







Exploring the Relationship Between Stress, Salivary C-Reactive Protein, and Embodied Physiological Responses in a Nigerian Population

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ABSTRACT

Objectives: The impacts of stress on inflammation, although hypothesized, have not been thoroughly examined, especially in relation to social and environmental factors and particularly within Black populations. This study aims to explore the biological mechanisms of embodiment linking stress and health to understand physiological changes in the body's response to psychological stress in a Nigerian population. Through a multidisciplinary approach, this study queries the relationship between stress, cortisol, and salivary C-reactive protein (sCRP), a biomarker of inflammation, while also validating the use of sCRP as a potential and accurate stress indicator in the field.

Methods: In this cross-sectional study, 138 passive drool saliva samples ($n_{\rm female} = 89$ $n_{\rm male} = 49$) were collected and assessed for sCRP and cortisol levels in adults. Participants also completed a short demographic survey and, to measure psychological stress, the General Health Questionnaire 12 (GHQ-12). Relationships between sCRP and stress-related variables (i.e., cortisol, GHQ-12, and demographic data) were assessed using Spearman's correlations, simple regression, multivariable linear regression, and exploratory factor analysis.

Results: sCRP levels ranged from 20.57 to 6879.41 pg/mL across all samples, with significant differences between female and male participants. The GHQ-12 was not a significant predictor of sCRP variability. However, socio-demographic factors such as body mass index (BMI), age, self-reported sex, ethnic identity, and cortisol were significant predictors, collectively explaining 24%–27% of the variation in sCRP.

Conclusion: Socio-demographic predictors like BMI, age, sex, and particularly ethnic group experience in Nigeria encapsulate aspects of embodied stress, that significantly affect sCRP variability.

1 | Introduction

Studies linking stress and disease have typically focused on traditional stress response pathways such as the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS) (Stephens and Wand 2012; Rohleder 2014). However,

scholars have noted that these traditional pathways alone are not adequate to explore mechanisms linking stress and disease, citing the need to incorporate other possible modifiers (Cohen et al. 2012; Miller, Chen, and Zhou 2007; Rohleder 2014; Liu, Wang, and Jiang 2017). Inflammation has emerged as a promising mediator between stress and chronic disease because of

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its ability to respond to stressors through quantifiable systemic measures in the body.

Inflammation is a biological process that promotes healing by fighting disease-causing agents and other stimuli (Szabo, Slavish, and Graham-Engeland 2020). Short-term responses to inflammation are necessary and healthy; however, when the inflammatory response is ongoing, the body is negatively affected. Responses to these stimuli can produce acute or chronic inflammatory stress responses throughout the body (Chen et al. 2018; Pahwa et al. 2018). Chronic inflammation in the body has been associated with cardiovascular disease (CVD) (Henein et al. 2022; Sorriento and Iaccarino 2019), diabetes (Tsalamandris et al. 2019), cancer (Singh et al. 2019), and other poor health outcomes (Emerging Risk Factors Collaboration 2010; Furman et al. 2019). It is also associated with increased risks of mental health disorders, such as depression and anxiety, due to the prolonged impact on the body's immune system and stress response.

The inflammatory response can be triggered by a range of infectious (i.e., bacteria and viruses) and noninfectious (i.e., physical, chemical, and psychological) factors (Pahwa et al. 2018). Among the psychological factors, stress plays a significant role in promoting inflammation. However, the impacts of stress on inflammation, although hypothesized, have not been thoroughly examined, especially in relation to social and environmental factors, particularly within Black populations (Goetz and Lucas 2020; Simons et al. 2021; Toussaint et al. 2022), and in low- or- middle-income countries (LMIC) (McDade 2012). Previous research underscores the importance of considering ecological and environmental contexts in understanding inflammatory processes and immune regulation (Aronoff et al. 2024; Vitzthum et al. 2024; Blackwell et al. 2016; McDade 2012; McDade et al. 2011; Blackwell et al. 2010; McDade et al. 2010). In response to these works, interest in assessing how local stressors become embodied and influence inflammatory and immune processes across varying socio-ecological contexts continues to grow (DeCaro and Helfrecht 2022).

Salivary C-reactive protein (sCRP) is increasingly recognized as a key biomarker for assessing different aspects of stress, reflecting how chronic and acute stressors can lead to inflammation. In the Nigerian context, however, literature examining the relationship between stress and sCRP is scarce, highlighting a significant gap in understanding how these stress-induced inflammatory processes manifest in this population. To address this gap, this paper explores the effects of physiological, psychological, and socio-demographic related stressors on sCRP in a Nigerian population. Embodiment theory is the orienting framework used to examine the relationship between sCRP and stressors. Broadly, this theory posits that life experiences can have biological consequences on the body (Engel 1977; Lock 1993; Nguyen and Peschard 2003; Kuzawa and Sweet 2009; Adler and Stewart 2010; Geronimus et al. 2006; Baluran and Winful 2021). These experiences can manifest through acute or chronic exposures to stress (Geronimus 1992; Geronimus et al. 2006), influenced by socioeconomic status (SES) (Yang et al. 2020), race (Forde et al. 2019), environment (Thayer and Kuzawa 2011; Leatherman and Hoke 2016), and psychosocial stress (Sapolsky 2021), leading to physiological responses (McEwen and Wingfield 2003; McDade 2012). Theoretical conceptions of embodiment are beneficial in grappling with how best to model the impacts of stress biologically and holistically, as they consider and contextualize how experiences, measured through social, behavioral, and psychosocial variables, impacts health outcomes. Anthropological approaches to embodiment further allow scholars to attach political frameworks to health (Adler and Stewart 2010). Political frameworks directly incorporate the need for social change and equity by drawing on concepts of embodiment and resilience to connect social inequalities to biological outcomes. Political frameworks for health can provide insight on cultures of inequality and the role they play in creating societies that are unhealthy (Nguyen and Peschard 2003; Adler and Stewart 2010). Using embodiment theory in addition to cognizance of the broader political context impacting the study participants, the current study considers biological pathways underlying how stress becomes internalized and impacts immune response. Furthermore, the specific focus on a Nigerian community, addresses the dearth of embodiment research in understudied communities.

In this study, the primary focus is on the role of stress on sCRP variability, as the impacts of stress on inflammation have not been thoroughly examined in a Nigerian context. To explore this relationship, we measure stress via the General Health Questionnaire 12 (GHQ-12), a validated measure of psychological distress in international populations, and salivary cortisol, a physiological measure of stress, in a Nigerian teaching hospital in Ikeja, Nigeria, among students, faculty, staff, and community members. The study also includes other SES (education status, self-reported sex, and employment), health-related (comorbidities, blood pressure, body mass index [BMI], and flow rate), and demographic/stigma related factors (ethnic group) as these fall under social stressors, which are thought to influence CRP variability. Specifically, the primary objectives of this study are

- 1. To query the validity of the use of sCRP as a potential and accurate stress indicator in the field.
- To assess the variability in sCRP levels in response to psychological and physiological stress.
- 3. To investigate the relationship between other identified stressors and sCRP variability.

2 | Background

2.1 | Salivary CRP Background

Systemic, chronic, inflammation is measured by a variety of biomarkers including pro-inflammatory (i.e., IL-6 and TNF-alpha), anti-inflammatory (i.e., IL-10 and TGF-beta), or acute phase proteins (CRP and Ferritin) that are influenced by behavioral, biological, and psychosocial factors. CRP is an acute-phase protein, secreted by the liver in response to IL-6, an inflammatory cytokine that is produced during the inflammatory response (Gonzalez-Jaramillo et al. 2019).

CRP is found and measured in the blood (serum, plasma) or saliva. Serum CRP is commonly used as a biomarker of inflammation in the body; however, interest in salivary CRP (sCRP) has

emerged as researchers are looking for less invasive, more effective ways of testing for inflammation when conducting fieldwork (Pay and Shaw 2019; Ouellet-Morin et al. 2011). Throughout this manuscript, the term "CRP" will refer specifically to C-reactive protein collected by blood serum and dried blood spots (DBS), while "sCRP" will denote salivary CRP. Other benefits to sCRP have been documented in the literature, including participant comfort, increased safety during data collection, and the lack of professional training required for collection (Ouellet-Morin et al. 2011; Goetz and Lucas 2020; Szabo and Slavish 2021). However, although utilizing sCRP offers advantages, validated methods for assessing salivary inflammation have not been published extensively. These validated methods are useful in developing more accurate approaches to ensure that sCRP reliably reflects systemic inflammation comparable to CRP, addressing existing concerns about its validity (Slavish et al. 2015). Nonetheless, some studies have shown promising correlations between plasma and sCRP levels (Ouellet-Morin et al. 2011; Pay and Shaw 2019; Wetterö et al. 2021; Szabo and Slavish 2021). Studies measuring the relationship between serum CRP and sCRP suggest a moderate correlation (R_s ranging from 0.17 to 0.73) that continues to make sCRP a method of interest in inflammation-related studies (Dillon et al. 2010; Ouellet-Morin et al. 2011; Punyadeera et al. 2011; Out et al. 2012). This moderate association may be explained by a lack of standardized methods in collecting sCRP. Yet, some studies have shown that under a particular set of conditions, (i.e., adjusting for salivary flow rate, accounting for oral health hygiene, etc.), sCRP, especially at lower levels, may improve the correlation between serum CRP and sCRP and thus reflect systemic inflammation (Out et al. 2012; Pay and Shaw 2019).

CRP enters saliva through passive diffusion or filtration from the blood. CRP levels are known to generally increase with age and vary by biological sex, with women having higher average levels than men (Reiner et al. 2012). Differences in CRP levels are also observed between racialized groups, where African, American, and Hispanic populations are reported to have higher CRP levels relative to white Americans (Emerging Risk Factors Collaboration 2010; Doumatey et al. 2012; Kong et al. 2012; Reiner et al. 2012). Even after accounting for confounding factors such as obesity, metabolic issues, and other atherosclerotic measures, CRP levels remain higher in African American populations compared to other racialized groups. Because of the higher CRP levels observed in African Americans, other factors, such as chronic psychosocial stress, acute stress, depression, and SES related variables are thought to contribute to CRP variability (Reiner et al. 2012; Farmer and Thomas Tobin 2022).

Internationally, and specifically in Nigeria, CRP variability between sexes shows patterns similar to those in the United States, with females consistently having higher CRP values relative to males. Moreover, studies measuring CRP in Nigeria are typically cross-sectional and focus on CRP levels in patients with chronic diseases such as sickle cell anemia and Type 2 diabetes (Baba et al. 2010; Baba et al. 2012). These studies illustrate a relationship where disease severity is correlated with increased CRP levels (Okocha et al. 2014; Agho et al. 2021). However, to our knowledge no studies to date have examined levels or predicators (i.e., socio-demographic and stress) of variability in CRP or sCRP among healthy Nigerian populations.

The association between chronic exposures to stress and CRP has caused increased interest among researchers to incorporate inflammatory-related biomarkers in efforts to understand the pathways between stress, inflammation, and eventual disease onset (Liu, Wang, and Jiang 2017). One lab-related study demonstrated that acute and psychological stress influences inflammatory markers (Szabo, Slavish, and Graham-Engeland 2020). Further, up until recently research explicitly demonstrating how these salivary markers respond to acute stress via upstream pathways has been scarce (McDade et al. 2011; Slavish et al. 2015).

