

Research Article

Assessment of Inflammatory and Oxidative Stress Biomarkers in Treated and Untreated Hypertensive Adults in Port Harcourt, Nigeria

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Abstract

Introduction: Hypertension is a leading global health concern, characterised by chronic low-grade inflammation and oxidative stress that drive a vicious cycle of vascular dysfunction, endothelial damage, and end-organ injury. **Aim:** This study evaluated serum levels of inflammatory and oxidative stress biomarkers among hypertensive adults in Port Harcourt, Nigeria, to examine the variation in these biomarkers between untreated and treated hypertensive subjects. **Methods:** This cross-sectional study enrolled 150 participants aged 25-65 years, divided into three groups: 50 treated hypertensives on medication, 50 newly-diagnosed untreated hypertensives, and 50 normotensive controls. All participants underwent anthropometric and blood pressure measurements. Venous blood (5mL) was collected for the laboratory quantification of serum levels of inflammatory markers: C-reactive protein (CRP) and tumour necrosis factor- α (TNF- α), and oxidative stress biomarkers: malondialdehyde (MDA), reduced glutathione (GSH), glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT). **Results:** Findings reveal that study participants were relatively age-matched across the groups. Our data show significantly elevated body mass index (BMI), MDA, CRP and TNF among the treated hypertensive subjects compared to both the untreated hypertensive and normotensive controls ($p < 0.05$). Conversely, we observed significantly reduced levels of GSH, GPx, CAT and SOD among the treated and untreated hypertensive groups compared to the normotensive control ($p < 0.05$). **Conclusion:** The current study demonstrates that hypertension is characterised by chronic immuno-inflammatory dysregulation mediated by reactive oxygen species (ROS), which drives endothelial dysfunction and arterial stiffness. The persistence of these inflammatory and oxidative stress markers in treated patients underscores the need for adjunct antioxidant and immunomodulatory supplementation to improve vascular outcomes in hypertension.

Keywords

Hypertension, Inflammation, C-reactive Protein, Tumour Necrosis Factor, Oxidative Stress, Antioxidant Enzymes

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1. Introduction

Blood pressure (BP) is the lateral haemodynamic force exerted by circulating blood against the walls of the arteries, generated by cardiac contraction against vascular resistance. It is quantified as the product of cardiac output (CO) and systemic vascular resistance (SVR), reflecting the interplay between heart function and arterial stiffness [1, 2]. Within physiologic limits, systemic blood pressure is tightly regulated by neural, hormonal, and local metabolic mechanisms. Neural control primarily involves the autonomic nervous system (ANS), with sympathetic activation increasing blood pressure via norepinephrine-mediated vasoconstriction and enhanced cardiac output, while parasympathetic input (via vagal tone) exerts counter-regulatory effects on heart rate [3, 4]. Hormonal regulation includes the renin-angiotensin-aldosterone system (RAAS), where angiotensin II induces vasoconstriction, and aldosterone promotes sodium retention [5, 6], alongside vasodilatory hormones such as atrial natriuretic peptide (ANP) and nitric oxide (NO) [7, 8]. Local metabolic factors, such as hypoxia-induced adenosine release, lactic acid, and endothelial-derived hyperpolarising factors (EDHFs), modulate regional vascular resistance to match tissue perfusion demands [9, 10]. High blood pressure (HBP), also known as hypertension (HTN), is a chronic cardiovascular disorder characterised by persistently elevated systemic arterial pressure ($\geq 140/90$ mmHg measured on more than two occasions) resulting from dysregulated neural, hormonal, and metabolic control mechanisms [11-13]. Hypertension arises from the failure of these key regulatory mechanisms that maintain vascular homeostatic systems, including sympathetic overactivity, RAAS hyperactivation, endothelial dysfunction, and impaired local vaso-regulation that collectively increase peripheral vascular resistance and/or cardiac output [6, 14, 15]. Although the pathophysiological basis of hypertension is not fully understood, blood pressure elevation is thought to arise from the complex, cumulative interaction of multiple biological, environmental and genetic determinants ranging from excessive dietary sodium, physical inactivity, excessive alcohol consumption, tobacco use, chronic stress and dyslipidaemia, insulin resistance and poor sleep quality and chronic inflammation [4, 16-21].

