



The Relationship Between Protein Types and hs-CRP on eGFR

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Abstract

Few studies have measured the relationship between protein types and inflammation on kidney function among US adults. This study's objective was to identify the relationship between protein types (animal, dairy, plant, seafood) and high-sensitivity C-reactive protein on estimated glomerular filtration rate (eGFR). A cross-sectional secondary analysis using NHANES 2017-2018 data was performed on 4252 adults with an eGFR of >15 ml/min/1.73m². At least one 24-hour recall was used to categorize the protein type. Descriptives, frequencies, Pearson correlation, and multiple linear regressions were conducted using SPSS v28 with a significance of $p < 0.05$. Participants were mostly female (50.1%), had a mean age of 50.1 years, and self-identified as non-Hispanic White (36.5%). A majority consumed animal and dairy products compared to seafood and plant products. A negative association was observed between consumption of plant proteins and inflammation on eGFR ($p < 0.05$). In the adjusted regression model, non-Hispanic Black race had a positive influence on eGFR, female and age had negative influences on eGFR ($p < 0.001$), with no statistical significance seen with one identifying as male or other races. Reduced consumption of plant proteins with elevated inflammation can decline kidney function. Future studies should focus on frequency and amount of proteins consumed and inflammation to reduce the progression of chronic diseases such as kidney disease.

Keywords: inflammation, protein, eGFR, chronic kidney disease

Introduction

Chronic Kidney Disease (CKD) is a prevalent issue in the United States (US), as an estimated 15% of adults have this disease. Furthermore, about 9 in 10 adults may be unaware that they have CKD due to the asymptomatic nature of the disease (CDC, 2021). CKD is categorized into five different stages and is defined as a persistent abnormality in kidney structure or function (e.g., estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m²) for more than 3 months (American Kidney Foundation, 2021). Based on the KDOQI (Kidney Disease Outcomes Quality Initiative) guidelines, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation should be used to determine eGFR, which is based on serum

creatinine, gender, and age (Miller et al., 2022). The rate at which CKD progresses can depend on factors such as race, gender, age, family history, comorbidities, inflammation, and diet, a modifying risk factor (NKF, 2015; Kazancıoğlu, 2011).

In the US, the Western dietary pattern is generally consumed, which is characterized as high consumption of animal foods and low consumption of fruits and vegetables (Kramer, 2019; Rakhra et al., 2020). Consuming high levels of animal protein (e.g., red meat) with low consumption of fruits and vegetables can lead to high levels of endogenous acid, resulting in an increased workload and deterioration of the kidneys (Kramer, 2019). Current literature supports consumption of plant-based diets such as the Mediterranean and vegetarian, as plant proteins reduce uric acid production and inflammation compared to animal proteins (Hou et al., 2022; Khatri, et al., 2019). However, to the authors' knowledge, no studies have been able to demonstrate a relationship between the type of protein and inflammation on kidney function as measured by eGFR among the US general adult population. The aim for this study was to examine the relationship between protein types and the inflammation marker hs-CRP on eGFR. The hypothesis was that participants who consume on average more plant and seafood proteins will have lower hs-CRP compared to those who consume more animal proteins.

Methods and Materials

Study population

A cross-sectional study was performed using the 2017-2018 NHANES data cycle. The Center for Disease Control and Prevention's National Center for Health Statistics conducts the National Health and Nutrition Examination Survey (NHANES) every two years to assess the health, nutrition, disease prevalence, and trends over time for the US civilian population (NHANES, 2022). Participants were included in this study if they 1) were 18 years of age or older, 2) had serum creatinine and hs-CRP measurements, 3) had eGFR values >15 mL/min/1.73m², and 4) completed at least 1–24-hour dietary recall. Participants were excluded if they did not meet the above criteria and identified that they were pregnant or that the pregnancy test was inconclusive (Figure 1). A total of 4252 adults were included for analysis with a near equal distribution of genders.

