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Dietary Carbohydrate Intake, Insulin Resistance, and Gastroesophageal Reflux Disease (GERD): A Pilot Study in European- and African-American Obese Women

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Abstract

Background—Although obesity rates are higher in African-American than European-American women, GERD and its comorbidities are more prevalent in European-American women. A common denominator for increased adiposity, and consequent insulin resistance, is excess dietary macronutrient intake – which may promote greater prevalence and severity of GERD in women.

Aim—We hypothesized that GERD would be more robustly associated with dietary carbohydrate intake, particularly dietary simple carbohydrate intake, and insulin resistance in European-American women.

Methods—144 obese women were assessed at baseline and 16 weeks after consuming a high-fat/low-carbohydrate diet. GERD diagnosis and medication usage was confirmed in medical records with symptoms and medications assessed weekly.

Results—33.3% (N=33) of European-American and 20.0% (N=9) of African-American women had GERD at baseline. Total carbohydrate ($r=0.34$, $P<0.001$), sugars ($r=0.30$, $P=0.005$), glycemic load ($r=0.34$, $P=0.001$) and HOMA-IR ($r=0.30$, $P=0.004$) were associated with GERD, but only in European-American women. In response to high-fat/low-carbohydrate diet, reduced intake of sugars was associated with reduced insulin resistance. By the end of diet week 10, all GERD symptoms and medication usage had resolved in all women.

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CONTRIBUTIONS: H.J. Silver conceived and designed the study. H.J. Silver was responsible for study implementation and supervision. S.D. Pointer and J. Rickstrew created tables and figures. C. Slaughter provided statistical analysis and interpretation. S.D. Pointer, J. Rickstrew, M.F. Vaezi and H.J. Silver, provided intellectual content, drafted the manuscript, and manuscript revisions.

Authorship Statement:

SDP, JR, MV and HJS were responsible for study concept and design. SDP, JR and HJS were responsible for data collection and data entry. JCS and HJS were responsible for data analyses and data interpretation. SDP, JR, JCS, MV and HJS participated in manuscript writing. All authors have approved the final manuscript.

Conclusions—GERD symptoms and medication usage was more prevalent in European-American women, for whom the relationships between dietary carbohydrate intake, insulin resistance and GERD were most significant. Nevertheless, high-fat/low-carbohydrate diet benefited all women with regard to reducing GERD symptoms and frequency of medication use.

INTRODUCTION

Gastroesophageal reflux disease (GERD), occurring in 20–30% of U.S. adults,¹ is the most common gastrointestinal diagnosis with over 9 million outpatient visits annually.^{2,3} Treatment is empirical and U.S. prescription drug spending for proton pump inhibitors (PPIs) and H₂ receptor antagonists (H₂RA) amounts to ~\$12.5 billion annually.^{1,3,4–6} Yet, 30–40% of patients are response failures and up to 60% report residual symptoms.^{5,7} Chronic inadequately treated GERD can lead to esophagitis, strictures, and Barrett's esophagus which predisposes to esophageal adenocarcinoma.^{1,7,8} The growth in incidence of GERD comorbidities parallels the rise in obesity prevalence over the past three decades,^{9,10} with the risk for GERD increasing three-fold for every 3.5 kg/m² increase in body mass index (BMI).¹¹ Indeed, excess adiposity increases the percentage of time that esophageal pH is acidic (<4.0) and the number of reflux episodes experienced.¹² Compared to normal weight adults, the odds of having GERD are three-fold greater in obese men and four-fold greater in obese women.^{10,13–16}

Although obesity rates are higher in U.S. women of African descent (56.6%) compared to those of European descent (32.8%),^{17,18} GERD comorbidities such as esophagitis are more prevalent in European-Americans who now have a four-fold higher incidence of esophageal adenocarcinoma.^{19,20} While the exact mechanism for this racial disparity remains undetermined, it is plausible that the accumulation of more visceral (*versus* subcutaneous) adipose tissue by European-Americans in the abdominal depot, and the degree of insulin resistance produced, has more profound metabolic effects on functional disorders - including GERD. Importantly, recent evidence links greater insulin resistance with increased prevalence and severity of GERD symptoms.²¹

A common denominator for the rising prevalence of obesity, intra-abdominal adiposity, and consequent insulin resistance, is higher dietary energy intake, now ~340 calories more per day - mostly from increased dietary carbohydrates.²² High carbohydrate intake, particularly simple carbohydrates (mono- and disaccharides), stimulates secretion of insulin and incretins like glucagon-like peptide 1 that promote postprandial glycemia, hyperinsulinemia, and insulin resistance. Notably, a case series of five adults reported resolution of GERD symptoms within two weeks of consuming a low carbohydrate/high fat (Atkins) diet.²³ Moreover, a crossover trial with 41 subjects showed that 70% had significant symptom improvement on low carbohydrate *versus* low fat diet, and only 6% reported no benefit from reduced carbohydrate intake.²⁴ Of concern, the published studies utilized severe carbohydrate restriction of 20g/day which limits applicability to the general adult population who typically consume 250g/day.²⁵ The lack of clarity regarding the interaction between dietary carbohydrates and GERD also continues due to long-held belief that high fat foods increase GERD symptoms, possibly by delaying gastric emptying.^{26,27} However, ingestion of high compared to low fat meals showed no difference in post-prandial lower esophageal

sphincter pressure or gastroesophageal reflux.²⁸ Moreover, systematic review shows no unequivocal relationship between dietary fat and GERD.²⁹ Further, low fat weight loss trials have not consistently demonstrated improvement in GERD symptoms or medication use.^{28,30,31}

