Associations of Socioeconomic Status and Processed Food Intake with Serum Phosphorus in Community-Living Adults: the Multi-Ethnic Study of Atherosclerosis (MESA)

Orlando M. Gutiérrez, MD, MMSc,1 Ronit Katz, DPhil,2 Carmen A. Peralta, MD, MAS,5 Jan H. de Boer, MD, MS,3,4 David Siscovick, MD, MPH,3,4 Myles Wolf, MD, MMSc,6 Ana Diez Roux, MD, MPH,7 Bryan Kestenbaum, MD, MS,3,4 Jennifer A. Nettleton, PhD,8 and Joachim H. Ix, MD, MAS9

1Departments of Medicine and Epidemiology, University of Alabama at Birmingham, Birmingham, AL
2Department of Biostatistics, University of Washington, Seattle, WA
3Department of Medicine, University of Washington, Seattle, WA
4Department of Epidemiology, University of Washington, Seattle, WA
5San Francisco Veterans Affairs Medical Center and Department of Medicine, University of California San Francisco, San Francisco, CA
6Department of Medicine, University of Miami, Miami, FL
7Department of Epidemiology, University of Michigan, Ann Arbor, MI
8Division of Epidemiology, Human Genetics and Environmental Sciences, University of Texas Health Sciences Center, Houston TX
9Department of Medicine, University of California San Diego and Nephrology Section, Veterans Affairs San Diego Healthcare System, San Diego, CA

Corresponding Author: Orlando M. Gutiérrez, MD, MMSc, University of Alabama at Birmingham, 35294-0006 phone: 205-996-2736 fax: 205-996-6465; Email: ogutierr@uab.edu

Abstract

Objective

Higher serum phosphorus concentrations are associated with cardiovascular disease events and mortality. Low socioeconomic status is linked with higher serum phosphorus, but the reasons are unclear. Poor individuals disproportionately consume inexpensive processed foods commonly enriched with phosphorus-based food preservatives. Accordingly, we hypothesized that excess intake of these foods accounts for a relationship between lower socioeconomic status and higher serum phosphorus.

Design

Cross-sectional analysis.

Setting and Participants

We examined a random cohort of 2,664 participants with available phosphorus measurements in the Multi-Ethnic Study of Atherosclerosis, a community-based sample of individuals free of clinically apparent cardiovascular disease from across the United States.

Predictor Variables

Socioeconomic status, the intake of foods commonly enriched with phosphorus additives (processed meats, sodas) and frequency of fast food consumption.

Outcomes
Fasting morning serum phosphorus concentrations.

Results

In unadjusted analyses, lower income and lower educational achievement categories were associated with modestly higher serum phosphorus (by 0.02 to 0.10 mg/dL, $P < 0.05$ for all). These associations were attenuated in models adjusted for demographic and clinical factors, almost entirely due to adjustment for female gender. There were no statistically significant associations of processed meat intake or frequency of fast-food consumption with serum phosphorus in multivariable-adjusted analyses. In contrast, each serving per day higher soda intake was associated with 0.02 mg/dL lower serum phosphorus (95% confidence interval, $-0.04, -0.01$).

Conclusions

Greater intake of foods commonly enriched with phosphorus additives was not associated with higher serum phosphorus in a community-living sample with largely preserved kidney function. These results suggest that excess intake of processed and fast foods may not impact fasting serum phosphorus concentrations among individuals without kidney disease.

Keywords: phosphorus, socioeconomic status, nutrition

INTRODUCTION

Higher serum phosphorus concentrations are associated with higher risks of cardiovascular disease events and death independently of established risk factors and kidney function.$^1$-$^5$ Higher serum phosphorus concentrations are also associated with elevated levels of parathyroid hormone (PTH) and fibroblast growth factor 23 (FGF23), both of which have emerged as important non-traditional risk factors for cardiovascular disease and mortality.$^6$-$^9$ These findings suggest that excess serum phosphorus may directly or indirectly impair cardiovascular health and survival, which has focused increased attention on identifying factors that lead to elevated serum phosphorus concentrations in the general population.