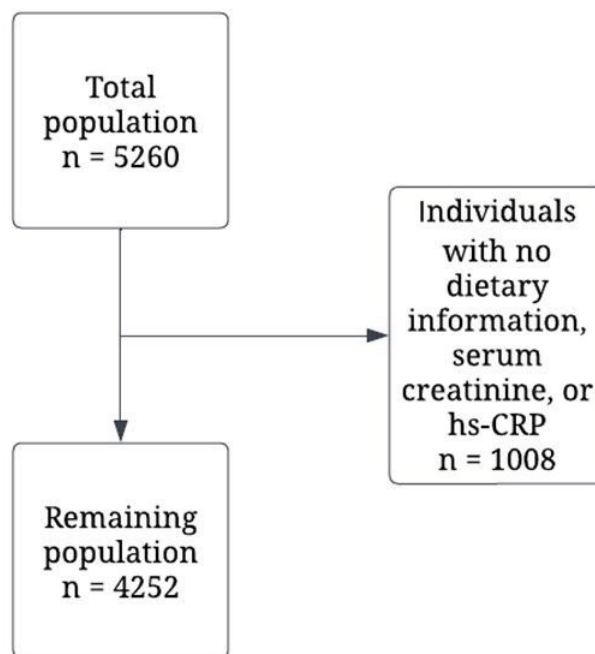


Figure 1. Study Population Exclusion Criteria

Data Collection

serum.

Serum creatinine and hs-CRP were collected; per the protocol from NHANES, serum creatinine was measured by the DxC800 modular chemistry side using the Jaffe rate method (kinetic alkaline picrate) (NHANES, 2022) and used to estimate eGFR using the CKD-EPI (Miller et al., 2022). Hs-CRP was analyzed using two reagents of the immunoturbidimetric system with a reference value of < 7.48 mg/L for both males and females (NHANES, 2022).

dietary.

Participants were interviewed by an NHANES representative for collection of two 24-hour dietary recalls, at day 0 and 3-10 days later, using a computer-based interview method (Ahluwalia et al., 2016). Codes were specified for the foods/beverages reported through these 24-hour recalls through NHANES based on the USDA's Food and Nutrient Database for Dietary Studies (FNDDS) (Ahluwalia et al., 2016). For this study, four protein groups were created: animal, dairy, plant, and seafood. As NHANES does not provide the amount consumed, if a protein type was consumed over the 2-day period, participants would receive a 1 (consumed) or

0 (not consumed). Table 1 depicts the types of foods counted for each protein type. Beans incorporated any consumed (e.g. pinto, black, kidney) as well as nuts/seeds. Both hard and soft cheeses were identified as dairy group, but cream cheese and sour cream were not included.

Table 1. Protein types and identified food groups

Animal	Seafood	Dairy	Plant
Beef	Fish	Cheese*	Beans
Egg	Crustaceans	Milk	Chickpeas
Game meat		Pizza	Nutritional bar (PB)**
Lamb/Goat		Whey	Nuts/Seeds
Poultry		Yogurt	Peanut Butter
Pork			Soy

Note. *Hard and soft cheeses; no cream cheese or sour cream; **PB: plant based

Statistical Analyses

Descriptive statistics had been obtained for the study variables. Mean and standard deviations were reported for the continuous variables (eGFR, hs-CRP, and age), and frequency and weighted percent reported for the categorical and dichotomous variables (race, gender). For analysis of the association between protein types, a dichotomous variable (0 or 1) was provided. A Pearson correlation was conducted to determine the association between a dichotomous variable, protein type, with a continuous variable, hs-CRP, and the outcome variable, eGFR. A multiple linear regression was performed to determine a relationship with protein type and hs-CRP on eGFR. Covariates (age, gender, and race) were included into the multiple regression model to detect influences on these relationships. A statistical significance was determined at $p < 0.05$ using SPSS v28.

Results

Study Participants

From the 4252 participants, a majority identified as female (50.1%) and self-identified as non-Hispanic White (36.5%) (Table 2). Not shown is age with a mean of 50.1 years.

