[1] It is well known that fatty fish and shellfish contain a higher content of n-3 LCPUFAs than lean fish.[2–4]

N-3 LCPUFAs, such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), pass through the placental circulation. The intake of n-3 LCPUFAs during pregnancy affects fetal development and extends the gestation time.[5] Moreover, n-3 LCPUFAs strongly affect fetal body composition.[6] Furthermore, a study conducted in Hong Kong reported that an average maternal consumption of 450 g of seafood per week during pregnancy could increase the IQ in the offspring.[7]

On the other hand, seafood is a source of contaminants. It contains dioxins, polychlorinated biphenyls (PCBs)—which are mainly found in cod liver and fish oils[8] and methylmercury (MeHg). It was reported that low levels of MeHg are found in clams and mussels and high levels are found in tuna, sea bass, sea bream, monkfish, hake

and octopus.[9] In addition, MeHg is generally present in large oily fish, it crosses the placenta and it can alter fetal neurodevelopment.[10] Based on those findings, the European Food Safety Authority Scientific Committee recommended that fish/seafood species with high mercury contents should be limited in the daily diet, in general, and particularly during the gestational period in pregnancy.[11]

The quantities of n-3 LCPUFAs and the concentrations of chemicals and toxic pollutants differ in different types of fish and shellfish. Consequently, there is some confusion about what amount of fish consumption would be suitable during pregnancy, to avoid damage from pollutants.[12] Therefore, the Spanish Agency for Consumer Affairs, Food Safety and Nutrition offered advice on the types of fish that should be consumed by pregnant women, as follows: 'eat a wide variety of fish, but avoid contaminated species (eg, swordfish, fresh tuna, pike and shark)'. They also included a statement that advocated eating fish three to four times a week, primarily oily fish, such as anchovies, sardines or red mullet.[13 14]

In addition, the European Food Safety Authority Scientific Committee recommended an intake of 1–4 servings of fish/week during pregnancy.[11] Other international organisations have variously recommended: ≥1–2 servings/week to provide nearly 200 mg of n-3 LCPUFAs (eg, DHA and EPA)[15–17]; 2–3 servings/week from the 'best choices' list, such as clams, cod, crab or shrimp; or 1 serving/week of the 'good choices list', such as monkfish and Spanish mackerel.[18]

Several longitudinal studies have evaluated the impact of maternal fish intake on the risk of small for gestational age (SGA) newborns. However, those studies have reported conflicting results; some reported positive effects,[3 19 20] some reported mixed effects[1 21] and others reported negative[12 22–25] or null effects.[26–28] Such inconsistencies might arise from differences in the types of fish assessed, which would lead to different contents of pollutants and polyunsaturated n-3 fatty acids.[21] Consequently, the relationships between fatty fish, lean fish or shellfish intake and the risk of having an SGA newborn remain unclear.

The present study aimed to determine how the consumption of different types of seafood during pregnancy affected the risk of having an SGA newborn.

METHODS
The study population included women who attended five hospitals in Eastern Andalusia (Spain): the University of Jaen Hospital (UJH), Ubeda Hospital, the University of Granada Hospitals (two centres) (UGH) and Poniente Hospital (PH). Taken together, these hospitals served 1.8 million people. The SGA and control groups were recruited from 15 May 2012 to 15 July 2015. .

We estimated the appropriate sample size, based on the results of a similar study.[25] To detect a significant (p<0.05) OR of 0.6 between extreme quintiles with a statistical power of 80%, we estimated that 447 pairs of cases and controls were required.

SGA group
Tables previously developed for the Spanish population[29] classified SGA newborns as infants with birth weights below the 10th percentile of infants at the same gestational age. Mothers were eligible for the SGA group when they had delivered a single live SGA newborn with no congenital malformation during the study period; they had to reside in the referral area of the hospital and they had to have an adequate understanding of the Spanish language. Nineteen women declined participation. A total of 533 women were selected for the SGA case group, from the following hospitals: UJH (n=79), UGH (n=369), UH (n=46) and PH (n=39).