We recently reported that lower socioeconomic status was independently associated with higher serum phosphorus in patients with chronic kidney disease (CKD) and also in individuals with largely preserved kidney function.$^{10, 11}$ While the mechanisms for these findings were unclear, individuals with low socioeconomic status often have limited access to healthy food choices, resulting in higher consumption of relatively inexpensive processed and fast foods that are rich in phosphorus-based food preservatives meant to enhance flavor, appearance, and shelf-life.$^{12}$-$^{15}$ High intake of additive-rich foods can nearly double total dietary phosphorus intake$^{16}$ and was associated with increased serum phosphorus in individuals across the spectrum of kidney function in prior studies.$^{16, 17}$ Moreover, interventions aimed at reducing the consumption of these foods lowered serum phosphorus concentrations in hemodialysis patients.$^{18}$ On the basis of these data, we hypothesized that greater intake of foods commonly enriched with phosphorus additives would be associated with higher serum phosphorus concentrations in a multi-ethnic, community-living population predominantly without CKD. In addition, we hypothesized that this association would partly explain the link between lower socioeconomic status and higher serum phosphorus. In order to test these hypotheses, we examined the associations of socioeconomic status and processed food intake with serum phosphorus in the Multi-Ethnic Study of Atherosclerosis (MESA), a community-based sample of individuals free of clinically apparent cardiovascular disease from across the United States.

METHODS

Study Population

MESA is a multi-center prospective cohort study established to examine the prevalence and progression of subclinical cardiovascular disease. The details of the study design have been reviewed elsewhere.$^{19}$ Briefly, 6,814 Caucasian, African-American, Hispanic, or Chinese individuals aged 45 to 84 years who were community-living and free of known cardiovascular disease were recruited from six U.S. communities: Baltimore, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles, California; Northern Manhattan and the Bronx, New York; and St. Paul, Minnesota. All participants underwent a baseline study visit during which socioeconomic characteristics, medical history, diet history, current medications, and anthropomorphic measurements were...
obtained. In addition, fasting (8-hour) morning blood and urine specimens were collected for measurement of study variables. The institutional review boards at each participating center, the data coordinating center, and the senior author’s institution approved the study, and all participants provided written informed consent.

A random subcohort of 2,774 MESA participants were selected for serum phosphorus measurement as part of an ancillary study focused on mineral metabolism and cardiovascular outcomes (PI: Ix). After excluding participants with missing serum phosphorus values (N=9) and missing data on indices of socioeconomic status (N=101), 2,664 participants were included in the final analytic sample for the present study.

**Measurements**

**Diet Characteristics** Diet was assessed via a 120-item, modified-Block food frequency questionnaire (FFQ) administered at the baseline visit. Participants reported the serving size and frequency of consumption of specific beverages and foods. These data were then converted to approximate daily intake of total energy, macronutrients and micronutrients using the Nutrition Data Systems for Research database (Nutrition Coordinating Center, University of Minnesota). The consumption of foods rich in organic or inorganic sources of phosphorus was assessed in all participants. Foods containing high quantities of organic sources of phosphorus included eggs, dairy, red meat, poultry, nuts/legumes, and fish. Foods assumed to contain high quantities of inorganic phosphorus (i.e., phosphorus-based food additives) included processed meats and sodas. Processed meat intake was determined from responses to “sausage, chorizo, scrapple, bacon,” “ham, hot dogs, bologna, salami, and other lunch meats,” and “ham hocks, pigs’ feet, chicarones.” Soda intake was determined from responses to “regular soft drinks, soda, sweetened mineral water (not diet), non-alcoholic beer” and “diet soft drinks, unsweetened mineral water.”

As an additional measure of additive-rich food exposure, we examined fast-food consumption among 2,655 participants in the subcohort who also participated in the MESA Neighborhood Study, an ancillary study that collected information on frequency of fast-food intake and reported opportunities to purchase fast foods. Overall fast-food consumption was assessed from responses to the following item: “in an average week how often do you eat (eat in or take out) a meal from a fast-food place such as McDonald’s, KFC, Taco Bell, or takeout pizza places?” In addition, self-reported neighborhood exposure to fast foods was assessed according to responses to: “There are many opportunities to purchase fast food in my neighborhood,” with potential answers ranging from strongly disagree to strongly agree.

**Phosphorus** Serum phosphorus concentrations were measured in morning specimens after an overnight (8-hour) fast using a Siemens Dimensions Vista 500 system, with coefficients of variation (CV) < 2%.

**Socioeconomic Variables** Annual household income and highest level of education achieved were the primary indices of socioeconomic status, determined from standardized questionnaires administered at the baseline visit. Participants selected their total annual family income from 13 possible income categories. For the purposes of this analysis, income categories were collapsed into four categories: < $25,000; $25,000 – $49,999; $50,000 – $75,000; and > $75,000. In addition, a continuous measure of family income was calculated by dividing the interval midpoint of family income in each category by the number of persons in the household (family per capita income). Educational attainment was categorized as less than a high school diploma, high school graduate, or greater than a high school diploma.

