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Dietary carbohydrate intake, glycaemic load, glycaemic index and ovarian cancer risk in African-American women

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Abstract

Epidemiological evidence regarding the association between carbohydrate intake, glycaemic load (GL) and glycaemic index (GI) and risk of ovarian cancer has been mixed. Little is known about their impact on ovarian cancer risk in African-American women. Associations between carbohydrate quantity and quality and ovarian cancer risk were investigated among 406 cases and 609 controls using data from the African American Cancer Epidemiology Study (AACES). AACES is an ongoing population-based case–control study of ovarian cancer in African-Americans in the USA. Cases were identified through rapid case ascertainment and age- and site-matched controls were identified by random-digit dialling. Dietary information over the year preceding diagnosis or the reference date was obtained using a FFQ. Multivariable logistic regression models were used to estimate odds ratios and 95 % CI adjusted for covariates. The OR comparing the highest quartile of total carbohydrate intake and total sugar intake *v.* the lowest quartile were 1·57 (95 % CI 1·08, 2·28; $P_{trend} = 0·03$) and 1·61 (95 % CI 1·12, 2·30; $P_{trend} < 0·01$), respectively. A suggestion of an inverse association was found for fibre intake. Higher GL was positively associated with the risk of ovarian cancer (OR 1·18 for each 10 units/4184 kJ (1000 kcal); 95 % CI 1·04, 1·33). No associations were observed for starch or GI. Our findings suggest that high intake of total sugars and GL are associated with greater risk of ovarian cancer in African-American women.

Key words: African-American women: Carbohydrate: Glycaemic load: Ovarian cancer: Epidemiology

Ovarian cancer is the leading cause of death from gynaecological cancers in developed counties including the USA[1,2], of which nearly 90 % are epithelial ovarian carcinomas[3]. Approximately 10 % of cases are thought to arise from inherited germline mutations while the rest are thought to be sporadic[3]. As at present there is no reliable screening available for ovarian cancer, most cases are diagnosed at an advanced stage, with a poor prognosis[4]. Moreover, compared with European-Americans, African-American women tend to have a worse 5-year survival rate[5], highlighting a critical need for identifying modifiable preventive factors. However, there is a scarcity of epidemiological studies in this area for African-American women.

Although there are a few established modifiable risk factors for ovarian cancer, the role of diet has been proposed. Carbohydrates in particular have been a focus of research[6], as long-term consumption of high levels of carbohydrates, especially sugars, could plausibly contribute to ovarian carcinogenesis[7,8]. The majority of epidemiological studies evaluating associations between intakes of carbohydrate[9–15], total sugars and added sugars[13,15–19] and fibre[9–14,20,21] and ovarian cancer risk have been conducted in European or European-American populations with mixed results. Inconsistencies in findings have been attributed to the different type, amount and rate of digestion of carbohydrates[13]. These factors may lead to varied blood glucose

Abbreviations: GI, glycaemic index; GL, glycaemic load; IGF-1, insulin-like growth factor-1.

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and postprandial insulin responses, which have been suggested to play critical roles in ovarian tumour development[13]. Therefore, it is necessary to evaluate the impact of both the quality and the quantity of carbohydrate intake on ovarian cancer risk.

Glycaemic index (GI) is a quality measure of carbohydrates, whereas glycaemic load (GL) reflects both the average quality and the quantity of carbohydrates. GI is a numerical index that is defined as the incremental area under the blood glucose response curve after a 50-g carbohydrate intake of a test food relative to an equivalent carbohydrate portion of bread or glucose[22]. Through combining the food's GI value and the carbohydrate content of the food's usual serving size, GL reflect the overall effects of a food on postprandial blood glucose concentrations[23]. A few studies have evaluated the relation between GL, GI and ovarian cancer risk, and the evidence is mixed[13,15,18,24,25]. In three of these studies, positive associations were observed for GL only or both GI and GL[13,15,25], and were stronger in postmenopausal women[15,25], or overweight and obese women[13]. Two other studies found a null relation[18] or an inverse association for GI[24].

