Environmental Health

RESEARCH

Open Access

Dietary bisphenols exposure as an influencing factor of body mass index

Yolanda Gálvez-Ontiveros[1,2,3†], Celia Monteagudo[1,2,3†], María Giles-Mancilla[1], José Joaquín Muros[4], Vega Almazán[5], María Alba Martínez-Burgos[3,6], Cristina Samaniego-Sánchez[1,2,3], Inmaculada Salcedo-Bellido[2,7,8*], Ana Rivas[1,2,3†] and Alberto Zafra-Gómez[2,3,9]

Abstract

Background Over the past three decades, there has been a significant increase in the prevalence and incidence of overweight and obesity worldwide. The obesogen hypothesis suggests that certain external agents may affect pathways related to fat accumulation and energy balance by stimulating fat cell differentiation and proliferation. Previous research has indicated that exposure to bisphenol A (BPA) and some of its analogues may influence fat accumulation by promoting the transformation of preadipocytes into adipocytes. This study aimed to assess the possible contribution of dietary bisphenol exposure to the odds of developing overweight and obesity in a sample of Spanish children according to sex.

Methods Dietary and anthropometric data were collected from 179 controls and 124 cases schoolchildren aged 3–12 years. Dietary exposure to BPA and bisphenol S (BPS) was assessed using a food consumption frequency questionnaire. Logistic regression models were used to assess the influence of dietary exposure to bisphenols on overweight and obesity stratified by sex.

Results For females, cases had significantly higher exposure to BPA from meat and eggs compared to controls (median = 319.55, interquartile range (IQR) = 176.39–381.01 vs 231.79 (IQR) = 162.11–350.19, *p*-value = 0.046). Diet quality was higher for controls (6.21 (2.14) vs 4.80 (2.24) $p < 0.001$) among males independently of a high or low exposure to bisphenols. However, higher diet quality was observed for female controls with an high exposure of total bisphenols (6.79 (2.04) vs 5.33 (2.02) $p = 0.031$). Females exposed to high levels of BPA from meat and eggs had higher likelihood of being overweight and obese (adjusted Odds Ratio = 2.70, 95% confidence interval = 1.00 – 7.32). However, no consistent associations were found in males.

Conclusions High BPA levels from meat and eggs were positively associated with overweight and obesity in females. The dietary intake of BPA in the schoolchildren in the present study was much higher than the acceptable daily intake established by EFSA for the last year.

Keywords Children, Overweight, Obesity, Bisphenol A, Bisphenol S, Weight excess

†Yolanda Gálvez-Ontiveros, Celia Monteagudo and Ana Rivas contributed equally to this work.

*Correspondence:
Inmaculada Salcedo-Bellido
isalcedo@ugr.es
Full list of author information is available at the end of the article

Background

The prevalence and incidence of overweight and obesity worldwide have increased significantly in the last three decades [1]. Diverse studies indicate that the etiology of this chronic disease is multifactorial and complex. The predisposing biological factors including genetic characteristics, prenatal determinants, pregnancy, intestinal microbiota and viruses [2]. In 2006, Grün and Blumberg postulated the obesogens hypothesis for the first time, where certain exogenous agents could alter adipogenic pathways and energy balance, promoting an increase in adipocyte differentiation and proliferation rates [3]. Some of the most known obesogens are endocrine-disrupting chemicals (EDCs), exogenous agents that may interfere with the hormonal system function in different ways, by influencing hormone synthesis, metabolism and/or cellular actions [4]. EDCs include compounds to which the human population is exposed in daily life through their use in pesticides/herbicides, a large variety of household and medical products (food, containers foodstuffs, clothes, drugs, sanitizers, cosmetics, personal care products, toys, construction materials, furniture), and in plant-based products [5, 6], becoming ubiquitous in our environment. They are considered as obesogenic compounds due to their capacity to alter lipid metabolism and inappropriately promote adipogenesis and fat accumulation [7, 8]. The prenatal period, infancy, and childhood are most vulnerable periods for the influence of these environmental contaminants due to the immaturity in metabolic enzymes and lower capacity to eliminate toxic compounds. This fact suggest that metabolism and detoxification are not as efficient as they are in adults [9].

Bisphenol A (BPA) is among the highest production volume chemicals detected in ecosystems, human fluids, and tissues [10]. To protect against BPA exposure, the European Commission has taken actions by banning the use of BPA in infant feeding bottles and restricting the use of BPA in certain food-contact materials [11]. Common exposure pathways include epoxy resins in canned foods/beverages, polycarbonate plastics, thermal paper, dental materials and consumer goods [6, 7, 12] being their main exposure oral ingestion through diet [13, 14]. As the use of BPA is decreasing, substitutes such as bisphenol S (BPS) is becoming more widely used. However, the current evidence shows that most alternative bisphenols are as hormonally active as BPA. Perinatal and chronic exposure to BPS induced obesogenic effects, even at low doses, and the obesogenic capacity of BPS was even higher than that of BPA in preadipocytes [15].

In vitro studies have shown also that exposure to BPA has a direct association with adipogenesis, promoting the conversion of preadipocytes into adipocytes and increasing lipid accumulation [16–18]. In vivo studies suggest the influence of bisphenols on fatty mass development, mainly when exposure occurred in the prenatal phase [11, 19, 20]. In spite of epidemiological studies have shown a positive association between childhood obesity and bisphenol exposure [21–23], the cross-sectional nature of most of them makes that causal links may be complex and consequently difficult to interpret. Thus, despite the significance of environmental obesogens in the pathogenesis of metabolic diseases, the contribution of synthetic chemical exposure to obesity epidemic remains largely unrecognised. Hence, the aim of the present study was to evaluate a possible contribution of dietary bisphenols exposure on likehood of developing overweight and obesity in a sample of Spanish children.

Materials and methods

Study design and population

The present research is a case–control study carried out to investigate the influence of environmental factors in the development of overweight and obesity in Spanish children. Both cases and controls were recruited from different primary care centers and schools randomly selected from the province of Granada, located in areas with different socioeconomic level. Participants were recruited from January 2020 to January 2022. Cases and controls must meet the following inclusion criteria: (1) prepuberal children aged between 3—12 years-old; (2) having resided continuously in the study areas for at least 6 months; (3) overweight or obesity diagnosis (only cases). The exclusion criteria were: obesity as a symptom of other pathologies, or as a side effect of pharmacological treatment. A total of 124 cases and 179 controls were recruited in this study.

Data collection

Face-to-face interviews were performed at baseline by trained interviewers to the participant's parents or legal tutors. In this way, sociodemographic information such as sex and age of children, and lifestyle data (smoking habits of family members, physical activity out-of-school and diet) were collected. In addition, anthropometric measurements such as height (in cm) and weight (in Kg) were obtained by qualified personnel. Concretely, participants with light clothing and without shoes were weighed using a portable Tanita scale (model MC 780-S MA). A stadiometer (model SECA 214 (20–107 cm) was used to measure the height in the sanding position. During height measurements, the participants' backs, buttocks, and heels should be in contact with the wall. Weight and height were used to obtain the body mass index (BMI) which was calculated as weight divided by height squared. Thus, subjects were classified as underweight, normal weight, overweight and obese as described by

Cole et al., 2000, 2007 [24, 25]. Also, we compare the proportion of cases according to methodology previously mentioned and using cut-off points given by WHO, using z-score (weight-to-age values from 3 to 5 years old and BMI-to-age values for children higher to 5 years old). We obtained a high agreement (kappa coefficient = 0.831; $p < 0.001$) between both methods.

Dietary information for the last 12 months prior to the interview was obtained through parents or legal tutors of participants using a semi-quantitative food frequency questionnaire (FFQ) state supervised by trained nutritionists. It collected information on the following 112 food items categorized in 13 groups: dairy products (11), eggs, meat and meat derivatives (9), fish and fish derivatives (7), vegetables (17), tubers (2), fruits and nuts (18), legumes (4), cereals (12), precooked or ultra-processed food (2), bakery products, pastries and sweets (13), fats and oils (5), non-alcoholic beverages (5) and miscellaneous (7). It was specified portion sized for each item and 8 consumption frequency options: never, 1–3 times for month, 2–4 times per week, 5–6 times per week, once a day, 2–3 times per day, 4–6 times per day and more than 6 times per day.

The Spanish version of KIDMED used in the study was taken from a previously performed research [26]. It is a self-administered instrument aimed at estimating adherence to the Mediterranean diet. This questionnaire consists of 16 questions, of which 4 questions reflected negative connotations associated with an adequate Mediterranean diet and scored negatively (-1 point), and 12 affirmative questions reflecting positive aspects related to the Mediterranean diet and scored positively (+1 point). Individuals are divided into three categories to follow: low adherence or low diet quality (score less than or equal to 3), medium adherence or medium diet quality (score 4–7) and high adherence or high diet quality (score greater than or equal to 8).