Table 2. Participant Demographics

Variables	No. of Responses (%)
Sex	
Male	2098 (49.3%)
Female	2154 (50.7%)
Race/Ethnicity	
Mexican-American	593 (13.9%)
Other Hispanic	390 (9.2%)
Non-Hispanic White	1554 (36.5%)
Non-Hispanic Black	967 (22.7%)
Other	748 (17.6%)

Dietary Intake

Out of the participants 93.7% consumed animal protein, 76.8% consumed dairy, 41.8% consumed plant proteins and 24.9% consumed seafood (Figure 2). Based on Pearson's correlation, a negative association was observed between consumption of plant proteins and inflammation ($r = -0.07$) with no other associations observed (Table 3).

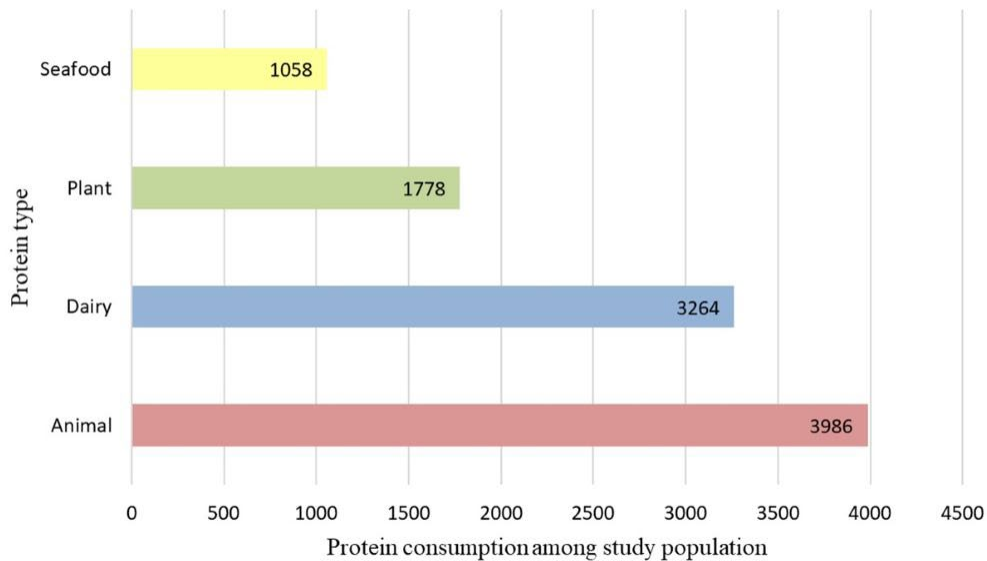


Figure 2. Protein Consumption Distribution Among Study Population (n = 4252)

Table 3. Pearson's correlation with protein types with inflammation (n = 4252)

Components	r	(CI 95%)*	p-Value**
eGFR - hsCRP	-0.009	(-1.000-0.016)	0.277
Animal - hsCRP	0.016	(-0.009-1.000)	0.143

Seafood - hsCRP	-0.021	(-1.000-0.004)	0.082
Plant - hsCRP	-0.069	(-1.000- 0.044)	0.000 **
Dairy - hsCRP	-0.001	(-1.000-0.024)	0.465

Note *CI = Confidence interval; ** $p < 0.05$

In an adjusted multiple-linear regression model, identifying as non-Hispanic Black had a positive influence on eGFR, while age and identifying as female had a negative influence on eGFR ($p < 0.00$) (Table 4). No other relationships were identified.