Inflammation is a biological response to harmful stimuli, characterised by heat, pain, redness, swelling, and loss of function. While acute inflammation is protective, chronic inflammation contributes to diseases like hypertension, rheumatoid arthritis, systemic lupus erythematosus and psoriasis [22-24]. Chronic Inflammation contributes to endothelial dysfunction, arterial stiffness, and renal impairment, exacerbating the pathogenesis of inflammation in a bidirectional manner and creating a vicious cycle that amplifies end-organ damage [25, 26]. Some of the key inflammatory biomarkers, such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumour necrosis factor-alpha (TNF- α), play roles in both

chronic inflammation and the pathogenesis of hypertension. IL-6 is a cytokine that is produced by macrophages, T cells, endothelial cells, and adipocytes and stimulates the hepatic production of CRP and other acute-phase proteins and facilitates leukocyte recruitment and T-cell differentiation. They promote vascular inflammation, oxidative stress dysfunction, with higher values linked to a 51% increased risk of hypertension [27-30]. C-reactive protein is produced in the liver in response to IL-6, serving as an acute-phase reactant that marks the presence of inflammation. They bind to pathogens and damaged cells to activate the complement system and promote phagocytosis. Elevated CRP levels are associated with endothelial dysfunction, vascular inflammation, and arterial stiffens, contributing to increased blood pressure. High CRP predicts the development and progression of hypertension [29, 31, 32]. TNF- α is a pro-inflammatory cytokine produced mainly by the macrophages, T lymphocytes, and adipose tissue, but also by endothelial and smooth muscle cells, where they promote the expression of adhesion molecules, chemokines, and other cytokines [33]. TNF- α impairs endothelial nitric oxide production, promoting vasoconstriction, vascular inflammation, vascular resistance and oxidative stress, contributing to the development and progression of hypertension [33-35]. Beyond its inflammatory functions, TNF- α also supports tissue repair, regeneration, and cellular proliferation. Under normal physiological conditions, circulating TNF- α levels are either undetectable or very low; however, its production and secretion increase significantly during inflammatory responses [28, 33]. In hypertension, chronic low-grade inflammation and oxidative stress form a vicious cycle that drives vascular dysfunction, endothelial damage, and end-organ injury [33, 36].

Oxidative stress occurs when there is an imbalance between reactive oxygen species (ROS) production and antioxidant defence mechanisms, leading to cellular damage. ROS, including superoxide (O_2^-), hydrogen peroxide (H_2O_2), and hydroxyl radicals ($OH^\cdot$), are natural byproducts of aerobic metabolism but become pathogenic when excessively generated or inadequately neutralised [37-39]. In hypertension, oxidative stress promotes endothelial dysfunction, vascular inflammation, and arterial stiffness, accelerating cardiovascular damage [40]. Inflammation-induced oxidative stress occurs when immune activation and pro-inflammatory signalling disrupt redox balance, leading to excessive reactive oxygen species (ROS) production and impaired antioxidant defences. This process plays a central role in hypertension development and progression [40-43].

Globally, hypertension represents the leading modifiable risk factor for premature mortality as epidemiologic data reveal that nearly one-third (33%) of adults aged 30–79 years are affected, with the global burden doubling from 650 million cases in 1990 to 1.3 billion by 2009 [11, 16, 19]. This alarming trajectory is expected to persist due to population

ageing and growth, with age-adjusted prevalence demonstrating significant gender disparities with higher values obtained in males when compared to females [44, 45]. The distribution of hypertension reflects global health inequities, with 78% of affected individuals living in low and middle-income countries (LMICs), where systemic barriers limit access to diagnosis and evidence-based management [19, 44]. Within these regions, blood pressure variations between rural and urban populations mirror distinct phases of epidemiological transition, driven by socioeconomic transformations that reshape cardiovascular risk profiles and disease patterns. In Nigeria, epidemiological data reveal a rise in prevalence, from 8.5% in 1995 to 32.5% by 2020 among adults aged ≥ 20 years [46]. A 2010 meta-analysis estimated 20.8 million affected individuals (28.0% prevalence), underscoring the condition's widespread impact [47]. Geographic and demographic disparities further characterise Nigeria's hypertension profile. Regional studies demonstrate prevalence rates ranging from 27.6% in rural southeastern communities to 38.1% in broader populations [17, 18], highlighting the significant impact of socio-demographic factors on both prevalence and management of hypertension in Nigeria [12]. Port Harcourt, Nigeria, exhibits a particularly high hypertension burden, with prevalence rates ranging from 33.97% to 49.7% in recent studies [48, 49], significantly exceeding national averages. This elevated risk profile likely reflects the confluence of urban lifestyle factors, characteristic dietary patterns unique environmental stressors such as air pollution from industrial activities.

