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Higher ultra-processed food intake is associated with higher DNA damage in healthy adolescents

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Abstract

Ultra-processed food is one of the main contributors to energy supply and consumption in food systems worldwide, and evidence of their detrimental health outcomes in humans is emerging. This study aimed to assess ultra-processed food intake and its association with urinary levels of 8-hydroxy-2′-deoxyguanosine (8-OHdG), a biomarker of DNA oxidative damage, in 139 healthy adolescents in Karaj City in Iran. Usual dietary intake was measured using a 168-item validated FFQ. The daily intake of ultra-processed food consumption was determined through the classification of NOVA, and general linear models were used to compare the urinary levels of 8-OHdG/creatinine (ng/mg creatinine) within tertiles of ultra-processed food intake. Adolescents in the higher tertile of ultra-processed food consumption had a significantly higher mean level of urinary 8-OHdG/creatinine in comparison with the lower tertiles in the crude model ($P_{\text{for trend}}$: 0·003) and after adjustment for confounding variables, including total energy intake, sex, age, BMI for age *Z*-score, obesity and physical activity ($P_{\text{for trend}}$: 0·004). This association was still significant after adjusting for dietary intake of whole grains, nuts, legumes, the ratio of MUFA:SFA (g/d) and Mediterranean dietary score ($P_{\text{for trend}}$: 0·002). More studies are needed to explore the determinants of ultra-processed food supply, demand, consumption and health effects; such studies should be applied to develop evidence-informed policies and regulatory mechanisms to improve children's and adolescents' food environment policymaking and legislation with special attention to ultra-processed food.

Key words: Ultra-processed food: Oxidative stress: 8-Hydroxy-2′-deoxyguanosine: Adolescents: DNA damage: Food-processing industry: Commercial determinants of health

Non-communicable diseases are the leading cause of death worldwide. They impose a remarkable economic burden, estimated at 7 trillion dollars during 2011–2025 in low- and middle-income countries[1]. Oxidative stress, an imbalance between the production of reactive oxygen species and antioxidant defence, can occur at an early age and lead to the development of several non-communicable diseases including cancer[2,3].

Children and adolescents seem to be more susceptible to exposure to accumulated reactive oxygen species and carcinogenic factors during development stages[4–7]. Moreover, unhealthy risk factors in children and adolescents could contribute to the long-term influence on non-communicable diseases in adult life based on the developmental origins of health and disease hypothesis[8]. Therefore, knowing dietary modifiable factors affecting oxidative damage is of great importance[9–12].

8-Hydroxy-2′-deoxyguanosine (8-OHdG), a biomarker of oxidative-generated DNA damage, has been widely used as a sensitive indicator of oxidative stress and carcinogenesis[13]. Several studies have reported higher levels of 8-OHdG in several non-communicable diseases including cancer[14–18]. Urinary 8-OHdG is a stable biomarker of oxidative stress, and the production of artifacts during its sampling is rare[19–21].

Abbreviations: 8-OHdG, 8-hydroxy-2′-deoxyguanosine; MDS, Mediterranean dietary score; MET, metabolic equivalent.

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Furthermore, its measurement is non-invasive, which makes it a suitable biomarker for assessing overall DNA oxidative damage[22], especially in the population of vulnerable children.

Ultra-processed food has become one of the main sources of food consumed in modern food systems in different countries[23–26]. Recently, several studies have revealed that consumption of ultra-processed food is associated with adverse health outcomes, including cancer, CVD and obesity[27–34]. Fiolet *et al.* assessed dietary intake of 104 980 adults enrolled in the prospective French NutriNet-Santé cohort study and found that a 10 % increase in dietary intake of ultra-processed food was associated with a significant 12 % increase in overall cancer risk[29,35]. Another report from the recent study by Srour *et al.*[36] showed that there was a higher risk of CVD associated with the consumption of ultra-processed food. Using secondary data analyses of the Seguimiento University of Navarra prospective cohort study in Spain, Rico-Campà *et al.*[27] reported that each additional serving of ultra-processed food increased all-cause mortality by 18 %.