Estimation of bisphenols dietary exposure

Bisphenol concentrations in the selected foodstuffs were described previously [27, 28]. Bisphenol levels were quantified using ultra-high-performance liquid chromatography-tandem mass spectrometry. From total of food samples analyzed, a 52% of them had bisphenol concentrations above quantification level.

The method used for the selection and analysis of food items has been described elsewhere [29]. Daily dietary exposure to BPA, BPS and total bisphenol (ng/day) for each participant was calculated by multiplying their daily food consumption (g/day) by the corresponding bisphenol content in each food (ng/g food). Mean intake (g/day) of foodstuffs was calculated multypliying the consumption frequency (servings/day) with portion size using the standard servings (g/serving) establish for the Spanish population [30].

Statistical analysis

The characteristics of cases and controls were summarized using median and interquartile range (IQR, percentil 25-percentil 75) for the continuous variables and percentages for categorical variables. To assess the level of significance of the differences observed among categorical variables used Chi-squared and Mann–Whitney U test or Kruskal–Wallis for continuous variables.

Logistic regression models were used to estimate odds ratios (OR) and 95% confidence intervals (95% CI) to assess the influence of BPA, BPS, and total bisphenol (BPA + BPS) dietary exposure on overweight and obesity. Then, BMI dichotomized as normal weight and overweight/obesity was the dependent variable. Dietary bisphenols exposure (BPA, BPS and total bisphenols) categorized according to tertiles (T) and later dichotomized as low (first and second T) and high (third T) exposure were the influencing factors, considering T1 and T2 as the reference category. An additional sensitivity logistic regression analysis was performed considering T1 as the reference category. Two models were used: (a) crude and (b) adjusted model for a priori potential confounders according to previous studies (age, energy intake, diet quality and parental education level) [22, 31–33], and those variables which produced changes > 10% in OR crude (smoking among members of the family unit, physical activity and body fat percentage). Moreover, we also performed sex-stratified due to biological, social and behavioural differences between men and women that may influence the prevalence of overweight and obesity [34]. Besides, it has been reported that sex may have an influence on the burden of overweight and/or obesity [22, 35]. The rationale for these approach is based on previously published literature where sex could modify the effect of bisphenol exposure on BMI [22]. Statistical analyses were performed with IBM SPSS (version 26.0, IBM® SPSS® Statistics, Armonik, NY, USA). The statistical significance set to $p \leq 0.05$.

Results

Table 1 shows the main characteristics of cases and controls stratified by sex. An additional description of the overall population is provided in Supplementary Table S1. Statistically significant differences were observed for most of the study variables, with the exception of energy intake for both, males and females. Cases were older, less physically active, family members smoked more frequently and parents' education level was lower. Body fat percentage was significantly higher for cases, both in males as females.

Table 1 General characteristics of cases and controls according to sex

		Males ($n=159$)			Females ($n=144$)		
		Controls ($n=93$)	Cases ($n=66$)	*p*-value	Controls ($n=86$)	Cases ($n=58$)	*p*-value
Age, years	Median	7.00	9.07	**<0.001**[a]	7.08	9.04	**0.002**[a]
	IQR	5.05 – 8.55	7.06 – 11–01		5.12 – 9.04	7.08 – 11.01	
Parental education level (%)				**<0.001**[b]			**<0.001**[b]
Up to primary		5.4	21.5		3.6	12.7	
Secondary		19.6	35.4		17.9	41.8	
University		75.0	43.1		78.6	45.5	
Energy intake, Kcal/day	Median	2070.49	2218.53	0.383[a]	2101.89	1889.10	0.120[a]
	IQR	1765.52 – 2335.86	1740.13 – 2558.93		1760.74 – 2451.22	1547.26 – 2277.57	
Physical activity (out-of-school) (%)	No	21.5	53	**<0.001**[b]	32.6	62.1	0.090[b]
	Yes	78.5	47		67.4	37.9	
Smoking among members of the family unit (%)	No	92.5	53	**<0.001**[b]	83.7	62.1	**0.003**[b]
	Yes	7.5	47		16.3	37.9	
Body fat percentage	Median	18.20	33.55	**<0.001**[a]	21.70	33.65	**<0.001**[a]
	IQR	15.65 – 20.70	28.63 – 38.08		19.70 – 23.50	30.18 – 39.10	

IQR interquartile range (percentile 25th – percentile 75th)

[a] U Mann–Whitney test

[b] Chi-square test

p-values ≤ 0.05 are highlighted in bold

Tables 2 and 3 show the daily food intake by food groups and mean exposure to bisphenols for case and controls, according to the sex. Among males, exposure to BPA from foods processed and to BPA, BPS and total bisphenols from legumes were significantly higher for cases (Table 2). However, male controls had significantly higher exposure to BPS from fruits (Table 3). For females and the overall population, cases had significantly higher exposure to BPA from meat and eggs and foods processed and BPA, BPS and total bisphenols for legumes, while BPS and total bisphenols exposure from dairy products was significantly higher among controls only in females (Table 3 and Supplementary Table S2). Non-significant differences among cases and controls were observed for total BPA, BPS and total bisphenols.

According to Table 4 and Supplementary Table S3, diet quality was significantly higher for controls for males (6.21 (2.14) vs 4.80 (2.24) $p<0.001$) and overall population (6.16 (2.37) vs 5.18 (2.18) $p<0.001$). Overall population and males with a BMI higher than 25 kg/m^2 had a significantly lower diet quality independently of a high or low exposure to BPA, BPS or total bisphenols. However, among females, significantly higher diet quality was observed for controls with a high exposure of total bisphenols (6.79 (2.04) vs 5.33 (2.02) $p=0.031$).

Table 5 and Supplementary Table S4 showed the influence of the highest (defined as T3) BPA, BPS and total bisphenols dietary exposure by food groups on overweight and obesity by sex and in the overall population. High exposure to BPA from processed foods and cereals and to BPA and BPS (separately and together) from legumes was positively associated to overweight and obesity, according to the results shown for crude model. Non-significant values were found for the adjusted model for males and overall population. On the other hand, a positive association between high exposure to BPA from meat and eggs and to BPA and BPS (separately and together) from legumes and weight excess (overweight and obesity) was observed in females and the overall population, according to crude model. Significance was only kept for BPA from meat and eggs in the adjusted model (OR adjusted by age, energy intake, diet quality, smoking among members of the family unit and body fat percentage) in females. When low exposure was used as the first tertile and medium and high exposure as separate categories, the direction of the associations remained similar although the statistical significance was lost (Supplementary Material, Table S5).

Discussion

The present study aimed to assess the association between dietary exposure to bisphenols and the likelihood of developing overweight and obesity in school children. The association between bisphenols and BMI depends on the food group and its consumption, independent of sex and age, among other factors. The results

Table 2 Dietary intake of bisphenols (ng/day) by foods groups according to cases and controls for males