Despite the growing global recognition of oxidative stress and inflammation as key pathophysiological mechanisms in hypertension [40, 41], there is a paucity of data on their pattern of variation among hypertensive adults in African populations, as current evidence derives predominantly from high-income countries. The present study, therefore, aims to address these knowledge gaps by evaluating inflammatory and oxidative stress biomarkers among hypertensive adults in Port Harcourt. This will further show the pattern of variation of these biomarkers among untreated and treated hypertensive subjects in this population in order to provide baseline data that could guide precision medicine approaches and support evidence-based public health policies to reduce the cardiovascular disease burden in pollution-affected urban populations.

2. Materials and Methods

2.1. Determination of Sample Size

The sample size was calculated using G*Power software (ver. 3.1.9.7) [50]. The calculation was based on the objective of detecting a statistically significant difference in biomarker levels among the three study groups: normotensive controls, treated hypertensive adults, and untreated hypertensive adults.

The analysis was set for a one-way analysis of variance (ANOVA) with three groups with a significance level (α) of 0.05, statistical power ($1-\beta$) of 80% and effect size (Cohen's f) of 0.4. The calculation yielded a minimum total sample size of 132 (44 participants per group). However, to account for a potential 10% attrition, the sample size was adjusted to 150 participants (50 participants per group).

2.2. Study Population and Design

A total of one hundred and fifty (150) participants (aged 25–65 years), residing in Port Harcourt for at least five years, were enrolled in this study. They comprised of fifty (50) known hypertensive subjects (HTN) receiving oral antihypertensive therapy, as documented in their medical records, fifty (50) newly diagnosed hypertensive subjects (naïve-HTN), identified based on elevated blood pressure readings across three separate clinic visits in accordance with WHO diagnostic criteria for hypertension [13] and fifty (50) normotensive individuals serving as the control group. The HTN participants were recruited from various private clinics in Port Harcourt, Nigeria, with a confirmed hypertension diagnosis and ongoing pharmacological management. The naïve-HTN group consisted of individuals newly diagnosed with hypertension, while the control group included apparently healthy individuals from the general population of Port Harcourt. Exclusion criteria for all participants included pregnancy, lactation, diabetes, chronic kidney disease (CKD), liver disease, malignancy, autoimmune disorders, or any serious hospitalisation within the preceding five months. All individuals on routine anti-inflammatory or antioxidant substances were excluded from the study.

2.3. Data and Sample Collection

Demographic and clinical information were obtained from all participants using a structured questionnaire. The weight and height were measured using a SECA scale, and the body mass index (BMI) was calculated. Blood pressure readings were obtained using an aneroid sphygmomanometer (Wuxi Yuqing Medical, China) and a Littmann stethoscope (USA) after the participants had rested for five minutes in a seated position. Three consecutive measurements were taken at one-minute intervals, and the average reading was recorded. Following a minimum of eight (8) hours fasting period, venous blood samples (5ml) were collected from the participants in sterile, additive-free vacutainers and allowed to clot at room temperature for 30 minutes. The samples were then centrifuged at 1000 rpm for 10 minutes at 4 °C using a swing-bucket centrifuge (Eppendorf, Germany). The supernatant serum fraction was carefully collected using calibrated micropipettes (Onilab Laboratory Instrument CO., Ltd, China) and immediately stored at 4 °C pending assay. Serum levels of inflammatory markers: tumour necrosis factor- α (TNF- α) and C-reactive protein (CRP) and oxidative stress biomarkers:

malondialdehyde (MDA), reduced glutathione (GSH), glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT) were quantified using commercially available laboratory assay kits (Elabscience Biotechnology Co., Ltd., China) according to the manufacturer's protocols.

2.4. Statistical Analysis

Statistical analysis was conducted using IBM SPSS Statistics (Version 27; IBM Corp., USA). Variables were expressed as mean $\pm$ standard deviation (SD). Differences in anthropometric measures, blood pressure and biomarker levels across study groups (normotensive controls, naïve hypertensive and treated hypertensive subjects) were assessed using one-way analysis of variance (ANOVA) with post-hoc LSD tests for multiple comparisons. Statistical significance was set at $p < 0.05$.