2.2 | Salivary Markers and Stress

Chronic exposure to psychosocial stress has been linked to chronic and elevated CRP and sCRP levels (Pace et al. 2006; Johnson, Abbasi, and Master 2013; Liu, Wang, and Jiang 2017; Nguyen et al. 2022). Elevated CRP levels have been associated with increased risk of depression, psychological distress—though results have been inconsistent—and poor lifestyle-related factors. Sex, SES, social stressors, and discrimination have also been associated with CRP variability. However, one study by Farmer and Thomas Tobin (2022), found that SES-related factors had less of an influence on CRP variability than other behavioral, psychosocial, and health-related factors. Farmer and colleagues reason that chronic exposure to stress results in maladaptive behaviors (alcohol consumption and smoking, poor physical activity) that lead to increased and prolonged inflammation.

Research on inflammation has proven to be a popular method of understanding the relationship between stress and health outcomes. While further exploration of these mechanisms is warranted, most scholars assess the impacts of stress on inflammation from a biological or socio-cultural perspective. Few studies integrate both biological and socio-cultural approaches, and the socio-cultural variables often examined are not comprehensive. The GHQ-12 is a comprehensive and effective tool for measuring stress in international populations for numerous reasons. It has been validated specifically in Nigeria (among other countries) and is easy to implement in primary care settings because of its feasible length and ease of administration (Makanjuola et al. 2014). Some literature suggests that the GHQ-12 does not accurately measure general distress but rather other "latent" variables: diminished confidence, social difficulties, and symptoms of anxiety and depression (Gao et al. 2004; Hankins 2008; Hystad and Johnsen 2020). Anxiety and depression are well-documented conditions associated with inflammation (Orsolini et al. 2022). CRP especially has been hypothesized to be a biomarker for major depressive disorder and higher levels of CRP have been shown in patients with depression (Orsolini et al. 2022). Although it has been noted that when considering the relationship between the two, it is necessary to account for possible confounding, as there are shared factors that influence both CRP and depression such as SES, BMI, chronic illness, and lifestyle factors (Pitharouli et al. 2021).

Other stress-related biological measures, such as cortisol, are also correlated with salivary and serum CRP (Fong, Ho, and Yau 2022; Sharpley et al. 2018). Salivary cortisol is a commonly used objective biomarker of stress (Pollard 1995). It is released

as part of the HPA axis in response to stress. Elevated levels of salivary cortisol have been linked to SES, job stress, depression, and other chronic exposures to stress (Crosswell and Lockwood 2020).

2.3 | Sociopolitical Context of Nigeria

Nigeria is a diverse country characterized by a complex sociopolitical landscape that has the potential to influence social stress among its population (Okudo, Nwudu, and Nwankwo 2023). The country's geographic regions, including the northern, southern, eastern, and western parts, each have distinct cultural, religious, and economic identities (Edewor, Aluko, and Folarin 2014; Omotosho, Ihekuna, and Fakoya 2020) (Figure 1). Though ethnic groups are not strictly confined to any one particular region of Nigeria, members of each ethnic group do tend to be more concentrated in specific regions of the country. For example, northern Nigeria has a predominantly Muslim population, while in the southwestern region the Yoruba ethnic group is predominant. In the eastern region, the Igbo ethnic group is most numerous, while the Hausa-Fulani ethnic group is predominantly located in the northern region of Nigeria (Udo 1970). Each of these ethnic groups has distinct, cultural, and religious identities (Central Intelligence Agency 2023). As it relates to health, stigma associated with the varied ethnic identities, cultural barriers, and beliefs potentially impact health outcomes by influencing access to care services, health related behaviors, and possibly influences stress experiences (Anti 2011; Odimegwu et al. 2018). However, capturing the ways in which these stress-related experiences are embodied in healthy Nigerian populations has not been studied as current stress-related studies in Nigeria are primarily centered around health care workers (Onigbogi and Banerjee 2019; Bolarinde, Aiyeyemi, and Ashawe 2023).

3 | Materials and Methods

This study was approved by the ethical review board of Lagos State University Teaching Hospital (LASUTH), included a local scholar, co-author M. Sorunke, and Vanderbilt University Institutional Review Board, Study # IRB 212222. Written informed consent was collected from each participant before data collection began.

3.1 | Study Participants

Participant recruitment occurred in Lagos State, one of Nigeria's biggest cities which have a dense Yoruba population that make up this region's demographic majority (Ojagbemi et al. 2017). Those who were over 18, not pregnant, did not report swelling or bleeding in the mouth, or had not consumed food or drink in the previous hour were encouraged to participate. Accordingly, saliva samples were collected from 160 participants ($n_{\rm female} = 105$,

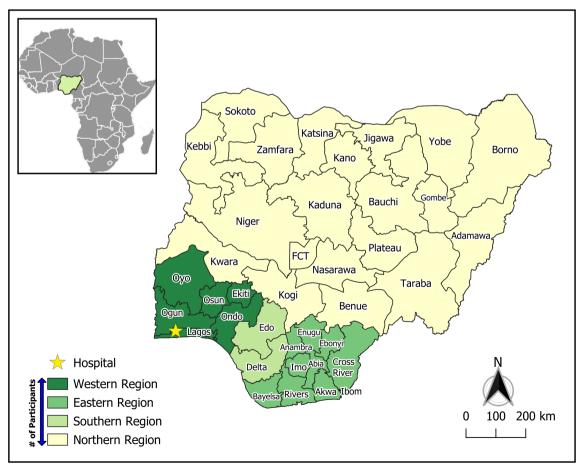


FIGURE 1 | Map of regional distribution of participant-identified ethnicity and LASUTH hospital location in western Nigeria.

 $n_{\text{male}} = 55$) ranging between 18 and 92 years of age between October 2022 and November 2022. Participants with no missing data (n=138) were included in data analysis. Table 1 summarizes the characteristics of these subset of individuals. Briefly, participants in this sample were on average 37.4 years old and female (64.5%). The sample was diverse, encompassing participants from 15 self-reported ethnic groups spanning all four regions of Nigeria. The majority of participants identified as Yoruba. The participants were a generally well-educated population with 63.8% attending University and 76.1% being employed. Mean blood pressure (126/78) and BMI (28.4) were slightly elevated in this population, in reference to World Health Organization (WHO) guidelines. Most participants, 84.1%, self-reported no presence of comorbidities like hypertension or diabetes. Likewise, 95.7% of the participants reported to be nonsmokers.

3.2 | Study Site

Data collection took place at Lagos State University Teaching Hospital (LASUTH) dental clinic between October 2022 and November 2022. LASUTH is a government-owned tertiary hospital in Ikeja, the capital city of Lagos State, located in the southwestern region of Nigeria (Figure 1). This hospital provides both medical and dental services for residents of Lagos State University and the broader community. LASUTH receives an average of 10,000 patients per month across all age groups due to its central location and being the recipient tertiary hospital for the 26 general hospitals in the state. The targeted population for the current study consisted of adult students, staff, and patients of the University. After written informed consent was obtained, demographic data and salivary samples were collected at patient appointment or pre-appointment times and during working and school hours for students and staff. As a public research University and teaching hospital, recruitment from students at the University relied on convenience and snowball sampling methods.

3.3 | Data Collection

Participants were first asked questions about oral health, food, and liquid consumption. They were then asked to complete two brief surveys emphasizing demographic (i.e., age, education status, and employment status) and stress-related responses via the GHQ-12 (Goldberg and Williams 1988). After completing the surveys, participants were asked to provide an unstimulated saliva sample via passive drooling into sterile polypropylene collection tubes using SalivaBio's 2mL cryovials and the Saliva Collection Aid from Salimetrics. Samples were stored at -80° C within 6 h of collection and kept until they were shipped in dry ice via World Courier to Salimetrics commercial lab for sCRP and cortisol analysis.

3.3.1 | Socio-Demographic Questionnaire

Socio-demographic data for each participant was recorded before saliva collection. Demographic information included education level, self-reported sex, employment status, self-reported ethnic group, income, smoking status, height (m), and weight (kg). BMI was calculated as weight (kg) divided by height squared (m²). Income data was collected but not included in any analysis, as most participants did not respond to this question. Blood pressure readings, measured using an Omron monitor cuff (Model # M3 HEM-7154-E), along with self-reported hypertension and diabetes status, were also collected for each participant.

3.3.2 | High-Sensitivity Salivary CRP

High-sensitivity sCRP samples were assayed at the Salimetrics' SalivaLab (Carlsbad, CA) using the Salimetrics Salivary C-Reactive Protein Assay Kit (Cat. No. 1-2102) in accordance with the manufacturers' protocol. Briefly, samples were thawed to room temperature, vortexed, and then centrifuged for 15 min at approximately 3000 RPM (1500×g) immediately before performing the assay. Samples were tested for salivary CRP using a high-sensitivity enzyme immunoassay (Cat. No. 1-2102). Sample test volume was $100\,\mu L$ of $2\times$ diluted saliva per determination. The assay has a lower limit of sensitivity of 19.44 pg/ mL (of ×2 dilution), a standard curve range from 25 to 1600 pg/ mL, and an average intra-assay coefficient of variation of 3.20%, and an average inter-assay coefficient of variation 2.6%, which meets the manufacturers' criteria for accuracy and repeatability in salivary bioscience, and exceeds the applicable (NIH) guidelines for enhancing reproducibility through rigor and transparency.

Flow rate, defined as the amount of liquid passed through a channel (e.g., tube and pipe) per unit of time, can influence the concentration of sCRP, among other salivary inflammatory biomarkers, present in the mouth. Flow rate was determined using the following equation: Flow rate = Volume (mL)/Time (min), as previously described by Mohamed et al. (2011) and Szabo and Slavish (2021).

3.3.3 | Stress Measures

3.3.3.1 | **General Health Questionnaire 12.** A 12 question GHQ-12 was administered after the demographic questionnaire to measure stress. Questions were scored using a 4-point Likert scale method, responses ranged from 0 ="less than usual," 1 = "no more than usual," 2 = "rather more than usual," and 3 = "much more than usual." The GHQ-12 can be scored by adding up the values associated with the participant's responses. Scoring was done on a continuous scale as there are no strict cut-offs for classification in the GHQ-12, however, higher scores on the assessment indicate higher levels of distress, with a maximum score of 36 (Gao et al. 2004). To prevent data skewing, positive questions (e.g., feeling you were playing a useful part in things) were reverse scored during analysis. This adjustment ensures that higher levels of distress are accurately measured by a higher total score. Cronbach's alpha was used to measure the reliability of the GHQ-12 in this population (Nunnally 1978).

3.3.3.2 | Salivary Cortisol. Salivary cortisol samples were assayed at the Salimetrics' SalivaLab (Carlsbad, CA) using the Salimetrics Salivary Cortisol Assay Kit (Cat. No. 1-3002),

1520,369,0,0, Downloaded from https://onlinelibrary.wile_com/doi/10_1002/ajhb_24158 by Taje Winful - University Of Illinois A., Wiley Online Library on [09/10/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/erms.ad-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 1 | Population characteristics by region.