Control group
Within a week after including each woman in the SGA group, a woman of similar age at delivery (±2 years) was selected at the same hospital for the control group. Women eligible for the control group delivered a non-SGA newborn (birth weight above the 10th percentile), but otherwise had to meet the same inclusion criteria required for the SGA group (residence in the referral area of the hospital, single pregnancy with no malformation and an adequate understanding of Spanish). Sixty-five women declined participation.

Patient involvement
Patients were informed of the study by providing a written document of the characteristics and objectives of the study. The health professionals involved in the recruitment and interview were available to clarify any doubts that might arise. Enrolled women were not involved in the recruitment of other participants. Personal identification data were not obtained; therefore, the results of this observational study could not be disseminated back to the individual participants.

Data collection
We used three sources of data. First, personal interviews were conducted by midwives within 2 days after delivery. Second, we reviewed clinical charts. Third, we reviewed prenatal care records.

We collected the following data: Mother's vital data, including age at pregnancy, race, education level, marital status, socioeconomic class and occupation; Obstetric history, including parity and abortions, previous adverse perinatal outcomes, and conditions during pregnancy (infections, pre-eclampsia, diabetes and other obstetric conditions); Birth weight measured (in grams) in the delivery room; drugs or medications, including prescribed drugs and over-the-counter medications; Social class, which included five main levels, ranging from I (the highest) to V (the lowest), according to the Spanish Society of Epidemiology classification system,[30] which was close to that of the Black Report[31]; the Kessner Index, a measure of prenatal care utilisation (number of visits and

date of first visit)[32] and toxic habits, including alcohol consumption during and before pregnancy (assessed with a structured questionnaire, which queried the number and type of drinks taken on weekdays, weekends, including Friday evening and holidays, including holiday eves); and smoking during pregnancy. The same data collection procedures were performed for SGA and control groups.

Dietary assessment

The midwives provided the Food Frequency Questionnaire (FFQ) to women after birth. The completion and return of the questionnaire confirmed participation in the study. The baseline questionnaire included a 137-item FFQ, previously validated in Spain, with open questions about the use of dietary supplements.[33 34] The questions were based on typical portion sizes, and nine options described the frequency of intake in the previous year for each food item (range: never or almost never to ≥6 times/day). For each FFQ food item, we estimated (1) the average amount of food consumed (grams) multiplied by the intake frequency; (2) the average total energy intake and (3) the average intake of macro and micronutrients, based on the latest available information from Spanish food composition tables.[35 36] Additionally, we asked each woman whether she had modified her intake of any items on the FFQ due to her pregnancy (ie, lower, higher or unchanged intake).

Fish and shellfish were included in the FFQ, as follows: lean fish (hake, whiting, grouper, flounder, monkfish, cod); fatty fish (anchovies, sardines, salmon, mackerel, fresh or frozen tuna, swordfish); salted and smoked fish (herring, salmon, anchovies); canned fish (canned tuna, canned fish in oil) and three different types of shellfish (1) bivalve molluscs: oysters, clams, mussels; (2) crustaceans: shrimp, prawns and (3) cephalopods: octopus, squid.

Seafood portion sizes were indicated in the FFQ, and the midwives were trained to give examples of portion sizes, as follows: 100–150 g for lean fish, 130 g for fatty fish, 60 g for salted and smoked fish, 50 g for canned fish (equivalent to a small can), 100–150 g for molluscs (six specimens), 200 g for crustaceans (4–5 specimens) and 200 g for cephalopods. The FFQ also asked whether supplements of n-3 LCPUFAs were used; subjects included information about the product brand and the frequency of intake (range: never or almost never to ≥6 times/day).

After computing the total energy intake, we excluded 15 matched pairs, due to unreliable dietary assessments (the total energy calculations indicated intakes above 4000 kcal/day). Thus, 518 matched SGA and control pairs were included in the final analysis.

Statistical analysis

Quantitative variables are expressed as the mean, SD and range, and frequencies are expressed in absolute and relative terms. The intake frequencies were derived from the FFQ; each respondent indicated intakes for the different types of seafood as: never; 1–3 servings/month; 1 serving/week or >1 serving/week).

We used the residuals method to adjust food and nutrient intakes to the total energy intake, for the SGA and control groups in separates ways, as recommended previously.[37] Nutrient intakes were stratified into quintiles, according to intakes observed in controls (which represent the general population); thus, the quintile bins used to stratify the n-3 fatty acid and fish intakes in the control group were applied to intakes reported in the SGA group.