Table 4. Multiple linear regression, unadjusted and adjusted models (n=4252)

Variables	Coef.	Std. Err.	t	p<t*	95% Conf. Interval	
Unadjusted model						
Hs-CRP	-0.02	0.01	-1.66	0.097	-0.03	0.00
Animal	0.19	0.32	0.60	0.55	-0.43	0.81
Dairy	0.21	0.18	1.19	0.24	-0.14	0.56
Seafood	-0.69	0.18	-0.39	0.70	-0.41	0.28
Plant	-0.06	0.15	-0.40	0.69	-0.36	0.24
Adjusted model						
Age	-0.04	0.00	-10.4	0.00*	-0.05	-0.035
Female gender	-1.36	0.15	-9.17	0.00*	-1.65	-1.069
Non-Hispanic Black	0.57	0.20	2.86	0.00*	0.18	0.952

Note. * $p < t = 0.05$

Discussion

This study focused on the relationship between protein types and the inflammation marker, hs-CRP, on eGFR. No relationships were found between protein types and hs-CRP on eGFR, thus, the hypothesis was rejected. Through an adjusted model, the covariates non-Hispanic Black had a positive influence on eGFR, whereas age and identifying as female had a negative influence on eGFR. There was a statistically significant negative association with plant products and hs-CRP, in which decreased consumption of plant products was associated with elevated hs-CRP.

Similar to results from other US based studies, animal and dairy products were consumed more than both plant and seafood products. In the US, the Western dietary pattern is normally consumed (Kramer, 2019; Rakhra et al., 2020), which increases one’s risk for inflammation and progression of chronic diseases (Kramer, 2019; Selamet et al., 2016). On the other hand, individuals who consume plant-based dietary patterns, such as Mediterranean and vegetarian,

were found to have lower risks of chronic diseases and CKD (Hou et al., 2022; Khatri, et al., 2019). In this current study, there was no association between animal and dairy proteins and hs-CRP or eGFR. This could be due to how the foods were assessed in the 24-hour recalls, in which all animal proteins were grouped together. Even though animal and dairy products are considered high-quality proteins, which contain all nine essential amino acids, certain amounts and types of amino acids may have an adverse effect upon digestion (Zha and Qian, 2017; Aihemaitijiang et al., 2020). Individuals with decreased kidney function are susceptible to accumulation of these acids causing metabolic acidosis (Zha and Qian, 2017; Haring et al., 2017; Mirmiran et al., 2020). A cross-sectional study was conducted among US men (n=6,932) and women (n=7,877) who were at least 20 years of age to determine protein types consumed and their impacts on serum uric acid. It was observed that, regardless of gender, consuming more total meat and seafood was associated with increased serum uric acid (Choi et al., 2005). However, consuming more dairy foods was associated with lower serum uric acid. There was no association between total protein intake and serum uric acid, thus the authors indicated that the type of protein consumed is what affects uric acid, rather than the total amount consumed (Choi et al., 2005).

Furthermore, fat content of meat may have an association with inflammation and eGFR. One cut of meat may be considered leaner than another; according to the United States Department of Agriculture (USDA), 3.5oz or 100g of lean meat, such as a cut of top sirloin steak or chicken breast without the skin, contains less than 10g of total fat, 4.5g of saturated fat and 95mg of cholesterol. A systematic review and meta-analysis which investigated 20 randomized control trials with a total of 1001 adults showed that increased red meat consumption resulted in increased serum lipid concentrations but ultimately had no significant effects on hs-CRP (Sun et al., 2022). However, excessive consumption of red meats high in saturated fatty acids may disrupt lipid metabolism, which can lead to increased secretion of CRP or hs-CRP (Saltiel and Olefsky, 2017; Sun et al., 2022). Additionally, increased lipid metabolism disruption may lead to oxidative stress, which can further induce inflammation (Leroy and Cofnas, 2020; Sun et al., 2022). Average red meat consumption per day was not identified within this review, thus future studies should be conducted on the frequency and amount of certain fats consumed on inflammation and ultimately kidney function.

