Research Article

Influence of Oxidative Stress in Hypertension with or without Obesity and its Correlation with MMP-9 and TIMP-1 - A Hospital-Based Cross-Sectional Study.

Shahida Byadagi[1], Basavaraj Devaranavadagi[2], Shweta Devaranavadagi[3], Gurushantappa S Kadakol[4]

[1] Department of Biochemistry, Jagadguru Jayadeva Murugarajendra Medical College, Bapuji Educational Association, Davangere, Karnataka, India
[2]Department of Biochemistry, S N Medical College, Bagalkote, Karnataka, India
[3]Department of Anaesthesia, KLE Jagadguru Gangadhar Mahaswamigalu Moorsavirmath Medical College and Hospital, Hubli, KLE Academy of Higher Education & Research Deemed-to-be-University Belagavi, Karnataka, India
[4] School of Applied Science and Technology, Genetics Laboratory, BLDE (Deemed to be University), Vijayapura, Karnataka, India.

(Received: 24-05-2025 Revised: 20-08-2025 Accepted: 07-09-2025)

Corresponding Author: ***Gurushantappa S Kadakol*** Email: gs.kadakol@bldedu.ac.in

ABSTRACT

Introduction and Aim: Hypertension (HTN) is a public health issue frequently linked with obesity. Both are connected with blood vessel remodelling, oxidative stress, and the imbalance of the matrix metalloproteinases (MMPs) and their inhibitor (TIMPs). The present study aims to explore the relationship between the markers of oxidative stress and biomarkers of extracellular matrix remodelling, MMP-9 and TIMP-1, in obese and non-obese patients with and without hypertension.

Material and Methods: A cross-sectional hospital-based study was conducted in 106 subjects classified into four groups: obese hypertensive (OHTN), non-obese hypertensive (NOHTN), obese controls (OC), and non-obese controls (NOC). Anthropometric parameters, blood pressure, markers of oxidative stress—Malondialdehyde (MDA), reduced Glutathione (GSH), Nitric oxide (NO)—and serum levels of MMP-9 and TIMP-1 were measured. ELISA and standardised biochemical assays were employed. MMP-9 and oxidative markers correlations were statistically compared.

Results: OHTN patients exhibited significantly elevated levels of MMP-9, TIMP-1, and MDA, but decreased levels of GSH and NO compared with the control group ($p < 0.001$). The MMP-9/TIMP-1 ratio was significantly increased in the OHTN group, representing extracellular matrix remodelling. In addition, MMP-9 levels were significantly correlated with MDA ($r = 0.56$) and inversely correlated with NO ($r = -0.42$) and GSH ($r = -0.49$), reflecting a close correlation between oxidative stress and hypertension-related vascular remodelling.

Conclusion: The results of the current study indicate the crucial involvement of oxidative and nitrosative stress in the vascular system dysfunction and extracellular matrix remodelling in hypertensive patients, especially in obese patients. Increased MMP-9 and TIMP-1 levels, as well as markers of oxidative stress, could represent potential biomarkers of early diagnosis and treatment of hypertension. Therapies targeting oxidative stress and the MMP/TIMP pathway could open new therapeutic perspectives.

Keywords: Obesity, Hypertension, Oxidative Stress, Nitric Oxide, Malondialdehyde, Glutathione, MMP-9, TIMP-1

1. INTRODUCTION

Hypertension (HTN) is a major and common worldwide health issue. According to the Joint National Committee-8 (JNC 8) guidelines, it is recognised when the diastolic blood pressure (DBP) is 90 mm Hg or higher, or when the systolic blood pressure (SBP) is 140 mm Hg or higher. Often presenting without symptoms,

HTN is frequently referred to as the "silent killer" because of its capacity to cause serious complications in the cardiovascular, renal, and cerebrovascular systems if not adequately managed. In India, approximately 29.8% of the population is affected by HTN, with its prevalence higher in urban areas at 33%. But only around one-third of people with hypertension can effectively regulate their blood pressure, which suggests that management and therapy are seriously lacking [1]. The increasing prevalence of fat exacerbates the risks of hypertension. Vascular dysfunction is closely associated with obesity, and it not only makes controlling blood pressure more difficult but also hastens the onset of several end-stage renal failure, stroke, and coronary artery disease, which are examples of cardiac conditions. Furthermore, vascular anomalies caused by obesity are often resistant to conventional antihypertensive treatments [2, 3].