Compared with European-Americans, African-Americans have similar total carbohydrate intake, but tend to have lower fibre consumption and higher intake of total sugars and added sugars[26–28]. Fibre intake has been hypothesised to be beneficial for ovarian cancer prevention, whereas sugar intake is suggested to play the opposite role[16,20]. Furthermore, there are important differences in the physiology of glucose homoeostasis between African-Americans and European-Americans, with higher insulin secretion and more insulin resistance in African-Americans[29,30]. Therefore, our study aimed to examine the associations between types of carbohydrate intake, GL and GI and ovarian cancer risk in African-American women. We specifically examined whether associations may be stronger in postmenopausal or overweight/obese women based on previous findings[13,15,25], and assessed whether there might be greater associations among diabetics as they may suffer from long-term higher insulin response to carbohydrate intake[8]. As some studies have suggested differences in ovarian cancer risk factors by histological subtypes[31,32], we also proposed to examine these associations by ovarian cancer subtypes (serous *v.* non-serous). To our knowledge, this is the first study that has examined the association between carbohydrate quality and quantity and ovarian cancer risk in African-Americans.

Methods

Study population

The African American Cancer Epidemiology Study (AACES) has been described in detail elsewhere[33]. In brief, AACES is an ongoing population-based case–control study of ovarian cancer in African-American women in eleven sites in the USA (Alabama, Georgia, Illinois, Louisiana, Michigan, North Carolina, New Jersey, Ohio, South Carolina, Tennessee and Texas). Cases were identified by rapid case ascertainment utilising state cancer registries, SEER (Surveillance, Epidemiology and End Results) registries or via hospitals' gynaecological oncology departments. Eligible cases included all self-identified African-American women aged between 20 and 79 years, with newly diagnosed, histologically confirmed invasive epithelial ovarian cancer. Controls who self-identified as African-American were selected using random-digit dialling and were matched to cases by 5-year age groups and state of residence. Women who had a previous history of ovarian cancer or a bilateral oophorectomy were ineligible controls. Only women able to complete an interview in English were eligible to participate. Among those who could be contacted, 66·5 % of potential cases and 72 % of potential controls agreed to participate in the main telephone interview[33]. The present study was approved by the Institutional Review Boards at all study sites.

We used data from AACES participants recruited from December 2010 to December 2014, which included 495 cases and 711 controls. Among them, 421 cases (85 %) and 635 controls (89 %) completed the FFQ for dietary assessment. We compared characteristics of women completing and not completing the FFQ and found no difference with respect to age, education, region, BMI and smoking status (results not shown). Participants were excluded from the analysis if they reported an extreme energy intake defined as greater than twice the interquartile range of the log energy intake (case, n 1; control, n 3) or if they were missing important covariates (case, n 14; control, n 23), such as tubal ligation and family history of ovarian/breast cancer. The final analytical sample comprised 406 cases and 609 controls.

Data collection

Upon signing informed consent, participants completed a computer-assisted telephone interview. The questionnaire included detailed questions on demographic information, personal and family history of cancer, reproductive history, medication use, lifestyle characteristics and other factors of particular relevance to African-American women such as perceived discrimination, access to healthcare facilities and cultural beliefs.

Dietary intake was assessed using a self-administered Block 2005 FFQ, which included questions on frequency and portion size on 110 food items. The FFQ was mailed to participants with portion size pictures to facilitate recall. Participants were asked to estimate their usual consumption of each of these food items during the year before their reference date. Nutrient intakes were derived from the FFQ through the Block Dietary Data Systems based on the US Department of Agriculture (USDA) Food and Nutrient Database for Dietary Studies, version 1.0. The validity of the Block FFQ has been evaluated[34,35]. The correlations between estimates from the questionnaire and 2-d food records were >0·50 for most nutrients. In particular, the correlation of energy-adjusted carbohydrate intake was 0·60 and 0·61, respectively, for women below or above age 65 years[35]. Total carbohydrate values consist of total sugars (including added sugars), starch and fibre intakes.

The GI and GL values for food items in our study were based on the published international tables of values[36], or from direct testing of food items at the University of North Carolina Nutrition Obesity Research Center, using glucose as the reference. The GL value of each food was calculated by multiplying the non-fibre carbohydrate contained in a specified serving size of the food by the GI value of that food, divided by 100. The daily GL value of each individual was the sum of all foods after multiplying the GL of each food by its frequency of consumption and portion size. An individual's daily GI value was determined by dividing the daily GL by the total amount of non-fibre carbohydrate consumed.