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368 (398) 1470 (2760) 900 (NA) 775 (1080) 671 (1300) 'Max) 187 (44.2, 1580) 263 (189, 6410) 900 (900, 900) 186 (374, 3160) 671 (1300) 'min) 1.17 (1.07) 0.653 (0.636) 0.192 (NA) 0.552 (0.375) 0.713 (0.906) 'Max) 0.855 (0.0233, 4.41) 0.448 (0.116, 1.66) 0.192 (0.192, 0.192) 0.426 (0.146, 1.15) 0.445 (0.0578, 6.81) itatus 25 (67.6%) 4 (80.0%) 1 (100%) 6 (66.7%) 0.445 (0.0578, 6.81) on 25 (57.6%) 1 (20.0%) 0 (0%) 0 (0%) 1 (11.6%) 1 (11.6%) on 2 (5.4%) 0 (0%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 1 (11.6%) on 1 (2.7%) 0 (0%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 9 (10.5%) on 1 (2.7%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 9 (10.5%) on 1 (2.7%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 9 (10.5%) on 1 (2.7%) <th< td=""><td>Median (Min, Max)</td><td>35.0 (18.0, 63.0)</td><td>30.0 (24.0, 41.0)</td><td>46.0 (46.0, 46.0)</td><td>25.0 (19.0, 59.0)</td><td>35.0 (19.0, 92.0)</td><td>34.0 (18.0, 92.0)</td></th<>	Median (Min, Max)	35.0 (18.0, 63.0)	30.0 (24.0, 41.0)	46.0 (46.0, 46.0)	25.0 (19.0, 59.0)	35.0 (19.0, 92.0)	34.0 (18.0, 92.0)
368 (398) 1470 (2760) 900 (NA) 775 (1080) 671 (1300) 187 (442, 1580) 263 (189, 6410) 900 (900, 900) 186 (374, 3160) 176 (20.6, 6880) 1.17 (1.07) 0.635 (0.636) 0.192 (NA) 0.552 (0.375) 0.713 (0.906) 25 (67.6%) 4 (80.0%) 1 (100%) 6 (66.7%) 69 (80.2%) 12 (32.4%) 0 (0%) 0 (0%) 1 (100%) 6 (66.7%) 69 (80.2%) 12 (32.4%) 0 (0%) 0 (0%) 0 (0%) 1 (10.6%) 1 (10.8%) 1 (10.8%) 1 (2.7%) 0 (0%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 19 (22.1%) 4 (10.8%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 1 (11.2%) 1 (12.7%) 1 (2.7%) 0 (0%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 1 (11.2%) 2 (70.3%) 1 (20.0%) 0 (0%) 0 (0%) 1 (11.1%) 2 (13.8%) 1 (2.7%) 4 (80.0%) 1 (100%) 0 (0%) 1 (10.5%) 2 (13.8%) 2 (70.3%) 15.6 (83.2%) </td <td>sCRP (pg/mL)</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	sCRP (pg/mL)						
1.17 (1.07) 0.635 (0.536) 0.192 (NA) 0.552 (0.375) 176 (20.6,6880) 1.17 (1.07) 0.635 (0.636) 0.192 (NA) 0.552 (0.375) 0.713 (0.906) 1.17 (1.07) 0.635 (0.636) 0.192 (NA) 0.552 (0.375) 0.713 (0.906) 1.17 (1.07) 0.635 (0.636) 0.192 (0.192, 0.192) 0.426 (0.146, 1.15) 0.445 (0.0578, 6.81) 1.2 (32.4%) 1 (20.0%) 0 (0%) 0 (0%) 0 (0%) 17 (19.8%) 1.2 (3.4%) 0 (0%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 19 (22.3%) 1.2 (3.4%) 1 (20.0%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 19 (22.1%) 1.2 (3.4%) 1 (20.0%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 19 (22.1%) 1.2 (3.4%) 1 (20.0%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 19 (23.1%) 1.2 (3.4%) 1 (3.0%) 1 (10.0%) 1 (10.0%) 1 (10.0%) 13.8 (5.45) 13.8 (5.45) 11.8 (6.20, 24.0) 13.0 (0.20, 24.0) 17.0 (0.20, 20.0)	Mean (SD)	368 (398)	1470 (2760)	900 (NA)	775 (1080)	671 (1300)	627 (1190)
1.17 (1.07) 0.635 (0.636) 0.192 (NA) 0.552 (0.375) 0.713 (0.906) 0.855 (0.0233, 4.41) 0.448 (0.116, 1.66) 0.192 (0.192, 0.192) 0.426 (0.146, 1.15) 0.445 (0.0578, 6.81) 0.25 (67.6%) 4 (80.0%) 1 (10.0%) 6 (66.7%) 6 (66.7%) 6 (9 (80.2%) 1.2 (32.4%) 1 (20.0%) 0 (0%) 3 (33.3%) 1 (10.8%) 0 (0%) 0 (0%) 0 (0%) 2 (2.3%) 1 (2.7%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 0 (0.5%) 1 (12.7%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 0 (0.5%) 1 (12.7%) 0 (0%) 0 (0%) 1 (11.1%) 0 (0%) 1 (11.2%) 2 (2.3%) 1 (2.7%) 1 (2.7%) 0 (0%) 1 (10.0%) 0 (0%) 1 (10.0%) 1	Median (Min, Max)	187 (44.2, 1580)	263 (189, 6410)	900 (900, 900)	186 (37.4, 3160)	176 (20.6, 6880)	187 (20.6, 6880)
x) 0.635 (0.636) 0.192 (NA) 0.552 (0.375) 0.713 (0.906) x) 0.855 (0.0233, 4.41) 0.448 (0.116, 1.66) 0.192 (0.192, 0.192) 0.426 (0.146, 1.15) 0.445 (0.0578, 6.81) 25 (67.6%) 4 (80.0%) 1 (100%) 6 (66.7%) 6 (66.7%) 69 (80.2%) 12 (32.4%) 1 (20.0%) 0 (0%) 0 (0%) 17 (19.8%) 17 (19.8%) 2 (5.4%) 0 (0%) 0 (0%) 0 (0%) 17 (19.8%) 17 (19.8%) 4 (10.8%) 0 (0%) 0 (0%) 1 (11.1%) 9 (10.5%) 1 (2.7%) 0 (0%) 0 (0%) 1 (11.1%) 9 (10.5%) 1 (2.7%) 0 (0%) 1 (11.0%) 7 (77.8%) 50 (58.1%) x) 15.7 (6.85) 15.8 (9.12) 22.0 (NA) 13.8 (5.45) 14.4 (5.80)	Flow rate (mL/min)						
x) 0.855 (0.0233, 4.41) 0.448 (0.116, 1.66) 0.192 (0.192, 0.192) 0.426 (0.146, 1.15) 0.445 (0.0578, 6.81) 25 (67.6%) 4 (80.0%) 1 (100%) 6 (66.7%) 69 (80.2%) 12 (32.4%) 1 (20.0%) 0 (0%) 17 (19.8%) 2 (5.4%) 0 (0%) 0 (0%) 5 (5.8%) 1 (2.7%) 0 (0%) 0 (0%) 2 (2.3%) 4 (10.8%) 0 (0%) 0 (0%) 1 (11.1%) 9 (10.5%) 3 (8.1%) 1 (20.0%) 0 (0%) 1 (11.1%) 9 (10.5%) 1 (2.7%) 0 (0%) 0 (0%) 1 (11.1%) 9 (10.5%) 2 (5.70.3%) 4 (80.0%) 1 (100%) 7 (77.8%) 50 (58.1%) x) 18.0 (0.290) 10.0 (9.00, 30.0) 22.0 (22.0, 22.0) 13.0 (700, 24.0) 17.0 (0.5.0)	Mean (SD)	1.17 (1.07)	0.635 (0.636)	0.192 (NA)	0.552 (0.375)	0.713 (0.906)	0.819 (0.936)
25 (67.6%) 4 (80.0%) 1 (100%) 6 (66.7%) 69 (80.2%) 12 (32.4%) 1 (20.0%) 0 (0%) 3 (33.3%) 17 (19.8%) 2 (5.4%) 0 (0%) 0 (0%) 5 (5.8%) 1 (2.7%) 0 (0%) 0 (0%) 2 (2.3%) 4 (10.8%) 0 (0%) 0 (0%) 2 (2.3%) 3 (8.1%) 1 (20.0%) 0 (0%) 1 (11.1%) 9 (10.5%) 1 (2.7%) 0 (0%) 0 (0%) 1 (11.1%) 9 (10.5%) 2 (70.3%) 4 (80.0%) 1 (100%) 7 (77.8%) 50 (58.1%) x) 18.0 (0.29.0) 10.0 (9.00, 30.0) 22.0 (22.0, 22.0) 13.0 (7.00, 24.0) 17.0 (0, 26.0)	Median (Min, Max)	0.855 (0.0233, 4.41)	0.448 (0.116, 1.66)	0.192(0.192, 0.192)	0.426 (0.146, 1.15)	0.445 (0.0578, 6.81)	0.493 (0.0233, 6.81)
25 (67.6%) 4 (80.0%) 1 (100%) 6 (66.7%) 69 (80.2%) 12 (32.4%) 1 (20.0%) 0 (0%) 3 (33.3%) 17 (19.8%) nn 2 (5.4%) 0 (0%) 0 (0%) 2 (2.3%) lool 4 (10.8%) 0 (0%) 0 (0%) 1 (11.1%) 19 (22.1%) lool 4 (10.8%) 0 (0%) 0 (0%) 1 (11.1%) 9 (10.5%) lool 4 (10.8%) 0 (0%) 0 (0%) 1 (11.1%) 9 (10.5%) lool 5 (10.5%) 1 (10.0%) 0 (0%) 1 (11.1%) 9 (10.5%) lool 6 (10.5%) 1 (10.0%)	Employment status						
nn 2 (5.4%)	Employed	25 (67.6%)	4 (80.0%)	1 (100%)	(%2'99) 9	69 (80.2%)	105 (76.1%)
nn 2 (5.4%) 0 (0%) 0 (0%) 5 (5.8%) 2 (2.3%) 1 (2.7%) 0 (0%) 0 (0%) 2 (2.3%) 2 (2.3%) ool 4 (10.8%) 0 (0%) 0 (0%) 1 (11.1%) 19 (22.1%) iool 3 (8.1%) 1 (20.0%) 0 (0%) 1 (11.1%) 9 (10.5%) ig 1 (2.7%) 0 (0%) 0 (0%) 0 (0%) 1 (11.1%) 9 (10.5%) 26 (70.3%) 4 (80.0%) 1 (100%) 7 (77.8%) 50 (58.1%) Max) 18.0 (0.29.0) 10.0 (9.00, 30.0) 22.0 (NA) 13.8 (5.45) 17.0 (0.26.0)	Unemployed	12 (32.4%)	1 (20.0%)	(%0)0	3 (33.3%)	17 (19.8%)	33 (23.9%)
ion 2 (5.4%) 0 (0%) 0 (0%) 5 (5.8%) iool 1 (2.7%) 0 (0%) 0 (0%) 2 (2.3%) iool 4 (10.8%) 0 (0%) 0 (0%) 10 (22.1%) inbool 3 (8.1%) 1 (20.0%) 0 (0%) 1 (11.1%) 9 (10.5%) ing 1 (2.7%) 0 (0%) 0 (0%) 1 (11.1%) 50 (58.1%) 26 (70.3%) 4 (80.0%) 1 (100%) 7 (77.8%) 50 (58.1%) 15.7 (6.85) 15.8 (9.12) 22.0 (0AA) 13.8 (5.45) 14.4 (5.80) 1, Max) 18.0 (0, 29.0) 10.0 (90.0, 30.0) 22.0 (22.0, 22.0) 13.0 (7.00, 24.0) 17.0 (0, 26.0)	Education level						
tool 4 (10.8%) 0 (0%) 0 (0%) 2 (2.3%) tool 4 (10.8%) 0 (0%) 1 (11.1%) 19 (22.1%) thool 3 (8.1%) 1 (20.0%) 0 (0%) 1 (11.1%) 9 (10.5%) ing 1 (2.7%) 0 (0%) 0 (0%) 1 (11.2%) 9 (10.5%) strong 1 (2.7%) 4 (80.0%) 1 (100%) 7 (77.8%) 50 (58.1%) strong 15.7 (6.85) 15.8 (9.12) 22.0 (NA) 13.8 (5.45) 14.4 (5.80) strong 18.0 (0.29.0) 10.0 (9.00, 30.0) 22.0 (22.0, 22.0) 13.0 (7.00, 24.0) 17.0 (0, 26.0)	Basic education	2 (5.4%)	0 (0%)	(%0)0	0 (0%)	5 (5.8%)	7 (5.1%)
tool 4 (10.8%) 0 (0%) 1 (11.1%) 19 (22.1%) thool 3 (8.1%) 1 (20.0%) 0 (0%) 1 (11.1%) 9 (10.5%) ting 1 (2.7%) 0 (0%) 0 (0%) 1 (1.2%) 1 (1.2%) 26 (70.3%) 4 (80.0%) 1 (100%) 7 (77.8%) 50 (58.1%) 15.7 (6.85) 15.8 (9.12) 22.0 (NA) 13.8 (5.45) 14.4 (5.80) h, Max) 18.0 (0, 29.0) 10.0 (9.00, 30.0) 22.0 (22.0, 22.0) 13.0 (7.00, 24.0) 17.0 (0, 26.0)	Diploma	1 (2.7%)	0 (0%)	(%0)0	0 (0%)	2 (2.3%)	3 (2.2%)
thool 3 (8.1%) 1 (20.0%) 0 (0%) 1 (11.1%) 9 (10.5%) ing 1 (2.7%) 0 (0%) 0 (0%) 1 (1.2%) 1 (1.2%) 26 (70.3%) 4 (80.0%) 1 (100%) 7 (77.8%) 50 (58.1%) 15.7 (6.85) 15.8 (9.12) 22.0 (NA) 13.8 (5.45) 14.4 (5.80) 4 Max) 18.0 (0, 29.0) 10.0 (9.00, 30.0) 22.0 (22.0, 22.0) 13.0 (7.00, 24.0) 17.0 (0, 26.0)	Graduate school	4 (10.8%)	(%0)0	(%0)0	1 (11.1%)	19 (22.1%)	24 (17.4%)
ing 1 (2.7%) 0 (0%) 0 (0%) 1 (1.2%) 1 (1.2%) 2 (70.3%) 4 (80.0%) 1 (100%) 7 (77.8%) 50 (58.1%) 2 (15.8 (9.12) 22.0 (NA) 13.8 (5.45) 14.4 (5.80) 10.0 (9.00, 30.0) 22.0 (22.0, 22.0) 13.0 (7.00, 24.0) 17.0 (0, 26.0)	Secondary school	3 (8.1%)	1 (20.0%)	(%0)0	1 (11.1%)	9 (10.5%)	14 (10.1%)
26 (70.3%) 4 (80.0%) 1 (100%) 7 (77.8%) 50 (58.1%) 50 (58.1%) 15.7 (6.85) 15.8 (9.12) 22.0 (NA) 13.8 (5.45) 14.4 (5.80) 17.0 (0, 26.0)	Some schooling	1 (2.7%)	(%0)0	(%0)0	(%0)0	1 (1.2%)	2 (1.4%)
15.7 (6.85) 15.8 (9.12) 22.0 (NA) 13.8 (5.45) 14.4 (5.80) 10.0 (9.00, 30.0) 22.0 (22.0, 22.0) 13.0 (7.00, 24.0) 17.0 (0, 26.0)	University	26 (70.3%)	4 (80.0%)	1 (100%)	7 (77.8%)	50 (58.1%)	88 (63.8%)
15.7 (6.85) 15.8 (9.12) 22.0 (NA) 13.8 (5.45) 14.4 (5.80) 10.0 (9.00, 30.0) 22.0 (22.0, 22.0) 13.0 (7.00, 24.0) 17.0 (0, 26.0)	GHQ-12 score						
18.0(0, 29.0) $10.0(9.00, 30.0)$ $22.0(22.0, 22.0)$ $13.0(7.00, 24.0)$ $17.0(0, 26.0)$	Mean (SD)	15.7 (6.85)	15.8 (9.12)	22.0 (NA)	13.8 (5.45)	14.4 (5.80)	14.8 (6.18)
	Median (Min, Max)	18.0 (0, 29.0)	10.0 (9.00, 30.0)	22.0 (22.0, 22.0)	13.0 (7.00, 24.0)	17.0 (0, 26.0)	17.0 (0, 30.0)