We implemented conditional logistic regression models to calculate crude ORs (cORs) and adjusted ORs (aORs) with their 95% CIs. The lowest quintile (Q1) was taken as the reference, and the main comparison was to the highest quintile (Q5). Trend analyses were performed with quintiles in logistic regression models, where the median intake for each quintile was introduced into the model. Intermediate variables were discarded, and to control for confounding variables, only variables that changed the diet coefficient by more than 10% were retained in the logistic models. A priori, we evaluated SGA risk factors in mothers that were related to diet (ie, tobacco use, pregestational body mass index (BMI), body weight, educational level, etc) as potential confounders. The model was adjusted for the following maternal factors: energy intake, educational level, smoking and pregestational BMI, and a previous preterm or low birthweight newborn. All p values are two tailed. Statistical significance was set at p<0.05. We repeated the analysis after including supplemental products that contained n-3 LCPUFAs. We performed all analyses with Stata V.14.

RESULTS

Table 1 describes the characteristics of women included in the SGA and control groups. Marital status was different between the SGA and control groups. More women were married in the control group than in the SGA group (p<0.036). Previous preterm deliveries and low birthweight newborns were more frequent in the SGA group than in the control group (p<0.001). The SGA group included more women who smoked during pregnancy, more cases of pre-eclampsia and more women with intrauterine growth restriction during pregnancy than observed in the control group (p<0.001). The mean weight gain during pregnancy and the pregestational BMI were higher in the control group than in the SGA group (p<0.001).

Some items on the FFQ were modified by women during pregnancy. Fish intake was increased during pregnancy in 27.03% of women in the SGA group and in 24.13% of the controls. Conversely, fish intake was reduced during pregnancy in 6.37% of women in the SGA group and in 6.76% of controls (p=0.563). At least a 50% increase in fish intake was reported by 5.6% of women in the SGA group and by 4.8% of controls (p=0.862; data not shown in tables).

Table 2 shows the frequency of consumption of several types of seafood in the two groups. We observed a higher

Table 1 Characteristics of the study population

Characteristic	SGA group	Controls	P values
Marital status, n (%)			0.036
Single	37 (7.1)	42 (8.1)	
Stable couple	161 (31.1)	124 (23.9)	
Married	320 (61.8)	352 (68.0)	
Education level, n (%)			0.084
Primary	112 (21.6)	93 (17.9)	
High school, not ended	42 (8.1)	28 (5.4)	
High school	185 (35.7)	190 (36.7)	
University	179 (34.6)	207 (40.0)	
Previous preterm/low birthweight newborn, n (%)	64 (12.4)	26 (5.0)	<0.001
Kessner Index (prenatal care), n (%)			0.737
Adequate	259 (50.0)	253 (48.8)	
Intermediate	185 (35.7)	182 (35.2)	
Inadequate	74 (14.3)	83 (16.0)	
Smoking during pregnancy, n (%)	149 (28.8)	80 (15.4)	<0.001
Pre-eclampsia, n (%)	46 (8.9)	11 (2.1)	<0.001
Intrauterine growth retardation, n (%)	141 (27.2)	8 (1.5)	<0.001
Weight gain during pregnancy (g/week), mean (SD)	278 (121)	310 (114)	<0.001
Pregestational body mass index, mean (SD)	23.1 (4.5)	23.9 (4.1)	<0.001
Alcohol intake (g/week), mean (SD)	4.2 (18.5)	3.1 (15.2)	0.312

SGA, small for gestational age.

intake of lean fish (>1 serving/week) in the control group than in the SGA group. In the adjusted analysis, we found no significant association between the risk of SGA newborns and the intake of lean fish, fatty fish or salted fish. Nevertheless, more than once/week intakes of shellfish molluscs, such as clams, common cockles and mussels, yielded a lower risk of SGA newborns (aOR 0.25, 95% CI 0.08 to 0.76), even though the intakes of this particular type of seafood were infrequent. We found that the occasional intake of shellfish, cephalopods, squid and octopus conferred a slight protective effect against an SGA birth (no more than 3 servings/month; aOR 0.62, 95% CI 0.44 to 0.87), but this association was not observed with more frequent intakes (ie, there was no trend). We also found that canned fish intake (>1/week) had an overall protective effect, and this association was similar in the multivariable analysis, although not significant (aOR 0.64, 95% CI 0.37 to 1.13). Thus, canned fish with oil (the typical intake) was unrelated to the risk of an SGA newborn.