**Other Measurements** Cystatin C concentrations were determined using a BNII nephelometer (Dade Behring, Deerfield, IL), with intra-assay CVs ≤ 3%. Measurements were used to calculate estimated glomerular filtration rate (eGFR) using the formula eGFR= 76.7 * cystatin C^{−1.19}. This equation has been validated in comparison to iothalamate-measured GFR in a pooled cohort of kidney disease studies and may be a more accurate marker of kidney function than creatinine-based methods at GFR levels > 60 ml/min/1.73m^2. Urine albumin and creatinine were measured in spot specimens by means of nephelometry and the rate Jaffé reaction, respectively.

**Statistical Analyses**

Demographic, clinical, dietary, and laboratory data were compared across annual family income categories using one-way ANOVA or Kruskal-Wallis tests for continuous variables and Pearson χ² tests for categorical variables, as appropriate.
Sequential linear regression models were fit to examine the associations of indices of socioeconomic status with serum phosphorus concentrations. The initial models were unadjusted. The second models adjusted for potential confounders including age, gender, race/ethnicity, clinical site, body mass index, eGFR, and urine albumin to creatinine ratio. The third models further adjusted for total caloric intake and phosphorus intake to evaluate whether the relationship between socioeconomic status and serum phosphorus was mediated by total energy or phosphorus consumption. In addition, since female gender modified the association of serum phosphorus with outcome variables in previous studies, we also tested the significance of interaction terms in the models (i.e., gender \times income, gender \times education).

The relationships between additive-rich food intake with serum phosphorus were examined in linear regression models using a similar analytic approach. For these analyses, frequency response items were aggregated within individual food groups (processed meats, sodas), and the consumption frequency of each was weighted by the reported serving size. The weighted frequencies were then converted to servings per day, modeled as a continuous variable. Frequency of fast food intake was categorized as never, \(< 1\) time/week, or \(\geq 1\) time/week, and self-reported neighborhood exposure to fast foods was categorized from strongly disagree to strongly agree. A \(P\) value of 0.05 was considered statistically significant for all analyses, including interaction terms. Analyses were performed with SAS software version 9.2 (SAS Institute, Cary, NC).

**RESULTS**

**Population Characteristics**

Table 1 depicts demographic, clinical, and laboratory characteristics of study participants according to annual family income. Lower income was associated with older age, female gender, non-white race, Hispanic ethnicity, greater prevalence of diabetes and hypertension, lower eGFR and higher albumin to creatinine ratio. In addition, participants with lower income were more likely to have lower educational achievement, and to be unemployed, employed only part-time or retired. Furthermore, fasting serum phosphorus concentrations increased as annual family income declined.

| Table 1 |
| Participant characteristics by category of annual family income. Results are presented as frequencies, mean (standard deviation), or median [interquartile range] |

Diet characteristics of study participants are summarized according to annual family income in Table 2. Lower income was associated with lower total energy intake and lower estimated phosphorus intake per day. In addition, participants with lower income on average consumed fewer servings per day of foods containing high quantities of organic forms of phosphorus such as red meat, poultry, nuts and fish, as well as fewer servings per day of foods typically enriched with inorganic forms of phosphorus, i.e., processed meats and sodas (\(P\) for trend < 0.001 for all).

| Table 2 |
| Diet characteristics of participants by category of family income. Results are presented as frequencies, mean (standard deviation), or median [interquartile range] |

**Socioeconomic Status and Serum Phosphorus**

Table 3 depicts linear regression models examining the association of socioeconomic status with serum phosphorus concentrations. In the crude analysis, as compared to participants with an annual family income of > $75,000, participants with annual family incomes of $50,000 – $75,000, $25,000 – $49,999, and < $25,000 had 0.02, 0.07 and 0.10 mg/dL higher serum phosphorus concentrations, respectively. After adjustment for age, gender, race/ethnicity, clinical site, body mass index, eGFR, and urine albumin to creatinine ratio, the relationship between lower income and higher serum phosphorus was attenuated. Female gender was the covariate that was responsible for most of the attenuation of the regression coefficients. Further adjustment for total caloric and phosphorus intake had minimal impact on these associations. When income was analyzed as a continuous
variable (family per capita income), analogous results were observed. In the unadjusted model, each $1,000 increase in family per capita income was associated with 0.002 mg/dL lower serum phosphorus (95% confidence interval [CI], −0.004, −0.001), but this association was attenuated after multivariable adjustment (0.000 mg/dL, 95% CI, −0.003, 0.001).