2.5. Ethical Consideration

All participants were fully informed about the study's objectives, procedures, and potential implications. They voluntarily provided written informed consent in accordance with ethical research guidelines. The research design and protocol were formally approved by the Research Ethics Committee of the University of Port Harcourt (UPH/CEREMAD/REC/MM75/101).

3. Results

Table 1 presents a cross-sectional analysis of demographic and body mass index parameters of the distinct study population: control, Naïve-hypertensive and treated hypertensive subjects. The sex distribution showed a slightly higher number of females (64.67%) compared to the males (57.33%). The gender distribution across the age groups is relatively balanced, with males constituting 33.72, 32.56 and 33.72% for the control, Naïve-hypertensive and treated hypertensive subjects, respectively. Similarly, female subjects accounted for 32.81, 34.38 and 32.81% of control, Naïve-hypertensive and treated hypertensive subjects, respectively. The data indicate no significant disparity in gender representation across the study population. Age distribution revealed pronounced variations across groups. The older adults (55–60 years) represented 36.7% of participants, while the middle-aged group (40–54 years) had the lowest representation at 17.33%, followed closely by young adults (25–39 years) at 37.67%. Among the young adults, the normotensive control had the highest representation at 40.00%, while the Naïve-HTN group had the lowest at 27.27%. The 40–54-year age group was most prevalent in the Naïve-HTN cohort (36.23%), whereas the 55–60-year age group was highest in the Naïve-HTN group as well (38.46%). BMI trends showed that the control group had the highest proportion of individuals with normal BMI (55.93%), compared to only 15.26% in the treated-HTN group. Overweight individuals were most prevalent in the Naïve-HTN group (48.64%), while obesity was disproportionately high in the treated-HTN group (61.11%).

Table 1. Demographic and anthropometric characteristics of the study population.

Parameters		Control n (%)	Naïve-HTN n (%)	Treated-HTN n (%)	Total
Sex	Male	29 (33.72)	28 (32.56)	29 (33.72)	86 (57.33)
	Female	21 (32.81)	22 (34.38)	21 (32.81)	64 (64.67)
Age	25–39 years	22 (40.00)	15 (27.27)	18 (32.73)	55 (36.67)
	40–54 years	20 (28.99)	25 (36.23)	24 (34.78)	69 (46.00)
	55–60 years	8 (30.77)	10 (38.46)	8 (30.77)	26 (17.33)
BMI	Normal	33 (55.93)	17 (28.81)	9 (15.26)	59 (39.33)
	Overweight	11 (29.73)	18 (48.64)	8 (21.63)	37 (24.67)
	Obese	6 (11.11)	15 (27.78)	33 (61.11)	54 (36.00)

Table 2 depicts the mean age, BMI and blood pressure parameters among the normotensive controls, untreated hypertensive (naïve-HTN), and treated hypertensive (treated-HTN) subjects in Port Harcourt, Nigeria. The data reveal that the age matched across the study group with only minor variations

(control: 43.48 ± 9.92 years; naïve-HTN: 44.28 ± 10.20 ; treated-HTN: 44.12 ± 8.59). However, the naïve-HTN and treated-HTN exhibited significantly higher body mass index (BMI) (+13% and +33%, respectively) compared to controls ($p < 0.05$). Similarly, blood pressure parameters showed sig-

nificant elevations among the naïve-HTN, with systolic blood pressure (SBP) 55.2% higher and diastolic blood pressure (DBP) 33.7% higher than controls ($p<0.05$). Treated-HTN showed improvements but remained elevated (SBP +46%, DBP +21% elevation when compared to the control group ($P<0.05$). Pulse rate was slightly lower in both hypertensive groups compared to controls ($p<0.05$). However, there was no

significant variation in pulse rate between the naïve-HTN and treated-HTN subjects. The mean arterial pressure (MAP) showed a similar trend with naïve-HTN and treated HTN subjects showing significantly elevated mean values (+43% and +32% respectively) when compared to the control ($p<0.05$).

Table 2. Age, body mass index and blood pressure characteristics of the study population.