Table 3 shows the associations (ORs) between the risk of an SGA newborn and different daily intakes of seafood and marine n-3 fatty acids (g/day), stratified into quintiles. We found that a higher daily intake of seafood or marine n-3 fatty acids yielded significant protection against an SGA newborn. The OR of delivering an SGA newborn was lower with seafood intakes of >29 g/day (Q5; aOR 0.63, 95% CI 0.41 to 0.98) compared with intakes of ≤8 g/day (Q1; p=0.025 for this trend). Moreover, the risk of having an SGA newborn was lower among women in Q5, with high daily intakes of marine n-3 fatty acids (>1 g/day; aOR 0.58, 95% CI 0.38 to 0.90) than in the Q1 group (≤0.4 g/day; p=0.025 for the trend).

We also investigated whether the intake of n-3 LCPUFA supplements was related to the risk of an SGA newborn. We found that 8.7% of women in the SGA group and 6.2% of controls used these supplements. Among these, all but one woman used the same pharmaceutical brand (Natalben). The average daily intake was 200 mg. The cOR was 1.46 (95% CI 0.91 to 2.37), and it remained unaltered after adjusting for confounders (aOR 1.51, 95% CI 0.90 to 2.52). The inclusion of these supplements in the multivariable analyses of fish and marine n-3 fatty acid intakes did not change the previous results.

DISCUSSION

Our results demonstrated that the risk of having an SGA newborn was not consistently associated with the intakes of specific types of seafood (lean fish, fatty fish and shellfish) during pregnancy, when these types were addressed separately. However, when we considered the entire seafood intake during pregnancy, women in the highest quintile (Q5) had a lower risk of an SGA newborn than those in the lowest quintile (Q1). This result was reinforced, when we analysed the total intake of marine n-3 fatty acids.

Table 2 Frequency of maternal intake of different seafood and ORs for the risk of an SGA infant