Food Group	Controls ($n=93$)			Cases ($n=66$)			p-value[b]
	n*	Food Intake (g/day), median (IQR)	Bisphenol Intake (ng/day), median (IQR)	n*	Food Intake (g/day), median (IQR)	Bisphenol Intake (ng/day), median (IQR)	
BPA							
Dairy products	66	452.22 (207.12 – 635.55)	3269.61 (1578.70 – 5727.51)	55	306.54 (145.39 – 603.63)	1945.89 (637.83 – 4434.08)	0.226
Meat and eggs	87	109.40 (90.29 – 140.87)	302.96 (166.16 – 369.05)	63	128.70 (105.44 – 156.05)	324.81 (173.75 – 410.31)	0.174
Fish	79	21.45 (7.15 – 31.95)	1530.30 (4.52 – 6510.93)	60	7.15 (0.00 – 21.45)	1529.45 (0.00 – 3255.71)	0.440
Vegetables	81	167.95 (108.73 – 227.25)	143.05 (21.19 -347.66)	48	158.98 (121.18 – 242.58)	37.71 (19.35 – 329.93)	0.355
Fruits	86	198.06 (131.78 – 279.89)	428.27 (224.87 – 685.37)	55	132.99 (88.48 – 209.53)	392.31 (136.90 – 678.83)	0.250
Legumes	93	7.15 (4.02- 8.58)	3.22 (1.81 – 3.86)	66	8.58 (7.15 – 10.01)	3.86 (3.22 – 4.50)	**0.029**
Cereals	90	38.97 (25.47 – 60.64)	8.79 (5.37 – 12.66)	57	41.47 (17.16 – 58.58)	11.47 (3.12 – 15.32)	0.410
Pastries	91	8.58 (4.02 – 22.66)	48.94 (0.91 – 104.46)	65	10.72 (4.02 – 25.74)	50.16 (4.80 – 105.78)	0.151
Processed	91	49.22 (28.03 – 70.03)	83.09 (42.11 – 126.88)	58	69.97 (42.72 – 95.97)	127.76 (84.64 – 282.82)	**<0.001**
Total BPA (ng/day), median (IQR)	93	6923.59 (4350.94 – 12,926.03)		66	6141.03 (3889.25 – 11,877.11)		0.499
BPS							
Dairy products	66	452.22 (207.12 – 635.55)	133.54 (73.87 – 217.54)	55	306.54 (145.39 – 603.63)	143.80 (72.50 – 208.90)	0.889
Meat and eggs	87	109.40 (90.29 – 140.87)	527.34 (131.33 – 557.47)	63	128.70 (105.44 – 156.05)	528.82 (183.32 – 573.08)	0.470
Fish	79	21.45 (7.15 – 31.95)	317.39 (1.51 – 1347.70)	60	7.15 (0.00 – 21.45)	317.11 (0.00 – 673.93)	0.440
Vegetables	81	167.95 (108.73 – 227.25)	3733.90 (1865.51 – 14,671.38)	48	158.98 (121.18 – 242.58)	3820.37 (1937.46 – 16,202.09)	0.727
Fruits	86	198.06 (131.78 – 279.89)	625.95 (407.69 – 844.57)	55	132.99 (88.48 – 209.53)	501.67 (239.05 – 744.04)	**0.047**
Legumes	93	7.15 (4.02- 8.58)	1.07 (0.60 – 1.29)	66	8.58 (7.15 – 10.01)	1.29 (1.07 – 1.50)	**0.029**
Cereals	90	38.97 (25.47 – 60.64)	6.00 (3.82 – 9.52)	57	41.47 (17.16 – 58.58)	5.80 (1.79 – 9.03)	0.296
Pastries	91	8.58 (4.02 – 22.66)	6.30 (5.70 – 11.98)	65	10.72 (4.02 – 25.74)	5.58 (1.29 – 9.74)	0.061
Processed	91	49.22 (28.03 – 70.03)	208.74 (98.65 – 1724.47)	58	69.97 (42.72 – 95.97)	215.18 (206.12 – 630.24)	0.171
Total BPS (ng/day), median (IQR)	93	9900.40 (4377.91 – 17,097.21)		66	8200.62 (3710.95 – 19,262.03)		0.912
Total Bisphenols							
Dairy products	66	452.22 (207.12 – 635.55)	3462.56 (1938.17 – 5788.65)	55	306.54 (145.39 – 603.63)	2140.08 (691.06 – 4849.06)	0.215
Meat and eggs	87	109.40 (90.29 – 140.87)	849.59 (291.53 – 918.30)	63	128.70 (105.44 – 156.05)	849.10 (351.28 – 985.52)	0.263
Fish	79	21.45 (7.15 – 31.95)	1847.69 (6.03 – 7858.64)	60	7.15 (0.00 – 21.45)	1846.56 (0.00 – 3929.64)	0.440
Vegetables	81	167.95 (108.73 – 227.25)	4466.05 (1983.23 – 14,857.90)	48	158.98 (121.18 – 242.58)	4388.35 (1986.72 – 16,268.10)	0.831
Fruits	86	198.06 (131.78 – 279.89)	1037.94 (657.29 – 1664.25)	55	132.99 (88.48 – 209.53)	974.71 (415.52 – 1541.65)	0.181
Legumes	93	7.15 (4.02- 8.58)	4.29 (2.41 – 5.15)	66	8.58 (7.15 – 10.01)	5.15 (4.29 – 6.01)	**0.029**
Cereals	90	38.97 (25.47 – 60.64)	15.29 (9.17 – 22.18)	57	41.47 (17.16 – 58.58)	17.57 (5.25 – 26.11)	0.748
Pastries	91	8.58 (4.02 – 22.66)	55.24 (6.20 – 114.09)	65	10.72 (4.02 – 25.74)	62.27 (33.87 – 117.90)	0.230
Processed	91	49.22 (28.03 – 70.03)	318.04 (141.60 – 1755.18)	58	69.97 (42.72 – 95.97)	347.36 (290.71 – 1010.10)	0.105
Total Bisphenols (ng/day), median (IQR)	93	20,499.84 (10,410.41 – 29,284.01)		66	17,378.90 (9112.18 – 28,427.09)		0.912

IQR interquartile range (percentile 25th – percentile 75th); [b]*p*-Values show bisphenols intake significant differences between cases and controls, by U de Mann–Whitney test; *p*-values ≤ 0.05 are highlighted in bold; *BPA* bisphenol A, *BPS* bisphenol S

* n for consumers

showed an increased likelihood of being overweight and obese in school children exposed to high levels of BPA from meat and eggs. This finding was observed only in females and no consistent associations were found in males.

To the best of our knowledge, no previous studies have supported the claim that females are at higher likelihood

Table 3 Dietary intake of bisphenols (ng/day) by foods groups according to cases and controls for females

Food Group	Controls (*n* = 86)			Cases (*n* = 58)			*p*-value[b]
	n*	Food Intake (g/day), median (IQR)	Bisphenol Intake (ng/day), median (IQR)	n*	Food Intake (g/day), median (IQR)	Bisphenol Intake (ng/day), median (IQR)	
BPA							
Dairy products	67	350.48 (188.51 – 645.51)	2894.15 (1435.76 – 4418.16)	43	169.12 (88.66 – 393.05)	1878.41 (105.65 – 4310.55)	**0.037**
Meat and eggs	80	113.69 (88.85 – 136.65)	231.79 (162.11 – 350.19)	46	130.14 (99.66 – 154.37)	319.55 (176.59 – 381.01)	**0.046**
Fish	77	20.51 (7.15 – 31.50)	1540.59 (7.72 – 3283.92)	51	21.45 (7.15 – 31.95)	3249.68 (1527.10 – 9749.03)	0.139
Vegetables	66	190.99 (114.40 – 271.98)	161.28 (24.50 – 345.31)	42	187.20 (114.91 – 261.85)	53.49 (21.74 – 331.14)	0.277
Fruits	77	188.65 (118.73 – 273.13)	499.77 (227.94 – 684.51)	49	155.72 (88.34 – 265.89)	665.86 (110.34 – 829.26)	0.729
Legumes	85	7.15 (4.02 – 8.58)	3.22 (1.81 – 3.86)	58	8.58 (4.69 – 10.01)	3.86 (2.11 – 4.50)	**0.040**
Cereals	82	33.43 (19.37 – 49.57)	7.47 (4.93 – 11–54)	56	29.90 (16.25 – 54.80)	8.69 (4.78 – 14.98)	0.270
Pastries	82	11.55 (4.02 – 21.56)	48.94 (0.75 – 103.89)	56	8.48 (3.35 – 17.81)	48.94 (0.50 – 103.95)	0.901
Processed	84	44.33 (27.58 – 63.09)	83.16 (44.25 – 125.40)	55	58.18 (38.62 – 81.77)	103.30 (80.94 – 163.40)	**0.016**
Total BPA (ng/day), median (IQR)	86	7145.99 (4897.58 – 11,475.55)		58	7753.50 (4199.40 – 11,572.26)		0.883
BPS							
Dairy products	67	350.48 (188.51 – 645.51)	128.67 (84.52 – 199.70)	43	169.12 (88.66 – 393.05)	110.40 (60.54 – 170.98)	0.333
Meat and eggs	80	113.69 (88.85 – 136.65)	228.94 (118.39 – 550.87)	46	130.14 (99.66 – 154.37)	530.23 (126.10 – 570.77)	0.211
Fish	77	20.51 (7.15 – 31.50)	320.82 (2.57 – 683.34)	51	21.45 (7.15 – 31.95)	671.92 (316.32 – 2015.76)	0.139
Vegetables	66	190.99 (114.40 – 271.98)	4499.82 (2043.49 – 15,006.69)	42	187.20 (114.91 – 261.85)	4153.59 (1878.64 – 14,942.34)	0.529
Fruits	77	188.65 (118.73 – 273.13)	634.01 (339.35 – 815.61)	49	155.72 (88.34 – 265.89)	622.20 (223.47 – 832.98)	0.447
Legumes	85	7.15 (4.02 – 8.58)	1.07 (0.60 – 1.29)	58	8.58 (4.69 – 10.01)	1.29 (0.70 – 1.50)	**0.040**
Cereals	82	33.43 (19.37 – 49.57)	5.01 (2.91 – 8.79)	56	29.90 (16.25 – 54.80)	4.46 (2.39 – 8.45)	0.419
Pastries	82	11.55 (4.02 – 21.56)	6.21 (1.61 – 8.18)	56	8.48 (3.35 – 17.81)	5.70 (1.36 – 7.78)	0.286
Processed	84	44.33 (27.58 – 63.09)	209.02 (101.62 – 620.04)	55	58.18 (38.62 – 81.77)	211.10 (102.56 – 1678.06)	0.339
Total BPS (ng/day), median (IQR)	86	8327.37 (4871.06 – 17,848.19)		58	8018.65 (4006.48 – 18,378.72)		0.896
Total Bisphenols							
Dairy products	67	350.48 (188.51 – 645.51)	3077.55 (1542.62 – 4648.94)	43	169.12 (88.66 – 393.05)	2007.60 (439.50 – 4385.58)	**0.047**
Meat and eggs	80	113.69 (88.85 – 136.65)	451.44 (287.68 – 889.87)	46	130.14 (99.66 – 154.37)	860.06 (329.93 – 954.74)	0.120
Fish	77	20.51 (7.15 – 31.50)	1861.42 (10.30 – 3967.26)	51	21.45 (7.15 – 31.95)	3921.60 (1843.42 – 11,764.79)	0.139
Vegetables	66	190.99 (114.40 – 271.98)	5041.14 (2175.03 – 15,615.46)	42	187.20 (114.91 – 261.85)	4455.23 (1962.18 – 14,997.39)	0.508
Fruits	77	188.65 (118.73 – 273.13)	1085.86 (521.59 – 1504.45)	49	155.72 (88.34 – 265.89)	1255.11 (412.61 – 1691.00)	0.653
Legumes	85	7.15 (4.02 – 8.58)	4.29 (2.41 – 5.15)	58	8.58 (4.69 – 10.01)	5.15 (2.81 – 6.01)	**0.040**
Cereals	82	33.43 (19.37 – 49.57)	14.16 (9.01 – 22.07)	56	29.90 (16.25 – 54.80)	13.65 (8.03 – 23.48)	0.916
Pastries	82	11.55 (4.02 – 21.56)	52.90 (6.20 – 110.87)	56	8.48 (3.35 – 17.81)	50.55 (6.20 – 108.64)	0.911
Processed	84	44.33 (27.58 – 63.09)	321.90 (182.62 – 910.17)	55	58.18 (38.62 – 81.77)	337.45 (187.10 – 1709.38)	0.240
Total Bisphenols (ng/day), median (IQR)	86	18,734.76 (12,035.54 – 27,467.75)		58	17,738.61 (11,309.29 – 28,467.20)		0.971