Top food sources that contribute to carbohydrates, sugars or GL in this sample are provided in online Supplementary Table S1.

Statistical analysis

Distributions of demographic and major risk factors for ovarian cancer, such as parity and tubal ligation, were compared between cases and controls using χ^2 tests. Student's *t* tests were used to compare the mean nutrient intakes by cases and controls.

Dietary variables under investigation – total carbohydrate, total sugars, added sugars, starch, fibre and GL, except GI – were adjusted for energy intake using the multivariate nutrient density approach[37]. Dietary variables were then categorised into quartiles based on the distributions among controls. Unconditional logistic regression models were used to calculate OR and 95 % CI for ovarian cancer risk by levels of energy-adjusted dietary intake. Linear trends were tested by modelling the median value of each quartile as a continuous variable. Dietary variables were also evaluated as a continuous increment based on the difference between the 75th and 25th percentile of the controls' distribution, rounded to one significant digit.

The first model adjusted for age, geographic region (south- and mid-Atlantic, south central, Midwest), education (high school or less, some post-high school training, college or graduate degree) and total energy intake[38]. Additional covariates selected for model 2 included risk factors for ovarian cancer that changed the effect estimate of each corresponding dietary variable by >10 %: parity (0, 1–2, >2), oral contraceptive use (never, <60, ≥60 months), menopause status (pre-, postmenopause), tubal ligation (no, yes) and first-degree family history of breast/ovarian cancer (no, yes). The second model additionally adjusted for vegetable consumption (servings, continuous) or alcohol consumption (drink-equivalent, continuous) when evaluating added sugars or fibre, respectively. As vegetable intake is an important source of fibre and affects GL and GI values, we did not adjust for vegetable consumption when evaluating their associations with ovarian cancer to avoid over-adjustment. Other potential confounders considered were age at menarche (<12, 12–13, >13 years), hormone therapy use (never, ever) and smoking (never, ever), but were not included in the final model as they did not change the effect estimate by 10 %.

Further analyses were conducted adjusting for BMI and diabetes, both of which may be either confounders or mediators in the causal pathway between carbohydrate intake and ovarian cancer. We also considered possible confounding effects by total sugars and added sugars when evaluating fibre intake and SFA and total fat intake as potential covariates for any of the associations under study.

We examined whether the associations were modified by menopausal status, obesity and diabetes by testing statistical interactions using product terms with the continuous variable of dietary intake. We also examined whether the associations were different by histological subtypes of ovarian cancer. As smoking may be related to mucinous tumours[39], we further adjusted for smoking when examining the associations by histological subtypes. A *P* value < 0·1 was defined as statistically significant for interaction, whereas $P < 0{\cdot}05$ was used for main effects. All the statistical analyses mentioned above were performed using STATA (version 11.2; StataCorp LP). We had excellent power for main analyses evaluating carbohydrate intake, GL, GI and ovarian cancer risk. As assessed by Epi Info (version 7.1.5), we could detect an OR of 1·49 using quartile exposures based on a power of 80 % and two-sided 95 % CI.

Results

Compared with controls, cases were slightly older (cases mean 57·5 years *v.* controls 54·5 years; *P* value 0·01), less likely to reside in the Midwest, to have children, to have used oral contraceptives or have had a tubal ligation (Table 1). Cases were more likely to have a family history of breast/ovarian cancer. Cases were similar to controls in total energy intake and energy-adjusted total and SFA intake. They had statistically significant higher intakes of carbohydrate, total sugars, fructose and added sugars, higher GL and lower protein intake and alcohol consumption, although the magnitude of difference was very small for carbohydrate or protein intakes comparing cases and controls (Table 2).