Parameters	Control n = 50	Naïve-HTN n = 50	Treated-HTN n = 50
Age (years)	43.48 ±9.92	44.28 ±10.20	44.12 ±8.59
Body mass index (kg/m ²)	23.73 ±4.25	26.84 ±4.05 ^a	31.65 ±8.21 ^a
Systolic blood pressure (mmHg)	107.20 ±9.47	166.40 ±23.44 ^a	156.10 ±30.95 ^{ab}
Diastolic blood pressure (mmHg)	72.26 ±9.43	96.64 ±8.48 ^a	87.68 ±17.51 ^{ab}
Pulse rate (b/min)	87.22 ±9.00	82.40 ±9.26 ^a	81.16 ±9.54 ^a
Mean arterial pressure (mmHg)	83.90 ±8.40	119.87 ±11.01 ^a	110.46 ±20.89 ^{ab}

Results are given as mean ±standard deviation

a=significantly different compared to normotensive control

b=significantly different compared to naïve hypertensives

Table 3. Inflammatory and oxidative stress parameters of the study population.

Parameters	Control n = 50	Naïve-HTN n = 50	Treated-HTN n = 50
C-Reactive protein (ng/ml)	270.60 ±112.89	1093.88 ±220.31 ^a	635.08 ±114.18 ^{ab}
Tumour necrosis factor – α (ng/L)	62.71 ±15.16	92.99 ±17.76 ^a	68.55 ±9.53 ^{ab}
Malondialdehyde (nmol/ml)	1.55 ±0.17	3.40 ±0.33 ^a	2.07 ±0.30 ^{ab}
Reduced glutathione (mmol/L)	5.01 ±0.82	3.39 ±0.68 ^a	4.43 ±0.72 ^{ab}
Glutathione peroxidase (u/L)	204.98 ±18.67	190.04 ±18.47 ^a	195.32 ±16.80 ^{ab}
Catalase (U/ml)	121.42 ±16.71	64.26 ±2.57 ^a	97.45 ±7.99 ^{ab}
Superoxide dismutase (U/ml)	58.41 ±3.89	36.48 ±8.20 ^a	53.51 ±11.34 ^{ab}

Results are given as mean ±standard deviation

a=significantly different compared to normotensive control

b=significantly different compared to naïve hypertensives

Table 3 shows the various changes in Inflammatory and oxidative stress among the study population. The data reveal that the naïve-HTN and treated-HTN groups had elevated mean levels of MDA, CRP and TNF- α compared to the control group and significantly reduced levels of GSH, GPx, CAT and SOD when compared to the control group ($P<0.05$). The untreated (Naïve-HTN) showed a dramatic increase in serum levels of CRP, surging 304% and TNF- α rising 48% above the control values ($P<0.05$). Though treatment significantly reduced the CRP levels, it did not normalise inflammation,

leaving CRP 135% higher and TNF- α 9% when compared to the control ($P<0.05$). Similarly, Oxidative stress markers mirrored this trend, with MDA increasing by 119% in naïve-HTN and remaining 33.5% elevated after treatment. The antioxidant system showed parallel disruption, with catalase activity plunging -47.1% in naïve-HTN and recovering only partially to 20% among the treated-HTN. The mean values of serum GPx, GSH and SOD were found to be 32, 7 and 38% lower, respectively, in naïve-HTN, while treated-HTN showed 12, 5 and 20% significant reduction ($p<0.05$), re-

spectively. This shows a partial recovery of the antioxidant enzymes in the treated-HTN. However, the mean values remained significantly lower compared to the control ($P < 0.05$).

4. Discussion

Hypertension is a major global public health issue due to its high prevalence and stands as the leading modifiable risk factor for disability and mortality worldwide. In Nigeria, the prevalence of hypertension is significantly influenced by socio-demographic factors that affect both its occurrence and management. Hypertension is characterised by chronic low-grade inflammation and oxidative stress, which create a vicious cycle that promotes vascular dysfunction, endothelial damage, and end-organ injury. This study evaluated serum levels of inflammatory and oxidative stress biomarkers among hypertensive adults in Port Harcourt, Nigeria, to examine the variation in these biomarkers between untreated and treated hypertensive subjects.

