

Investigating Racial and Ethnic Variation in High Sensitivity C-Reactive Protein Levels Among Individuals with Prediabetes

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Abstract

Background: High sensitivity C-reactive protein (hs-CRP) is a marker of inflammation linked to chronic health conditions, including prediabetes. Many factors, including social determinants of health such as socioeconomic status, food insecurity, chronic stress and many others, can affect hs-CRP levels. Given the well-documented health disparities across racial and ethnic minority groups regarding social determinants of health, it's crucial to investigate how hs-CRP levels vary in people with prediabetes to uncover possible contributing factors that could predispose an individual to develop prediabetes and its sequelae. This study investigated whether hs-CRP levels differ among racial and ethnic groups with prediabetes, potentially reflecting the role of health inequalities.

Methods: Data from the National Health and Nutrition Examination Survey (NHANES) were utilized for adults age 18 and older with prediabetes. Participants were grouped into racial and ethnic minority populations (Mexican American, Other Hispanic, Non-Hispanic Black, Non-Hispanic Asian, and Other Race) and non-minority populations (Non-Hispanic White). A Wilcoxon rank-sum test was performed to compare the distribution of hs-CRP levels after adjusting for sample weights. Further subgroup analyses were conducted comparing CRP levels by minority status for the following subgroups: sex, insurance status, and education status.

Results: In the unweighted sample, racial and ethnic minority populations had significantly higher hs-CRP levels than non-minority populations ($p=0.03$). However, after adjusting for survey weights, this

difference approached but did not reach statistical significance ($p=0.09$). The median hs-CRP level for minority populations was 2.99 (IQR: 1.22, 5.74), compared to 1.94 (IQR: 1.03, 4.67) in non-minority populations ($p = 0.09$). Non-Hispanic Black individuals had the highest hs-CRP levels, with a median hs-CRP level of 3.93. CRP levels only seemed to significantly differ in the combined subgroup of high school graduates and individuals with some college or AA degree. In this subgroup, the minority group had higher median CRP levels than the non-minority group (3.10 versus 2.10; p -value = 0.0048).

Conclusion: Our findings present disparities in hs-CRP levels among different racial and ethnic populations with prediabetes, especially in Non-Hispanic Black individuals. Understanding and addressing possible social determinants of health, such as food insecurity or chronic stress, is essential for accurately assessing individual risk and implementing patient-centered preventive strategies.

Introduction

Prediabetes is a significant public health concern in the United States, affecting an estimated 97.6 million adults as of 2021, according to the Centers for Disease Control and Prevention (1). This condition is characterized by blood glucose levels that are elevated above the normal range but have not met the threshold for a diagnosis of Type 2 diabetes (1). The CDC defines prediabetes based on glycated hemoglobin (HbA1C) levels ranging from 5.7% to 6.4%, reflecting average blood glucose concentrations over approximately 3 months (1). Several studies have shown that diagnosis of prediabetes is linked to an increased

risk of developing early forms of nephropathy and chronic kidney disease (2). Additionally, individuals with prediabetes are at markedly increased risk of progression to Type 2 diabetes and its cardiovascular sequelae including coronary heart disease and stroke (3). Large prospective cohorts further demonstrate that prediabetes confers an elevated risk of all-cause mortality relative to normoglycemia, underscoring its clinical significance (3). Thus, early identification of individuals at risk for prediabetes is critical, as timely intervention can delay or prevent the progression to Type 2 diabetes and development of its associated risks (4, 5).

One biomarker that has garnered increased attention for use as a diagnostic test for prediabetes is high-sensitivity C-reactive protein (hs-CRP), an acute-phase protein produced by the liver in response to systemic inflammation (6, 7). Elevated hs-CRP levels have been associated with prediabetes, suggesting a potential role for inflammatory processes in its pathogenesis (8). While elevated hs-CRP levels have been linked to the development of prediabetes, limited research has explored how this relationship may vary across different racial and ethnic groups. Existing knowledge indicates that among adults in the United States, there is a disparity of diabetes diagnoses, with minority groups having a higher prevalence in comparison to non-minority groups (9). These disparities have been linked to social determinants of health, for example limited access to care, increased exposure to chronic stress, and residence in poorer neighborhood environments (10–14). Though a social construct, race and ethnicity have notable impacts upon the equity of healthcare outcomes, thus a relevant relationship to explore. This study aims to address this gap in the literature by examining the association between hs-CRP and prediabetes within the context of racial and ethnic variation. There is a focus on examining whether racial and ethnic minority groups (e.g. Non-Hispanic Black, Hispanic) have higher hs-CRP levels than non-minority populations (Non-Hispanic White), potentially reflecting the role of health inequities in the development of prediabetes.