IQR interquartile range (percentile 25th – percentile 75th); [b]*p*-Values show bisphenols intake significant differences between cases and controls, by U de Mann–Whitney test; *p*-values ≤ 0.05 are highlighted in bold; *BPA* bisphenol A, *BPS* bisphenol S

[*] n for consumers

of developing overweight or obesity due to exposure to BPA from meat and eggs. BPA is a chemical compound used in the production of plastics and resins, and its presence in food may occur due to certain packaging and storage processes [27, 36]. It is important to note that research on the association between BPA and health is

Table 4 Diet quality (KIDMED) according to high and low BPA, BPS and total bisfenols exposure for controls and cases by gender

		Boys ($n=159$)			Girls ($n=144$)		
		Controls ($n=93$)	Cases ($n=66$)	*p-value*[a]	Controls ($n=86$)	Cases ($n=58$)	*p-value*[a]
		Mean (SD)			Mean (SD)		
KIDMED		6.21 (2.14)	4.80 (2.24)	**<0.001**	6.11 (2.60)	5.63 (2.03)	0.243
BPA	High exposure (Tertil 3)	6.22 (2.04)	4.92 (2.47)	**0.028**	6.00 (2.50)	5.24 (1.94)	0.219
	Low exposure (Tertil 1 + 2)	6.20 (2.22)	4.72 (2.13)	**0.002**	6.18 (2.67)	5.94 (2.08)	0.669
BPS	High exposure (Tertil 3)	6.38 (1.74)	5.36 (2.15)	**0.042**	6.76 (2.25)	5.60 (2.25)	0.065
	Low exposure (Tertil 1 + 2)	6.10 (2.37)	4.36 (2.26)	**0.001**	5.67 (2.74)	5.64 (2.07)	0.950
Total bisphenols	High exposure (Tertil 3)	6.50 (1.88)	5.26 (2.24)	**0.031**	6.79 (2.04)	5.33 (2.02)	**0.031**
	Low exposure (Tertil 1 + 2)	6.04 (2.27)	4.54 (2.24)	**0.002**	5.76 (2.79)	5.73 (2.05)	0.958

SD standard deviation, *BPA* bisphenol A, *BPS* bisphenol S. aStudent T-test

[a] *p*-Values show diet quality significant differences between cases and controls

p-values ≤ 0.05 are highlighted in bold

ongoing, and there are conflicting debates and findings in the scientific literature.

That the present research only found a consistent association in the females may be due to the sexual dysmorphic effect where females may be more susceptible to BPA due to differences in hormonal response or greater sensitivity to hormonal changes that may be influenced by BPA exposure [22, 37]. Previous epidemiological studies also found a positive association between dietary exposure to BPA and overweight and obesity in females, but not in males [22]. A research [22] found that overweight/obese females were 3.38 times more likely to have high BPA exposure compared to normal-weight females. Other epidemiological studies also observed sex differences [38, 39]. Li et al. (2013) [38] observed a positive association between high urinary BPA levels and overweight in females; but they found no association in males. However, a work [39] found a negative association between urinary BPA and lower BMI and adiposity measures in females.

Some studies have examined how exposure to BPA and some analogues may be associated with changes in metabolism, body fat distribution, adipose tissue function and other metabolic processes that could contribute to the development of obesity. In vitro studies show that BPA, bisphenol F (BPF), BPS and bisphenol AF (BPAF) promote preadipocyte to adipocyte proliferation, due to their ability to bind to nuclear receptor in the murine cell line 3T3-L1 and in human preadipocytes [17, 18, 40]. BPA is also associated with the induction of inflammatory responses, lipogenesis and decreased insulin sensitivity in adipose tissue cells, leading to a dysfunctional adipocyte [41, 42]. In a recent in vitro study, we observed the association between combined exposure to BPA, BPF and BPS on the differentiation of preadipocytes to adipocytes in human adipose tissue. Concretely, in cells exposed to a bisphenol mix (10 nM to 10 mM BPA, BPF and BPS) for 14 days, it was observed a promotion of intracellular lipid accumulation in a dose-independent manner that resulted in significant changes in gene expression of adipogenic markers, such as peroxisome proliferator-activated receptor-γ (PPARγ), CCAAT/enhancer-binding protein (C/EBPα), lipoprotein lipase and fatty acid-binding protein 4 (FABP4) [43]. In animal models, exposure to bisphenols has also been shown to induce alterations in lipid metabolism. Several studies in zebrafish (Danio rerio) showed that chronic exposure to BPA and BPS induced dysregulation of genes involved in lipid metabolism, triggering hepatic steatosis [44–46]. In addition, exposure to environmental doses of BPA in zebrafish was found to be associated with the development of obesity [47]. Studies in rodents show that exposure to BPA during developmental stages was associated with alterations in hormones involved in satiety and appetite, increased food intake, altered adipocyte numbers, glucose and insulin, leading to weight gain [48–50].

To our knowledge, we have not found any studies that have assessed the association between dietary factors of BPA and BPS exposure (by food source) and childhood overweight/obesity. A limited number of epidemiological studies have studied the relationship between dietary bisphenol and obesity in childhood with not conclusive results. Thus Heinsberg et al. didn't found association between dietary BPA levels and adiposity in Samoan children [51] whereas in other study observed that Spanish adolescent females with overweight and obesity had a more dietary BPA exposure compared to normal weight [22].

Biomonitoring studies have addressed the association between bisphenol levels and overweight/obesity with

Table 5 Influencing of the highest (tertil 3 *vs* tertil 1 + 2) BPA, BPS and total bisphenols dietary exposure by food groups on overweight/obesity for males and females