To our knowledge, the association between oxidative stress and dietary ultra-processed food has not been investigated; however, a limited number of studies have reported that advanced glycation end products in ultra-processed food could adversely affect oxidative stress in animal or *in vitro* cell studies[37,38]. Heterocyclic amine intakes were also associated with high levels of DNA damage levels in adults[39].

Until now, studies linking 8-OHdG and dietary factors mostly focused on antioxidant nutrients and the Mediterranean diet and its food components, in which some studies showed protective effects of antioxidant components[9,39,40] while others did not[41,42]. For example, Aline de Carvalho *et al.* found that a lower intake of fruit was associated with higher DNA damage levels in 146 Brazilian adults[39]. Kim *et al.*[42], however, did not find any association between Mediterranean diet and 8-OHdG in 976 Korean adults.

Examining the association between DNA oxidative damage and ultra-processed food intake gained from a regular diet in different populations can unravel the mechanisms underlying the detrimental effects of ultra-processed food intakes on health outcomes. The present study, for the first time, aimed to assess the association between ultra-processed food intake and DNA oxidative damage in healthy adolescents in Iran.

Methods

Study population

Totally, 139 students aged 13–19 years were recruited through a multi-stage random cluster sampling process from ten public high schools in five different districts in Karaj City. For detection of the weakest correlation (r 0·3) between ultra-processed food intake and urinary considerations of 8-OHdG, with α error = 0·05 and β error = 0·1, the total sample size required was 114. However, for improving the precision of the study, the sample size was increased[43].

The involvement of oxidative stress in chronic disease is well documented in several studies and having a chronic disease may affect dietary modifications[2]. As this factor may confound the association between ultra-processed food intake and oxidative DNA damage, we controlled for these confounding variables as exclusion criteria and excluded children with known metabolic diseases. The exclusion criteria were as follows: history of any chronic diseases which may induce oxidative stress affect and alter dietary intakes or including diabetes mellitus, hypertension, hypo-and hyperthyroidism, kidney disease, hepatic disorders and being on a restrictive diet. All eligible participants signed written informed consent at the baseline.

Dietary intake assessment

Usual adolescent dietary intake over the past year was evaluated using a 168-item validated FFQ specifically tailored to the Iranian population[44]. Study participants were asked to report how often, on average, she or he had consumed every food item on a daily, weekly, monthly or yearly basis over the previous year, followed by a question about the amount of food consumed each time in standard or household units. Portion sizes of consumed food were converted to grams by using household measures[45]. Then, the consumed amount for every food item was calculated by multiplying the frequency/d and grams of consumption. We estimated the daily dietary intake of ultra-processed food based on NOVA food group classification[46] by summing the daily intake of thirty-seven food and beverage items included in FFQ that classified as ultra-processed food and categorised as seven food groups and expressed as intake in g/d (online Supplementary file 1). To understand the contribution of each food group to total ultra-processed food intake, the mean daily intake from each seven subgroups of ultra-processed food divided by the daily intake of total ultra-processed food multiplied by 100. The energy intake was analysed using the US Department of Agriculture's food composition tables[47]. To define over and under-reporting, we used the method suggested by Banna *et al.*[48]. Therefore, boys with energy intake out of 3347 kJ/d (800 kcal/d) or 16 736 kJ/d (4000 kcal/d) and girls with energy intake out of 2092 kJ/d (500 kcal/d) or 14 664 kJ/d (3500 kcal/d) were excluded (six people).