Methods

Data Collection

Data were obtained from the National Health and Nutrition Examination Survey (NHANES), a cross-sectional, multistage probability survey conducted

by the Centers for Disease Control and Prevention to assess the health and nutritional status of the non-institutionalized U.S. population (15). This study used publicly available, de-identified data and was determined not to constitute human subjects research by the Geisinger Institutional Review Board (Study #2024-0576).

Patient Population

Participants included adults age 18 years and older who met the criteria for prediabetes, defined by HbA1c levels of 5.7% to 6.4%. Race and ethnicity were self-reported by participants during standardized NHANES interviews and categorized as Non-Hispanic White, Non-Hispanic Black, Mexican American, Other Hispanic, Non-Hispanic Asian, or Other Race, including multiracial individuals. Categories were selected based on those provided in the NHANES dataset. Race and ethnicity were assessed in this study to evaluate potential disparities in systemic inflammation among individuals with prediabetes, as prior literature suggests associations between race and ethnicity, and chronic disease risk.

Statistical Analysis

To produce nationally representative estimates, we utilized the survey weights developed by NHANES to account for the complex, multistage probability design. Specifically, fasting subsample weights were applied, as hs-CRP is a laboratory variable derived from the fasting blood draw component. For the single NHANES cycle used, weights were adjusted according to the National Center for Health Statistics analytic guidelines. The R “survey” package was used to apply appropriate weights in all statistical components.

Descriptive statistics were performed on the unweighted and weighted samples. Medians, interquartile ranges (IQR), and ranges were reported for continuous variables and frequencies, and percentages for categorical variables. Weighted population characteristics were further examined across race and ethnicity status, and descriptive statistics were provided. A Wilcoxon rank sum test was performed on the unweighted and weighted samples. Further subgroup analyses were conducted comparing hs-CRP levels by minority status for the following subgroups: sex, insurance status, and education status. For education status, the groups were combined to create the following 3 groups (unknown were not considered): less than high school, high school

graduate/some college or associate's degree (AA), and college graduate or above. A p-value of 0.05 was used to determine significance. Analyses were performed using SAS version 9.4 (Cary, North Carolina, USA) and R v4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

The unweighted study sample consisted of 675 participants, representing a weighted population of 19,280,268 individuals. The median age was 61.0 years (IQR: 50.0 - 70.0) in the unweighted sample and 57.1 years (IQR: 43.7-65.9) in the weighted population, with an age range of 18–80 years in both samples. Median hs-CRP levels were consistent across both samples at 2.30 mg/L, with similar interquartile ranges (unweighted: 1.03-5.45 mg/L; weighted: 1.08-5.31 mg/L). The gender distribution was 41.3% male and 58.7% female in the unweighted sample, compared to 45.7% male and 54.3% female in the weighted population (Table 1).

Educational attainment varied, with the largest proportion of participants being a college graduate or above (unweighted: 37.3%; weighted: 35.3%). The majority of the unweighted and weighted sample had health insurance coverage, with 94.8% of the unweighted sample and 94.0% of the weighted population reporting coverage (Table 1).

Racial and ethnic composition showed that Non-Hispanic Whites comprised the majority (unweighted: 60.0%; weighted: 59.2%), followed by Non-Hispanic Blacks (unweighted: 11.1%; weighted: 11.0%). Approximately 40% of both the weighted and unweighted samples were identified as belonging to a minority population.