The involvement of matrix metalloproteinases (MMPs), particularly MMP-9, is crucial in degrading the extracellular matrix (ECM), contributing to vascular remodelling and dysfunction observed in hypertension. The activity of MMP-9 is modulated by tissue inhibitors of metalloproteinases (TIMPs), such as TIMP-1, which maintain vascular integrity. An imbalance between MMPs and TIMPs has been associated with numerous cardiovascular disorders, including HTN. Although previous research has investigated the roles of MMP-9 and TIMP-1 in hypertension, their interplay with oxidative stress markers remains insufficiently studied, particularly in Indian populations [4,5]. Vascular damage in hypertension is primarily caused by the hallmarks of oxidative stress, including an excess of reactive oxygen species (ROS) and a compromised antioxidant defence mechanism. It is commonly known that biomarkers like Nitric oxide (NO), Glutathione (GSH), and Malondialdehyde (MDA) participate in the aetiology of hypertension. Nevertheless, the connection among oxidative stress, MMP-9, TIMP-1, and anthropometric parameters in hypertensive individuals, particularly those with obesity, is poorly understood. Furthermore, a dearth of research investigating these biomarkers in conjunction with oxidative stress within Indian cohorts [6, 7].

Studies suggest elevated MMP-9 levels are linked to blood pressure and endothelial dysfunction. At the same time, oxidative stress biomarkers such as MDA and NO are closely associated with vascular remodelling and hypertension progression [8]. However, integrative studies investigating how MMP-9, TIMP-1, oxidative stress, and anthropometric parameters are interrelated in hypertensive individuals, both obese and non-obese, are still limited in Indian populations. This study was conducted in Northern Karnataka, India, to address these research gaps. It evaluates serum levels of MMP-9 and TIMP-1 while examining their correlations with oxidative stress markers and anthropometric parameters in hypertensive and non-hypertensive individuals with and without obesity. The findings aim to offer novel insights into the function that oxidative stress performs in the development of hypertension, especially in obesity. Additionally, this research may pave the way for developing targeted therapeutic approaches to improve hypertension management.

2. Materials and Methods

Study Design

In Vijayapura, Karnataka, India, at the Shri B. M. Patil Medical College, Hospital, and Research Centre of BLDE University, a cross-sectional hospital-based study was carried out. The research explored the association between hypertension, obesity, and biomarkers MMP-9, also known as matrix metalloproteinase, and TIMP-1, as a tissue inhibitor of metalloproteinases [4]. The institution's ethical committee provided ethical approval prior to the start of the research (clearance number: IEC/BLDE/2022/26). Every participant provided written informed consent. The Joint National Committee (JNC 8) guidelines were followed throughout the study.

Study Population

A total of **106 participants** were selected and categorised into four groups:

- Obese Hypertensive (OHTN, n = 27)
- Non-Obese Hypertensive (NOHTN, n = 26)

- Obese Control (OC, n = 26)
- Non-Obese Control (NOC, n = 27)

Both male and female participants aged 51 ± 14 years were included.

Inclusion Criteria

- Individuals newly diagnosed with hypertension (SBP≥ 140 mmHg and DBP ≥90 mmHg). [1]
- Normotensive individuals (SBP ≤120 mmHg and DBP ≤80 mmHg) formed the control group.

Exclusion Criteria

Patients diagnosed with renal failure, stroke, diabetes, liver diseases, or gout. Individuals unwilling to provide blood samples. Subjects with thyroid disorders, smokers, alcohol consumers, pregnant women, and menstruating females [4].

Note on Grouping and Sample Size Justification: Notes on Grouping and Sample Size Justification: 106 participants were registered to meet the goal sample size of about 25 people per group. Strict inclusion & exclusion criteria resulted in smaller final group sizes.

OHTN (n=27), NOHTN (n=26), OC (n=26), and NOC (n=27). The technique incorporates four distinct groups to evaluate the impact of obesity and hypertension on biomarkers. Including obese and non-obese control groups enables baseline comparisons for each phenotype, verifying that observed differences are due to the disease rather than body composition alone. Based on a power analysis of the pilot data, the sample size was determined to be 100 people (25 in each group).