The method described by Trichopoulou *et al.*[49] has been used to measure adherence to the Mediterranean dietary score (MDS). In this method, food is divided into nine food groups including fruits, fish, vegetables, whole grains, legumes, nuts, the ratio of grams of MUFA:SFA, meats (red meat, poultry and processed meat) and dairy products. MDS is represented by a scale where a value of 1 was assigned to the consumption of food groups considered beneficial to health at or above the median (vegetables, legumes, fruits and nuts, cereals, fish and ratio of MUFA:SFA) and below the median for food groups presumed to be detrimental to health (meats and dairy products). The MDS was calculated for each participant by summing of scores from the nine components for a total MDS within a range of zero (minimal adherence) to nine (maximal adherence)[49,50]. A higher score represented more adherence to the Mediterranean diet.

Measurement of 8-hydroxy-2′-deoxyguanosine

Spot morning urine samples were taken and centrifuged at 1000 ***g*** for 10 min. The clear supernatant was used for measuring 8-OHdG concentration. The concentration of 8-OHdG was

measured using ELISA using a commercially available standard kit and based on the manufacturer's instructions (Cusabio; Catalog no. CSB-E10140h). 8-OHdG (ng/ml) levels were then adjusted for urinary creatinine (mg/ml) levels, measured by a kinetic colorimetric method, and expressed as 8-OHdG/creatinine (ng/mg creatinine) before statistical analysis.

Demographic, anthropometric and physical activity assessment

Demographic variables including information on age, sex, exposure to smoking and medical history were obtained from a self-administrated questionnaire. Height was measured using a stadiometer (Seca, model 206) fixed to the wall, without shoes and headdress using the Frankfort technique. Weight was measured using a digital scale to the nearest 0·1 kg (Seca 707), while the person was in light clothing and barefoot. BMI was calculated by dividing weight by height squared (kg/m^2). BMI for age *Z*-score was calculated according to the 2007 WHO standard using Anthro Plus software version 1.0.4 by the WHO-2007 growth reference standard. BMI for age (*Z*-score > +1) described being obese or overweight[51].

Physical activity was measured using a self-reported questionnaire expressed as an equivalent metabolic h/d (MET-h/d)[52]. The physical activity questionnaire based on metabolic equivalent (MET) data, including nine levels of activity from sleep and rest (MET 0·9) to vigorous activity (more than six MET), was used to evaluate the students' level of physical activity. The validity and reliability of the questionnaire have been previously confirmed in Iran[52,53].

Statistical analysis

Statistical analysis was conducted using the SPSS version 16 software (SPSS Inc.). The distribution of variables in all and across the tertiles of ultra-processed food was assessed using a Kolmogorov–Smirnov test. Demographic characteristics and dietary intakes in all participants and within different tertiles of ultra-processed food were reported as mean values and standard deviations for normally distributed variables and geometric means and 95 % CI for ones with skewed distribution. Categorical variables were presented as numbers and percentages. To compare baseline characteristics and dietary intake within tertiles of ultra-processed food, we used χ^2 tests for categorical variables (sex, obesity or overweight, exposure to smoking) and general linear models after adjustment for total energy intake.

General linear models were also used to compare the geometric mean concentration of urinary 8-OHdG/creatinine within tertiles ultra-processed food intake in the uni- and multivariate models. The inclusion of variables as confounding factors was based on previous literature and known or suspected variables that affect 8-OHdG, such as the MDS and its food components[40]. Model 1 was adjusted for total energy intake (kcal/d), sex (female, male), age (years), BMI for age *Z*-score, obesity and physical activity (MET). In model 2, additional adjustments for whole grains (g/d), nuts (g/d), legumes and the ratio of MUFA:SFA (g/d) were carried out. Model 3 adjusted for the same covariates in model 2 plus MDS. The $P_{\text{for trend}}$ was calculated from generalised linear models in different models. All tests were two-sided, and $P < 0{\cdot}05$ was considered statistically significant.