	Males ($n = 159$)						Females ($n = 144$)					
	Crude model			Adjusted model			Crude model			Adjusted model		
Food Group	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p-value***	**OR**	**95% CI**	***p*-value**
BPA												
Dairy products (Ref. Low exposure*) High exposure**	0.79	0.42 – 1.50	0.469	1.31[b]	0.50 – 3.42	0.579	0.58	0.28 – 1.17	0.127	0.37[f]	0.06 – 2.21	0.273
Meat and eggs (Ref. Low exposure) High exposure	1.47	0.77 – 2.78	0.240	1.42[d]	0.29 – 7.00	0.670	2.10	1.04 – 4.23	**0.038**	3.43[b]	1.13 – 10.36	**0.029**
Fish (Ref. Low exposure) High exposure	0.75	0.39 – 1.48	0.412	0.09[c]	0.01 – 1.37	0.083	1.46	0.73 – 2.92	0.281	1.22[f]	0.23 – 6.50	0.817
Vegetables (Ref. Low exposure) High exposure	0.93	0.48 – 1.79	0.825	0.63[b]	0.22 – 1.81	0.393	0.74	0.37 – 1.45	0.378	0.48[d]	0.08 – 3.05	0.439
Fruits (Ref. Low exposure) High exposure	0.77	0.40 – 1.51	0.450	0.67[d]	0.12 – 3.78	0.639	1.50	0.76 – 2.94	0.239	1.30[b]	0.49 – 3.44	0.595
Legumes (Ref. Low exposure) High exposure	2.22	1.16 – 4.24	**0.016**	1.18[d]	0.14 – 9.86	0.881	2.06	1.05 – 4.06	**0.036**	1.44[f]	0.17 – 12.29	0.740
Cereals (Ref. Low exposure) High exposure	2.13	1.11 – 4.06	**0.022**	1.69[f]	0.36 – 7.85	0.506	1.49	0.75 – 2.96	0.255	2.32[a]	0.83 – 6.45	0.107
Pastries (Ref. Low exposure) High exposure	1.85	0.87 – 3.93	0.112	0.58[d]	0.12 – 2.93	0.513	1.04	0.47 – 2.27	0.929	2.90[f]	0.39 – 21.67	0.299
Processed (Ref. Low exposure) High exposure	3.19	1.65 – 6.18	**0.001**	1.42[b]	0.50 – 4.03	0.506	2.13	1.06 – 4.26	**0.033**	1.51[a]	0.55 – 4.13	0.425
Total BPA (Ref. Low exposure) High exposure	0.92	0.48 – 1.76	0.808	1.30[c]	0.25 – 6.84	0.757	1.31	0.66 -2.56	0.440	1.09[b]	0.43 – 2.79	0.857
BPS												
Dairy products (Ref. Low exposure) High exposure	0.82	0.44 – 1.55	0.542	1.22[f]	0.20 – 7.35	0.831	0.76	0.37 – 1.54	0.446	4.50[d]	0.56 – 36.37	0.158
Meat and eggs (Ref. Low exposure) High exposure	1.24	0.65 – 2.36	0.509	0.85[a]	0.34 – 2.12	0.848	1.46	0.73 – 2.92	0.281	1.53[d]	0.23 – 10.14	0.659
Fish (Ref. Low exposure) High exposure	1.23	0.65 – 2.31	0.529	0.74[c]	0.12 – 4.44	0.742	1.48	0.76 – 2.91	0.250	0.53[f]	0.10 – 2.69	0.442
Vegetables (Ref. Low exposure) High exposure	1.00	0.53 – 1.90	0.995	3.54f	0.66 – 18.95	0.139	0.77	0.38 – 1.53	0.452	0.70[f]	0.12 – 4.06	0.688
Fruits (Ref. Low exposure) High exposure	0.70	0.36 – 1.38	0.307	0.77[d]	0.15 – 4.02	0.759	0.85	0.43 – 1.67	0.638	0.24[f]	0.04 – 1.66	0.149
Legumes (Ref. Low exposure) High exposure	2.08	1.02 – 4.26	**0.044**	1.24[d]	0.11 – 14.29	0.863	2.48	1.16 – 5.32	**0.019**	0.78[f]	0.06 – 10.87	0.851
Cereals (Ref. Low exposure) High exposure	10.12	0.59 – 2.12	0.739	2.15[f]	0.44 – 10.53	0.343	1.12	0.55 – 2.30	0.748	1.08[e]	0.09 – 12.87	0.953

Table 5 (continued)

	Males ($n = 159$)						Females ($n = 144$)					
	Crude model			Adjusted model			Crude model			Adjusted model		
Food Group	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p-value***	**OR**	**95% CI**	***p*-value**
Pastries (Ref. Low exposure) High exposure	0.85	0.44 – 1.63	0.620	2.33[c]	0.40 – 13.64	0.349	0.75	0.37 – 1.50	0.409	0.61[f]	0.10 – 3.68	0.591
Processed (Ref. Low exposure) High exposure	1.24	0.65 – 2.36	0.509	0.38[d]	0.06 – 2.37	0.301	1.19	0.60 – 2.35	0.615	1.89[d]	0.27 – 13.36	0.525
Total BPS (Ref. Low exposure) High exposure	1.17	0.61 – 2.22	0.638	2.53[f]	0.52 – 12.29	0.251	0.83	0.42 – 1.64	0.588	0.68[f]	0.10 – 4.44	0.688
Total bisphenols												
Dairy products (Ref. Low exposure) High exposure	0.79	0.42 – 1.50	0.469	1.02[a]	0.41 – 2.51	0.969	0.58	0.28 – 1.17	0.127	0.37[f]	0.06 – 2.21	0.273
Meat and eggs (Ref. Low exposure) High exposure	1.47	0.77 – 2.78	0.240	2.06[d]	0.39 – 10.95	0.396	1.68	0.85 – 3.34	0.137	2.27[d]	0.36 – 14.54	0.387
Fish (Ref. Low exposure) High exposure	0.75	0.39 – 1.48	0.412	0.09[c]	0.01 – 1.37	0.083	1.46	0.73 – 2.92	0.281	1.22[f]	0.23 – 6.50	0.817
Vegetables (Ref. Low exposure) High exposure	1.02	0.58 – 2.09	0.780	3.69[f]	0.70 – 19.54	0.125	0.83	0.42 – 1.64	0.588	0.82[f]	0.14 – 4.81	0.829
Fruits (Ref. Low exposure) High exposure	0.61	0.31 – 1.20	0.154	0.74[c]	0.12 – 4.55	0.743	1.33	0.68 – 2.61	0.404	1.12[b]	0.43 – 2.90	0.813
Legumes (Ref. Low exposure) High exposure	2.08	1.02 – 4.26	**0.044**	1.24[d]	0.11 – 14.29	0.863	2.48	1.16 – 5.32	**0.019**	0.77[f]	0.06 – 10.87	0.851
Cereals (Ref. Low exposure) High exposure	1.68	0.89 – 3.18	0.110	1.79[b]	0.69 – 4.68	0.232	1.29	0.65 – 2.58	0.468	1.21[a]	0.42 – 3.49	0.725
Pastries (Ref. Low exposure) High exposure	1.41	0.74 – 2.65	0.290	0.96[d]	0.18 – 5.11	0.962	0.78	0.39 – 1.58	0.492	0.90[a]	0.34 – 2.39	0.839
Processed (Ref. Low exposure) High exposure	1.30	0.68 – 2.47	0.425	0.40[d]	0.06 – 2.51	0.328	1.19	0.60 – 2.35	0.615	1.89[d]	0.26 – 13.36	0.525
Total bisphenols (Ref. Low exposure) High exposure	0.97	0.50 – 1.88	0.934	0.77[d]	0.15 – 4.04	0.757	0.75	0.36 – 1.55	0.437	0.36[f]	0.05 – 2.39	0.290

[a] Analytes in foods were adjusted for age, energy intake, diet quality and parental educational level

[b] Analytes in foods were adjusted for age, energy intake, diet quality, parental educational level and smoking among members of the family unit

[c] Analytes in foods were adjusted for age, energy intake, diet quality, parental educational level, smoking among members of the family unit, physical activity and body fat percentage

[d] Analytes in foods were adjusted for age, energy intake, diet quality, parental educational level, smoking among members of the family unit and body fat percentage

[e] Analytes in foods were adjusted for age, energy intake, diet quality, parental educational level, physical activity and body fat percentage

[f] Analytes in foods were adjusted for age, energy intake, diet quality, parental educational level and body fat percentage

p-values ≤ 0.05 are highlighted in bold; BPA: bisphenol A; BPS: bisphenol S; Ref: reference category. * = low exposure (tertiles 1 + 2); ** = high exposure (tertile 3)

contradictory findings. In this sense, a study derived from the National Health and Nutrition Examination Survey (NHANES) in the United States, involving 745 children and adolescents, showed a statistically significant positive association between urinary BPA and BPF levels with increased body fat. However, no significant association was found with BPS [52]. Another research performed in 212 children from the Health Outcomes and Measures of the Environment (HOME) study showed no significant association between childhood urinary BPA and BPS concentrations with increased adiposity [53]. Another NHAMES-derived study in children and adolescents showed a modest positive association between urinary BPS levels and increased BMI and abdominal fat. However, urinary BPA concentrations were not significantly associated with any body mass findings [54]. A Korean study involving 2,351 children and adolescents who participated in the Korean National Environmental Health Survey (KoNEHS) found no statistically significant positive association between urinary BPA and obesity in Korean children [55].

In relation to dietary exposure, our findings are consistent with previous research that also highlights food intake as the main source of bisphenol exposure, with 90% of exposure estimated to come from diet [13, 14, 22, 56, 57]. Most of the fresh foods in the present study were found to contain BPA and BPS, the selected foods are packaged foods, although some foods are fresh (Supplementary Material, Table S6). Consumption of fresh food is considered a healthy dietary habit and is associated with lower exposure to bisphenols or other environmental chemical contaminants compared to other foods. However, studies show that exposure to bisphenols from these foods comes mainly from packaged and ready-to-eat foods [27, 58]. The presence of bisphenols in food may be due to the presence of bisphenols in the environment in which they originate (air, dust, water, etc.) or due to the presence of bisphenols in the composition of food packaging [36, 59, 60]. In relation to contamination by the environment in which they are ingested, the presence of BPA has been detected in fresh foods such as meat, fish, eggs, cereals, vegetables and fresh fruit, demonstrating the possibility of contamination prior to processing and packaging [27, 61]. The presence of these compounds in fresh foods points to the ubiquity of bisphenols throughout the food production chain, beyond packaging.