Our study reveals that untreated hypertensive subjects (naïve-HTN) and treated hypertensive subjects (treated-HTN) had significantly elevated body mass index (BMI) compared to the normotensive controls ($p < 0.05$). Elevated BMI, as observed in overweight and obesity, is independently and positively associated with a higher risk of morbidity and mortality from hypertension, cardiovascular disease, type II diabetes mellitus, and other chronic conditions [19, 51]. Several pathophysiological mechanisms explain the link between increased BMI and hypertension. Overweight and obesity are characterised by overactivation of the sympathetic nervous system, resulting in heightened vasoconstriction, increased heart rate, and elevated cardiac output, all of which contribute to raised blood pressure levels [52, 53]. Additionally, obesity impairs endothelial function through reduced bioavailability of nitric oxide (NO) and heightened oxidative stress, causing vasoconstriction and increased peripheral resistance that promote hypertension [54, 55]. Furthermore, adipose tissue secretes pro-inflammatory cytokines such as leptin, tumour necrosis factor- α (TNF- α), and interleukin-6 (IL-6), which exacerbate oxidative stress and endothelial dysfunction, further driving the development of hypertension [40, 56]. Our data also show that treated-HTN subjects had significantly higher BMI compared to the naïve-HTN subjects ($P < 0.05$). Weight has been demonstrated as one of the side effects of some antihypertensive drug classes, particularly beta-blockers and thiazolidinediones (TZDs). TZDs cause insulin resistance and reduce metabolic rate, leading to weight gain [57, 58], while beta blockers cause weight gain by impairing lipid oxidation and promoting central adiposity [59, 60]. Also, studies have shown that some patients on antihypertensives may reduce physical activity or dietary vigilance under the assumption that medication alone suffices for risk control. This behavioural change can contribute to weight gain [61-63]. This association between obesity and hypertension underscores the potential role of weight management in

mitigating hypertensive risks. These findings align with recent studies demonstrating that higher BMI is a significant risk factor in the development and progression of hypertension in Port Harcourt, Nigeria [48, 64, 65].

Expectedly, both the untreated and treated hypertensive subjects showed significantly elevated systolic blood pressure, diastolic blood pressure and mean arterial pressure when compared to the control ($P < 0.05$). However, the pulse rate was significantly lower in both naïve-HTN and untreated-HTN compared to ($p < 0.05$), with no significant variation between the two hypertensive groups. It has been suggested that hypertension causes a reduction in the spontaneous baroreflex control of heart rate (HR-SBRS), making it less effective at adjusting heart rate in response to changes in arterial pressure in regulating blood pressure [66]. Also, neurohumoral mechanisms, including suppressed cardiac sympathetic activity and increased parasympathetic tone, reduce heart rate in hypertension and during baroreflex activation [66, 67]. The use of beta-blockers by hypertensive patients has been observed as a major cause of reduced pulse rate despite elevated blood pressure [68, 69].

Hypertension is associated with chronic inflammation, a key driver of endothelial dysfunction and arterial stiffness, which creates a bidirectional vicious cycle that exacerbates the progression of hypertension [20, 27]. The present study found significantly elevated CRP and TNF- α levels in both treated and untreated hypertensive subjects compared to normotensive controls ($p < 0.05$). Although treated hypertensive patients showed a significant reduction in CRP and TNF- α levels relative to untreated hypertensives, their values remained higher than baseline normotensive levels. Research indicates that hypertension and vascular diseases are fundamentally inflammatory conditions. Evidence suggests that inflammation plays a key role in triggering and advancing vascular disorders, such as endothelial dysfunction, atherosclerosis, vascular remodelling, and high blood pressure. This inflammatory process involves intricate interactions among immune cells, signalling molecules (cytokines, chemokines), adhesion proteins, and the renin-angiotensin-aldosterone system [29, 32]. C-reactive protein (CRP) is an acute-phase reactant predominantly produced by the liver hepatocytes. It serves as a key mediator of the inflammatory response, with levels rising within 6–8 hours following infection, tissue injury, or other inflammatory triggers, peaking at approximately 48 hours [30, 70]. The elevated CRP levels observed in both treated and untreated hypertensive patients may result from the effects of high blood pressure, which increases mechanical stress on arterial walls and promotes vascular inflammation, subsequently raising CRP, which is a systemic marker of inflammation [30, 71, 72]. CRP has been shown to reduce nitric oxide (NO) production by inhibiting the AMP-activated protein kinase (AMPK) and endothelial nitric oxide synthase (eNOS) phosphorylation pathways. This reduction in NO bioavailability contributes to endothelial dysfunction, vasoconstriction, and worsening of existing hyper-