Results

The characteristics and dietary intakes of the study participants in all and across tertiles categories of ultra-processed food intake are presented in Table 1. Boys significantly showed a higher intake of dietary ultra-processed food intake than girls. No significant difference was observed in the percentage of students who exposed to secondary smoke within tertiles of ultra-processed food intake. Individuals in the highest tertile of ultra-processed food consumption had significantly lower daily intakes of whole grains ($P < 0{\cdot}05$), higher daily intakes of nuts ($P < 0{\cdot}05$), total energy intake and ratio of MUFA:SFA ($P < 0{\cdot}001$). Total MDS and daily intake of vegetables, fruits, fish, legumes, dairy products, poultry, meat and Na did not significantly differ across the tertiles of ultra-processed food intake. The prevalence of overweight/obesity was greater in the highest tertile compared with the lowest one, although the difference was not statistically significant.

The main two food group contributors to ultra-processed food intake are shown in Table 2, which were non-dairy beverages (coffee, cola and lemon juice), following cookies and cakes group (cookies, biscuits, pastries (creamy and non-creamy), cake, pancake, doughnut, industrial bread, toasted bread, noodles and pasta). The relation between ultra-processed food intake and geometric mean urinary 8-OHdG damage is shown in Table 3. As dietary ultra-processed food intake rose from the lowest to the highest tertile, the geometric mean concentration of urinary 8-OHdG creatinine concentrations significantly increased from 2·6 to 4·4 in the crude model ($P_{\text{for trend}}$: 0·003). The positive association between dietary ultra-processed food intake and 8-OHdG concentration was significant in model 1 (adjusted for total energy intake (kcal/d), sex (female, male), age (years), BMI for age *Z*-score, obesity and physical activity (MET)) ($P_{\text{for trend}}$: 0·004). This relationship was stronger and still significant in model 2 (additionally adjusted for dietary intake of whole grains, nuts, legumes and ratio of MUFA:SFA (g/d)) and model 3 (additionally adjusted for MDS) ($P_{\text{for trend}}$: 0·002).

Discussion

The present study is the first one which showed that higher ultra-processed food intake is associated with a higher urinary biomarker of DNA oxidative damage in healthy adolescents. This association was still significant after taking into consideration factors like sex, obesity, BMI for age *Z*-scores, physical activity, MDS and food components that are known or suspected to affect 8-OHdG[40].

Table 1. Participant characteristics and dietary intakes in total population and according to tertiles (T) of ultra-processed food intake in adolescents in the present study
(Mean values and standard deviations; geometric mean values and 95 % confidence intervals; numbers and percentages)