In the present study, cases of both sexes showed slightly higher but significant exposure to BPA and BPS through intake of legumes and BPA from processed foods compared to controls due to their higher daily intake. On the other hand, exposure to BPS from fruit and BPA from dairy products was found to be higher in the control group in males and females respectively. These differences may be related to assimilation behaviour during childhood, as diet is a dietary pattern determined by direct food experience, imitation, food availability, economic income, emotional symbols and cultural traditions [62, 63].

In our study, dietary exposure to BPA was below the limit of 4 μg/kg bw/day set by the European Food Safety Authority [64]; however, a new limit of 0.2 ng/kg bw/day has recently been set [65] which is lower than the dietary exposure of our study participants (average intake of BPA = 306.74 ± 263.64 ng/kg bw/day, data not shown). International organisations have not yet established a specific limit for BPS and the other analogues.

Dietary exposure to BPA and analogues is highest in early life. This is due to the unequal relationship between body weight and food consumption [66]. The effect of EDCs has been shown to be more intense, pronounced and at lower doses in early life. Since the detoxifying mechanisms present in adulthood are not fully functional in the developmental stages. The metabolic rate during early life is higher than during adulthood, leading to an increase in their effects on the organism, such as their obesogenic effect [67]. Due to these findings it is important to protect the most vulnerable groups from exposure to bisphenols and to obtain more evidence on the possible on weight gain or other adverse results in these age groups.

Among our findings, diet quality (KIDMED) is not associated with exposure to BPA, BPS and total bisphenols in both sexes. However, statistically significant differences by weight and diet quality were observed for males, with the control group scoring higher on the KIDMED compared to the cases. On the other hand, the present study shows that exposure to total BPA and total BPS in both sexes is slightly higher in the control group, although these differences do not reach statistical significance. A study published in 2022 by Melough et al. observed that healthy diets commonly recommended for disease prevention do not appear to reduce exposure to many EDCs, including bisphenols [68]. This may be due to the dietary intake of bisphenols from fresh produce such as fruits, vegetables, meats and fish among others [2, 61].

The present study has two strengths. The first is that, to our knowledge it is the first study to evaluate the association between dietary factors of BPA and BPS exposure (according to food source) and childhood overweight/obesity. And the second strength is that qualified personnel were available to take the anthropometric measurements and to collect the data by means of questionnaires, thus achieving greater accuracy in obtaining the data. In relation to the limitations of the study, the main limitation is a relatively small sample size, that could contribute

to the variability of the results, which is why most of the findings have not shown statistically significant associations. In addition, the analyses were not adjusted for multiple comparisons by the exploratory nature of our study. Nevertheless, we are interested in detecting the greatest number of possible associations that need to be confirmed in further studies. Of note, the use of retrospective FFQs could introduce inaccuracies, leading to potential information biases, particularly recall bias and social desirability bias. In the latter case, where participants' parents might report the frequency of their children's food intake based on what they believe that should children consume, rather than the actual frequency. Although the FFQs are not free from errors in estimating dietary intake, they are considered the reference dietary instrument in nutrition studies [69] and no ideal method without limitations exists.

The results obtained in this explorative study can serve as a basis to confirm hypotheses in further research. Despite the fact that BPA remains the main bisphenol detected in food samples and it has been found to be the most important [27, 70], the present study shows that the total daily dietary intake of BPS in schoolchildren is higher than that of BPA. This result reflects that analogues are replacing BPA and exposure to BPA is expected to continue to increase. The current lack of legal regulation of analogues and the failure to set toxicological limits are the reason why analogues are increasingly detected in both food and biological samples [27, 70–73]. Since BPA analogues have a similar chemical structure to BPA, they can be said to exhibit similar endocrine disrupting and obesogenic activity [19, 42, 74, 75].

Conclusions

The present investigation shows a statistically significant positive association between dietary exposure to BPA from meat and eggs and overweight and obesity in females. Furthermore, it has been observed that the dietary intake of BPA in the schoolchildren in the present study was much higher than the acceptable daily intake established by EFSA for the last year.

The ubiquity of bisphenols and the results found in the present study represent a public health concern. However, further epidemiological studies are needed to assess the obesogenic activity of bisphenols in the most vulnerable age groups, to confirm the present findings.

Abbreviations

EDCs	Endocrine-Disrupting Chemicals:
BPA	BisPhenol A
BPS	BisPhenol S
BMI	Body Mass Index
FFQ	Food Frequency Questionnaire
IQR	InterQuartile Range
OR	Odds Ratio
CI	Confidence Interval
T	Tertiles
BPF	BisPhenol F
BPAF	BisPhenol AF
PPARγ	Peroxisome Proliferator-Activated Receptor-γ
C/EBPα	CCAAT/Enhancer-Binding Protein
FABP4	Lipoprotein Lipase and Fatty Acid-Binding Protein 4
NHANES	National Health and Nutrition Examination Survey
HOME	Health Outcomes and Measures of the Environment
KoNEHS	Korean National Environmental Health Survey

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12940-024-01134-7.

Supplementary Material 1.

Acknowledgements

The results presented in this article are part of a doctoral thesis by Yolanda Gálvez-Ontiveros, Nutrition and Food Sciences Doctorate Program of the University of Granada. The authors are grateful to the Spanish Ministry of Education, Culture and Sports for the pre-doctoral fellowship granted to Yolanda Gálvez-Ontiveros (FPU19/05989).

Authors' contributions

YG-O: Data curation, Methodology, Formal analysis, Writing -original draft, Writing – review & editing, CM: Data curation, Methodology, Formal analysis, Writing -original draft, Writing – review & editing, MVG-M: Investigation, Writing – review & editing, JJM: Investigation, Writing – review & editing, VAFB: Investigation, Writing – review & editing, MAM-B: Investigation, Writing – review & editing, CS-S: Investigation, Writing – review & editing, IS-B: Formal analysis, Writing -original draft, Writing – review & editing, AR: Conceptualization, Project administration, Funding acquisition, Supervision, Writing – review & editing, AZ-G: Conceptualization, Project administration, Funding acquisition, Supervision, Writing – review & editing. All authors read and approved the final manuscript.

Funding

This study has been funded by Instituto de Salud Carlos III (ISCIII) through the project "PI20/01278" and "PI23/01359" and co-funded by the European Union; co-funded project FEDER-Consejería de Salud y Familias, Junta de Andalucía "PE-0250–2019"; co-funded project FEDER/Junta de Andalucía-Consejería de Transformación Económica, Industria, Conocimiento y Universidades/Proyecto "P18-RT-4247"; and project I + D + i del Programa Operativo FEDER 2020 "CTS-252-UGR20".

Data availability

The data used in the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All parents or legal tutors of the study participants were fully informed about the present study and signed the informed consent. The present study has been approved by the ethics committees of the University of Granada and of the Provincial Biomedical Research of Granada (CEI), Spain (reference 1939-M1–22, Andalusian Biomedical Research Ethics Portal), and has been performed following the ethical standards.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details
[1]Department of Nutrition and Food Science, University of Granada, Granada 18071, Spain. [2]Instituto de Investigación Biosanitaria Ibs. GRANADA, Granada 18014, Spain. [3]"José Mataix Verdú" Institute of Nutrition and Food Technology (INYTA), Biomedical Research Centre (CIBM), University of Granada, Granada 18100, Spain. [4]Department of Didactics and Corporal Expression, University of Granada, 18071 Granada, Spain. [5]Maracena Health Center, Andalusian Health Service, Granada 18200, Spain. [6]Department of Physiology, University of Granada, Granada 18071, Spain. [7]Department of Preventive Medicine and Public Health, University of Granada, Granada 18071, Spain. [8]Consortium for Biomedical Research in Epidemiology & Public Health (CIBER en Epidemiología y Salud Pública-CIBERESP), Madrid 28029, Spain. [9]Department of Analytical Chemistry, University of Granada, Granada 18071, Spain.