tension [30, 73]. The observed reduction in CRP levels among treated hypertensive patients compared to untreated individuals suggests that effective blood pressure control attenuates the underlying inflammatory drive. Since CRP levels correlate positively with the severity of inflammation, this trend toward baseline values further supports its utility as a widely used, though nonspecific, biomarker in clinical practice [28-31, 71]. Our findings are consistent with prior studies demonstrating elevated CRP levels among hypertensives and a reduction in CRP levels following antihypertensive therapy [74-76]. Similarly, elevated TNF- α levels in both treated and untreated hypertensives further support hypertension's inflammatory and immunologic nature. Multiple hypertensive stimuli, like endothelial cell stretch, elevated sodium concentrations, sympathetic nervous system (SNS) activation, and angiotensin II, trigger the activation of innate immune cells such as monocytes, macrophages, dendritic cells, and natural killer cells. These immune cells initiate rapid, non-specific reactions to tissue injury. Once activated, they migrate to arterial walls, where they release pro-inflammatory cytokines like TNF- α that contribute to blood pressure elevation, vascular remodelling, and impaired nitric oxide (NO) bioavailability. This cascade promotes endothelial dysfunction, increases vascular contractility, and exacerbates hypertension, creating a self-perpetuating cycle of inflammation and vascular damage [77, 78]. Beyond its inflammatory functions, TNF- α also supports tissue repair, regeneration, and cellular proliferation. Under normal physiological conditions, circulating TNF- α levels are either undetectable or very low; however, their production and secretion increase significantly during inflammatory responses [33]. Elevated TNF- α levels have been observed in both human studies and experimental models of hypertension, where they contribute to inflammatory renal tissue injury. TNF- α promotes renal vasoconstriction and reduces glomerular filtration rate (GFR), further implicating its role in hypertensive kidney damage [28, 34, 79-81]. Our study demonstrates that TNF- α levels remained elevated compared to untreated hypertensives and normotensive controls, suggesting the persistence of low-grade inflammation despite therapy. Similar findings have been shown in elevated TNF- α levels in both prehypertensive and established hypertensive populations [82, 83] and a reduction in blood pressure with antihypertensive or treatment with TNF- α inhibitors [84, 85].

As discussed, hypertension induces immuno-inflammatory activation, promoting the release of pro-inflammatory cytokines like TNF- α , which in turn elevates CRP levels. This mechanism is driven by reactive oxygen species (ROS), leading to endothelial dysfunction and arterial stiffness and ageing [25, 38, 40]. The oxidative stress theory of disease posits that an excess of reactive oxygen species (ROS) disrupts cellular macromolecules like DNA, RNA, proteins, lipids, and carbohydrates, leading to cellular damage and death [86, 87]. As a protective mechanism, cellular antioxidant defence systems (GSH, GPx, CAT and SOD) work syn-

ergistically to maintain redox homeostasis by scavenging reactive oxygen species (ROS) and preventing their pathological accumulation. Our findings reveal that the cellular antioxidant defence systems (GSH, GPx, CAT and SOD) were significantly reduced among untreated and treated hypertensives compared to the normotensive controls. Glutathione (GSH) serves as the primary intracellular antioxidant, neutralising reactive oxygen species (ROS), regenerating other antioxidants such as vitamins C and E, and preserving cellular redox balance. In hypertension, GSH depletion exacerbates oxidative stress, leading to the depletion of nitric oxide, dysregulation of vascular smooth muscle and the activation and release of pro-inflammatory (TNF- α , IL-6), which sustains vascular inflammation and further elevates blood pressure [86, 88, 89]. Our findings demonstrated elevated glutathione (GSH) levels in treated hypertensive patients compared to both untreated hypertensive controls and normotensive controls. This aligns with prior studies reporting increased GSH levels in treated hypertension, likely attributable to enhanced antioxidant capacity mediated by antihypertensive therapy [88, 89]. Glutathione Peroxidase (GPx) catalyses the reduction of hydrogen peroxide and lipid peroxides using GSH as a substrate, thus preventing ROS accumulation. Depleted levels of GPx, as observed in hypertension, reduce this ability to detoxify hydrogen peroxide, promoting oxidative damage. Lower GPx activity enhances angiotensin II-induced endothelial dysfunction and impairs vascular relaxation, promotes vascular fibrosis and stiffness, worsening the hypertension [43, 88]. Catalase (CAT) is a critical antioxidant enzyme that detoxifies hydrogen peroxide (H_2O_2) into water and oxygen. Our findings reveal significantly reduced CAT activity in both treated and untreated hypertensive subjects compared to normotensive controls, indicating systemic impairment of hydrogen peroxide clearance. This catalase deficiency promotes pathological accumulation (H_2O_2), which directly contributes to oxidative stress-mediated endothelial dysfunction, exacerbates vascular inflammation and remodelling, and further perpetuates hypertensive pathophysiology [43, 90]. It has been shown that catalase depletion precedes hypertension onset, suggesting that CAT dysfunction may be both a biomarker and pathogenic contributor to disease development [86]. Notably, the persistence of CAT depletion in treated hypertensives shows the incomplete restoration of redox balance by current antihypertensive therapies. Superoxide dismutase (SOD) catalyses the dismutation of superoxide radicals ($O_2^{\cdot -}$) into hydrogen peroxide (H_2O_2), which is subsequently detoxified by GPx and CAT. In our present study, both treated and untreated hypertensive subjects had diminished SOD activity, which could have resulted from persistent $O_2^{\cdot -}$ accumulation, leading to direct nitric oxide (NO) inactivation, impaired vasodilation and consequent vasoconstriction, oxidative stress-mediated vascular remodelling, and increased peripheral vascular resistance [43, 90]. Among all antioxidant enzymes evaluated in this study, superoxide dismutase (SOD) exhibited the most pronounced reduction in