TABLE 1 | (Continued)

(5000000)						
	East $(n=37)$	North $(n=5)$	Other $(n=1)$	South $(n=9)$	West $(n = 86)$	Overall $(n=138)$
$BMI (kg/m^2)$						
Mean (SD)	27.6 (5.80)	27.3 (2.98)	26.2 (NA)	26.9 (8.76)	29.0 (7.76)	28.4 (7.17)
Median (Min, Max)	27.0 (15.4, 47.5)	28.7 (23.3, 30.4)	26.2 (26.2, 26.2)	22.2 (20.2, 44.1)	27.5 (16.5, 62.3)	27.0 (15.4, 62.3)
BP systolic						
Mean (SD)	124 (14.6)	131 (16.6)	124 (NA)	116 (15.2)	127 (19.8)	126 (18.2)
Median (Min, Max)	125 (100, 156)	128 (116, 159)	124 (124, 124)	111 (98.0, 141)	122 (96.0, 202)	122 (96.0, 202)
BP diastolic						
Mean (SD)	77.2 (13.9)	89.6 (16.9)	81.0 (NA)	65.6 (11.5)	78.6 (17.3)	77.8 (16.3)
Median (Min, Max)	77.0 (45.0, 102)	84.0 (76.0, 119)	81.0 (81.0, 81.0)	70.0 (44.0, 81.0)	76.0 (53.0, 177)	76.0 (44.0, 177)
Weight (kg)						
Mean (SD)	77.6 (17.1)	70.6 (8.91)	84.0 (NA)	76.0 (20.9)	78.1 (18.0)	77.6 (17.5)
Median (Min, Max)	74.0 (49.0, 121)	70.0 (57.0, 80.0)	84.0 (84.0, 84.0)	69.0 (56.0, 120)	75.5 (50.0, 160)	74.5 (49.0, 160)
Height (m)						
Mean (SD)	1.67 (0.0802)	1.61 (0.140)	1.79 (NA)	1.69 (0.0809)	1.65 (0.122)	1.66 (0.111)
Median (Min, Max)	1.68 (1.52, 1.80)	1.67 (1.37, 1.72)	1.79 (1.79, 1.79)	1.70 (1.59, 1.78)	1.65 (1.08, 2.03)	1.66 (1.08, 2.03)
Comorbidities						
0	33 (89.2%)	5 (100%)	1 (100%)	8 (88.9%)	69 (80.2%)	116 (84.1%)
1	4 (10.8%)	(%0)0	(%0)0	(%0)0	15 (17.4%)	19 (13.8%)
2	(%0)0	(%0)0	(%0)0	1 (11.1%)	2 (2.3%)	3 (2.2%)
Smoking status						
No	34 (91.9%)	5 (100%)	1(100%)	9 (100%)	83 (96.5%)	132 (95.7%)
Yes	3 (8.1%)	(%0)0	(%0)0	(%0)0	3 (3.5%)	6 (4.3%)
^a Mean cortisol (μg/dL)						
Mean (SD)	0.119 (0.0693)	0.109(0.0408)	0.209 (NA)	0.108 (0.0420)	0.128 (0.0614)	0.124(0.0616)
Median (Min, Max)	0.110(0.0360,0.346)	0.121 (0.0540, 0.141)	0.209 (0.209, 0.209)	0.106(0.0670,0.201)	0.118 (0.0190, 0.309)	0.112 (0.0190, 0.346)
Abbraviations: BMI hody mass is	ndex: BD blood pressure: GHO12	Abhravistions: BMI hody mass inday: BD blood pressure: GHO12 Ganaral Haalth quastionnaire 12: CD standard daviation	SD standard deviation			

Abbreviations: BMI, body mass index; BP, blood pressure; GHQ12, General Health questionnaire 12; SD, standard deviation. "Sub sample of 109 participants.

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following the manufacturers' protocol for a subset of samples $(n\!=\!109,\ n_{\rm female}\!=\!70\ n_{\rm male}\!=\!39)$. Samples were thawed to room temperature, vortexed, and then centrifuged for 15 min at approximately 3000 RPM (1500×g) immediately before performing the assay. Samples were tested for salivary cortisol using a high-sensitivity enzyme immunoassay (Cat. No. 1-3002). Sample test volume was 25 μ L of saliva per determination. The assay has a lower limit of sensitivity of 0.007 μ g/dL, a standard curve range from 0.012 to 3.0 μ g/dL, and an average intra-assay coefficient of variation of 4.60%, and an average inter-assay coefficient of variation 6.00%, which meets the manufacturers' criteria for accuracy and repeatability in salivary bioscience and exceeds the applicable NIH guidelines for enhancing reproducibility through rigor and transparency.

3.4 | Analytical Approach

Descriptive statistics are provided for the total sample (n = 138), while descriptive statistics for cortisol measurements reference only the subset that had cortisol data (n = 109). Spearman's non-parametric tests (r_s), multivariable linear regression (MVLR), and exploratory factor analysis (EFA) were then applied to address each objective. All data analysis was done using R (4.3.3), using the "corrplot," "stats," and "psych" packages, respectively.

To validate the use of sCRP as a potential and accurate stress indicator in the field, Spearman's nonparametric (r_s) tests and scatter plots were employed to examine the relationship between sCRP, stress-related variables, and established correlates of inflammation. MVLR and EFA were used to assess sCRP variability in response to psychological and physiological stress and to further identify the relationship between other sociodemographic stressors. MVLR analysis was employed to investigate the relationship between stress (measured by the GHQ-12

and salivary cortisol) and variability in sCRP. Prior to regression analyses, sCRP and salivary cortisol data were log and square root transformed, respectively to meet assumptions of linear regression. Additionally, education status was dichotomized as "below a bachelor's degree" (i.e., some schooling, basic education, secondary school, and diploma) or "bachelor's degree and above" (i.e., university and graduate school), due to small sample size.

Questions from the GHQ-12 were initially included in regression analysis either as a direct assessment (via total sum scores) or an indirect evaluation (via EFA, see Table 2). EFA is a statistical technique that combines observed variables (e.g., SES and income) into a scale to measure an unobserved, latent factor (e.g., stress, health, and quality of life). The use of EFA provides a more nuanced assessment of how several aspects of stress impact CRP variability, going beyond a simple total score. This was employed to see which measure of stress (total sum score vs. latent measures) more accurately described CRP variability (see Table S1 for regression outcomes of incorporating latent variables). For EFA, screen plots of eigenvalues values, along well-established literature determined the number of factors extracted from the GHQ-12 (Graetz 1991; Gao et al. 2004). Factor loadings above 0.4 were retained.