As shown in Table 3, total carbohydrate intake was strongly positively associated with ovarian cancer risk. The multivariable-adjusted OR comparing the highest *v.* the lowest quartile of total carbohydrate intake was 1·57 (95 % CI 1·08, 2·28; $P_{trend} = 0{\cdot}03$). In continuous analyses, we estimated a 32 % increase in OR (95 % CI 1·09, 1·61) per 30 g/4184 kJ (1000 kcal) of carbohydrate consumption. The positive association between carbohydrate intake and ovarian cancer risk seemed to be attributable to total sugar intake, with an OR of 1·61 (95 % CI 1·12, 2·30; $P_{trend} < 0{\cdot}01$) for those in the highest quartile compared with the lowest. Each additional 20 g/4184 kJ (1000 kcal) per d of sugar intake was associated with a 22 % increased OR (95 % CI 1·08, 1·37). For a 8368 kJ (2000 kcal) diet, such an increment represents approximately a can of soda or one cup of ice-cream. When further evaluating types of sugars, we observed that fructose intake was positively associated with the risk of ovarian cancer (OR 1·23 for each 10 g/4184 kJ (1000 kcal); 95 % CI 1·05, 1·43). Added sugar intake was positively associated with ovarian cancer risk but was not statistically significant. We did not find an association between starch intake and ovarian cancer risk. There was a suggestion of decreased risk for higher total fibre intake but the risk estimate was only significant for the third quartile compared with the lowest. A *post hoc* analysis that evaluated fibre from various sources (from vegetable and fruit, from beans, from grains) as either quartiles or continuous variables did not find any association, except a marginally significant 12 % decrease in the OR (95 % CI 0·74, 0·99) per 3 g/4184 kJ (1000 kcal) of fibre from vegetable and fruit sources (data not shown).

We found a positive linear association between GL and ovarian cancer risk (OR 1·18 for each 10 units/4184 kJ (1000 kcal); 95 % CI 1·04, 1·33). However, we only observed a significant association when comparing the third quartile *v.* the lowest (OR 1·57; 95 % CI 1·09, 2·28) but not for the highest quartile of GL. There was no evidence of an association between GI and ovarian cancer, with OR near the null and not statistically significant.

Our results were not materially altered with further adjustment for BMI or diabetes. Results for fibre were not altered after adjusting for total or added sugar intake.

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Table 1. Descriptive characteristics of African-American women with and without ovarian cancer, African American Cancer Epidemiology Study 2010–2014 (Number and percentages)

	Cases (*n* 406)		Controls (*n* 609)		
Variables	*n*	%	*n*	%	*P**
Age (years)					
<50	88	21·7	172	28·2	0·01
50–59	146	36·0	230	37·8	
≥60	172	42·4	207	34·0	
Education					
High school or less	180	44·3	224	36·8	0·06
Some post-high school training	131	32·3	222	36·5	
College or graduate degree	95	23·4	163	26·8	
Region†					
South- and mid-Atlantic	228	56·2	321	52·7	0·02
South central	109	26·9	141	23·2	
Midwest	69	17·0	147	24·1	
Parity					
0	79	19·5	80	13·1	0·02
1–2	177	43·6	273	44·8	
>2	150	37·0	256	42·0	
Oral contraceptive use					
Never	116	28·6	118	19·4	<0·01
<60 months	163	40·2	275	45·2	
≥60 months	127	31·3	216	35·5	
Use of hormone-replacement therapy among postmenopausal women					
Never	219	74·5	321	76·8	0·48
Ever	75	25·5	97	23·2	
Age at menarche (years)					
<12	90	22·2	165	27·1	0·21
12–13	212	52·2	300	49·3	
>13	104	25·6	144	23·7	
Menopause status					
Premenopausal	109	26·9	189	31·0	0·15
Postmenopausal	297	73·2	420	69·0	
Tubal ligation					
No	271	66·8	364	59·8	0·02
Yes	135	33·3	245	40·2	
Family history of breast/ovarian cancer (first-degree relative)					
No	297	73·2	494	81·1	<0·01
Yes	109	26·9	115	18·9	
Diabetes					
No	318	78·3	468	76·9	0·58
Yes	88	21·7	141	23·2	
BMI 1 year before (kg/m^2)‡					
<25	54	13·3	108	17·7	0·17
25– <30	106	26·1	151	24·8	
≥30	246	60·6	350	57·5	
Smoking					
Never	231	56·9	349	57·3	0·90
Current/former	175	43·1	260	42·7	

* χ^2 tests.
† South- and mid-Atlantic includes Georgia, North Carolina, New Jersey, South Carolina; South central includes Alabama, Louisiana, Tennessee, Texas; and Midwest includes Illinois, Michigan, Ohio.
‡ 1 year before diagnosis (cases)/interview (controls).