Considering the racial disparities in obesity and insulin resistance in women, the insufficient evidence supporting a role for dietary fats in GERD, and the lack of efficacy from low fat diets, we hypothesized that carbohydrates, rather than fats, were associated with GERD in obese women. We further hypothesized that decreased dietary carbohydrate intake would be associated with reduced GERD symptoms and medication use, and would do so most robustly in European- *versus* African-American women. To shed light on a plausible underlying mechanism, we also hypothesized that relationships between dietary carbohydrates, GERD, and race would be influenced by the degree of insulin resistance present. To test these hypotheses, we conducted a case-control analysis with data from a 16-week intervention designed to determine metabolic effects of consuming a diet wherein the amount of carbohydrate was lower than typical (35% *vs* 45% energy), the amount of fat was higher than typical (48% *vs* 38% energy), and the amount of protein remained unchanged (17% energy).³² This study was approved by the Vanderbilt University Institutional Review Board and registered in the U.S. National Institutes of Health ClinicalTrials.gov registry (NCT00696228).

METHODS

Subjects

European-American and African-American women aged 21–50 years with Class I/II obesity (BMI 30–39.9 kg/m²) were recruited through E-mail announcements and fliers posted in the local vicinity. All subjects were born in the U.S. and race was self-identified with confirmation that both parents originated from the same racial group. Consistent with current American College of Gastroenterology guidelines for diagnosis and empiric treatment of GERD (i.e., esophageal pH monitoring and endoscopy not being required in typical patients),^{1,33,34} GERD diagnosis and prescription for GERD medications were obtained from electronic medical record review. A baseline clinic visit was conducted by a study nurse and dietitian (RD) to obtain a comprehensive diet, weight, and gastrointestinal health history. To assess GERD frequency and severity, items from the NIH Promis System³⁵ and the Frequency Scale for the Symptoms of GERD³⁶ were used. Additional questionnaires included the Eating Attitudes Test,³⁷ the Three Factor Eating Questionnaire,³⁸ and the Impact of Weight on Quality of Life.³⁹ The RD also performed random 24-hour diet recall interviews using Nutrition Data System for Research (NDSR version 2011, Nutrition Coordinating Center, Minn., MN) to quantify current energy, macronutrient and micronutrient intakes.

Physical measures were obtained in triplicate and averaged for seated blood pressure (after a 5-minute rest using a calibrated sphygmomanometer with a large size cuff), height ($\pm$ 0.1cm via wall-mounted stadiometer), weight ($\pm$ 0.1kg via digital platform scale), and waist and hip circumferences ($\pm$ 0.1cm via flexible measuring tape above the right iliac crest and at the full extension of the buttocks, respectively). A venous blood sample was obtained to rule out

acute illness by assessing complete blood count, basic metabolic panel, liver enzymes and lipid profile via standard assays performed at the Vanderbilt Department of Pathology Clinical Laboratory.

Potential subjects were excluded if GERD symptoms (heartburn, reflux, regurgitation) occurred less than one day per week during the prior 3 months; if they had a history of tobacco use; alcohol or substance abuse; gastrointestinal disease other than GERD; hypertension; hyperlipidemia (serum triglycerides >200mg/dL or LDL-cholesterol >130mg/dL); were pregnant or lactating; had evidence of disordered eating by Eating Attitudes Test score ≥ 20 and/or Three Factor Eating Questionnaire score <14; were taking appetite stimulating or reducing medications; used daily aspirin, Coumadin or ACE inhibitors; consumed dietary supplements other than a multivitamin/mineral supplement; and had excessive caffeinated beverage intake (>240mg/d).

Intervention

Subjects were provided with instructions and 14-day cycle menu plans for the diet intervention. Caloric goal was individualized based on measured resting energy expenditure multiplied by a modest 1.2 activity factor.⁴⁰ Recipes for meals and snacks were calculated using NDSR software. Total carbohydrate was categorized as complex (total starch) or simple (total sugars: mono- and disaccharides)⁴¹ and balanced within menu plans as $\frac{1}{2}$ complex and $\frac{1}{2}$ simple. Total fat was balanced as $\frac{1}{3}$ saturated, $\frac{1}{3}$ monounsaturated, $\frac{1}{3}$ polyunsaturated and standardized across subjects by providing all sources of fats (oils, spreads, nuts and seeds) at weekly clinic visits in pre-portioned containers. Weekly visits included assessment of weight, anthropometrics, and occurrence of heartburn, reflux, regurgitation, other gastrointestinal symptoms, and GERD medication use over the prior week.