In Model 1 (n = 138), the GHQ-12 total sum score was the main predictor variable and sCRP was the main response variable. All variables listed in Table 1, with the exception of height, weight, and smoking status was incorporated into the model as control variables or covariates. Model 2 included only those participants who consented to have their samples used for analyses beyond sCRP, resulting in a slightly downsized sample size (n = 109). In Model 2, cortisol was the main predictor variable, and the GHQ-12 total sum score was included as a covariate. Similarly, in Model 2, all measures in Table 1, aside from height, weight,

TABLE 2 | Exploratory factor analysis of GHQ-12.

		Factor 1	Factor 2	Factor 3
Anxiety/depression	Felt constantly under strain		0.634	
	Feeling unhappy and depressed ^a		0.448	
	Lost sleep over worry		0.638	
	Could not overcome difficulties		0.512	
Social dysfunction	Feeling reasonably happy	0.735		
	Playing a useful part	0.57		
	Capable of making decisions	0.694		
	Able to face problems	0.603		
	Able to enjoy day-to-day activities	0.638		
	Able to concentrate	0.704		
Confidence loss	Feeling unhappy and depressed ^a			0.408
	Losing confidence			0.697
	Thinking of self as worthless			0.75

Note: Numbers represent factor loadings.

^aLoaded onto two latent variables, which differs from the Graetz model. Factor loadings above 0.4 were retained.

and smoking status were incorporated into the model as control variables or covariates.

4 | Results

4.1 | High-Sensitivity Salivary CRP

Salivary CRP levels ranged from 20.57 to 6879.41 pg/mL; with a mean level of 627 pg/mL, and a standard deviation (SD) of 1190 pg/mL. The regional variations in sCRP levels were notable, with the highest mean observed in participant from northern Nigeria (1470 pg/mL) and the lowest in participants from eastern Nigeria (368 pg/mL). Saliva flow rate ranged from 0.02 to 6.81 ug/mL and was significantly correlated with sCRP levels ($r_{\rm s}=-0.23$). The mean flow rate across the entire sample was 0.819 mL/min, with a SD of 0.936 mL/min. There were notable regional variations, with the highest mean flow rate observed in participants from eastern Nigeria (1.17 mL/min) and the lowest in participants from the "Other Region" category (0.192 mL/min) (Table 1).

4.2 | Stress Measures

4.2.1 | General Health Questionnaire 12

The GHQ-12 is a reliable measure of stress in this community with a Cronbach's alpha of 0.80. The mean GHQ-12 score across the sample was 14.8, with a SD of 6.18. The median score was 17.0, with a range from 0 to 30. The scores varied slightly by region, with participants from "Other Region" category having the highest mean score of 22.0 and participants from southern Nigeria the lowest at 13.8.

4.2.2 | Salivary Cortisol

Among the participants that consented to participate in the portion of the study on cortisol ($n\!=\!109$), salivary cortisol levels ranged from 0.02 to 0.35 $\mu g/dL$; with a mean level of 0.12 $\mu g/dL$. The highest mean cortisol level was observed in participants from the "Other Region" category (0.209 $\mu g/dL$), while the lowest was in participants from eastern Nigeria (0.110 $\mu g/dL$).

4.3 | Validation of sCRP

Figures 2 and 3 show the linear correlation between sCRP and known correlates of systemic inflammation. Results from the scatter plot and simple regression line of log sCRP by BMI (Figure 2) were as expected, the relationship between BMI and sCRP was significant and positive (Adjusted R^2 :0.1772, p-value=1.64e -07). Salivary CRP levels differed significantly between sexes, with females having higher levels relative to males (Khera et al. 2005; Lakoski et al. 2006; Begum et al. 2021) (Figure 3). There was also a significant positive relationship with age. Spearman's nonparametric tests indicated a significant and negative correlation between sCRP levels and both the total sum of the GHQ-12 and its three factors: social dysfunction, anxiety/depression, and confidence loss (Figure 4).

Scatter Plot of BMI and Log10 sCRP

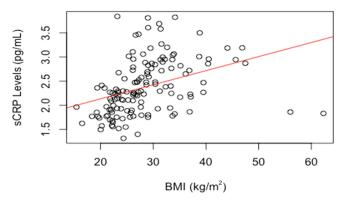


FIGURE 2 | Scatter plot between Log10 sCRP and a known correlate of inflammation, BMI. Individual participant data is represented by the black dots.

Scatter Plot of Log10 sCRP by age and sex

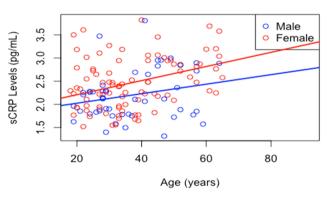


FIGURE 3 | Scatter plot of Log10 sCRP levels by age and self-reported sex.

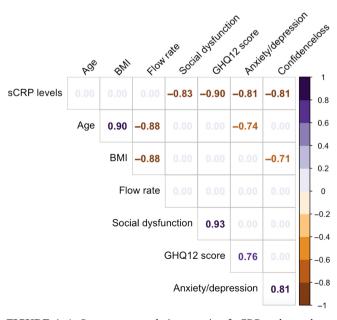


FIGURE 4 | Spearman correlation matrix of sCRP and correlates of inflammation. Only significant correlations are shown. The significance threshold was set at a *p*-value of 0.05.

4.4 | sCRP Variability in Response to Psychological, Physiological, and Sociodemographic Stressors

4.4.1 | Model 1

The MVLR analysis revealed an overall significant fit between sCRP and the GHQ-12 (Table 3), holding other variables constant (p < 0.001). Predictor variables consisted of demographic and social-related variables from Table 1 (excluding smoking status and ethnicity). Model 1 accounted for a moderate variance in sCRP (Adjusted $R^2 = 0.267$). Within the model, the GHQ-12 did not have a significant association with sCRP (b = -0.01, p = not significant (ns)), but BMI (b = 0.02, p < 0.001), age (b = 0.01, p < 0.01), self-reported sex (b = -0.21, p < 0.05) and region, specifically northern Nigerian ethnic groups (b = 0.53, p < 0.05) were all significant predictors of sCRP (Table 3). The significance threshold was set at a p-value of 0.05. While most regions were not significant predictors of sCRP variability, on average region had the greatest effect of sCRP variability. Sex also had a significant effect, with males having a lower sCRP compared to females (b = -0.21, p < 0.05). Although having one comorbidity (b = 0.23) showed some effect, it was not statistically significant.

4.4.2 | Model 2

MVLR revealed an overall significant fit between salivary sCRP and cortisol, holding other variables constant (p < 0.001). The model accounted for a moderate variance in sCRP (Adjusted R^2 =0.2433). Within Model 2, cortisol, the main independent variable, was a significant predictor of sCRP and had the largest effect (b = 1.36, p < 0.05). Self-reported sex (male) (b = -0.33, p < 0.01) had a negative but significant effect. In contrast, age (b=0.01, p<0.01), region, specifically northern Nigeria ethnic groups (b = 0.62, p < 0.05), and BMI (b = 0.02, p < 0.01), were all significant and positive predictors of sCRP in Model 2 (Table 4). Similar to Model 1, ethnicity, self-reported sex, and having one comorbidity (b = 0.21, p = ns). had the largest effect on sCRP.

5 | Discussion

This exploratory study investigates how stressors become embodied and impact sCRP variability in a Nigerian context, expanding upon the growing interest on the impacts of local stressors on inflammatory processes among different environmental contexts (DeCaro and Helfrecht 2022). In this study, measuring stress with two different variables, the GHQ-12 and salivary cortisol, was twofold, serving as a way to validate the use of sCRP as an accurate measurement of systemic inflammation and as a means to explore the effectiveness of using the GHQ-12 as an accurate and effective model of understanding stress in this specific population. The findings of this study suggest a moderate but significant relationship between sCRP and stress, measured both by the GHQ-12 (Adjusted $R^2 = 0.267$, p < 0.001) and cortisol (Adjusted $R^2 = 0.2433$, p < 0.001) when social factors are considered.

TABLE 3 | Linear regression of coefficients for Model 1.

	Model 1
(Intercept)	2.48***
	[1.72, 3.24]
GHQ-12 total score	-0.01
	[-0.02, 0.00]
Sex (Male)	-0.21*
	[-0.41, -0.01]
Age	0.01**
	[0.00, 0.02]
North region	0.53*
	[0.05, 1.00]
Other region	0.73
	[-0.27, 1.74]
South region	0.15
	[-0.23, 0.54]
West region	-0.04
	[-0.24, 0.16]
Unemployed	0.05
	[-0.17, 0.27]
Below university degree	0.01
	[-0.22, 0.23]
Comorbidities1	0.23
	[-0.07, 0.53]
Comorbidities2	0.10
	[-0.49, 0.69]
BMI (kg/m²)	0.02***
	[0.01, 0.04]
Flow rate (mL/min)	-0.05
	[-0.15, 0.04]
BP systolic	-0.01
	[-0.02, 0.00]
BP diastolic	0.00
	[-0.01, 0.01]
N	138
R^2	0.35
Adjusted R ²	0.267

Note: Mixed impact of socio-demographic, anthropometric, and stress related predicators on salivary CRP with varying significance. Ranges represent 95% confidence intervals (low CI, and high CI).

^{***}p<0.001. **p < 0.01.

p < 0.05

TABLE 4 | Linear regression of coefficients for Model 2.

	Model 2
(Intercept)	2.35***
	[1.38, 3.31]
Cortisol (µg/dL)	1.36*
	[0.04, 2.68]
GHQ-12 total score	-0.01
	[-0.03, 0.01]
Sex (Male)	-0.33**
	[-0.56, -0.09]
Age	0.01**
	[0.00, 0.02]
Unemployed	0.07
	[-0.20, 0.34]
North region	0.62*
	[0.04, 1.19]
Other region	0.66
	[-0.42, 1.75]
South region	0.09
	[-0.36, 0.54]
West region	-0.06
	[-0.31, 0.19]
Below university degree	-0.08
	[-0.36, 0.20]
Comorbidities1	0.21
	[-0.16, 0.57]
Comorbidities2	0.01
	[-0.63, 0.65]
BMI (kg/m^2)	0.02**
	[0.01, 0.04]
Flow rate (mL/min)	0.00
	[-0.12, 0.12]
BP systolic	-0.01
	[-0.02, 0.00]
BP diastolic	-0.00
	[-0.02, 0.01]
N	109
R^2	0.36
Adjusted R ²	0.2433

Note: Mixed impact of socio-demographic, anthropometric, and stress related predicators on salivary CRP with varying significance on a smaller subset population with cortisol as an additional predicator. Ranges represent 95% confidence intervals (low CI and high CI).