activity (-47%), indicating that hypertension preferentially disrupts this critical first-line defence against oxidative stress. This finding suggests a systemic impairment of the antioxidant enzymatic cascade, with SOD dysfunction representing a central feature of hypertensive pathophysiology. The inability to normalise SOD activity in treated hypertensives suggests ongoing oxidative stress despite blood pressure control, and hence the need for targeted antioxidant therapies in hypertension management. Malondialdehyde (MDA) is a byproduct of lipid peroxidation, where reactive oxygen species (ROS) attack polyunsaturated fatty acids in cell membranes, producing MDA as a final product. MDA is recognised as a marker of oxidative stress, with elevated levels reflecting increased oxidative damage in various diseases and conditions [91, 92]. The elevated MDA levels observed in both treated and untreated hypertensive subjects compared to normotensive controls demonstrate significant lipid peroxidation and oxidative damage. This MDA accumulation directly contributes to structural and functional impairment of endothelial and vascular smooth muscle cells, disruption of vascular homeostasis through nitric oxide (NO) depletion, and increased peripheral vascular resistance [91, 92]. These pathological alterations establish a vicious cycle of endothelial dysfunction and hemodynamic stress, which reinforces hypertension progression. Though antihypertensive therapy significantly reduced MDA levels compared to untreated patients, values remained elevated relative to normotensive controls. This persistent lipid peroxidation suggests residual oxidative damage despite blood pressure control.

5. Conclusion

The current study demonstrates that hypertension is characterised by chronic immuno-inflammatory dysregulation mediated by reactive oxygen species (ROS), which drives endothelial dysfunction and arterial stiffness. The present study shows significantly elevated levels of CRP, TNF- α , and MDA, coupled with reduced activity of SOD, CAT, and GSH in both treated and untreated hypertensive groups. Notably, the persistence of these inflammatory and oxidative stress markers in treated patients suggests that conventional antihypertensive therapy alone is insufficient to fully restore redox balance or resolve chronic inflammation. These findings underscore the need for adjunct therapies such as antioxidant and immunomodulatory supplementation to improve vascular outcomes in hypertension. Furthermore, the measurable alterations in these biomarkers (CRP, TNF- α , MDA, SOD, CAT, and GSH) may serve as cost-effective, accessible tools for monitoring disease progression and predicting cardiovascular complications in Nigerian populations, where resource limitations often hinder advanced diagnostics.

Abbreviations

IL-6	Interleukin-6
TNF- α	Tumour Necrosis Factor-alpha
ROS	Reactive Oxygen Species
LMICs	Low and Middle-income Countries
ANOVA	Analysis of Variance
CKD	Chronic Kidney Disease
BMI	Body Mass Index
MDA	Malondialdehyde
GSH	Reduced Glutathione
GPx	Glutathione Peroxidase
SOD	Superoxide Dismutase
CAT	Catalase
IBM	International Business Machine
SPSS	Statistical Product and Service Solutions
LSD	Least Significant Difference
SD	Standard Deviation
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
MAP	Mean Arterial Pressure
HR-SBRS	Spontaneous Baroreflex Control of Heart Rate
AMPK	Adenosine Monophosphate-activated Protein Kinase
eNOS	Endothelial Nitric Oxide Synthase
SNS	Sympathetic Nervous System
GFR	glomerular Filtration Rate
H ₂ O ₂	Hydrogen Peroxide
O ₂ ⁻	Superoxide

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Conflicts of Interest

The authors declare no conflicts of interest.

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