Clinical Testing

Subjects were admitted to the Vanderbilt Clinical Research Center for testing at baseline and study weeks 2, 9 and 16. They were reminded to avoid alcohol, excess caffeine intake, and non-routine physical activities during the two days before, and to fast from 9:00pm until arrival at 7:00am. Resting energy expenditure was measured in thermoneutral conditions using a mobile metabolic cart system (ParvoMedics TrueOne 2400®, Sandy, UT).⁴² Next, a certified densitometrist performed dual energy x-ray absorptiometry (DXA) using a Lunar iDXA™ (GE Healthcare) scanner, which was phantom calibrated before each use, to acquire whole and regional body composition. Finally, a venous blood sample was obtained to measure fasting levels of glucose (colorimetric timed endpoint method), insulin (chemiluminescent immunoassay) and high sensitivity C-reactive protein (partial enhanced turbidimetric assay). The homeostatic model assessment of insulin resistance (HOMA_{IR}) was calculated as $[\text{fasting glucose (mmol/L)} \times \text{fasting insulin (mU/L)}] / 22.5$.⁴³

Data Analysis

Data analysis was performed using SPSS (version 19.0, IBM, Armonk, NY). Data were assessed for normality by visual inspection of Q-Q plots (i.e., plotting the quantiles of the variable against the theoretical normal quantiles for that variable). Nonparametric

approaches were employed to compare characteristics between women by GERD status and race at baseline when plots depicted deviation from normality. Univariate relationships between variables were assessed using Spearman's rho correlation coefficients. Binary and multivariate logistic regression models were fit adjusting for age, weight, and BMI to assess relationships between nutrients, adipose tissue depots, and GERD status in order to identify correlates that significantly increase the odds of having GERD and to generate predictive probability plots. Within nutrients, the category of carbohydrates was categorized by molecular size (simple: mono- and disaccharides; complex: oligo- and polysaccharides) and by digestibility (total *versus* available carbohydrate). Within simple carbohydrates, we analyzed both total simple carbohydrate (total sugars) and added simple carbohydrate (added sugars), defined as those sugars and syrups used as ingredients in processed or prepared foods, as well as each individual simple carbohydrate.^{41,44} For analysis of dietary fats, we analyzed total fat intake, fat intake classified by saturation status (saturated, monounsaturated, polyunsaturated) and individual fatty acids. To assess changes over time, repeated measures ANOVA was performed. Overall statistical significance was set at $P < 0.05$. Values are expressed as means $\pm$ standard deviation (SD). All authors had access to the study data and have reviewed and approved the final manuscript.

RESULTS

Baseline GERD Status

Of the 144 women, 50 (34.7%) reported GERD symptoms. In the present analyses we excluded 8 who did not meet the criteria of having GERD diagnosis in their medical record and taking prescribed medications to treat GERD symptoms more than one day per week during the three months prior to enrollment. Of the 42 women, 21 were taking over-the-counter medications for GERD (TUMS®) in addition to their prescribed medications, although the proportion taking over-the-counter medications did not differ significantly by race at baseline or at any other study time-point. In the 42 women, the frequency of experiencing GERD symptoms (heartburn and/or regurgitation/reflux) averaged 1.1 ± 0.5 times per day (Table 1).

Baseline Differences by GERD Status

Overall, women with GERD were about 3 years older on average ($P = 0.004$) than those without GERD (Table 2). No significant differences were detected at baseline in body weight, waist circumference, waist/hip ratio, total body fat or android region (truncal) fat between women with and without GERD. Average daily total amount (grams) of food consumed daily and total fat intake did not differ in women with and without GERD. There were also no differences in the average amounts of dietary fiber (soluble or insoluble), alcohol or caffeine consumed. While total carbohydrate intake also did not differ, women with GERD consumed significantly more available (digestible) carbohydrates ($P = 0.002$). Women with GERD also had significantly higher intakes of sucrose (GERD: 48.9 ± 37.0 g vs non-GERD: 37.3 ± 23.6 g, $P = 0.03$), added sugars (GERD: 73.7 ± 47.8 g vs non-GERD: 60.6 ± 40.8 g, $P = 0.03$), and total sugars (GERD: 99.5 ± 49.5 g vs non-GERD: 82.3 ± 40.8 g, $P = 0.03$). In contrast, there were no differences between women with and without GERD in the intake of lactose or fructose (Table 2). Interestingly, the types of foods being consumed at

baseline that comprised simple carbohydrate (mono- and disaccharides) intake differed by group; in women with GERD most (>60%) of their intake of total sugars derived from sweet solids (cakes, pies, frozen desserts, cookies, brownies, granola bars), whereas in women without GERD most of total sugars intake was from sweet liquids (soda, fruit flavored beverages, sweetened milk, sweet tea).

Thus, overall dietary glycemic load was higher in women with GERD (GERD: 193.6 ± 51.4 vs non-GERD: 166.5 ± 60.0 , $P = 0.005$) and women with GERD had higher HOMA_{IR} scores (GERD: 2.9 ± 2.3 vs non-GERD: 2.3 ± 2.1 , $P = 0.04$), indicating greater insulin resistance. In multivariate analysis, the factors significantly associated with increased odds for having GERD at baseline were older age, higher total sugars intake, and European-American race. No other factors significantly accounted for the variability in having GERD. Figure 1 presents the relationship between having GERD based on total sugars intake adjusted for age ($P = 0.01$). Notably, the odds of having GERD would increase 13% for every additional teaspoon (4.2g) of sugars consumed (Table 3).

Baseline Differences in Women with GERD by Race

At baseline, 33.3% of European-American and 20.0% of African-American women had GERD. There were no significant differences by race in age, body weight, BMI, waist circumference, waist/hip ratio, total body fat, android region fat, or in the average amount of food consumed daily or average energy intake (Table 4). Yet, European-American women with GERD tended to have lower fat intake (36.0 ± 5.0 vs 43.4 ± 9.0 %kcal, respectively, $P = 0.05$) and higher carbohydrate intake than African-American women with GERD ($P = 0.03$). European-American women with GERD also had higher intakes of available carbohydrate ($P = 0.004$), total and added sugars (P s = 0.01), and they tended to have greater insulin resistance (HOMA_{IR} 3.2 ± 2.5 vs 1.9 ± 1.2 , $P = 0.05$).