NHANES is unable to provide the exact quantity of animal and dairy products consumed, aside from the total protein, which may have contributed to the limited relationship between

protein types and inflammation on eGFR. A cross-sectional study was conducted to determine an association between type and amount of protein consumed and the inflammation marker CRP among 312 men and 911 women ($n = 1223$) with a mean age of 68.9 ± 7.6 (Chai et al., 2017). Results showed that there was an association between consumption of an average of 50g daily of processed meat and red meat and CRP in women (Chai et al., 2017). Additionally, a cross-sectional study was conducted with 391 overweight and obese ($BMI > 25 \text{ kg/m}^2$) Iranian women aged between 18-56 years old. Results showed a positive association between consuming, on average, 40.2g daily of red meat and hs-CRP (Shiraseb et al., 2022). Moreover, an observational study that assessed habitual dietary intake of 4881 participants indicated that consuming two or more servings of total red meat or processed meat daily led to increased risk of CKD or expedited progression in individuals with the disease (Mirmiran et al., 2020). These studies indicate that consuming at least 280g or more of red meat weekly is associated with inflammation as well as adverse kidney functions. This is confirmed by the World Health Organization (WHO), which recommends consuming no more than 12-18 ounces or 350-500g of red or processed meat weekly to reduce risk for certain cancers and non-communicable chronic diseases (WHO, n.d.). Further research should explore quantities of different animal proteins consumed and their effects on hs-CRP and eGFR.

In this present study, results showed decreased plant product consumption was associated with elevated hs-CRP. Consuming plant products may reduce inflammation due to the terpenes and terpenoids found in these plants (Stromsnes et al., 2021). Terpenes and terpenoids have demonstrated anti-inflammatory properties *in vitro* and *in vivo*. This is due to their ability to reduce the activity of the NF- κ B pathway, which is a main transcription factor involved in inflammatory processes (Stromsnes et al., 2021). Furthermore, upon metabolism, plant proteins do not produce as much acid compared to red meats due to plant products containing fewer acidic amino acids compared to animal and dairy based products. Additionally, plant products contain more fiber; evidence shows diets rich in fiber may minimize inflammation by altering gut pH (Berrazaga et al., 2019; Swann et al., 2020; Yusuf et al., 2022). Additionally, it has been reported that a higher consumption of gluten from plant protein can reduce serum uric acid and oxidized low density lipoprotein (LDL) (Jenkins et al., 2001). Several studies indicate that an increased consumption of plant proteins has a positive effect on weight reduction, LDL and high-density lipoprotein (HDL), as well as lower inflammation markers in adults with chronic diseases

(Dinu et al., 2017; Aycart et al., 2021). Therefore, future studies should focus on consumption of plant foods and their impact on inflammation.

As illustrated, results from this study show that identifying as non-Hispanic Black had a positive influence on eGFR. The National Kidney Foundation (NKF) provides a set of risk factors for kidney disease, which include being 60 years of age or older, as well as identifying as Black, African American, Hispanic, or Latino (NKF, 2020). As of 2021, eGFR equations have been updated to remove race in order to reduce bias and improve precision and accuracy (Parekh et al., 2022). This may explain this study's observation that there is a positive influence of identifying as non-Hispanic Black on eGFR as compared to studies conducted before the equation adjustments. Furthermore, in this study, age was found to have a negative influence on eGFR. As noted by the NKF and the current literature, as individuals age, the structure of the kidneys change, which impacts the glomeruli, tubules, interstitium, and vasculature (Laster et al., 2018). The NKF advises individuals over the age of 60 to be screened for kidney disease, as it is most prevalent in older populations, especially in populations with diabetes and high blood pressure (NKF, 2014).

Limitations

This study is not without limitations. First, NHANES is nationally representative of the US population, yet self-reporting bias may have occurred within those who decided to participate, especially with the 24-hour recall. Second, the serum creatinine and hs-CRP were only collected at one point in time. Both of these biochemical values could have been abnormal due to various factors that were unknown to the researchers. It is recommended that at least three months of serum creatinine is collected to determine if eGFR is reduced from kidney decline.

Conclusion

In conclusion, results from this cross-sectional study showed that consuming less plant products was associated with elevated hs-CRP. Factors including race, age, and sex were found to influence eGFR. However, no relationships with protein types and hs-CRP on eGFR were observed. Future studies should focus on frequency and amount of proteins consumed and its influence on inflammation and in relationship to inflammation as a mechanism to reduce the progression of chronic kidney disease for both researchers and practitioners.

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