5.1 | Validation of sCRP

BMI, a known correlate of systemic inflammation, was used to validate this study's findings in relation to previously reported studies on CRP and other inflammatory markers. Results from the scatter plot and simple regression line of sCRP by BMI were as expected, showing a significant positive relationship between BMI and sCRP (Figure 2). Higher BMI across the life course has been associated with chronic inflammation and stress (Ellulu et al. 2017; Cooper et al. 2019). Similarly, both age and self-reported sex exhibited patterns that were consistent with the existing literature, further supporting the robustness of our findings. Specifically, our results aligned with previous research indicating that older age and specific sex-related differences are associated with variations in CRP levels, underscoring the relevance of these factors in assessing chronic inflammation and stress. This consistent relationship supports the validity of using sCRP as a reliable biomarker for chronic inflammation and stress, similar to blood-based CRP, thereby reinforcing the applicability of sCRP in field related settings. However, the negative correlation between sCRP and the GHQ-12 along with its latent factors was unexpected (Figure 4), as the correlation between CRP and distress is prevalent in the literature (Farmer and Thomas Tobin 2022; Nguyen and Peschard 2003; McEwen 1998). This may suggest that other psychosocial factors, such as social support, coping mechanisms, or resilience, are mitigating the expected positive relationship between distress and sCRP, leading to the observed negative correlation.

5.2 | sCRP Variability in Response to Psychological, Physiological, and Sociodemographic Stressors

Results from both regression Models 1 and 2 (Tables 3 and 4) show that the GHQ-12 score, on its own, did not significantly predict sCRP variability. These models were intended to assess the variability in sCRP levels in response to psychological and psychological stress and investigate the relationship between other identified stressors and sCRP variability. This was surprising as the Cronbach's alpha of the GHQ-12 for this study was 0.8, meaning the questionnaire was highly reliable in measuring distress. Other GHQ-12 uses in Nigerian populations have shown positive reliability and validity outcomes (Okokon et al. 2012; Makanjuola et al. 2014; Audu et al. 2021; Aloba, Opakunle, and Ogunrinu 2019). Presumably, the GHQ-12 may not be enough to measure the ways in which stress is embodied in this population. These results conflict with what the literature says about psychosocial factors, anxiety/depression, and its influence on CRP in African Americans, as these factors play a significant role in CRP variability (Farmer and Thomas Tobin 2022). This discrepancy potentially illuminates differences in the ways in which anxiety and depression are understood, expressed, or experienced between populations.

Conversely, salivary cortisol was a significant predictor of sCRP variability (Table 4). This was not surprising as the literature has shown a strong relationship between cortisol and stress (Pollard 1995; Hellhammer, Wüst, and Kudielka 2009; Kandhalu 2013), and a hypothetical relationship between CRP and cortisol (Almadi, Cathers, and Chow 2013). Comorbidities

^{***}p<0.001.

^{**}p < 0.01.

^{*}p < 0.05.

were not a significant predictor of sCRP variability although they did have a larger effect on it. In the current study's population, most respondents reported neither diabetes nor hypertension. However, over 40% of diabetes throughout sub-Saharan Africa is undiagnosed, so this self-report may not accurately reflect reality of the prevalence of diabetes among study participants (Agho et al. 2021).

The results from the regression analyses indicate a significant impact of ethnicity on sCRP variability. Notably, individuals from ethnic groups not belonging to the dominant group of the region, especially those from northern Nigeria or ethnic groups associated with other countries had a greater effect on sCRP variability. These findings suggest that ethnic group experiences in Nigeria encapsulate aspects of embodied stress that significantly affect sCRP variability. The specificities of how these experiences impact health outcomes require further research, as most studies on health outcome variability by ethnic group in Nigeria have focused on child mortality rates (Adedini et al. 2015). Given that associated socio-ecological stressors may contribute to elevated sCRP levels, it is essential to investigate the specific factors driving this variability.

The use and interest of sCRP as (1) a biomarker for systemic inflammation and (2) a predictor of stress is lacking but steadily increasing as support of sCRP has emerged over the last decade (Bosch 2014; Goetz and Lucas 2020). Results from both regression models support that distress when considered with other social predictors, can be a significant predictor of sCRP variability (24%–27%). Results from both regressions also highlight that social variables alone are not enough to account for sCRP variability although they do largely affect it (Tables 3 and 4). From the literature, it is known that genetic factors make up roughly 40% of CRP variability (Carlson et al. 2005). Other behavioral and lifestyle factors predicting sCRP variability should be explored further (e.g., diet and oral health, cultural beliefs, and affiliated behaviors) (Calle and Andersen 2019; Pay and Shaw 2019).

6 | Limitations

6.1 | Cross Sectional Approach

While this study is able to explore the relationship between sCRP and stress there are a few limitations. One, the study uses a cross-sectional model, with only one sCRP measurement. Other studies on CRP note that taking multiple measures gives researchers the ability to correlate CRP and disease risk (Macy, Hayes, and Tracy 1997; Ockene et al. 2001; McDade 2012). It is recommended that CRP samples are collected once every 7-14 days for up to 3 months (Braga and Panteghini 2012). These recommendations could be applied to sCRP studies as well. In the current study, this limitation is not a major problem because disease risk is not explicitly investigated. However, repeated measures could still benefit this study by giving additional context to the already limited amount of research on stress and sCRP in this population. Further, the sole focus on the impacts of psychological and socio-demographic related factors on sCRP in Nigerian population, to our knowledge, is the first study of its kind. Future studies looking to validate the use of sCRP in stress-related

studies could benefit from including better measures of social inequality, including genetic data, and continuing to study these relationships in underrepresented communities.

6.2 | Sample Size

The limitations of this study include the small sample size, which suggests that while preliminary conclusions can be hypothesized, additional testing is required to identify clear patterns. Including more ethnic groups and a more balanced distribution of male and females will help determine if these initial patterns hold true. Further, these results should be contextualized as ethnic groups were self-reported and thus may not resonate with the ways the state acknowledges them, but this approach is valuable for capturing how individuals embody their lived experiences as it can often reflect personal identity, social stressors, language, and cultural practices, which may not align with categories of the government who in turn may miss the nuances.

7 | Conclusion

The present study explored how different stress measures relate to sCRP variability in a Nigerian population, aiming to understand the embodiment of stress. This paper demonstrated that stress significantly and moderately correlates with sCRP levels in a Nigerian population. On their own, sCRP and GHQ-12 stress scores have a negative but significant association; similarly, while salivary cortisol has a greater association, on its own, it is still weak. However, when other social and demographic factors are accounted for, the relationship between sCRP and the GHQ-12 (Model 1) and sCRP and salivary cortisol (Model 2) strengthens significantly. Future studies assessing embodied stress in Nigerian populations should focus on capturing societal, behavioral, and cultural related factors that may contribute to this experience.

Incorporating genetic data, including associated SNPs or methylation patterns in the CRP promoter region, could help account for a greater proportion of the observed variability in CRP levels within the population. CRP is known to be influenced by both genetic and nongenetic factors. Further, while the GHQ-12 has been validated in Nigerian communities, a survey that merges SES-related questions alongside psychological well-being could be more beneficial. Surveys that go beyond income are ideal for Nigerian communities as asking direct questions about income appear to be socially unacceptable (Ibadin and Akpede 2021). In the current study, 90% of participants skipped the income question in the demographic survey. Factors relating to SES (i.e., job security, education, and marriage status) play a huge role in the everyday stressors of the Nigerian community and should be incorporated to indirectly gauge income (Olusanya 1985; Oyedeji 1985; Ibadin and Akpede 2021).

Overall, findings from this study generally highlight the complexity of measuring stress among study participants. Approaches to measuring stress that may be beneficial among participants in the United States, do not fully encapsulate or

translate to the experiences of stress in this particular Nigerian population. Conversely, while stress is present, the measures used to accurately capture what participants are experiencing are lacking. Additional bioculturally informed research geared toward understanding how participants view, understand, and experience stress are needed in embodiment research. Engaging with these questions, no matter the population, can also strengthen our understanding of the nuance of biological mechanisms of embodiment.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Access to the data from participants who provided consent for future use $(n\!=\!130)$ is available upon request, subject to the approval of the corresponding author and co-author M. Sournke. The GHQ-12 is copyrighted, and access typically requires permission or the purchase of a license for use in research or clinical settings. Code is available upon reasonable request to the corresponding author.

References

Adedini, S. A., C. Odimegwu, N. S. Imasiku, and D. N. Ononokpono. 2015. "Ethnic Differentials in Under-Five Mortality in Nigeria." *Ethnicity & Health* 20, no. 2: 145–162. https://doi.org/10.1080/13557858.2014.890599.

Adler, N., and J. Stewart. 2010. "Preface to the Biology of Disadvantage: Socioeconomic Status and Health." *Annals of the New York Academy of Sciences* 1186: 1–4.

Agho, E. T., F. J. Owotade, B. A. Kolawole, E. O. Oyetola, and T. A. Adedeji. 2021. "Salivary Inflammatory Biomarkers and Glycated Hemoglobin Among Patients With Type 2 Diabetic Mellitus." *BMC Oral Health* 21: 1–8.

Almadi, T., I. Cathers, and C. M. Chow. 2013. "Associations Among Work-Related Stress, Cortisol, Inflammation, and Metabolic Syndrome." *Psychophysiology* 50, no. 9: 821–830. https://doi.org/10.1111/psyp.12069.

Aloba, O., T. Opakunle, and K. Ogunrinu. 2019. "Alternative Models Examination and Gender Measurement Invariance of the 12-Item General Health Questionnaire Among Nigerian Adolescents." *Psychiatry Investigation* 16, no. 11: 808.

Anti, M. 2011. "Ethnic Disparities in Health Care Access and Outcomes in Nigeria." *Journal of Health Disparities Research and Practice* 4, no. 1: 1–15.

Aronoff, J. E., S. M. Koning, L. S. Adair, et al. 2024. "Intimate Partner Violence, Depression, and Chronic Low-Grade Inflammation Among Middle-Aged Women in Cebu, Philippines." *American Journal of Human Biology* 36: e24053.

Audu, I. A., T. L. Sheikh, V. O. Olisah, and M. A. Amedu. 2021. "Validity of the Use of GHQ- 12 in Primary Health Care Setting in Northern Nigeria." *Journal of Medical and Basic Scientific Research* 2, no. 2: 51–55.

Baba, M. M., B. A. Kolawole, M. O. Balogun, et al. 2012. "C-Reactive Protein in Healthy Adult Nigerians." *Nigerian Quarterly Journal of Hospital Medicine* 22, no. 4: 288–290.

Baba, M. M., B. A. Kolawole, R. T. Ikem, F. A. Arogundade, H. Yusuph, and I. D. Gezawa. 2010. "Serum C-Reactive Protein in Nigerians With

Type II Diabetes Mellitus." Nigerian Quarterly Journal of Hospital Medicine 20, no. 3: 108–113.

Baluran, D., and T. Winful. 2021. Covid-19 and America's Epidemic of Social Inequality: Lessons From Social Science.

Begum, K., G. D. Cooper, N. Akhter, P. Nahar, A. Kasim, and G. R. Bentley. 2021. "Early Life, Life Course and Gender Influences on Levels of C-Reactive Protein Among Migrant Bangladeshis in the UK." *Evolution, Medicine, and Public Health* 10, no. 1: 21–35. https://doi.org/10.1093/emph/eoab041.

Blackwell, A. D., J. J. Snodgrass, F. C. Madimenos, and L. S. Sugiyama. 2010. "Life History, Immune Function, and Intestinal Helminths: Trade-Offs Among Immunoglobulin E, C-Reactive Protein, and Growth in an Amazonian Population." *American Journal of Human Biology* 22, no. 6: 836–848.