Table 3
Unadjusted and multivariable-adjusted linear regression models examining differences in serum phosphorus (mg/dL) as a function of indices of socioeconomic status. Results are depicted as regression coefficients (95% confidence intervals)

Lower educational achievement was similarly associated with modestly higher serum phosphorus concentrations as compared to higher educational achievement in unadjusted, but not in multivariable-adjusted analyses. As with family income, female gender was the variable responsible for the majority of the attenuation. There was no evidence of effect modification by gender in the analyses of the associations of diet categories, income, or education with serum phosphorus concentrations (P for interaction > 0.1 for all).

Processed Food Intake and Serum Phosphorus

Table 4 depicts linear regression models examining the associations of processed food intake with serum phosphorus. Greater processed meat intake was associated with lower serum phosphorus levels in the unadjusted model, but this association was attenuated after multivariable adjustment. Each serving per day increase in soda intake was associated with 0.02 mg/dL lower serum phosphorus in unadjusted analysis, and, in contrast to processed meat intake, this association remained statistically significant after multivariable adjustment. Since soda intake often comes at the expense of milk intake, an important source of dietary phosphorus in westernized diets, we further adjusted for milk intake and found that this had no material effect on the direction, magnitude, or strength of the association of higher soda intake with lower serum phosphorus (data not shown).

Table 4
Unadjusted and multivariable-adjusted linear regression models examining differences in serum phosphate (mg/dL) as a function of frequency of food group intake (cumulative services per day) and fast food intake. Results are...
concentrations independently of demographic, clinical, and biochemical factors in 14,261 adult participants of the Third National Health and Nutrition Examination Survey (NHANES). In contrast, an association of lower socioeconomic status with higher serum phosphorus was attenuated after multivariable adjustment in the present study, almost entirely due to adjustment for female gender. Several possibilities could explain this discrepancy. First, it is possible that the sample size of this study provided insufficient power to detect an association of socioeconomic status with serum phosphorus that was as modest as we observed in the NHANES study, which had a nearly 5-fold larger sample size. Second, the mean age of the NHANES study sample was 45 years, whereas it was 62 years in this study. It is recognized that estradiol has phosphaturic properties, and that the transition through menopause is associated with declining estradiol levels, resulting in higher serum phosphorus in older women than in older men. Thus, the association of female gender with higher serum phosphorus may have been stronger in the current study than in the much younger NHANES cohort, potentially resulting in more substantial attenuation of the association of socioeconomic status with serum phosphorus after adjustment for gender in MESA. Last, NHANES is a population-based survey, whereas MESA participants were from 6 centers and were recruited for racial/ethnic diversity and absence of clinically apparent cardiovascular disease. These differences may have further influenced the nature of the observed associations and the magnitude of attenuation by gender. Future studies that span a wider age spectrum should evaluate the associations of socioeconomic status with serum phosphorus in men and women separately, and consider stratifying women based on menopausal status to evaluate these possibilities.

Higher intake of foods commonly enriched with phosphorus-based food preservatives was not associated with higher serum phosphorus. The simplest explanation for this finding is that food additives do not meaningfully impact fasting serum phosphorus in the general population, perhaps because the contribution of phosphorus-based food additives to total dietary phosphorus intake is negligible. While possible, prior studies showed that diets rich in phosphorus additives can increase phosphorus intake by 400 to 1000 mg per day, indicating that, when consumed in excess, additive-rich foods can substantially augment daily phosphorus intake. Still, if consumed in smaller quantities more typical of the general population, the intake of these foods may not be sufficient to markedly increase overall phosphorus intake. Indeed, the mean servings per day of processed meats was a fraction of that of other major sources of dietary phosphorus such as dairy, red meat or poultry in this study, especially in the lower income categories, supporting the possibility that additive-rich foods are not consumed in high enough quantities to substantially augment phosphorus intake in the general population. In addition, as the vast majority of participants in this study had preserved kidney function, any impact of high additive intake on serum phosphorus levels may have been mitigated by compensatory increases in the secretion of phosphaturic hormones including PTH and FGF23. This hypothesis is consistent with the observation that estimated dietary phosphorus intake and the intake of high-phosphorus foods were only weakly associated with serum phosphorus in a prior analysis of individuals with mostly preserved kidney function in NHANES.