				Tertiles of ultra-processed food intake						
	Total (*n* 139)			T1 (*n* 46)		T2 (*n* 47)		T3 (*n* 46)		
Variables	Mean		SD	Mean	SD	Mean	SD	Mean	SD	*P**
Age (years)	15·7		1·7	15·6	1·8	15·7	1·6	15·8	1·7	0·720
MET (h/d)	43·4		24·9	42·8	26·4	42·0	24·8	45·4	24·0	0·628
Sex										0·017
Female										
n		62		28		15		19		
%		44·6		60·9		31·9		41·3		
Male										
n		77		18		32		27		
%		55·4		39·1		68·1		58·7		
Exposure to smoking										0·954
Yes										
n		55		18		18		19		
%		39·6		39·1		38·3		41·3		
No										
n		84		28		29		27		
%		60·4		60·9		61·7		58·7		
Being obese or overweight										0·438
n		29		7		10		12		
%		20·9		15·2		21·3		26·1		
UPF (% of total energy intake)	24·8		9·2	17·9	6·2	25·8	6·8	34·3	7·4	<0·001
Total energy intake (kcal)†	2571·5		700·2	2034·0	418·7	2538·5	567·2	3142·8	607·6	<0·001
UPF (g/d)‡										
Geometric mean		264·2			141·8		279·7		464·9	<0·001
95 % CI		237·4, 294·1			128·1, 156·9		256·7, 305·2		419·4, 515·4	
MDS	4·4		1·4	4·0	1·2	4·2	1·5	5·0	1·1	0·070
Vegetables (g/d)‡										
Geometric mean		200·2			184·7		190·7		228·1	0·232
95 % CI		177·5, 225·9			149·1, 228·8		158·8, 229·0		183·6, 283·7	
Fruits (g/d)‡										
Geometric mean		112·2			112·2		116·9		109·0	0·859
95 % CI		101·7, 124·9			93·2, 135·2		99·7, 137·1		90·2, 131·7	
Nuts (g/d)‡										
Geometric mean		4·8			3·1		4·5		7·7	0·023
95 % CI		3·7, 6·3			1·9, 5·1		3·0, 6·9		4·7, 12·6	
Fish (g/d)‡										
Geometric mean		9·2			7·4		10·4		10·0	0·231
95 % CI		7·8, 10·9			5·4, 10·2		8·0, 13·5		7·3, 13·8	
Whole grains (g/d)‡										
Geometric mean		82·3			105·5		79·5		68·5	0·044
95 % CI		71·3, 95·0			80·9, 137·4		63·4, 99·7		52·4, 89·7	
Legumes (g/d)‡										
Geometric mean		20·4			24·0		22·08		16·4	0·062
95 % CI		17·9, 23·3			24·0, 30·7		17·8, 27·3		12·8, 21·1	
Dairy products (g/d)	561·5		252·9	460·4	224·4	589·8	260·4	633·8	244·6	0·706
Poultry (g/d)‡										
Geometric mean		22·1			18·8		22·7		24·8	0·320
95 % CI		18·4, 26·4			13·2, 26·7		17·0, 30·3		17·6, 34·9	
Meat (g/d)‡										
Geometric mean		27·0			26·7		28·1		26·1	0·909
95 % CI		23·5, 31·0			21·3, 33·6		23·1, 34·1		20·7, 32·9	
MUFA:SFA ratio	0·78		0·1	0·70	0·1	0·78	0·1	0·87	0·1	<0·001
Na (g/d)	7528·2		3493·1	7095·1	3442·0	7326·9	3038·9	8166·9	3934·3	0·142

MET, metabolic equivalents; UPF, ultra-processed food; MDS, Mediterranean dietary score.
* *P* values based on χ^2 tests for categorical variables (sex, obesity or overweight, exposure to smoking), and $P_{\text{for trend}}$-for trend for age, MET and dietary intakes using general linear model adjusted for total energy intake.
† To convert energy values from kcal to kJ, multiply by 4·184.
‡ Geometric mean and 95 % CI were calculated since data were not normally distributed.

Studies investigating the association between DNA damage and ultra-processed food intake are not common. However, a study by de Carvalho *et al.*[39] has shown that dietary intake of heterocyclic amine, a contaminant, seems to be high in ultra-processed food[29]; this has been associated with increased DNA damage in adults. There has been also some evidence showing that advanced glycation end products have detrimental effects on oxidative stress in animal or *in vitro* studies[37,38].

The mechanisms behind the effect of ultra-processed food on oxidative damage are not clear. Several studies have shown that different ultra-processed food in the food market, such as cereals including cookies and cakes[54,55], biscuits[56,57], industrial bread[58–60], potato chips[57,61,62] and coffee[63], contain a high concentration of acrylamide[64]. Based on laboratory data, this chemical has been shown to have a carcinogenic effect[63,65–69], although the epidemiological evidence has not been consistent in this regard[70]. Acrylamide has been declared a human health concern by the European Food Safety Authority Panel on contaminants in the food chain as well as join the FAO/WHO expert committee on food additives[71].