Estimates for total carbohydrates, total sugars and GL were strengthened after adjusting for total fat or SFA intake (online Supplementary Table S2), although the interpretation should be cautious as this isoenergetic model estimates the effect of substituting carbohydrates for the same amount of non-fat sources of energy. Results for added sugars, fibre or GI remained unchanged.

Results for carbohydrate intake, GL and GI as continuous variables were stratified by diabetes status in addition to interaction tests as the number of women with diabetes was small (online Supplementary Table S3). Although interaction tests were not statistically significant, the positive association between carbohydrate intake, total sugars, added sugars and GL with ovarian cancer risk appeared to be stronger among participants with diabetes. We also evaluated effect modification by menopausal status and BMI. No significant interaction was found. Associations were also evaluated by histological subtype. Given the small number of non-serous subtypes, they were combined for analysis. The findings did not seem to be different for serous *v.* non-serous subtypes of ovarian cancer (data not shown). Further adjusting for smoking did not alter this result.

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Table 2. Energy-adjusted dietary factors of African-American women with and without ovarian cancer, African American Cancer Epidemiology Study 2010–2014* (Mean values and standard deviations)

	Cases (*n* 406)		Controls (*n* 609)		
Daily nutrient intakes	Mean	SD	Mean	SD	*P*†
Total energy intake (kJ)	7472·6	5107·8	7275·9	4609·5	0·44
Total energy intake (kcal)	1795·9	1220·8	1739·0	1101·7	
Total carbohydrate (g/4184 kJ (1000 kcal))	122·8	19·6	119·6	20·2	0·01
Total sugars (g/4184 kJ (1000 kcal))	65·4	22·2	61·5	20·6	0·005
Fructose (g/4184 kJ (1000 kcal))	17·2	8·8	16·0	8·2	0·03
Sucrose (g/4184 kJ (1000 kcal))	23·0	11·4	22·1	11·8	0·23
Added sugars (tsp/4184 kJ (1000 kcal))	9·0	4·5	8·5	4·3	0·04
Starch (g/4184 kJ (1000 kcal))	48·5	10·3	48·9	10·7	0·55
Fibre (g/4184 kJ (1000 kcal))	8·9	3·6	9·1	3·9	0·31
Glycaemic load (units/4184 kJ (1000 kcal))	59·4	10·3	57·6	11·3	0·01
Glycaemic index (units)	52·2	3·7	52·1	4·0	0·60
Total fat (g/4184 kJ (1000 kcal))	41·5	6·5	41·7	6·7	0·67
SFA (g/4184 kJ (1000 kcal))	12·3	2·5	12·3	2·5	0·86
Protein (g/4184 kJ (1000 kcal))	37·0	7·7	37·9	8·2	0·05
Alcohol, drink-equivalent‡	0·30	0·07	0·47	0·05	0·05

Tsp, teaspoon.
* Glycaemic index and alcohol intake is not further energy adjusted.
† Student's *t* test.
‡ One drink equivalent is defined as 12 fl oz of beer, 5 fl oz of wine or 1·5 fl oz of distilled spirits.

Discussion

In this first population-based study of carbohydrate intake and ovarian cancer risk in African-American women, we observed that high carbohydrate and sugar intakes were associated with a greater risk of ovarian cancer, independent of several relevant non-dietary and dietary factors. There was also a suggestion of a positive association between GL and ovarian cancer risk. The association between carbohydrate intake, sugar (total and added) intakes or GL and ovarian cancer appeared to be stronger for women with diabetes, although the interaction tests were not statistically significant.

Total carbohydrate intake is a combination of sugars, starch and fibre consumption. Our results suggested that the positive association between carbohydrate intake and ovarian cancer risk was primarily driven by sugar intake. In support of our findings, a previous study found that higher consumption of bread, pasta and rice and more total sugar intakes were associated with an increased risk of ovarian cancer[16]. However, other studies reported an inverse association[19] or no association between sugar intake and ovarian cancer risk[13,15,17,18].