Received: 11 April 2024 Accepted: 17 October 2024
Published online: 29 October 2024

References

1. Boudalia S, Bousbia A, Boumaaza B, Oudir M, Canivenc Lavier MC. Relationship between endocrine disruptors and obesity with a focus on bisphenol a: a narrative review. Bioimpacts. 2021;11:289–300.
2. González-Casanova JE, Pertuz-Cruz SL, Caicedo-Ortega NH, Rojas-Gomez DM. Adipogenesis regulation and endocrine disruptors: emerging insights in obesity. Biomed Res Int. 2020;2020:7453786.
3. Murro I, Lisco G, Di Noia C, Lampignano L, Zupo R, Giagulli VA, et al. Endocrine disruptors and obesity: an overview. Endocr Metab Immune Disord Drug Targets. 2022;22:798–806.
4. Di Pietro G, Forcucci F, Chiarelli F. Endocrine disruptor chemicals and children's health. Int J Mol Sci. 2023;24: 2671.
5. Groh KJ, Geueke B, Martin O, Maffini M, Muncke J. Overview of intentionally used food contact chemicals and their hazards. Environ Int. 2021;150:106225.
6. Micić D, Polovina S, Micić D, Macut D. Endocrine disrupting chemicals and obesity: the evolving story of obesogens. Acta Endocrinol (Buchar). 2021;17:503–8.
7. Agencia Española de Seguridad Alimentaria y Nutrición (AESAN). Informe del Comité Científico de la Agencia Española de Seguridad Alimentaria y Nutrición (AESAN) sobre las evidencias disponibles en relación a la potencial actividad obesogénica de determinados compuestos químicos que pueden estar presentes en los alimentos. 2023. Available from: https://www.aesan.gob.es/AECOSAN/docs/documentos/publicaciones/revistas_comite_cientifico/OBESOGENOS.pdf
8. Ribeiro CM, Beserra BTS, Silva NG, Lima CL, Rocha PRS, Coelho MS, et al. Exposure to endocrine-disrupting chemicals and anthropometric measures of obesity: a systematic review and meta-analysis. BMJ Open. 2020;10: e033509.
9. Ghassabian A, Vandenberg L, Kannan K, Trasande L. Endocrine-disrupting chemicals and child health. Annu Rev Pharmacol Toxicol. 2022;62:573–94.
10. Haverinen E, Fernandez MF, Mustieles V, Tolonen H. Metabolic syndrome and endocrine disrupting chemicals: an overview of exposure and health effects. Int J Environ Res Public Health. 2021;18: 13047.
11. Biemann R, Blüher M, Isermann B. Exposure to endocrine-disrupting compounds such as phthalates and bisphenol A is associated with an increased risk for obesity. Best Pract Res Clin Endocrinol Metab. 2021;35: 101546.
12. European Food Safety Authority (EFSA): Bisfenol A. 2023. https://www.efsa.europa.eu/es/topics/topic/bisphenol. Accessed 5 Feb 2024.
13. González-Casanova JE, Bermúdez V, Caro Fuentes NJ, Angarita LC, Caicedo NH, Rivas Muñoz J, et al. New Evidence on BPA's role in adipose tissue development of proinflammatory processes and its relationship with obesity. Int J Mol Sci. 2023;24: 8231.
14. Ni L, Zhong J, Chi H, Lin N, Liu Z. Recent advances in sources, migration, public health, and surveillance of bisphenol a and its structural analogs in canned foods. Foods. 2023;12: 1989.
15. Predieri B, Iughetti L, Bernasconi S, Street ME. Endocrine disrupting chemicals' effects in children: what we know and what we need to learn? Int J Mol Sci. 2022;23: 11899.
16. Huc L, Lemarié A, Guéraud F, Héliès-Toussaint C. Low concentrations of bisphenol A induce lipid accumulation mediated by the production of reactive oxygen species in the mitochondria of HepG2 cells. Toxicol In Vitro. 2012;26:709–17.
17. Martínez MÁ, Blanco J, Rovira J, Kumar V, Domingo JL, Schuhmacher M. Bisphenol A analogues (BPS and BPF) present a greater obesogenic capacity in 3T3-L1 cell line. Food Chem Toxicol. 2020;140: 111298.
18. Skledar DG, Carino A, Trontelj J, Troberg J, Distrutti E, Marchianò S, et al. Endocrine activities and adipogenic effects of bisphenol AF and its main metabolite. Chemosphere. 2019;215:870–80.
19. Darbre PD. Endocrine disruptors and obesity. Curr Obes Rep. 2017;6:18–27.
20. Desai M, Ferrini MG, Jellyman JK, Han G, Ross MG. In vivo and in vitro bisphenol A exposure effects on adiposity. J Dev Orig Health Dis. 2018;9:678–87.
21. Kim KY, Lee E, Kim Y. The association between bisphenol a exposure and obesity in children-a systematic review with meta-analysis. Int J Environ Res Public Health. 2019;16: 2521.
22. Robles-Aguilera V, Gálvez-Ontiveros Y, Rodrigo L, Salcedo-Bellido I, Aguilera M, Zafra-Gómez A, et al. Factors associated with exposure to dietary bisphenols in adolescents. Nutrients. 2021;13: 1553.
23. Wu W, Li M, Liu A, Wu C, Li D, Deng Q, et al. Bisphenol a and the risk of obesity a systematic review with meta-analysis of the epidemiological evidence. Dose Response. 2020;18:1559325820916949.
24. Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut offs to define thinness in children and adolescents: international survey. BMJ. 2007;335:194.
25. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ. 2000;320:1240–3.
26. López-Gajardo MA, Leo FM, Sánchez-Miguel PA, López-Gajardo D, Soulas C, Tapia-Serrano MA. KIDMED 2.0, An update of the KIDMED questionnaire: Evaluation of the psychometric properties in youth. Front Nutr. 2022;9: 945721.
27. Gálvez-Ontiveros Y, Moscoso-Ruiz I, Rodrigo L, Aguilera M, Rivas A, Zafra-Gómez A. Presence of Parabens and Bisphenols in Food Commonly Consumed in Spain. Foods. 2021;10: 92.
28. García-Córcoles MT, Cipa M, Rodríguez-Gómez R, Rivas A, Olea-Serrano F, Vílchez JL, et al. Determination of bisphenols with estrogenic activity in plastic packaged baby food samples using solid-liquid extraction and clean-up with dispersive sorbents followed by gas chromatography tandem mass spectrometry analysis. Talanta. 2018;178:441–8.
29. Monteagudo C, Robles-Aguilera V, Salcedo-Bellido I, Gálvez-Ontiveros Y, Samaniego-Sánchez C, Aguilera M, et al. Dietary exposure to parabens and body mass index in an adolescent Spanish population. Environ Res. 2021;201: 111548.
30. Moreiras O, Carbajal Á, Cabrera L, Cuadrado C. Tablas de composición de alimentos. Guía de prácticas. 19ª ed. Pirámide; 2018.
31. Charisiadis P, Andrianou XD, van der Meer TP, den Dunnen WFA, Swaab DF, Wolffenbuttel BHR, et al. Possible Obesogenic Effects of Bisphenols Accumulation in the Human Brain. Sci Rep. 2018;8:8186.
32. Song Y, Hauser R, Hu F, Franke A, Liu S, Sun Q. Urinary concentrations of bisphenol A and phthalate metabolites and weight change: a prospective investigation in US women. Int J Obes (Lond). 2014;38:1532–7.
33. Zhang Y, Dong T, Hu W, Wang X, Xu B, Lin Z, et al. Association between exposure to a mixture of phenols, pesticides, and phthalates and obesity: Comparison of three statistical models. Environ Int. 2019;123:325–36.
34. Kapoor N, Arora S, Kalra S. Gender Disparities in People Living with Obesity - An Unchartered Territory. J Midlife Health. 2021;12:103–7.
35. Moon MK, Kim MJ, Lee I, Kim S, Choi S, Park J, et al. Exposure to Bisphenol A, S, and F and its Association with Obesity and Diabetes Mellitus in General Adults of Korea: Korean National Environmental Health Survey (KoNEHS) 2015–2017. Expo Health. 2023;15:53–67.
36. Barboza LGA, Cunha SC, Monteiro C, Fernandes JO, Guilhermino L. Bisphenol A and its analogs in muscle and liver of fish from the North East Atlantic Ocean in relation to microplastic contamination. Exposure and risk to human consumers. Journal of Hazardous Materials. 2020;393: 122419.
37. Wang H, Zhou Y, Tang C, Wu J, Chen Y, Jiang Q. Association between bisphenol A exposure and body mass index in Chinese school children: a cross-sectional study. Environ Health. 2012;11:79.