In univariate analyses, total carbohydrate intake ($r = 0.34$, $P < 0.001$), added sugars intake ($r = 0.30$, $P = 0.005$), sucrose intake ($r = 0.33$, $P = 0.001$), glycemic load ($r = 0.34$, $P = 0.001$), and HOMA_{IR} score ($r = 0.30$, $P = 0.004$) were associated with GERD status in European-American women. These relationships were not significant in African-American women (Figure 2).

Response to High-Fat/Low-Carbohydrate Diet by GERD Status

Overall, women with and without GERD at baseline had similar reductions in body weight, BMI, waist circumference, total body fat, android and gynoid region fat (Table 5). As prescribed, percentage of energy from dietary fat intake increased similarly in both groups (14.5 ± 6.3 vs 14.6 ± 6.1 %kcal, $P = 0.91$). However, the corresponding decrease in dietary carbohydrate differed as women with GERD had significantly greater decreases in available carbohydrate ($P = 0.001$), total sugars ($P = 0.002$) and sucrose intake ($P = 0.009$), but not in dietary fiber ($P = 0.10$), fructose ($P = 0.68$) or lactose intake ($P = 0.26$). Indeed, women with GERD reduced their intake of total sugars by 61% from baseline. Accordingly, overall glycemic load was reduced more in women with GERD ($P = 0.001$) as was insulin resistance (HOMA_{IR}, $P = 0.02$). There were no other differences by baseline GERD status with regard

to changes in dietary intakes, including no differences in the reduction in caffeine ($P = 0.54$) or alcohol ($P = 0.47$) consumed.

Response to High-Fat/Low-Carbohydrate Diet in Women with Baseline GERD by Race

In comparing the response to the diet in women who had GERD at baseline by race (Table 6), European-American and African-American women had similar decreases in total energy intake ($P = 0.93$), but European-American women had a greater decrease in the intake of available carbohydrates ($P = 0.03$) and total sugars intake ($P = 0.03$). Hence, European-American women tended to have a significantly greater reduction in insulin resistance (HOMA_{IR} : $P = 0.05$). In European-American women, the reduction in total sugars ($r = 0.64$, $P = 0.002$), added sugars ($r = 0.52$, $P = 0.01$), and sucrose ($r = 0.63$, $P = 0.003$) intake were significantly associated with reduced insulin resistance. However, these relationships were not significant in African-American women (Figure 2). The degree of insulin resistance reduced three times greater in European-American than African-American women.

Final GERD Status

Overall, we observed resolution of GERD symptoms and discontinuation of GERD medication usage in European-American women by end of study week 9 and in African-American women by the end of study week 10. This improvement in GERD status persisted in all women to the end of study week 16 (Figure 3).

DISCUSSION

Consistent with the known epidemiology of GERD,^{1,45,46} 29.2% of the obese women had GERD diagnosis and medication use at baseline. In this cohort, the factor most strongly associated with having GERD was dietary simple carbohydrates. In evaluating the simple carbohydrates (mono- and disaccharides) comprising subjects' intake, it was the amount of sucrose that was greater in the dietary intakes of women with GERD. Some insight on the potential role of simple carbohydrates might be revealed from prior work where infusions of a disaccharide and of oligosaccharides increased the number of reflux episodes in a 24-hour period.⁴⁷ As the number of transient lower esophageal sphincter relaxations increased, it is possible that simple carbohydrates affect mediators of lower esophageal sphincter function. One potential mechanism for dietary sugars influencing lower esophageal sphincter function is by stimulating the secretion of gut hormones, such as gastrin, to promote gastric acid secretions, reduce sphincter pressure, and/or increase transient sphincter relaxations.⁴⁸ While other gut peptides (cholecystokinin, intestinal peptide YY, glucagon, glucagon-like peptide 1) have also been investigated in relation to GERD, there remains need for direct investigation of dietary carbohydrates on hormonal mediators, lower esophageal sphincter function, and GERD.

Another potential mechanism may be related to influence on gastric distention and motility. It is intriguing that the food sources of simple carbohydrates at baseline differed between women with and without GERD; women with GERD derived most of theirs from solid foods whereas the women without GERD consumed most from liquids. By occupying greater stomach volume and slowing gastric emptying, solid foods retained in the proximal

stomach may potentiate greater number of transient lower esophageal sphincter relaxations.⁴⁹ While it is unclear to what extent delayed emptying and impaired motility actually influence GERD symptoms, both have been described previously in GERD patients.

It is intriguing that the relationship between simple carbohydrates and GERD was significant only in the European-American because some nationally representative data suggest African-American women consume more simple carbohydrates than European-American women.⁵⁰ However, the present data showed that despite similar energy (kcal) and protein intake, European-American women had significantly greater consumption of total carbohydrate, available carbohydrate, added sugars and total sugars at baseline. Congruous with the baseline findings, dietary simple carbohydrate was the factor most strongly associated with resolution of GERD symptoms and medication use after 16 weeks of consuming the high-fat/low-carbohydrate diet. This finding is consistent with an experiment in 8 obese women showing a 44% symptom improvement, 51% decrease in time esophageal pH was <4.0, and a reduction in Johnson-DeMeester score similar to that expected with pharmaceutical treatment, just 6 days after commencing low carbohydrate diet.⁵¹