Blackwell, A. D., B. C. Trumble, I. Maldonado Suarez, et al. 2016. "Immune Function in Amazonian Horticulturalists." *Annals of Human Biology* 43, no. 4: 382–396.

Bolarinde, S. O., T. H. Aiyeyemi, and T. E. Ashawe. 2023. "Occupational Stress and Coping Strategies Among Healthcare Workers at Federal Medical Center, Owo, Ondo State, Nigeria." *Journal of Community Medicine and Public Health Reports* 4, no. 9.

Bosch, J. A. 2014. "The Use of Saliva Markers in Psychobiology: Mechanisms and Methods." *Saliva: Secretion and Functions* 24: 99–108.

Braga, F., and M. Panteghini. 2012. "Biologic Variability of C-Reactive Protein: Is the Available Information Reliable?" *Clinica Chimica Acta* 413, no. 15–16: 1179–1183.

Calle, M. C., and C. J. Andersen. 2019. "Assessment of Dietary Patterns Represents a Potential, Yet Variable, Measure of Inflammatory Status: A Review and Update." *Disease Markers* 2019, no. 1: 3102870.

Carlson, C. S., S. F. Aldred, P. K. Lee, et al. 2005. "Polymorphisms Within the C-Reactive Protein (CRP) Promoter Region Are Associated With Plasma CRP Levels." *American Journal of Human Genetics* 77, no. 1: 64–77.

Central Intelligence Agency. 2023. "The World Factbook." https://www.cia.gov/the-world-factbook/countries/nigeria/.

Chen, L., H. Deng, H. Cui, et al. 2018. "Inflammatory Responses and Inflammation-Associated Diseases in Organs." *Oncotarget* 9, no. 6: 7204–7218. https://doi.org/10.18632/oncotarget.23208.

Cohen, S., D. Janicki-Deverts, W. J. Doyle, et al. 2012. "Chronic Stress, Glucocorticoid Receptor Resistance, Inflammation, and Disease Risk." *Proceedings of the National Academy of Sciences of the United States of America* 109: 5995–5999.

Cooper, R., M. Popham, A. J. Santanasto, R. Hardy, N. W. Glynn, and D. Kuh. 2019. "Are BMI and Inflammatory Markers Independently Associated with Physical Fatigability in Old Age?" *International Journal of Obesity* 43, no. 4: 832–841. https://doi.org/10.1038/s41366-018-0087-0.

Crosswell, A. D., and K. G. Lockwood. 2020. "Best Practices for Stress Measurement: How to Measure Psychological Stress in Health Research." *Health Psychology Open* 7, no. 2: 205510292093307. https://doi.org/10.1177/2055102920933072.

DeCaro, J. A., and C. Helfrecht. 2022. "Applying Minimally Invasive Biomarkers of Chronic Stress Across Complex Ecological Contexts." *American Journal of Human Biology* 34, no. 11: e23814.

Dillon, M. C., D. C. Opris, R. Kopanczyk, et al. 2010. "Detection of Homocysteine and C-Reactive Protein in the Saliva of Healthy Adults: Comparison With Blood Levels." *Biomarker Insights* 5: BMI-S5305.

Doumatey, A. P., G. Chen, F. Tekola Ayele, et al. 2012. "C-Reactive Protein (CRP) Promoter Polymorphisms Influence Circulating CRP Levels in a Genome-Wide Association Study of African Americans." *Human Molecular Genetics* 21, no. 13: 3063–3072.

Edewor, P. A., Y. A. Aluko, and S. F. Folarin. 2014. "Managing Ethnic and Cultural Diversity for National Integration in Nigeria." *Developing Country Studies* 4, no. 6: 70–76.

Engel, G. L. 1977. "The Need for a New Medical Model." *Science* 196: 129–136.

Ellulu, M. S., I. Patimah, A. Rahmat, and Y. Abed. 2017. "Obesity and Inflammation: The Linking Mechanism and the Complications." *Archives of Medical Science: AMS* 13, no. 4: 851–863. https://doi.org/10.5114/aoms.2016.58928.

Emerging Risk Factors Collaboration. 2010. "C-Reactive Protein Concentration and Risk of Coronary Heart Disease, Stroke, and Mortality: an Individual Participant Meta-Analysis." *Lancet* 375, no. 9709: 132–140.

Farmer, H. R., and C. S. Thomas Tobin. 2022. "Correlates of Elevated C-Reactive Protein Among Black Older Adults: Evidence From the Health and Retirement Study." *Journals of Gerontology Series B: Psychological Sciences and Social Sciences* 77, no. 11: 1964–1977. https://doi.org/10.1093/geronb/gbac033.

Fong, T. C. T., R. T. H. Ho, and J. C. Y. Yau. 2022. "Longitudinal Associations Between Salivary Cortisol to C-Reactive Protein Ratios and Psychological Well-Being in Chinese Adults." *Psychoneuroendocrinology* 143: 105824. https://doi.org/10.1016/j.psyneuen.2022.105824.

Forde, A. T., D. M. Crookes, S. F. Suglia, and R. T. Demmer. 2019. "The Weathering Hypothesis as an Explanation for Racial Disparities in Health: A Systematic Review." *Annals of Epidemiology* 33: 1–18.

Furman, D., J. Campisi, E. Verdin, et al. 2019. "Chronic Inflammation in the Etiology of Disease Across the Life Span." *Nature Medicine* 25, no. 12: 1822–1832.

Gao, F., N. Luo, J. Thumboo, C. Fones, S. C. Li, and Y. B. Cheung. 2004. "Does the 12-item General Health Questionnaire Contain Multiple Factors and Do We Need Them?" *Health and Quality of Life Outcomes* 2: 1–7.

Geronimus, A., M. Hicken, D. Keene, and J. Bound. 2006. ""Weathering" and Age Patterns of Allostatic Load Scores Among Blacks and Whites in the United States." *American Journal of Public Health* 96: 826–833.

Geronimus, A. T. 1992. "The Weathering Hypothesis and the Health of African–American Women and Infants: Evidence and Speculations." *Ethnicity and Disease* 2: 207–221.

Goetz, S. M., and T. Lucas. 2020. "C-Reactive Protein in Saliva and Dried Blood Spot as Markers of Stress Reactivity in Healthy African-Americans." *Biomarkers in Medicine* 14, no. 5: 371–380. https://doi.org/10.2217/bmm-2019-0391.

Goldberg, D. P., and P. Williams. 1988. A User's Guide to the General Health Questionnaire. Berkshire, UK: NFER-Nelson.

Gonzalez-Jaramillo, V., E. Portilla-Fernandez, M. Glisic, et al. 2019. "Epigenetics and Inflammatory Markers: A Systematic Review of the Current Evidence." *International Journal of Inflammation* 19: 1–14.

Graetz, B. 1991. "Multidimensional Properties of the General Health Questionnaire." *Social Psychiatry and Psychiatric Epidemiology* 26: 132–138.

Hankins, M. 2008. "The Reliability of the Twelve-Item General Health Questionnaire (GHQ-12) Under Realistic Assumptions." *BMC Public Health* 8, no. 1: 1–7.

Henein, M. Y., S. Vancheri, G. Longo, and F. Vancheri. 2022. "The Role of Inflammation in Cardiovascular Disease." *International Journal of Molecular Sciences* 23, no. 21: 12906.

Hellhammer, D. H., S. Wüst, and B. M. Kudielka. 2009. "Salivary Cortisol as a Biomarker in Stress Research." *Psychoneuroendocrinology* 34, no. 2: 163–171.

Hystad, S. W., and B. H. Johnsen. 2020. "The Dimensionality of the 12-Item General Health Questionnaire (GHQ-12): Comparisons of Factor Structures and Invariance Across Samples and Time." Frontiers in Psychology 11: 1300.

Ibadin, M. O., and G. O. Akpede. 2021. "A Revised Scoring Scheme for the Classification of Socio-Economic Status in Nigeria." *Nigerian Journal of Paediatrics* 48, no. 1: 26–33.

Johnson, T. V., A. Abbasi, and V. A. Master. 2013. "Systematic Review of the Evidence of a Relationship Between Chronic Psychosocial Stress and C-Reactive Protein." *Molecular Diagnosis & Therapy* 17: 147–164.

Kandhalu, P. 2013. "Effects of Cortisol on Physical and Psychological Aspects of the Body and Effective Ways By Which One Can Reduce Stress." *Berkeley Scientific Journal* 18, no. 1.

Khera, A., D. K. McGuire, S. A. Murphy, et al. 2005. "Race and Gender Differences in C-Reactive Protein Levels." *Journal of the American College of Cardiology* 46, no. 3: 464–469.

Kong, H., Y. S. Qian, X. F. Tang, et al. 2012. "C-Reactive Protein (CRP) Gene Polymorphisms, CRP Levels and Risk of Incident Essential Hypertension: Findings From an Observational Cohort of Han Chinese." *Hypertension Research* 35, no. 10: 1019–1023.

Kuzawa, C. W., and E. Sweet. 2009. "Epigenetics and the Embodiment of Race: Developmental Origins of US Racial Disparities in Cardiovascular Health." *American Journal of Human Biology: The Official Journal of the Human Biology Association* 21, no. 1: 2–15.

Lakoski, S. G., M. Cushman, M. Criqui, et al. 2006. "Gender and C-Reactive Protein: Data From the Multiethnic Study of Atherosclerosis (MESA) Cohort." *American Heart Journal* 152, no. 3: 593–598.

Leatherman, T., and M. Hoke. 2016. "Critical Biocultural Anthropology: A Model for Anthropological Integration." In *The Routledge Companion to Contemporary Anthropology*, 283–302. London: Routledge. https://doi.org/10.4324/9781315743950.

Liu, Y. Z., Y. X. Wang, and C. L. Jiang. 2017. "Inflammation: The Common Pathway of Stress-Related Diseases." *Frontiers in Human Neuroscience* 11: 316.

Lock, M. 1993. "Cultivating the Body: Anthropology and Epistemologies of Bodily Practice and Knowledge." *Annual Review of Anthropology* 22, no. 1: 133–155.

Makanjuola, V. A., M. Onyeama, F. T. Nuhu, L. Kola, and O. Gureje. 2014. "Validation of Short Screening Tools for Common Mental Disorders in Nigerian General Practices." *General Hospital Psychiatry* 36, no. 3: 325–329. https://doi.org/10.1016/j.genhosppsych.2013.12.010.

Macy, E. M., T. E. Hayes, and R. P. Tracy. 1997. "Variability in the Measurement of C-Reactive Protein in Healthy Subjects: Implications for Reference Intervals and Epidemiological Applications." *Clinical Chemistry* 43, no. 1: 52–58.

McDade, T. W. 2012. "Early Environments and the Ecology of Inflammation." *Proceedings of the National Academy of Sciences of the United States of America* 109: 17281–17288. https://doi.org/10.1073/pnas.1202244109.

McDade, T. W., J. Rutherford, L. Adair, and C. W. Kuzawa. 2010. "Early Origins of Inflammation: Microbial Exposures in Infancy Predict Lower Levels of C-Reactive Protein in Adulthood." *Proceedings of the Royal Society B: Biological Sciences* 277, no. 1684: 1129–1137.

McDade, T. W., P. S. Tallman, L. S. Adair, J. Borja, and C. W. Kuzawa. 2011. "Comparative Insights Into the Regulation of Inflammation: Levels and Predictors of Interleukin 6 and Interleukin 10 in Young Adults in The Philippines." *American Journal of Physical Anthropology* 146, no. 3: 373–384.