38. Li D-K, Miao M, Zhou Z, Wu C, Shi H, Liu X, et al. Urine bisphenol-A level in relation to obesity and overweight in school-age children. PLoS ONE. 2013;8: e65399.
39. Vafeiadi M, Roumeliotaki T, Myridakis A, Chalkiadaki G, Fthenou E, Dermitzaki E, et al. Association of early life exposure to bisphenol A with obesity and cardiometabolic traits in childhood. Environ Res. 2016;146:379–87.
40. Boucher JG, Husain M, Rowan-Carroll A, Williams A, Yauk CL, Atlas E. Identification of mechanisms of action of bisphenol a-induced human preadipocyte differentiation by transcriptional profiling. Obesity (Silver Spring). 2014;22:2333–43.
41. Ariemma F, D'Esposito V, Liguoro D, Oriente F, Cabaro S, Liotti A, et al. Low-Dose Bisphenol-A Impairs Adipogenesis and Generates Dysfunctional 3T3-L1 Adipocytes. PLoS ONE. 2016;11: e0150762.
42. Boucher JG, Ahmed S, Atlas E. Bisphenol S Induces Adipogenesis in Primary Human Preadipocytes From Female Donors. Endocrinology. 2016;157:1397–407.
43. Reina-Pérez I, Olivas-Martínez A, Mustieles V, Salamanca-Fernández E, Molina-Molina JM, Olea N, et al. The Mixture of Bisphenol-A and Its Substitutes Bisphenol-S and Bisphenol-F Exerts Obesogenic Activity on Human Adipose-Derived Stem Cells. Toxics. 2022;10: 287.
44. Qin J, Ru S, Wang W, Hao L, Ru Y, Wang J, et al. Long-term bisphenol S exposure aggravates non-alcoholic fatty liver by regulating lipid metabolism and inducing endoplasmic reticulum stress response with activation of unfolded protein response in male zebrafish. Environ Pollut. 2020;263: 114535.
45. Santangeli S, Notarstefano V, Maradonna F, Giorgini E, Gioacchini G, Forner-Piquer I, et al. Effects of diethylene glycol dibenzoate and Bisphenol A on the lipid metabolism of Danio rerio. Sci Total Environ. 2018;636:641–55.
46. Sun L, Ling Y, Jiang J, Wang D, Wang J, Li J, et al. Differential mechanisms regarding triclosan vs. bisphenol A and fluorene-9-bisphenol induced zebrafish lipid-metabolism disorders by RNA-Seq. Chemosphere. 2020;251: 126318.
47. Tian S, Yan S, Meng Z, Huang S, Sun W, Jia M, et al. New insights into bisphenols induced obesity in zebrafish (Danio rerio): Activation of cannabinoid receptor CB1. J Hazard Mater. 2021;418: 126100.
48. Angle BM, Do RP, Ponzi D, Stahlhut RW, Drury BE, Nagel SC, et al. Metabolic disruption in male mice due to fetal exposure to low but not high doses of bisphenol A (BPA): evidence for effects on body weight, food intake, adipocytes, leptin, adiponectin, insulin and glucose regulation. Reprod Toxicol. 2013;42:256–68.
49. Desai M, Ferrini MG, Han G, Jellyman JK, Ross MG. In vivo maternal and in vitro BPA exposure effects on hypothalamic neurogenesis and appetite regulators. Environ Res. 2018;164:45–52.
50. Stoker C, Andreoli MF, Kass L, Bosquiazzo VL, Rossetti MF, Canesini G, et al. Perinatal exposure to bisphenol A (BPA) impairs neuroendocrine mechanisms regulating food intake and kisspetin system in adult male rats. Evidences of metabolic disruptor hypothesis. Molecular and Cellular Endocrinology. 2020;499: 110614.
51. Heinsberg LW, Bui CNN, Hartle JC, Sereika SM, Choy CC, Wang D, et al. Estimated Dietary Bisphenol-A Exposure and Adiposity in Samoan Mothers and Children. Toxics. 2020;8: 67.
52. Liu B, Lehmler HJ, Sun Y, Xu G, Sun Q, Snetselaar LG, et al. Association of Bisphenol A and Its Substitutes, Bisphenol F and Bisphenol S, with Obesity in United States Children and Adolescents. Diabetes Metab J. 2019;43:59–75.
53. Gajjar P, Liu Y, Li N, Buckley JP, Chen A, Lanphear BP, et al. Associations of mid-childhood bisphenol A and bisphenol S exposure with mid-childhood and adolescent obesity. Environ Epidemiol. 2021;6: e187.
54. Jacobson MH, Woodward M, Bao W, Liu B, Trasande L. Urinary bisphenols and obesity prevalence Among U.S. children and adolescents. J Endocr Soc. 2019;3:1715–26.
55. Seo MY, Moon S, Kim S-H, Park MJ. Associations of phthalate metabolites and bisphenol a levels with obesity in children: The Korean National Environmental Health Survey (KoNEHS) 2015 to 2017. Endocrinol Metab (Seoul). 2022;37:249–60.
56. Chen D, Kannan K, Tan H, Zheng Z, Feng Y-L, Wu Y, et al. Bisphenol analogues other than BPA: environmental occurrence, human exposure, and toxicity-a review. Environ Sci Technol. 2016;50:5438–53.
57. Martínez MA, Rovira J, Prasad Sharma R, Nadal M, Schuhmacher M, Kumar V. Comparing dietary and non-dietary source contribution of BPA and DEHP to prenatal exposure: A Catalonia (Spain) case study. Environ Res. 2018;166:25–34.
58. Pacyga DC, Sathyanarayana S, Strakovsky RS. Dietary Predictors of Phthalate and Bisphenol Exposures in Pregnant Women. Adv Nutr. 2019;10:803–15.
59. Careghini A, Mastorgio AF, Saponaro S, Sezenna E. Bisphenol A, nonylphenols, benzophenones, and benzotriazoles in soils, groundwater, surface water, sediments, and food: a review. Environ Sci Pollut Res Int. 2015;22:5711–41.
60. Mercogliano R, Santonicola S. Investigation on bisphenol A levels in human milk and dairy supply chain: a review. Food Chem Toxicol. 2018;114:98–107.
61. Liao C, Kannan K. Concentrations and profiles of bisphenol A and other bisphenol analogues in foodstuffs from the United States and their implications for human exposure. J Agric Food Chem. 2013;61:4655–62.
62. Qiu C, Hatton R, Li Q, Xv J, Li J, Tian J, et al. Associations of parental feeding practices with children's eating behaviors and food preferences: a Chinese cross-sectional study. BMC Pediatr. 2023;23:84.
63. Sánchez-García R, Reyes-Morales H, González-Unzaga MA. Preferencias alimentarias y estado de nutrición en niños escolares de la Ciudad de México. Bol Med Hosp Infant Mex. 2014;71:358–66.
64. EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF). Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs. EFSA J. 2015;13:3978.
65. EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP), Lambré C, Barat Baviera JM, Bolognesi C, Chesson A, et al. Re-evaluation of the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs. EFSA J. 2023;21:e06857.
66. Agencia Española de Seguridad Alimentria y Nutrición (AESAN). Preguntas y Respuestas sobre el Bisfenol A. 2021. Available from: https://www.aesan.gob.es/AECOSAN/docs/documentos/seguridad_alimentaria/gestion_riesgos/Preguntas_respuestas_bisfenol_A.pdf.
67. García-Mayor RV, Larrañaga Vidal A, Docet Caamaño MF, Lafuente iménez A. Disruptores endocrinos y obesidad: obesógenos. Endocrinol Nutr. 2012;59:261–7 A.
68. Melough MM, Maffini MV, Otten JJ, Sathyanarayana S. Diet quality and exposure to endocrine-disrupting chemicals among US adults. Environ Res. 2022;211: 113049.
69. Martínez-González MA, De la Fuente-Arillaga C, Wärnberg J. Epidemiologia nutricional. In: Conceptos de Salud Pública y Estrategias Preventivas. Un Manual Para Ciencias de la Salud, 1st ed.; Martínez-González, M.A., Ed.; Elsevier España SL: Barcelona, Spain; 2013; pp. 337–341.
70. Lucarini F, Gasco R, Staedler D. Simultaneous Quantification of 16 Bisphenol Analogues in Food Matrices. Toxics. 2023;11: 665.
71. Gálvez-Ontiveros Y, Moscoso-Ruiz I, Almazán Fernández de Bobadilla V, Monteagudo C, Giménez-Martínez R, Rodrigo L, et al. Levels of Bisphenol A and its analogs in nails, saliva, and urine of children: a case control study. Front Nutr. 2023;10:1226820.
72. Pan Y, Zhu J, Zhu Z, Wei X, Zhou X, Yin R, et al. Occurrence of multiple bisphenol S analogues in children from Shantou. China Environ Int. 2023;174:107926.
73. Wan Y-P, Ma Q-G, Hayat W, Liu Z-H, Dang Z. Ten bisphenol analogues in Chinese fresh dairy milk: high contribution ratios of conjugated form, importance of enzyme hydrolysis and risk evaluation. Environ Sci Pollut Res Int. 2023;30:88049–59.
74. Andújar N, Gálvez-Ontiveros Y, Zafra-Gómez A, Rodrigo L, Álvarez-Cubero MJ, Aguilera M, et al. Bisphenol a analogues in food and their hormonal and obesogenic effects: a review. Nutrients. 2019;11: 2136.
75. Rochester JR, Bolden AL. Bisphenol S and F: a systematic review and comparison of the hormonal activity of bisphenol a substitutes. Environ Health Perspect. 2015;123:643–50.

Publisher's Note