In the European-American women, the reduction in sucrose, added sugars, and total sugars was associated with an overall decrease in dietary glycemic load. The reduction in dietary sugars and glycemic load appeared to drive the significant improvement in insulin resistance (measured by HOMA_{IR} score) in the European-American women – especially considering that reductions in body weight, BMI, waist circumference, and android region fat did not differ in women with and without GERD. A relationship between HOMA_{IR} and GERD was first reported in a cross-sectional study wherein the association was strongest in male subjects.²¹ The present finding of a robust relationship in women, which improved with diet intervention, suggests that insulin resistance is an under-explored risk factor for occurrence of GERD in all individuals. Notably, the relationship between insulin resistance and GERD at baseline, as well as the relationship between improved insulin resistance and GERD resolution after high-fat/low-carbohydrate diet, was not detected in African-American women. The relationship between insulin resistance and race is considered complex and paradoxical; although African-American women tend to have higher insulin resistance in general, when matched to European-Americans they do not have higher levels of known risk factors including visceral adipose tissue and blood lipids, and thus, present a different metabolic profile.

The most unusual finding was that all women with GERD had resolution of their symptoms, and thus, discontinued GERD medications within 10 weeks of consuming the high-fat/low-carbohydrate diet, a novel outcome that persisted through the end (week 16) of the diet intervention. It is important to note that the response to this diet also included significantly reduced body weight. Indeed, high body mass is associated with increased esophageal acid exposure.⁵² Although the American Gastroenterological Association guidelines advise weight loss for overweight/obese people with GERD,¹ the few studies investigating the effects of nonsurgical weight loss have yielded mixed results. While some show a positive association between lower esophageal pH and weight loss, comparing calorically restricted *versus* unrestricted diet showed no significant decrease in GERD symptoms despite a 10% weight loss.⁵³ As the amount of weight loss in the present study was similar between women

with and without GERD, it does not appear that resolution of GERD symptoms and medication use was due solely to weight loss. Moreover, a significant relationship between BMI and GERD was not observed in these women at baseline. It is possible this inconsistency in the relationship between body mass and GERD reflects a gender-specific difference in the presentation of GERD.⁵⁴

A major strength of this study was the meticulous calculation, standardization, and balancing of the high-fat/low-carbohydrate diet with total carbohydrate as ½ complex, ½ simple and total fat as 1/3 saturated, 1/3 monounsaturated, and 1/3 polyunsaturated. Diet assessment reliability was enhanced by in-depth subject training of 24-hour recall methodology and portion size estimation using standardized measuring utensils, along with RD use of the USDA multiple-pass technique, a standardized script and software-generated probes.⁵⁵ Objective measurement of fatty acid oxidation rate, respiratory quotient, and 24-hour urinary urea nitrogen concentrations confirmed that average daily consumption met prescribed goals. Moreover, frequency of clinic visits and duration of the diet intervention provided adequate exposure and time to observe persistent resolution of symptoms and medication use.

With regard to study limitations, it might have been informative to confirm GERD diagnosis with 24-hour esophageal pH monitoring or PPI testing. However, standard practice is to treat empirically, as presented in American College of Gastroenterology guidelines,³³ unless patients are unresponsive to pharmaceutical treatment.⁵⁶ Indeed a symptom based approach is considered efficacious.⁵⁷ Yet, interpretation of the present findings is limited by the sample size of the case-control design which had unequal numbers of European-American and African-American women. Future prospective work is needed using randomized designs with large samples to investigate effects of promising diets on GERD. As this study was performed in obese females it remains unknown whether similar responses would occur in males. It is noteworthy that gender related differences have been identified in the gene expression, clinical outcome, and progression of GERD.⁵⁸

CONCLUSION

GERD is a major public health problem with high medication use (PPIs being a top three highest selling pharmaceutical agent), health care costs, lost worker productivity, and overall quality of life burden. While food intake should have a buffering effect reducing stomach acidity, reflux most often occurs postprandially. Yet, results from prior diet interventions are conflicting, and thus, no evidence based dietary recommendations are available for standard practice. Contrary to long-held belief that higher fat intake promotes GERD symptoms; nationally representative data do not show a strong association between dietary fat and GERD.⁵⁹ Thus, the present study provides important insights that contribute to the accumulating evidence of a role for dietary simple carbohydrates in GERD pathophysiology. We found that simple carbohydrates, particularly sucrose, contribute to GERD in obese women and the likelihood of having GERD was predicted by simple carbohydrate (total sugars) intake. The finding that the probability of having GERD increases with each additional teaspoon of simple carbohydrates is highly relevant considering per capita consumption of added sugars has increased 20–30% over the past three decades.⁶⁰ The

discontinuance of GERD symptoms and medication use in all women within ten weeks of the high-fat/low-carbohydrate diet suggests that further research is warranted to determine potential mechanisms underlying the relationship between carbohydrates and GERD. As low fat weight loss interventions have not consistently improved GERD status, a more balanced approach to dietary fat and carbohydrate may offer potential to impact clinical practice, assist pharmaceutical treatment, and improve GERD patients' quality of life.

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ABBREVIATIONS

BMI	body mass index
RD	dietitian
DXA	dual energy x-ray absorptiometry
HOMA_{IR}	homeostatic model assessment of insulin resistance
GERD	gastroesophageal reflux disease
H₂RA	H ₂ receptor antagonists
LES	lower esophageal sphincter
PPIs	proton pump inhibitors

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Figure 1.

The probability of having GERD was predicted by the average amount of total sugars (all mono- and disaccharides in foods and beverages) consumed per day at baseline in 144 women with obesity. Shading in gray displays the 95% confidence interval.