An alternative explanation may be that an association of additive-rich food intake with serum phosphorus was missed because phosphorus was measured in fasting morning blood samples. Detailed feeding studies involving healthy volunteers demonstrated that, when measured in fasting morning blood samples, serum phosphorus concentrations did not differ or were in fact lower in subjects undergoing dietary phosphorus loading as compared to subjects consuming a standard phosphorus diet. However, when comparing mean serum phosphorus concentrations averaged over 24-hours, phosphorus-loaded subjects had significantly higher serum phosphorus than control subjects, primarily because of greater diurnal increases in serum phosphorus during afternoon/evening hours in the loaded group. These studies provide important empirical evidence that dietary phosphorus loading—using phosphorus salts biochemically similar to commercial food additives—can measurably increase time-integrated serum phosphorus concentrations in healthy individuals, even in the face of compensatory increases in PTH and FGF23. However, in order to capture this effect, multiple serum phosphorus measurements during the day are required. In light of these findings, future studies evaluating the systemic effects of phosphorus-based food additives may require multiple measurements of serum phosphorus throughout the day, even when using large sample sizes. Still, it is noteworthy that prior epidemiologic studies have shown independent associations of single fasting morning serum phosphorus concentrations with cardiovascular disease. As such, further studies are needed to identify factors other than dietary intake that might explain differences in fasting morning serum phosphorus and their associations with clinical outcomes.

Our study had several important limitations. Diet was assessed using a single FFQ which was not specifically...
designed to ascertain the intake of additive-rich food items. This may have reduced precision in our estimates of diet intake and thus, limited our ability to detect an association of processed foods with serum phosphorus. Moreover, prior studies showed that the accuracy of self-reported dietary intake from FFQs may be diminished in individuals with lower socioeconomic status, which may have also adversely impacted the precision of our diet intake estimates. Next, given the cross-sectional nature of the study, the assumption that the food groups we examined were enriched with phosphorus additives was not independently verified, potentially resulting in exposure misclassification. Nevertheless, studies have consistently documented that processed and fast foods are replete with phosphorus additives. In addition, it is possible that these food groups provided only a partial assessment of cumulative additive exposure among study participants. Phosphorus additives are also commonly found in baking goods and cheese products, many of which are inexpensive, filling, and widely available in convenience and discount stores. As a result, individuals consuming large quantities of these foods—for example, because they cannot afford healthier options—may have been exposed to substantial amounts of unrecognized dietary phosphorus even if they infrequently consumed the processed and fast foods we focused on. Finally, because the proportion of participants with an eGFR < 60 ml/min/1.73m² was small, we were limited in our ability to examine the association of processed and fast-food intake with serum phosphorus concentrations among individuals with an impaired ability to excrete phosphorus. Given that decreased intake of processed and fast foods lowered serum phosphorus in hemodialysis patients, future studies should examine the extent to which our findings extend to CKD patients.

In conclusion, we found no associations of higher intake of processed and fast foods with higher fasting serum phosphorus concentrations in individuals with preserved kidney function. Given the link between elevated serum phosphorus and adverse health outcomes, further studies will need to examine potential biological or environmental mechanisms that may account for the association of low socioeconomic status with increased serum phosphorus observed in previous studies.

Acknowledgments

SUPPORT

This study was supported by grants K23DK081673 (OMG), R21HL091217 and an associated ARRA supplement R21HL091217-01A2S1 (JHI), and contracts N01-HC95159 through N01-HC-95165 and N01-HC-95169 from the National Institutes of Health. A full list of participating MESA investigators and institutions can be found at http://www.mesa-nhlbi.org.

Footnotes

FINANCIAL DISCLOSURES DELARATION:

None.

PRACTICAL APPLICATION

Higher intake of processed foods commonly enriched with phosphorus-based food additives was not associated with higher serum phosphorus concentrations in a sample of community-living adults with largely preserved kidney function. These results suggest that high intake of processed and fast foods may not impact fasting serum phosphorus concentrations in individuals without kidney disease.

Publisher’s Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

References


12. Baker EA, Schootman M, Barnidge E, Kelly C. The role of race and poverty in access to foods that enable individuals to adhere to dietary guidelines. Prev Chronic Dis. 2006 Jul;3(3):A76. [PMC free article] [PubMed]