The inconsistencies in findings between our study and most of the previous studies, which were mainly conducted in European or European-American women, may be due to differences in consumption of sugar types or glucose metabolism of African-Americans. Although the range of carbohydrate and total sugar intake in our study is comparable with those reported in other studies[19], the differences in the intake of sugar subtypes have been noticed comparing African-Americans and European-Americans. According to the National Health and Nutrition Examination Survey III, African-Americans have a higher consumption of fructose compared with non-Hispanic whites[40]. Evidence is accumulating that compared with other sugars, fructose is more involved in the development of insulin resistance[41], a hypothesised mechanism for ovarian cancer[42]. Consistently, we found a positive association between fructose consumption and ovarian cancer risk. Furthermore, African-Americans are more hyperinsulinaemic and insulin resistant compared with European-Americans[30], suggesting that they may have a higher ovarian cancer risk for a given amount of sugar intake. Another reason to explain the inconsistent findings may be due to the different energy-adjustment methods. It was suggested that the nutrient density method as used in our study, or residual method, may be more powerful than the standard energy-adjustment model employed in most of the previous studies[13,15,18] to detect the relative odds when the nutrient variables were categorised[43].

The evidence regarding the association between fibre intake and ovarian cancer risk has been inconsistent. Although some studies found no association between fibre intake and the risk of ovarian cancer[10,14,21,44], others found an inverse association[9,11–13,20]. Two of these studies further examined types of fibre intake and showed that the inverse association was observed only for vegetable fibre but not for fruit or cereal fibre[11,20]. Our data, which observed an inverse association with dietary fibre from vegetable and fruit but not with fibre from grains, support the fact that the effects of dietary fibre on ovarian cancer may vary depending on the food sources.

Among the few previous studies examining the associations of GL and GI with ovarian cancer risk[13,15,18,24,25], our results are consistent with those of a prospective cohort study and a population-based case–control study that showed positive associations with GL but not with GI[13,15]. The null findings with GI suggested that it may not be as good as GL to reflect the overall glycaemic effect of the diet, as GL also takes the amount of carbohydrate intake into consideration in addition to carbohydrate quality as for GI[24].

Potential mechanisms linking carbohydrate-rich foods to ovarian tumour development have been proposed. Long-term consumption of carbohydrate-rich foods can result in chronic hyperinsulinaemia, which can indirectly promote the production

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Table 3. Association between daily dietary carbohydrate intake and ovarian cancer risk in African American Cancer Epidemiology Study 2010–2014 (Numbers and percentages; odds ratios and 95 % confidence intervals)