Figure 2.

The relationship between the change in total sugars intake and the change in insulin resistance after 16 weeks of consuming high fat/low carbohydrate diet was significant in European-American (EA) women but not African-American (AA) women.

Figure 3.
The prevalence of GERD medication use (prescribed and over-the-counter) reduced consistently from baseline to week 16 in European-American and African-American women who consumed high fat/low carbohydrate diet.

Table 1

Frequency of Symptoms and Prescription Medication Use at Baseline in 42 Women with Obesity and GERD

	European-American (N = 33)	African-American (N = 9)
<u>Symptoms</u>		
1–2 times/week	4	1
3–5 times/week	10	2
Once a day	13	4
2 or more times/day	6	2
<u>Medication</u>		
Prilosec	15 (45.5%)	4 (44.4%)
Protonix	10 (30.3%)	2 (22.2%)
Prevacid	4 (12.1%)	1 (11.1%)
Nexium	2 (6.0%)	1 (11.1%)
Pepcid	2 (6.0%)	1 (11.1%)
TUMs®	17 (51.2%)	4 (44.4%)

Table 2

Baseline Comparisons in 144 Women with Obesity by GERD status

	GERD	No GERD	P value
	(N = 42)	(N = 102)	
Demographics			
Age (y)	39.3 ± 5.9	35.7 ± 6.9	0.004
Race			0.10
European-American	33 (78.6%)	70 (68.6%)	
African-American	9 (21.4%)	32 (31.4%)	
Body Composition			
Height (cm)	164.4 ± 6.3	163.3 ± 6.5	0.34
Weight (kg)	92.3 ± 10.4	93.7 ± 11.1	0.51
BMI (kg/m ²)	34.1 ± 2.9	35.1 ± 2.6	0.06
Waist (cm)	102.8 ± 7.6	102.7 ± 8.1	0.74
Waist/Hip ratio	0.9 ± 0.1	0.9 ± 0.1	0.76
Android Fat (%)	57.2 ± 4.4	57.3 ± 4.1	0.94
Gynoid Fat (%)	54.3 ± 3.7	55.7 ± 3.9	0.06
Total Body Fat (%)	47.1 ± 3.3	47.2 ± 3.4	0.75
Daily Nutrient Intake			
Amount of Food (g)	2675.7 ± 610.1	2778.1 ± 815.9	0.60
Energy (kcal)	2103.1 ± 435.1	1840.1 ± 435.0	0.002
Protein (% kcal)	15.6 ± 3.0	16.9 ± 4.6	0.16
Total Fat (% kcal)	37.2 ± 6.0	38.7 ± 7.8	0.42
Saturated Fat (g)	31.0 ± 10.3	28.9 ± 9.5	0.12
Monounsaturated Fat (g)	32.1 ± 8.4	29.5 ± 9.7	0.18
Polyunsaturated Fat (g)	19.8 ± 9.3	17.7 ± 8.7	0.17
Total Carbohydrate (% kcal) ¹	46.5 ± 6.1	44.0 ± 9.6	0.10
Available Carbohydrate (g)	224.9 ± 55.7	190.6 ± 64.9	0.002
Total Dietary Fiber (g)	16.8 ± 6.5	15.2 ± 5.8	0.45
Total Starch (g)	117.7 ± 30.9	109.1 ± 37.9	0.003
Total Sugars (g)	99.5 ± 49.5	82.3 ± 40.8	0.03
Added Sugars (g)	73.7 ± 47.8	60.6 ± 40.8	0.03
Sucrose (g)	48.9 ± 37.0	37.3 ± 23.6	0.03
Fructose (g)	16.3 ± 12.6	16.8 ± 12.0	0.87
Glucose (g)	18.3 ± 11.2	17.9 ± 11.1	0.79
Lactose (g)	10.3 ± 8.6	9.1 ± 9.8	0.25
Maltose (g)	3.2 ± 2.9	2.9 ± 2.0	0.08
Glycemic Load ²	193.6 ± 51.4	166.5 ± 60.0	0.005
Caffeine (mg)	160.1 ± 112.6	133.7 ± 102.6	0.22

	GERD	No GERD	P value
	(N = 42)	(N = 102)	
Alcohol (oz)	2.2 ± 4.2	1.8 ± 3.1	0.31
Metabolic/Inflammation			
HOMA _{IR} (score) ³	2.9 ± 2.3	2.3 ± 2.2	0.04
C-Reactive Protein (mg/dl)	6.7 ± 8.3	5.8 ± 6.3	0.64

¹Total carbohydrate is all starches and sugars (the term sugars refers to mono- and di-saccharides in food and beverages); Available carbohydrate is total carbohydrate minus dietary fiber (indigestible carbohydrates); Total sugars includes all sources of mono- and di-saccharides; Added sugars include sugars and syrups added as a result of food processing or preparation.

²Glycemic load is the grams of available carbohydrate in foods multiplied by the glycemic index and divided by 100.

³Homeostatic model assessment of insulin resistance.