Intake frequency	SGA group n (%)	Controls n (%)	cOR (95% CI)	aOR* (95% CI)
Lean fish (100–150 g)				
Never	47 (9.1)	32 (6.2)	1 (ref.)	1 (ref.)
1–3 a month	108 (20.9)	105 (20.3)	0.68 (0.40 to 1.15)	0.70 (0.39 to 1.26)
1 a week	301 (58.1)	291 (56.2)	0.67 (0.41 to 1.09)	0.70 (0.41 to 1.20)
>1 a week	62 (12.0)	90 (17.4)	0.45 (0.25 to 0.80)	0.53 (0.28 to 1.01)
Fatty fish (130 g)				
Never	77 (14.9)	73 (14.1)	1 (ref.)	1 (ref.)
1–3 a month	130 (25.1)	113 (21.8)	1.09 (0.72 to 1.68)	1.22 (0.76 to 1.96)
1 a week	258 (49.8)	263 (50.8)	0.93 (0.64 to 1.36)	0.96 (0.62 to 1.47)
>1 a week	53 (10.2)	69 (13.3)	0.73 (0.45 to 1.19)	0.69 (0.40 to 1.20)
Salted-smoked fish (60 g)				
Never	312 (60.2)	321 (62.0)	1 (ref.)	1 (ref.)
1–3 a month	149 (28.8)	125 (24.1)	1.21 (0.92 to 1.62)	1.28 (0.93 to 1.75)
1+ a week	57 (11.0)	72 (13.9)	0.82 (0.56 to 1.21)	0.73 (0.48 to 1.11)
Shellfish-bivalves molluscs (6 units; 100–150 g)				
Never	183 (35.3)	162 (31.3)	1 (ref.)	1 (ref.)
1–3 a month	228 (44.0)	228 (44.0)	0.88 (0.66 to 1.17)	0.90 (0.66 to 1.22)
1 a week	102 (19.7)	113 (21.8)	0.77 (0.55 to 1.09)	0.73 (0.50 to 1.06)
>1 a week	5 (1.0)	15 (2.9)	0.28 (0.10 to 0.80)	0.25 (0.08 to 0.76)
Shellfish-cephalopods (200 g)				
Never	149 (28.8)	116 (22.4)	1 (ref.)	1 (ref.)
1–3 a month	237 (45.8)	282 (54.4)	0.61 (0.45 to 0.84)	0.62 (0.44 to 0.87)
1+ a week	132 (25.5)	120 (23.2)	0.85 (0.60 to 1.20)	0.93 (0.64 to 1.37)
Shellfish-crustacean (4–5 units; 200 g)				
Never	164 (31.7)	144 (27.8)	1 (ref.)	1 (ref.)
1–3 a month	256 (49.4)	279 (53.9)	0.80 (0.61 to 1.07)	0.85 (0.62 to 1.16)
1+ a week	98 (18.9)	95 (19.3)	0.90 (0.62 to 1.29)	0.92 (0.62 to 1.37)
Canned fish-raw (small can; 50 g)				
Never	175 (33.8)	147 (28.4)	1 (ref.)	1 (ref.)
1–3 a month	149 (28,8)	152 (29.3)	0.82 (0.60 to 1.14)	0.87 (0.62 to 1.24)
1 a week	160 (30.9)	171 (33.0)	0.78 (0.58 to 1.07)	0.81 (0.58 to 1.12)
>1 a week	34 (6.6)	48 (9.3)	0.57 (0.34 to 0.96)	0.64 (0.37 to 1.13)
Canned fish with oil (small can; 50 g)				
Never	161 (31.1)	150 (29.0)	1 (ref.)	1 (ref.)
1–3 a month	143 (27.6)	170 (32.8)	0.78 (0.57 to 1.08)	0.82 (0.58 to 1.16)
1 a week	176 (34.0)	158 (30.5)	1.04 (0.76 to 1.42)	0.99 (0.71 to 1.38)
>1 a week	38 (7.3)	40 (7.7)	0.89 (0.54 to 1.46)	1.00 (0.58 to 1.73)

*Adjusted for energy intake, educational level, smoking, pregestational BMI and previous preterm or low birthweight newborn.
aOR, adjusted OR; BMI, body mass index; cOR, crude OR; SGA, small for gestational age.

One of the strengths of this study was the low likelihood that biases might have affected our findings. A selection bias was unlikely, because the number of women who refused to participate was rather small (3% for the SGA group and 11% for the control group). Moreover, the FFQ used to measure, the diet was previously validated.[33 34] This tool was acceptable, but some misclassification bias could not be ruled out. Nevertheless, the likelihood of a differential bias was low, because currently, there are no special recommendations on seafood intake for women with intrauterine growth retardation, low weight gain during pregnancy, or signs of an SGA infant detected during obstetric explorations (mainly ultrasonic scans). Another strength was that the controls were density matched to women in the SGA

Table 3 Associations between quintiles of daily seafood and marine n-3 fatty acids intakes and the birth of an SGA infant

Intake amounts (g/day)	SGA group n (%)	Controls n (%)	OR (95% CI)	OR* (95% CI)
Seafood intake				
Q1 (≤8)	129 (24.9)	104 (20.1)	1 (ref.)	1 (ref.)
Q2 (8–14)	111 (21.4)	104 (20.1)	0.84 (0.57 to 1.22)	0.96 (0.63 to 1.46)
Q3 (14–21.2)	108 (20.9)	103 (19.9)	0.83 (0.56 to 1.21)	0.94 (0.61 to 1.43)
Q4 (21.2–29)	99 (19.1)	104 (20.1)	0.78 (0.53 to 1.15)	0.83 (0.54 to 1.28)
Q5 (>29)	71 (13.7)	103 (19.9)	0.56 (0.38 to 0.84)	0.63 (0.41 to 0.98)
P for trend			0.010	0.025
Marine n-3 fatty acids				
Q1 (≤0.4 g/day)	135 (26.1)	104 (20.1)	1 (ref.)	1 (ref.)
Q2 (0.4–0.6)	105 (20.3)	104 (20.1)	0.79 (0.54 to 1.17)	0.88 (0.56 to 1.35)
Q3 (0.6–0.7)	86 (16.6)	103 (19.9)	0.64 (0.43 to 0.95)	0.70 (0.45 to 1.09)
Q4 (0.7–1)	116 (22.4)	104 (20.1)	0.86 (0.59 to 1.25)	0.93 (0.61 to 1.41)
Q5 (>1)	76 (14.7)	103 (19.9)	0.58 (0.39 to 0.85)	0.58 (0.38 to 0.90)
P for trend			0.028	0.024