Table 2 stratifies the weighted patient characteristics by racial and ethnic groups. Non-Hispanic Black and Mexican American individuals had the highest median hs-CRP values (3.93 mg/L and 3.64 mg/L, respectively), while education levels and insurance coverage

varied significantly across groups. Insurance coverage was highest among Non-Hispanic Whites (61.0%) and lowest among Mexican Americans (7.0%). The elevated hs-CRP levels observed in the Non-Hispanic Black population contributed substantially to the overall trend of higher systemic inflammation seen within racial and ethnic minority groups.

Hs-CRP levels were compared between racial and ethnic minority and non-minority populations using survey weighted data in Table 3. In the unweighted sample (not represented in Table 3), minority populations had significantly higher hs-CRP levels ($p=0.03$). In the weighted sample, although median hs-CRP levels were higher in minority groups (2.99

Variables	Unweighted (N = 675)	Weighted (N = 19,280,268)
Age		
Median (IQR)	61.0 (50.0, 70.0)	57.1 (43.7, 65.9)
Range	18.0, 80.0	18.0, 80.0
CRP		
Median (IQR)	2.30 (1.03, 5.45)	2.30 (1.08, 5.31)
Range	0.11, 110.98	0.11, 110.98
Gender		
Male	279 (41.3%)	8,812,300 (45.7%)
Female	396 (58.7%)	10,467,968 (54.3%)
Education Level		
Less than 9th grade	19 (2.8%)	520,255 (2.7%)
9th-11th grade	40 (5.9%)	1,010,166 (5.2%)
High school graduate/GED or equivalent	127 (18.8%)	4,237,389 (22.0%)
Some college or AA degree	233 (34.5%)	6,593,090 (34.2%)
College graduate or above	252 (37.3%)	6,811,308 (35.3%)
Unknown	4 (0.6%)	108,060 (0.6%)
Covered by Insurance		
Yes	640 (94.8%)	18,126,879 (94.0%)
No	35 (5.2%)	1,153,389 (6.0%)
Race/Ethnicity		
Mexican American	52 (7.7%)	1,632,483 (8.5%)
Other Hispanic	66 (9.8%)	1,857,021 (9.6%)
Non-Hispanic White	405 (60.0%)	11,405,304 (59.2%)
Non-Hispanic Black	75 (11.1%)	2,127,216 (11.0%)
Non-Hispanic Asian	37 (5.5%)	1,195,707 (6.2%)
Other Race - Including Multiracial	40 (5.9%)	1,062,537 (5.5%)
Minority Population		
Yes	270 (40.0%)	7,874,964 (40.8%)
No	405 (60.0%)	11,405,304 (59.2%)