Table 3

Factors Significantly Increasing the Odds of Having GERD (Symptoms and Medication Use) in 144 Women with Obesity

	OR	95% CI	P Value
Age (y)	1.08	1.03 – 1.14	0.003
Race is European-American	2.40	1.07 – 6.19	0.04
Total Sugar Intake (g)	1.13	1.01 – 1.21	0.007
Gynoid Fat (%)	0.87	0.85 – 0.98	0.02

Table 4

Baseline Comparisons in 42 Women with Obesity and GERD by Race

	European-American	African-American	P value
	(N = 33)	(N = 9)	
Demographics			
Age (y)	39.4 ± 6.3	38.9 ± 3.9	0.77
Body Composition			
Height (cm)	164.6 ± 6.4	162.2 ± 6.3	0.63
Weight (kg)	92.9 ± 10.7	90.8 ± 8.6	0.50
BMI (kg/m ²)	34.1 ± 3.0	33.9 ± 1.7	0.65
Waist (cm)	101.1 ± 7.6	100.4 ± 7.7	0.81
Waist/Hip ratio	0.9 ± 0.1	0.8 ± 0.1	0.75
Android Fat (%)	57.2 ± 3.9	55.5 ± 5.5	0.49
Gynoid Fat (%)	54.4 ± 3.9	54.2 ± 2.8	0.91
Total Body Fat (%)	47.3 ± 3.2	45.9 ± 2.5	0.21
Daily Nutrient Intake			
Amount of Food (g)	2661.7 ± 616.8	2373.10 ± 594.0	0.24
Energy (kcal)	2085.6 ± 446.4	1945.8 ± 415.5	0.63
Protein (% kcal)	15.7 ± 2.6	16.0 ± 4.2	0.91
Total Fat (% kcal)	36.0 ± 5.0	43.4 ± 9.0	0.05
Saturated Fat (g)	30.2 ± 8.9	29.6 ± 7.7	0.53
Monounsaturated Fat (g)	30.9 ± 7.8	34.0 ± 9.3	0.45
Polyunsaturated Fat (g)	18.6 ± 9.6	21.69 ± 4.4	0.15
Total Carbohydrate (% kcal) ¹	47.6 ± 5.9	39.7 ± 7.1	0.03
Available Carbohydrate (g)	233.2 ± 53.6	189.7 ± 50.2	0.004
Total Dietary Fiber (g)	16.4 ± 6.7	16.4 ± 5.1	0.88
Total Starch (g)	106.0 ± 35.9	98.6 ± 39.5	0.44
Total Sugars (g)	106.2 ± 53.1	74.8 ± 20.5	0.01
Added Sugars (g)	80.6 ± 50.5	48.4 ± 23.9	0.01
Sucrose (g)	52.1 ± 40.3	37.1 ± 18.2	0.11
Fructose (g)	16.1 ± 13.0	15.2 ± 8.2	0.72
Glucose (g)	19.0 ± 11.0	14.5 ± 6.5	0.35
Lactose (g)	10.8 ± 9.2	8.4 ± 3.6	0.28
Maltose (g)	4.0 ± 2.9	1.8 ± 1.2	0.10
Glycemic Load ²	142.1 ± 36.5	124.5 ± 32.4	0.16
Caffeine (mg)	75.8 ± 72.4	49.6 ± 46.5	0.15
Alcohol (oz)	2.6 ± 4.1	1.3 ± 2.7	0.49
Metabolic/Inflammation			
HOMA _{IR} (score) ³	3.2 ± 2.5	1.9 ± 1.2	0.05

	European-American	African-American	P value
	(N = 33)	(N = 9)	
C-Reactive Protein (mg/dl)	6.9 ± 8.5	6.5 ± 5.8	0.92

¹Total carbohydrate is all starches and sugars (the term sugars refers to mono- and di-saccharides in food and beverages); Available carbohydrate is total carbohydrate minus dietary fiber (indigestible carbohydrates); Total sugars includes all sources of mono- and di-saccharides; Added sugars include sugars and syrups added as a result of food processing or preparation.

²Glycemic load is the grams of available carbohydrate in foods multiplied by the glycemic index and divided by 100.

³Homeostatic model assessment of insulin resistance.

Table 5

Response to High Fat/Low Carbohydrate Diet at Week 16 in 144 Women with Obesity by GERD Status

	GERD (N = 42)	No GERD (N = 102)	P-Value
<u>Body Composition</u>			
Weight (kg)	-5.6 ± 3.3	-5.4 ± 3.2	0.81
BMI (kg/m ²)	-2.8 ± 1.2	-2.1 ± 1.5	0.46
Waist (cm)	-5.4 ± 4.5	-5.2 ± 4.4	0.92
Total Body Fat (%)	-2.8 ± 1.5	-2.4 ± 2.3	0.48
Android Fat (%)	-3.8 ± 2.7	-3.4 ± 2.5	0.57
Gynoid Fat (%)	-2.6 ± 1.6	-2.5 ± 2.5	0.76
<u>Dietary Intake</u>			
Amount of Food (g)	-141.8 ± 573.7	-179.2 ± 721.5	0.49
Energy (kcal)	-372.7 ± 400.1	-145.7 ± 374.6	0.01
Protein (% kcal)	2.7 ± 3.6	2.2 ± 4.1	0.46
Total Fat (% kcal)	14.5 ± 6.3	14.6 ± 6.7	0.91
Saturated Fat (g)	-2.4 ± 7.9	-2.9 ± 10.3	0.25
Polyunsaturated Fat (g)	3.1 ± 10.0	3.9 ± 9.6	0.18
Monounsaturated Fat (g)	3.2 ± 8.4	4.0 ± 8.8	0.86
Total Carbohydrate (% kcal) ¹	-15.5 ± 6.2	-13.3 ± 6.5	0.05
Available Carbohydrate (g)	-123.6 ± 46.3	-86.7 ± 41.8	0.001
Total Dietary Fiber (g)	3.3 ± 8.4	3.2 ± 5.7	0.10
Total Starch (g)	-56.5 ± 31.7	-41.9 ± 34.4	0.01
Total Sugars (g)	-63.1 ± 43.9	-42.0 ± 41.6	0.002
Added Sugars (g)	-59.9 ± 40.4	-45.7 ± 42.0	0.04
Sucrose (g)	-36.7 ± 27.2	-21.9 ± 25.8	0.009
Fructose (g)	-9.6 ± 10.7	-9.2 ± 10.8	0.68
Glucose (g)	-10.5 ± 11.4	-9.9 ± 10.8	0.52
Lactose (g)	-3.0 ± 7.5	-2.8 ± 5.4	0.26
Maltose (g)	-1.4 ± 3.1	-1.4 ± 2.6	0.89
Glycemic Load ²	-82.5 ± 30.0	-72.9 ± 33.3	0.001
Alcohol (oz)	-1.0 ± 2.0	-0.8 ± 1.7	0.47
Caffeine (mg)	-13.3 ± 8.9	-11.9 ± 4.7	0.54
<u>Metabolic</u>			
HOMA _{IR} (score) ³	-1.1 ± 1.7	-0.6 ± 1.2	0.02
C-Reactive Protein (mg/dl)	-1.9 ± 8.0	-0.4 ± 2.5	0.27