McEwen, B. S. 1998. "Protective and Damaging Effects of Stress Mediators." *New England Journal of Medicine* 338, no. 3: 171–179.

McEwen, B. S., and J. C. Wingfield. 2003. "The Concept of Allostasis in Biology and Biomedicine." *Hormones and Behavior* 43, no. 1: 2–15. https://doi.org/10.1016/S0018-506x(02)00024-7.

Miller, G. E., E. Chen, and E. S. Zhou. 2007. "If It Goes Up, Must It Come Down? Chronic Stress and the Hypothalamic-Pituitary-Adrenocortical Axis in Humans." *Psychological Bulletin* 133, no. 1: 25–45. https://doi.org/10.1037/0033-2909.133.1.25.

Mohamed, R., L. Campbell, J. Cooper-White, G. Dimeski, and C. Punyadeera. 2011. "The Impact of Saliva Collection and Processing Methods on CRP, IgE, and Myoglobin Immunoassays." *Clinical and Translational Medicine* 1: 19. https://doi.org/10.1186/2001-1326-1-19.

Nguyen, A. W., H. O. Taylor, K. D. Lincoln, et al. 2022. "Neighborhood Characteristics and Inflammation Among Older Black Americans: The Moderating Effects of Hopelessness and Pessimism." *Journals of Gerontology: Series A* 77, no. 2: 315–322.

Nguyen, V., and K. Peschard. 2003. "Anthropology, Inequality, and Disease: A Review." In *Annual Review of Anthropology*, vol. 32, 447–474. California, US: Annual Reviews. http://search.proquest.com/docview/37808296/.

Nunnally, J. C. 1978. *Psychometric Theory*. 2nd ed. New York, NY: McGraw-Hill.

Ockene, I. S., C. E. Matthews, N. Rifai, P. M. Ridker, G. Reed, and E. Stanek. 2001. "Variability and Classification Accuracy of Serial High-Sensitivity C-Reactive Protein Measurements in Healthy Adults." *Clinical Chemistry* 47, no. 3: 444–450.

Odimegwu, C. O., O. Alabi, N. D. Wet, and J. O. Akinyemi. 2018. "Ethnic Heterogeneity in the Determinants of HIV/AIDS Stigma and Discrimination Among Nigeria Women." *BMC Public Health* 18: 763. https://doi.org/10.1186/s12889-018-5668-2.

Ojagbemi, A., T. Bello, Z. Luo, and O. Gureje. 2017. "Living Conditions, Low Socioeconomic Position, and Mortality in the Ibadan Study of Aging." *Journals of Gerontology Series B: Psychological Sciences and Social Sciences* 72, no. 4: 646–655. https://doi.org/10.1093/geronb/gbv093.

Okocha, C. E., P. O. Manafa, J. O. Ozomba, T. O. Ulasi, G. O. Chukwuma, and J. C. Aneke. 2014. "C-Reactive Protein and Disease Outcome in Nigerian Sickle Cell Disease Patients." *Annals of Medical and Health Sciences Research* 4, no. 5: 701–705.

Okokon, I. B., U. E. Asibong, V. A. Inem, et al. 2012. "Use of the General Health Questionnaire as a Screening Tool for Geriatric Patients in Calabar, Nigeria." *Nigerian Journal of Medicine* 21, no. 4: 432–437.

Okudo, O. C., N. T. Nwudu, and I. T. Nwankwo. 2023. "The Family Psychological Wellbeing as Correlate to Socio Political and Economic Climate Among Indigenes of South Eastern States of Nigeria." Sapientia Global Journal of Arts, Humanities and Development Studies 6, no. 4.

Olusanya, O. 1985. "The Importance of Social Class in Voluntary Fertility Control in Developing Country." *West African Journal of Medicine* 4: 205–212.

Omotosho, M., L. Ihekuna, and O. Fakoya. 2020. "Cultural Diversity and the Challenge of Inter-Ethnic Conflict in Nigeria." *EAS Journal of Humanities and Cultural Studies* 2, no. 3: 165–171.

Onigbogi, C. B., and S. Banerjee. 2019. "Prevalence of Psychosocial Stress and Its Risk Factors Among Health-Care Workers in Nigeria: A Systematic Review and Meta-Analysis." *Nigerian Medical Journal* 60, no. 5: 238–244.

Orsolini, L., S. Pompili, S. T. Valenta, V. Salvi, and U. Volpe. 2022. "C-Reactive Protein as a Biomarker for Major Depressive Disorder?" *International Journal of Molecular Sciences* 23, no. 3: 1616. https://doi.org/10.3390/ijms23031616.

Ouellet-Morin, I., A. Danese, B. Williams, and L. Arseneault. 2011. "Validation of a High-Sensitivity Assay for C-Reactive Protein in Human Saliva." *Brain, Behavior, and Immunity* 25, no. 4: 640–646.

Out, D., R. J. Hall, D. A. Granger, G. G. Page, and S. J. Woods. 2012. "Assessing Salivary C-Reactive Protein: Longitudinal Associations With Systemic Inflammation and Cardiovascular Disease Risk in Women Exposed to Intimate Partner Violence." *Brain, Behavior, and Immunity* 26, no. 4: 543–551.

Oyedeji, G. A. 1985. "Socio-Economic and Cultural Background of Hospitalised Children in Ilesha." *Nigerian Journal of Paediatrics* 12, no. 4: 111–117.

Pace, T. W., T. C. Mletzko, O. Alagbe, et al. 2006. "Increased Stress-Induced Inflammatory Responses in Male Patients With Major Depression and Increased Early Life Stress." *American Journal of Psychiatry* 163, no. 9: 1630–1633.

Pahwa, R., A. Goyal, P. Bansal, and I. Jialal. 2018. Chronic Inflammation.

Pay, J. B., and A. M. Shaw. 2019. "Towards Salivary C-Reactive Protein as a Viable Biomarker of Systemic Inflammation." *Clinical Biochemistry* 68: 1–8.

Pitharouli, M. C., S. P. Hagenaars, K. P. Glanville, et al. 2021. "Elevated C-Reactive Protein in Patients With Depression, Independent of Genetic, Health, and Psychosocial Factors: Results From the UK Biobank." *American Journal of Psychiatry* 178, no. 6: 522–529.

Pollard, T. M. 1995. "Use of Cortisol as a Stress Marker: Practical and Theoretical Problems." *American Journal of Human Biology* 7, no. 2: 265–274.

Punyadeera, C., G. Dimeski, K. Kostner, P. Beyerlein, and J. Cooper-White. 2011. "One-Step Homogeneous C-Reactive Protein Assay for Saliva." *Journal of Immunological Methods* 373, no. 1–2: 19–25.

Reiner, A. P., S. Beleza, N. Franceschini, et al. 2012. "Genome-Wide Association and Population Genetic Analysis of C-Reactive Protein in African American and Hispanic American Women." *American Journal of Human Genetics* 91, no. 3: 502–512.

Rohleder, N. 2014. "Stimulation of Systemic Low-Grade Inflammation by Psychosocial Stress." *Psychosomatic Medicine* 76, no. 3: 181–189.

Sapolsky, R. M. 2021. "Glucocorticoids, the Evolution of the Stress-Response, and the Primate Predicament." *Neurobiology of Stress* 14: 100320. https://doi.org/10.1016/j.ynstr.2021.100320.

Sharpley, C. F., R. Hussain, S. G. Wark, M. McEvoy, and J. Attia. 2018. "The Association Between Cortisol:C-Reactive Protein Ratio and Depressive Symptoms: A Cross-Sectional Study of a Community Sample." *Neuropsychiatric Disease and Treatment* 14: 2105–2114.

Simons, R. L., M. K. Lei, E. Klopack, Y. Zhang, F. X. Gibbons, and S. R. Beach. 2021. "Racial Discrimination, Inflammation, and Chronic Illness Among African American Women at Midlife: Support for the Weathering Perspective." *Journal of Racial and Ethnic Health Disparities* 8: 339–349.

Singh, N., D. Baby, J. P. Rajguru, P. B. Patil, S. S. Thakkannavar, and V. B. Pujari. 2019. "Inflammation and Cancer." *Annals of African Medicine* 18, no. 3: 121–126.

Slavish, D. C., J. E. Graham-Engeland, J. M. Smyth, and C. G. Engeland. 2015. "Salivary Markers of Inflammation in Response to Acute Stress." *Brain, Behavior, and Immunity* 44: 253–269.

Sorriento, D., and G. Iaccarino. 2019. "Inflammation and Cardiovascular Diseases: The Most Recent Findings." *International Journal of Molecular Sciences* 20, no. 16: 3879.

Stephens, M. A., and G. Wand. 2012. "Stress and the HPA Axis: Role of Glucocorticoids in Alcohol Dependence." *Alcohol Research: Current Reviews* 34, no. 4: 468–483.

Szabo, Y. Z., and D. C. Slavish. 2021. "Measuring Salivary Markers of Inflammation in Health Research: A Review of Methodological Considerations and Best Practices." *Psychoneuroendocrinology* 124: 105069. https://doi.org/10.1016/j.psyneuen.2020.105069.

Szabo, Y. Z., D. C. Slavish, and J. E. Graham-Engeland. 2020. "The Effect of Acute Stress on Salivary Markers of Inflammation: A Systematic Review and Meta-Analysis." *Brain, Behavior, and Immunity* 88: 887–900. https://doi.org/10.1016/j.bbi.2020.04.078.

Thayer, Z. M., and C. W. Kuzawa. 2011. "Biological Memories of Past Environments: Epigenetic Pathways to Health Disparities." *Epigenetics* 6, no. 7: 798–803.

Toussaint, L. L., D. P. Moriarity, S. Kamble, D. R. Williams, and G. M. Slavich. 2022. "Inflammation and Depression Symptoms Are Most Strongly Associated for Black Adults." *Brain, Behavior, & Immunity—Health* 26: 100552. https://doi.org/10.1016/j.bbih.2022.100552.

Tsalamandris, S., A. S. Antonopoulos, E. Oikonomou, et al. 2019. "The Role of Inflammation in Diabetes: Current Concepts and Future Perspectives." *European Cardiology Review* 14, no. 1: 50–59.

Udo, R. K. 1970. Geographical Regions of Nigeria. Los Angeles, CA: Univ of California Press.

Vitzthum, V. J., J. Thornburg, T. W. McDade, et al. 2024. "C-Reactive Protein (CRP) in High Altitude Bolivian Peri-Urban Adolescents Varies by Adiposity, Current Illness, Height, Socioeconomic Status, Sex, and Menarcheal Status: The Potential Benefits and Costs of Adipose Reserves in Arduous Environments." *American Journal of Human Biology* 36, no. 9: e24107.

Wetterö, J., S. Von Löhneysen, F. Cobar, M. Kristenson, P. Garvin, and C. Sjöwall. 2021. "Pronounced Diurnal Pattern of Salivary C-Reactive Protein (CRP) With Modest Associations to Circulating CRP Levels." *Frontiers in Immunology* 11: 607166.

Yang, Y. C., K. Schorpp, C. Boen, M. Johnson, and K. M. Harris. 2020. "Socioeconomic Status and Biological Risks for Health and Illness Across the Life Course." *Journals of Gerontology: Series B* 75, no. 3: 613–624.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.