Table 1. Patient Characteristics

	Mexican American (N = 1,632,483)	Other Hispanic (N = 1,857,021)	Non-Hispanic White (N = 11,405,304)	Non-Hispanic Black (N = 2,127,216)	Non-Hispanic Asian (N = 1,195,707)	Other Race-Including Multi-Racial (N = 1,062,537)
Age						
Median (IQR)	49.5 (35.2, 55.9)	52.0 (42.6, 60.5)	59.9 (45.7, 67.8)	54.3 (40.8, 63.2)	50.8 (43.4, 60.6)	55.3 (46.7, 65.2)
Range	18.0, 73.0	20.0, 79.0	19.0, 80.0	19.0, 78.0	21.0, 79.0	20.0, 77.0
CRP						
Median (IQR)	3.64 (1.63, 6.24)	3.07 (1.36, 5.53)	1.94 (1.02, 4.66)	3.93 (1.06, 7.07)	1.13 (0.70, 3.27)	2.39 (1.33, 4.16)
Range	0.41, 16.41	0.22, 14.47	0.11, 110.98	0.15, 36.65	0.20, 35.52	0.20, 43.91
Gender						
Male	646,878 (7.3%)	867,772 (9.5%)	5,520,379 (62.6%)	663,096 (7.5%)	583,239 (6.6%)	530,937 (6.0%)
Female	985,605 (9.4%)	989,249 (9.5%)	5,884,925 (56.2%)	1,464,120 (14.0%)	612,468 (5.9%)	531,601 (5.1%)
Education Level						
Less than 9th grade	128,482 (24.7%)	274,463 (52.8%)	25,378 (4.9%)	48,310 (9.3%)	0 (0.0%)	43,621 (8.4%)
9th-11th grade	141,498 (14.0%)	207,857 (20.6%)	437,396 (43.3%)	116,985 (11.6%)	44,926 (4.5%)	61,505 (6.1%)
High school graduate/ GED or equivalent	476,526 (11.2%)	466,597 (11.0%)	2,569,501 (60.6%)	401,223 (9.47%)	131,661 (3.1%)	191,882 (4.5%)
Some college or AA	595,653 (9.0%)	466,683 (7.1%)	4,068,327 (61.7%)	852,700 (12.9%)	128,258 (1.9%)	481,469 (7.3%)
College graduate or above	270,027 (4.0%)	441,421 (6.5%)	4,240,612 (62.3%)	684,327 (10.1%)	890,861 (13.1%)	284,061 (4.2%)
Unknown	20,297 (18.8%)	0 (0.0%)	64,090 (59.3%)	23,672 (21.9%)	0 (0.0%)	0 (0.0%)
Covered by Insurance						
Yes	1,260,625 (7.0%)	1,587,170(8.8%)	11,061,036(61.0%)	2,014,090(11.1%)	1,177,206(6.5%)	1,026,751 (5.7%)
No	371,858 (32.2%)	269,851 (23.4%)	344,268 (29.9%)	113,126 (9.8%)	18,500 (1.6%)	35,786 (3.1%)

Table 2. Patient Characteristics by Race and Ethnicity, Presented with Row Percentages

vs. 1.94 mg/L in non-minority), the difference was not statistically significant ($p=0.09$). Within the subgroup analysis, CRP levels only seemed to significantly differ in the combined subgroup of high school graduates and individuals with some college or AA degree. In this subgroup, the minority group had higher median CRP levels than the non-minority group (3.10 versus 2.10; p -value = 0.0048).

Discussion

Overall, our study found that persons identifying as Non-Hispanic Black had higher median hs-CRP levels compared to non-minority population groups. While these differences were statistically significant in the unweighted analysis, they were not significant after applying survey weights ($p = 0.09$), though a clear trend persisted. These results, when considered with previous studies that linked elevated hs-CRP to impaired glucose regulation, allow us to hypothesize that Non-Hispanic Black populations may have higher impairments of glucose regulation (6–7,16).

Interestingly, in our subgroup analysis our study found significant differences in hs-CRP levels among

people who had completed high school, attended some college, or received an AA degree. Within this group, minority population groups had significantly higher median hs-CRP levels than non-minority population groups. This finding suggests that other social factors may influence and contribute to systemic inflammation even among those with similar education levels, reinforcing the importance of considering how race and other social factors influence health outcomes.

By exploring how hs-CRP levels vary among diverse racial and ethnic groups rather than relying solely on broad demographic categorizations, our findings emphasize the importance of examining prediabetes through the lens of health equity. Social determinants of health such as socioeconomic status (SES), food insecurity, chronic stress, residential segregation, environmental exposure, and unequal healthcare access may contribute to systemic inflammation in these populations, producing biomarker-level disparities, specifically hs-CRP disparities (10–14). For instance, Muscatell et al. demonstrated this in their meta-analysis which found a significant association between lower SES and elevated levels of