	Cases (*n* 406)		Controls (*n* 609)		Model 1*		Model 2†	
	n	%	*n*	%	OR	95 % CI	OR	95 % CI
Total carbohydrate (g/4184 kJ (1000 kcal))								
Q1 (≤106·9)	83	20·4	153	25·1	1·00	Ref.	1·00	Ref.
Q2 (107·0–120·1)	105	25·9	153	25·1	1·31	0·90, 1·90	1·32	0·90, 1·92
Q3 (120·2–133·1)	97	23·9	152	25·0	1·18	0·81, 1·73	1·17	0·80, 1·72
Q4 (≥133·2)	121	29·8	151	24·8	1·58	1·10, 2·28	1·57	1·08, 2·28
P_{trend}						0·03		0·03
Per 30 g/4184 kJ (1000 kcal)‡					1·33	1·09, 1·61	1·32	1·09, 1·61
Total sugars (g/4184 kJ (1000 kcal))								
Q1 (≤48·2)	92	22·7	153	25·1	1·00	Ref.	1·00	Ref.
Q2 (48·3–60·9)	96	23·7	152	25·0	1·04	0·72, 1·51	1·03	0·70, 1·50
Q3 (61·0–72·7)	81	20·0	152	25·0	0·91	0·62, 1·33	0·90	0·61, 1·33
Q4 (≥72·8)	137	33·7	152	25·0	1·57	1·11, 2·24	1·61	1·12, 2·30
P_{trend}						0·01		<0·01
Per 20 g/4184 kJ (1000 kcal)‡					1·21	1·08, 1·37	1·22	1·08, 1·37
Fructose								
Q1 (≤10·1)	89	21·9	153	25·1	1·00	Ref.	1·00	Ref.
Q2 (10·2–14·8)	98	24·1	153	25·1	1·14	0·79, 1·65	1·10	0·76, 1·61
Q3 (14·9–20·0)	102	25·1	151	24·8	1·20	0·83, 1·74	1·16	0·79, 1·68
Q4 (≥20·1)	117	28·8	152	25·0	1·42	0·99, 2·03	1·42	0·98, 2·05
P_{trend}						0·06		0·06
Per 10 g/4184 kJ (1000 kcal)‡					1·23	1·05, 1·43	1·23	1·05, 1·43
Sucrose								
Q1 (≤14·0)	78	19·2	153	25·1	1·00	Ref.	1·00	Ref.
Q2 (14·1–19·9)	116	28·6	152	25·0	1·53	1·05, 2·22	1·51	1·03, 2·21
Q3 (20·0–27·5)	105	25·9	152	25·0	1·38	0·94, 2·02	1·33	0·90, 1·96
Q4 (≥27·6)	107	26·4	152	25·0	1·37	0·94, 1·99	1·39	0·95, 2·04
P_{trend}						0·28		0·24
Per 10 g/4184 kJ (1000 kcal)‡					1·07	0·96, 1·19	1·07	0·96, 1·19
Added sugars (tsp/4184 kJ (1000 kcal))								
Q1 (≤5·3)	85	20·9	153	25·1	1·00	Ref.	1·00	Ref.
Q2 (5·4–7·7)	92	22·7	152	25·0	1·14	0·78, 1·66	1·12	0·76, 1·65
Q3 (7·8–10·9)	118	29·1	153	25·1	1·42	0·98, 2·05	1·39	0·95, 2·04
Q4 (≥11·0)	111	27·3	151	24·8	1·40	0·97, 2·03	1·33	0·90, 1·98
P_{trend}						0·06		0·13
Per 6 tsp/4184 kJ (1000 kcal)‡					1·23	1·03, 1·46	1·20	0·99, 1·44
Starch (g/4184 kJ (1000 kcal))								
Q1 (≤42·7)	122	30·1	156	25·6	1·00	Ref.	1·00	Ref.
Q2 (42·8–48·8)	82	20·2	150	24·6	0·75	0·52, 1·08	0·75	0·52, 1·09
Q3 (48·9–54·9)	105	25·9	151	24·8	0·89	0·63, 1·27	0·86	0·60, 1·23
Q4 (≥55·0)	97	23·9	152	25·0	0·83	0·58, 1·18	0·84	0·59, 1·21
P_{trend}						0·39		0·41
Per 10 g/4184 kJ (1000 kcal)‡					0·96	0·85, 1·09	0·97	0·85, 1·09
Total fibre (g/4184 kJ (1000 kcal))								
Q1 (≤6·5)	117	28·8	163	26·8	1·00	Ref.	1·00	Ref.
Q2 (6·6–8·3)	104	25·6	142	23·3	0·92	0·64, 1·32	0·85	0·58, 1·22
Q3 (8·4–10·8)	86	21·2	156	25·6	0·69	0·46, 1·01	0·64	0·43, 0·94
Q4 (≥10·9)	99	24·4	148	24·3	0·88	0·60, 1·30	0·79	0·53, 1·17
P_{trend}						0·51		0·27
Per 4 g/4184 kJ (1000 kcal)‡					0·92	0·79, 1·06	0·88	0·76, 1·03
Glycaemic load (units/4184 kJ (1000 kcal))								
Q1 (≤50·8)	83	20·4	155	25·5	1·00	Ref.	1·00	Ref.
Q2 (50·9–57·9)	90	22·2	152	25·0	1·10	0·75, 1·60	1·16	0·79, 1·71
Q3 (58·0–64·9)	125	30·8	150	24·6	1·53	1·07, 2·21	1·57	1·09, 2·28
Q4 (≥65·0)	108	26·6	152	25·0	1·31	0·91, 1·90	1·35	0·93, 1·97
P_{trend}						0·06		0·05
Per 10 units/4184 kJ (1000 kcal)‡					1·17	1·04, 1·32	1·18	1·04, 1·33
Glycaemic index (units)								
Q1 (≤49·9)	96	23·7	155	25·5	1·00	Ref.	1·00	Ref.
Q2 (50·0–52·2)	108	26·6	152	25·0	1·10	0·77, 1·58	1·17	0·81, 1·69
Q3 (52·3–54·8)	103	25·4	156	25·6	0·97	0·68, 1·40	0·95	0·66, 1·38
Q4 (≥54·9)	99	24·4	146	24·0	0·97	0·67, 1·40	1·03	0·70, 1·50
P_{trend}						0·73		0·86
Per 5 units‡					0·99	0·84, 1·17	1·00	0·84, 1·18

Q, quartile; Ref., referent values; tsp, teaspoon.