*Adjusted for energy intake, educational level, smoking, pregestational BMI and previous preterm or low birthweight newborn.
BMI, body mass index; SGA, small for gestational age.

group; thus, seasonal influences on the responses to the FFQ were unlikely to affect our results, and a cohort effect on diet was avoided (younger women consumed a Westernised diet more frequently than older women). Moreover, age matching between cases and controls ensured that the reported preference for seafood among older women[38 39] would not alter the results. Therefore, any potential misclassification bias was likely to be non-differential, which would cause an underestimation of the strength of an association, that is, when an association was observed in the data, the actual association was likely to be higher than that calculated. We also reduced biases due to confounding factors by collecting data on the most important determinants of SGA and considering them in multivariable analyses. However, this study also had some limitations. First, it was unlikely that our results were completely free of biases, and residual confounding could not be totally ruled out. Moreover, although we found that the total seafood intake and marine n-3 fatty acid intake were associated with a lower probability of delivering an SGA newborn, we could not demonstrate causality. However, some causality items were fulfilled, including the strength of the association and consistency. Finally, our study was limited by the inability to adjust for environmental contaminants in the seafood.

One advantage of our study, which increased our statistical power, was that the Spanish population has a relatively high seafood intake, and a wide variety of species are typically included in the Spanish diet.[40 41] Additionally, we found that, in our sample, women were more likely to increase, rather than decrease, fish intake during pregnancy. Nevertheless, in our study, a substantial proportion of women (about 30%) displayed little (1–3 servings/month) or no seafood intake, which allowed us to assess whether dietary fish was associated with a lower risk of an SGA newborn. The use of n-3 LCPUFA supplements was

scarce in our population (200 mg/day in Q2), much lower than the amounts consumed in the diet (>460 mg/day in Q2). It has been pointed out that supplements taken in the last half of the gestation period could provide a modest increase in measures at birth (eg, a higher birth weight) and reduce the probability of delivering before week 34.[5 42] Nevertheless, those reports remarked that most randomised trials of prenatal n-3 LCPUFA supplementation had been conducted in high-income countries, and therefore, the findings were not generalisable to populations in low-income and middle-income settings.

Several previous studies have analysed the impact of seafood intake on the risk of delivering SGA newborns. Most studies were conducted with European cohorts,[1 3 23 26 27] but two were conducted in Spanish Mediterranean populations.[20 21] The sample sizes of those studies ranged from 657 women[21] to 62 099 women.[23] In general, almost all studies measured seafood intake with a validated FFQ, but the responses were collected at different times during pregnancy, that is, at the beginning of pregnancy,[1] at mid-pregnancy[3 19 21 23 26 27 43] and at birth[22 25]; the latter studies were conducted in Italian[25] and Japanese women.[22] However, many of those studies provided inconsistent results. In the present study, we collected all FFQ responses at birth.

The reported associations between the risk of an SGA newborn and seafood intake appeared to depend on the FFQ collection period. When the FFQ was completed at the beginning of pregnancy, for example, Halldorsson et al[3] found that, among 44 824 Danish women, the risk of an SGA newborn was positively associated with more than 4 servings of fatty fish/month. Similarly, in a cross-sectional study of Indian women with a low birthweight prevalence of 20%, weekly fish consumption increased the risk of having a low birthweight infant by 26%.[19] The Omega Study, conducted in Seattle Washington, showed that, in the

pregnancy cohort, higher intakes of shellfish (more than 1 serving/week) and lean fish (more than 1 serving/week) were associated with a higher risk of low birth weight.[43]

Conversely, when the FFQ was completed at mid-pregnancy, a protective effect was found with seafood intake. One study in 62 099 Norwegian women showed that the relative risk of delivering a low birthweight baby (<2500 g) in full-term pregnancies was significantly lower in women who consumed >60 g/day of seafood than in women who consumed ≤5 g/day of seafood.[23] Finally, an Italian retrospective case–control study (n=555 women) and a Turkish study (n=553 healthy pregnant women), reported that eating more fish reduced the odds of delivering an SGA newborn.[25 44] However, those studies were limited by small numbers of SGA cases.