Table 2. Main contribution of ultra-processed food intake in adolescents in the present study
(Percentages)

Food items	Contribution of each food subgroup intake to total ultra-processed food intake (%)
Non-dairy beverages	31·5
Cookies and cakes	23·6
Dairy beverages	13·9
Potato chips and salty snacks	13·7
Processed meat and fast food	7·8
Oil and sauces	5·3
Sweets	3·9

Moreover, ultra-processed foods may contain substantial acellular nutrients, emulsifiers and non-energetic artificial sweeteners that could adversely affect the gut microbiota and induce oxidative stress and inflammation based on laboratory evidence[72–74]. Dietary advanced glycation end products produced during the heating and processing of food products might contribute to risk factors associated with chronic diseases, such as inflammation and oxidative stress too[75,76]. Some ultra-processed foods are high in fructose, and the detrimental effects of fructose-rich diet have been noticed on mitochondrial DNA damage in the liver and in the case of metabolic diseases as shown in animal studies[77]. A study by Jones *et al.*[78] showed that the high dietary fructose intake was associated with a lower abundance of the beneficial microbe *Eubacterium* and *Streptococcus* in healthy adolescents.

Food processing led to the production of Maillard reaction products, which have been associated with DNA oxidative damage[79] and unhealthy gut microflora[80] in cell and animal studies. The high glycaemic index of ultra-processed foods[81,82] may also affect oxidative stress, as the positive relationship between high dietary glycaemic index and oxidative stress has been reported. The oxidative potential of high dietary glycaemic index, simple carbohydrates and sugar to DNA oxidative damage sugar has been documented[41].

In the present study, participants in the higher tertiles of ultra-processed food consumption have been seen to be more obese or overweight; however, this difference is NS. Our results are in line with the study of Enes *et al.* who found no association between ultra-processed food intake and obesity of 200 adolescents aged 10–18 years in Brazil[83]. However, a recent systematic review reported a direct association between some ultra-processed food groups and body fat in children and adolescents[31]. In the present study, this null association might be because the participants in the higher tertiles of ultra-processed food intake were those who had higher intakes of vegetables, nuts and total MDS, too. The Mediterranean diet is high in phytochemicals with anti-obesity effects[84,85]. It may attenuate the obesity potential effects of ultra-processed food intake with high energetic intake and may affect the null relationship between ultra-processed food intake and obesity. The low sample size might be a factor for this null association too.

Previous studies have shown detrimental effects of ultra-processed food consumption on human health and the environment[30], highlighting the need for future research and policy efforts to attenuate it. The positive relationship between high intake of ultra-processed food and DNA oxidative damage in adolescents in the present study adds to earlier research. The detrimental effects of ultra-processed food for health and environment should provide a wakeup call for legislators, food and nutrition policymakers, food scientists, academics, civil society and food activists to improve and to reform food environment policy-making and ultra-processed food regulations.

As dietary exposure to ultra-processed food and beverages is high in children and adolescents, they might be more prone to the detrimental effects of acrylamide and other processing ingredients[66,86–88]. Therefore, the development of a food safety monitoring and guidance system to define the content of acrylamide and other processing ingredients of industrial food mainly consumed by children and adolescents and to investigate the technological methods to reduce them while maintaining sensory quality in the industry[89] is highly recommended in Iran as well as other countries.

Table 3. Urinary concentration of 8-hydroxy-2′-deoxyguanosine (8-OHdG8)/creatinine according to tertiles of ultra-processed food group consumption in adolescents in the present study
(Geometric mean (GM) values and 95 % confidence intervals)

	Urinary 8-OHdG/creatinine (ng/mg creatinine)*							
	Crude model		Model 1†		Model 2‡		Model 3§	
Ultra-processed food intake (g/d)	GM	95 % CI	GM	95 % CI	GM	95 % CI	GM	95 % CI
Tertile 1	2·6	2·0, 3·3	2·4	1·8, 3·2	2·2	1·6, 3·0	2·2	1·6, 3·1
Tertile 2	3·3	2·6, 4·2	3·2	2·5, 4·0	3·2	2·5, 4·1	3·2	2·5, 4·1
Tertile 3	4·4	3·4, 5·6	4·8	3·6, 6·4	5·1	3·7, 7·0	5·1	3·7, 7·0
$P_{\text{for trend}}$‖	0·003		0·004		0·002		0·002	