* Model 1 adjusted for age, education, region and total energy intake.

† Model 2 adjusted for age, education, region, total energy intake, parity, oral contraceptive use, menopause status, tubal ligation and family history of breast/ovarian cancer (first-degree relative). For added sugars, model additionally adjusted for vegetable intake. For fibre, model additionally adjusted for alcohol consumption.

‡ Increment used in continuous analyses based on the difference between 75th and 25th percentile of the control distribution, rounded to one significant digit.

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of insulin-like growth factor-1 (IGF-1)[7]. IGF-1 is recognised to play a critical role in promoting cell proliferation and inhibiting apoptosis[45]. Higher circulating concentrations of IGF-1 were found in several cancer types such as prostate cancer and breast cancer[46], but the evidence for ovarian cancer is inconsistent[47–49]. Insulin and IGF-1 may also promote tumourigenesis through stimulating the production of sex hormones, especially androgens[50], which has been implicated in the pathogenesis of ovarian cancer[51]. In addition, the acute glucose fluctuations were found to evoke oxidative stress[52], with subsequent oxidative DNA damage[53], which was suggested to be involved in cancer development[53].

Our results of a stronger association between sugars, GL and ovarian cancer among diabetic participants are biologically plausible, although we had limited power to detect a significant statistical interaction. Type II diabetic patients may suffer from long-term higher compensatory rise in insulin[8], which in turn may increase cancer risk or growth via elevated IGF[7]. In addition, the cross-talk between the advanced glycation end products (AGE) and receptor for AGE system and oxidative stress are suggested to further increase the risk for cancers in diabetic patients[54]. Although our results can be chance findings and need to be replicated, given the high prevalence of diabetes among African-Americans and that ovarian cancer patients with diabetes exhibit poorer survival[55], primary dietary interventions may be especially important for this vulnerable population.

A number of limitations of the current study should be considered. First, residual confounding is possible, even with adjusting for a wide array of covariates. Second, there is a concern that undetected ovarian cancer may influence dietary choices in the year before diagnosis, leading to an issue of reverse causation. However, this is unlikely for ovarian cancer, considering that the median pre-diagnostic symptom duration for invasive cases is 4 months[56]. In addition, we found no difference in any dietary variables under study between cases at early stages *v.* advanced stages, which argues against undetected disease influencing dietary choices. Third, recall bias is always possible in case–control studies, but the largely unknown relationship between sugary foods and ovarian cancer and, as a result, lack of awareness of this link in this population should minimise this problem. Fourth, self-reported carbohydrate intake may be subject to under-reporting[57], and may limit our confidence to estimate the absolute amount of intake. However, FFQ have been shown to be a useful tool to rank individuals reliably based on their nutrient intakes, as in the present study[38]. FFQ-measured dietary GI and GL have also been shown to be valid and reliable tools to investigate their relationships with disease risks[58,59]. Furthermore, participation rates in population-based epidemiological studies are declining; however, although this is of concern, we found that the distribution of main risk factors among AACES ovarian cancer cases and controls were similar to other studies among African-Americans[60]. Reduced response rates do not necessarily compromise the internal validity of the study, as representative samples could still be achieved with proper study designs[61].

Major strengths of this study include the largest sample for this under-studied population and carefully collected information, which provides an unprecedented opportunity for studying the modifiable risk factors in this minority population.

In conclusion, the present study supports a detrimental role of a carbohydrate-rich diet in ovarian cancer. Considering the poorer survival among African-American ovarian cancer patients and no effective screening tool for ovarian cancer, prevention is especially important, particularly through dietary modification, which is relatively low cost and low risk compared with medical treatments. In addition, our findings suggest even greater risk from high carbohydrate intake among diabetics, although no significant statistical interaction was identified. As diabetes is more common among African-American women[62], this finding may have important implications for ovarian cancer prevention in this population.

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Supplementary material

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