¹Total carbohydrate is all starches and sugars (the term sugars refers to mono- and di-saccharides in food and beverages); Available carbohydrate is total carbohydrate minus dietary fiber (indigestible carbohydrates); Total sugars includes all sources of mono- and di-saccharides; Added sugars include sugars and syrups added as a result of food processing or preparation.

²Glycemic load is the grams of available carbohydrate in foods multiplied by the glycemic index and divided by 100.

³Homeostatic model assessment of insulin resistance.

Table 6

Response to 16 Weeks of High Fat/Low Carbohydrate Diet in Women with Obesity and GERD by Race

	European-American (N = 33)	African-American (N = 9)	P-Value
<u>Body Composition</u>			
Weight (kg)	-6.9 ± 3.3	-6.5 ± 2.8	0.58
BMI (kg/m ²)	-2.9 ± 1.2	-2.6 ± 1.1	0.54
Waist (cm)	-5.5 ± 4.4	-5.1 ± 4.7	0.72
Total Body Fat (%)	-2.9 ± 1.4	-2.8 ± 1.5	0.83
Android Fat (%)	-3.9 ± 2.3	-3.7 ± 4.0	0.64
Gynoid Fat (%)	-2.9 ± 1.6	-1.8 ± 1.7	0.18
<u>Dietary Intake</u>			
Amount of Food (g)	-183.5 ± 582.4	-231.1 ± 621.5	0.49
Energy (kcal)	-367.5 ± 404.3	-344.1 ± 346.6	0.93
Protein (% kcal)	1.7 ± 0.9	2.2 ± 2.5	0.46
Total Fat (% kcal)	14.5 ± 5.2	14.6 ± 8.9	0.81
Saturated Fat (g)	-2.9 ± 8.1	-2.6 ± 8.3	0.65
Polyunsaturated Fat (g)	4.1 ± 11.2	3.9 ± 9.6	0.48
Monounsaturated Fat (g)	4.4 ± 8.9	4.0 ± 10.2	0.46
Total Carbohydrate (% kcal) ¹	-15.0 ± 5.9	-15.0 ± 5.8	0.95
Total Available Carbohydrate (g)	-128.8 ± 45.8	-101.9 ± 44.7	0.03
Total Dietary Fiber (g)	2.6 ± 6.1	2.7 ± 5.7	0.75
Total Starch (g)	-56.7 ± 30.1	-53.2 ± 38.5	0.01
Total Sugars (g)	-68.9 ± 47.9	-43.2 ± 15.9	0.03
Added Sugars (g)	-64.9 ± 44.1	-43.2 ± 16.9	0.006
Sucrose (g)	-37.8 ± 29.9	-32.4 ± 15.2	0.56
Fructose (g)	-11.5 ± 13.9	-10.9 ± 10.11	0.54
Glucose (g)	-8.2 ± 8.2	-6.1 ± 6.7	0.52
Lactose (g)	-3.1 ± 5.1	-1.9 ± 5.4	0.49
Maltose (g)	-1.8 ± 3.1	-1.3 ± 2.1	0.31
Glycemic Load ²	-86.3 ± 28.3	-69.6 ± 28.6	0.001
Alcohol (oz)	-1.0 ± 2.0	-0.8 ± 2.1	0.74
Caffeine (mg)	-13.6 ± 7.9	-11.9 ± 4.7	0.67
<u>Metabolic</u>			
HOMA _{IR} (score) ³	-1.3 ± 1.8	-0.6 ± 1.0	0.05
C-Reactive Protein (mg/dl)	-1.6 ± 4.4	-2.2 ± 3.9	0.27

¹Total carbohydrate is all starches and sugars (the term sugars refers to mono- and di-saccharides in food and beverages); Available carbohydrate is total carbohydrate minus dietary fiber (indigestible carbohydrates); Total sugars includes all sources of mono- and di-saccharides; Added sugars include sugars and syrups added as a result of food processing or preparation.

²Glycemic load is the grams of available carbohydrate in foods multiplied by the glycemic index and divided by 100.

³Homeostatic model assessment of insulin resistance.