In our study, intakes of 2–3 seafood servings/week were observed two times as frequently in the control group as in the SGA group. This finding was supported by data from 19 European birth cohort studies, which showed that the average birth weight was 15.2 g higher (95 % CI 8.9 to 21.5 g) among women with a high fish intake during pregnancy (>3 servings/week) than among women with low fish intakes (<1 serving/week), independent of gestational age.[12] Recently, a meta-analysis of the same data investigated fish intake effects on the growth rate in infancy.[24] They found that, among mothers with high fish intakes (>3 serving/week) during pregnancy, the offspring BMI values were higher from infancy through middle childhood compared with offspring from mothers with low fish intakes (≤3 servings/week); this association was slightly stronger in female than in male newborns.

Other previous studies did not find any association between fish intake and the risk of an SGA newborn. This occurred in the study by Heppe et al[27] in a sample of 3380 pregnant women from Rotterdam, characterised by a low fish intake (median fish consumption, 75 g/week). Additionally, Drouillet et al[26] found no association between a seafood intake of >2 servings/week before pregnancy and the risk of an SGA newborn in a sample of 1805 women from the French Eden mother–child cohort. However, among women with BMIs ≥25 kg/m^2 in that cohort, women with pregestational seafood intakes of <5 servings/month had a threefold higher risk of an SGA newborn than women with intakes ≥9 servings/month.

Studies on specific types of seafood and the risk of SGA newborns have produced controversial results. For example, among Spanish women in Barcelona, canned tuna or crustacean intakes >1 serving/week increased the risk of SGA newborns.[20] Our results were inconsistent with the results of that study. In the Pelagie Cohort study, Guldner et al[1] studied a sample of 2398 French pregnant women. They found that 2 servings/week of fish and shellfish protected against SGA newborns; however, when considered individually, the effects were contradictory: fish reduced the risk, and shellfish increased the risk of SGA newborns. In our study, women who consumed more than 1 serving/week of bivalve molluscs had a lower risk of SGA newborns than women who consumed less than 1 serving/week. This

finding might be explained by the rich content of vitamin B_{12} and fatty acids and the low percentage of heavy metals in molluscs.[45] In addition, in the present case–control study, we observed that controls consumed more fatty fish, cephalopod shellfish and canned fish during pregnancy than women with SGA newborns.

Some of the observed discrepancies between studies might be due to the different fish species considered. We did not find a consistent pattern of association between the risk of SGA newborns and the isolated fish types, except for bivalve molluscs. However, a protective effect was evident for seafood consumption, in general. This phenomenon was previously described in other studies on seafood consumption in pregnancy[1] and in studies that analysed the effect of a Mediterranean diet on cardiovascular risk: the overall diet pattern, but not any individual food, showed a preventive effect.[46] We must consider that, in Spain, seafood intake is high and varied. Thus, an alternative type of seafood might compensate for low intake of a specific type of seafood, by contributing n3-fatty acids to the diet; for example, women with a low intake of molluscs might have a high intake of fatty fish and vice versa. This situation suggested that, instead of recommending the consumption of specific types of seafood during pregnancy, we should consider recommending all seafood, except known contaminated species (ie, swordfish, fresh tuna, pike and shark). Thus, pregnant women should consume 3–4 servings of seafood (fish and shellfish)/week, as recommended,[13] to protect against the risk of SGA newborns.

In summary, we found that an intake of at least 29 g/day of seafood, or at least 1 g/day of n3-fatty acids, was observed nearly two times as frequently in controls than in women with SGA newborns. This finding suggested that an intake of 3–4 seafood servings/week, according to recommendations, could reduce the frequency of SGA newborns. In our sample, less than 20% of pregnant women followed this recommendation; therefore, a nutritional educational intervention is required to target the general population, and specifically, pregnant women.

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