	Minority (N = 270)	Non-minority (N = 405)	P-value
Overall CRP levels			0.0885
Median (IQR)	2.99 (1.22, 5.74)	1.94 (1.03, 4.67)	
Range	0.15, 43.91	0.11, 110.98	
Female CRP levels			0.3648
Median (IQR)	3.68 (1.30, 6.62)	2.94 (1.41, 6.56)	
Range	0.15, 43.91	0.11, 31.44	
Male CRP levels			0.0755
Median (IQR)	2.05 (1.13, 4.15)	1.56 (0.77, 3.02)	
Range	0.15, 14.47	0.16, 110.98	
Covered by insurance			0.2044
Median (IQR)	2.38 (1.13, 5.52)	1.95 (1.04, 4.90)	
Range	0.15, 43.91	0.11, 110.98	
Not covered by insurance			0.0739
Median (IQR)	3.80 (3.17, 7.73)	1.70 (0.74, 2.67)	
Range	0.24, 14.13	0.22, 53.28	
Less than high school			0.1281
Median (IQR)	3.68 (1.82, 5.11)	1.56 (1.55, 3.09)	
Range	0.22, 13.01	0.15, 76.02	
High school graduate/some college			0.0048
Median (IQR)	3.10 (1.61, 6.43)	2.10 (1.03, 4.90)	
Range	0.15, 43.91	0.19, 110.98	
College graduate or above			0.5788
Median (IQR)	1.46 (0.81, 4.37)	1.84 (0.90, 4.65)	
Range	0.15, 35.52	0.11, 109.34	

Table 3. Median CRP Levels (mg/L) by Race/Ethnicity, Stratified by Sex, Insurance Coverage, and Education Level. Median and interquartile range (IQR) values are reported for minority (N = 270) and non-minority (N = 405) participants. P-values reflect group differences within each stratum.

inflammatory markers (17). These findings underscore the need to further explore upstream structural factors and to implement culturally tailored public health and clinical interventions (18).

Rationale for incorporating social determinants of health into hs-CRP interpretation is further supported by recent work from Modisette et al., who conducted a stratified analysis of hs-CRP predictors across racial and ethnic groups using NHANES data. Their study identified consistent predictors of elevated hs-CRP levels including increased BMI and female sex across most racial and ethnic groups, while also highlighting the influence of socioeconomic factors like poverty, particularly increased among Non-Hispanic Asian populations. These results reinforce the importance of interpreting hs-CRP levels through a race-conscious and equity-informed lens, as they

suggest that systemic inflammation is not solely biologically driven but also shaped by social determinants of health. Incorporating these insights strengthens the rationale for using hs-CRP as a biomarker in prediabetes risk stratification, while emphasizing the need for clinical interpretation that accounts for social and environmental exposures (19).

Considering these disparities, our findings also support the potential utility of hs-CRP testing as a widely accessible and affordable biomarker for identifying individuals with prediabetes who may be at greater risk of progression to overt Type 2 diabetes. This is supported by findings from Cheng et al., who demonstrated in a prospective cohort study that elevated hs-CRP levels were significantly associated with increased risk of progression from prediabetes to Type 2 diabetes among middle-aged and older adults (20). However, the clinical interpretation of hs-CRP levels should be approached with caution, integrating frameworks that consider social determinants of health to contextualize differences, rather than solely attributing variations to race (21–22). Such interpretation is essential to avoid misclassification or underestimation of risk, particularly in historically marginalized minority populations (23–24).

Despite the strengths of this study, including use of a nationally representative NHANES dataset and stratification by race/ethnicity, several limitations must be acknowledged. First, the NHANES dataset is cross-sectional in nature, which limits causal inference. Second, we did not control potential confounding variables such as smoking status, physical activity, obesity (BMI), or recent infections, all of which can elevate hs-CRP independently of glycemic status (25). These uncontrolled confounders may have contributed to the attenuation of statistical significance in the weighted analysis, masking underlying relationships.

Future studies should adopt longitudinal designs to track changes in hs-CRP and glycemic control over time, and mechanistic studies should be pursued to better understand the interplay between systemic inflammation and glucose metabolism. Additionally,

incorporating direct measures of socioeconomic status (e.g., income, education, occupation) and environmental exposures would strengthen our ability to delineate the root causes of observed disparities and guide equitable interventions.

Conclusion

This study highlights racial and ethnic differences in hs-CRP levels among individuals with prediabetes, with higher levels observed in minority populations, specifically Non-Hispanic Black populations. These differences persisted even after accounting for demographic factors such as insurance status or education level, underscoring the impact of social determinants of health on systemic inflammation. These findings emphasize the importance of critically interpreting hs-CRP levels with a perspective that acknowledges health disparities; an essential skill to accurately assess patient risk and to develop inclusive, patient-centered intervention strategies.

Disclosures

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