* GM and 95 % CI were calculated on the basis of log (ln)-transformed of urinary 8-OHdG/creatinine (ng/mg creatinine).
† Model 1 adjusted for total energy intake (kcal/d), sex (female, male), age (years), BMI for age *Z*-score, obesity and physical activity (MET).
‡ Model 2 adjusted for variables in model 1 plus whole grains (g/d), nuts (g/d), legumes (g/d) and the ratio of MUFA:SFA (g/d).
§ Model 3 adjusted for variables in model 2 plus Mediterranean dietary score.
‖ *P* value for linear trend over tertiles of ultra-processed food intake.

More research is needed to develop ground-breaking innovative methods and patents to reformulate and substitute ultra-processed food with healthier and safer ingredients[90]. Restricting ultra-processed food advertising and marketing to children and adolescents is of great importance[91,92]. As a result of the lack of legislation or weak implementation of policies regarding the healthy food supply in school cafeterias, higher consumption of ultra-processed food in adolescents in different countries has been reported[93]. Although all strategies and policies supposed to decrease ultra-processed food consumption might not be achieved without improving the good governance components of health policies[94,95] regarding the food environment.

The low energy cost of ultra-processed foods has been shown to be one of its determinants in its consumption[96]. Keeping in mind the social determinants of health, developing agent-based policies and educational approaches to decrease ultra-processed food consumption might be important, but surely not enough[97,98]. Therefore, future research using mixed-method and whole-food system approaches[99] should be seriously recommended in order to know the broad behavioural, social and political-economic factors associated with the high intake of ultra-processed food that should be applied to develop policies and regulatory mechanisms to decrease ultra-processed food consumption, especially in children and adolescents.

The present study is an attempt to control other covariates that seem to affect 8-OHdG, such as physical activity. In a recent meta-analysis study done by Tryfidou *et al.*[100], it was found that there was a substantial increase in DNA damage immediately following acute aerobic exercise, which remained between 2 h and 1 d, but not within 5–28 d post-exercise phase. In the present study, the participants were not athletes, and they did not do acute aerobic exercise before sampling.

Several limitations need to be considered when interpreting the results of the present study. First, we measured urinary 8-OHdG with the ELISA method. The ELISA technique has been widely used to measure urinary 8-OHdG in several previous studies and has shown to be correlated with measurements based on the HPLC method[101,102]. However, there are some concerns that ELISA frequently overestimates the urinary concentrations of 8-OHdG in comparison with chromatography-based methods[103–105]. Therefore, further studies are needed to assess the link between ultra-processed food and DNA oxidative damage using HPLC.

Another limitation was the relatively small sample size as the consumption has been classified into three categories, which can reduce the power of analysis. Moreover, this study was cross-sectional and no conclusion about causality can be drawn. DNA damage may also be affected by other environmental factors such as outdoor or indoor air pollution and therefore needs to be addressed in future studies[106,107]. Furthermore, although the FFQ used in the present study was developed and validated for the Iranian population, developing specified FFQ for assessing ultra-processed food consumption[108] may be needed for more accurate measurement in future studies in adolescents.

In conclusion, the present study showed that higher ultra-processed food intake was associated with higher DNA oxidative damage in healthy adolescents. Future research is needed to confirm these results.

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S. E. was involved in formulating the research question, data analysis, data interpretation, writing and finalising of the manuscript. F. B. was involved in data collection and data entry process. M. E.-M. and M. A. J. supervised the project. All the authors read and approved the final manuscript.

The authors declare that there are no conflicts of interest.

Supplementary material

For supplementary material referred to in this article, please visit https://doi.org/10.1017/S0007114520001981

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