A power analysis of the pilot data revealed that 100 participants (25 in each group) would be enough to detect a medium effect size (Cohen's d = 0.5) at 80% power and 5% significance level.

Data Collection and Measurements: Anthropometric and Hemodynamic Measurements

Anthropometric measurements were taken of participants when they were dressed lightly and without shoes. A calibrated digital weighing scale determined the weight to the nearest 0.1 kg. The Body Mass Index (BMI) was determined by dividing weight (kg) by height (m^2) using a stadiometer that was accurate to 0.1 cm. With a non-stretchable measuring tape, the waist circumference (WC) Measurement was taken halfway between the top of the iliac crest and the final visible rib. The hip circumference (HC) was measured from the broadest part of the buttocks. WC/HC was used to determine the Waist-to-Hip Ratio (WHR), and WC/height was used to get the Waist-to-Height Ratio (WHtR).[9] After at least five minutes of relaxation, the subject was seated and their blood pressure was taken using a calibrated mercury sphygmomanometer (Diamond Deluxe BP device, Pune, India). The average of two measurements that were collected two minutes apart was noted. Arm circumference was utilised to determine the proper cuff size. Diastolic and systolic blood pressure have been taken to the nearest 2 mmHg.

Blood Collection and Sample Processing:

Participants were given thorough research information and were asked for their consent before collecting samples. Under aseptic circumstances, venepuncture took 5 mL of fasting blood from a vein. The samples were centrifuged at 3000 rpm for 10 minutes to extract serum, which was then transferred to polyethene tubes and stored at -80°C until analysis. To make sure accuracy and repeatability, all samples were immediately brought to the laboratory and evaluated within 24 hours.

Biochemical Analysis

1. Extracellular matrix biomarkers:

MMP-9 and TIMP-1 Levels: Utilising enzyme-linked immunosorbent assay (ELISA) kits, serum concentrations were determined (E-lab-science, Human MMP-9 and TIMP-1) following the manufacturer's protocol [10].

2. Oxidative Stress Biomarkers:

Malondialdehyde (MDA): Buege and Aust (1978) described the thiobarbituric acid reactive substances (TBARS) technique for estimating serum and tissue malondialdehyde (MDA), a marker of lipid peroxidation. The test is based on the reaction of MDA, a subsequent product of polyunsaturated fatty acid peroxidation, with thiobarbituric acid (TBA) in acidic conditions and at high temperature, resulting in a pink chromogen detectable at 535 nm. To experiment, 100 µl of serum was diluted with 500 µl of distilled water and combined with 1 ml of TCA-TBA-HCl reagent (15% trichloroacetic acid,

0.375% thiobarbituric acid in 0.25 N hydrochloric acid). The mixture was incubated in a boiling water bath for 15 minutes, then cooled to room temperature and centrifuged. The absorbance of the supernatant was measured at 535 nm with a UV-visible spectrophotometer (Shimadzu, UV-1800).10]

Glutathione(GSH):

The reduced glutathione in whole blood was calculated using the Beutler et al. (1963) technique. The test is based on the reduction of 5, 5'-dithiobis (2-nitrobenzoic acid) (DTNB) by thiol groups to create a yellow-colored 5-thio-2-nitrobenzoic acid (TNB), which is detected at 412 nm. A solution including EDTA, NaCl, and metaphosphoric acid was employed to precipitate whole blood samples. After centrifugation, the supernatant was mixed with phosphate buffer and DTNB reagent. The absorbance was measured at 412 nm in 5 minutes. A standard curve was built using known levels of reduced glutathione (0.5 mg/mL stock solution), and GSH values in test samples were expressed as mg/dL of whole blood. 11]

Total Nitric Oxide (NO):

Total nitrite and nitrate (NOx) levels, which are stable nitric oxide metabolites, were determined using the Griess reaction and the cadmium reduction technique (Green et al., 1982; Cortas and Wakid, 1990; Moshage et al., 1995). Serum samples were initially deproteinized using zinc sulphate and sodium hydroxide. Nitrate was converted to nitrite using activated cadmium granules covered with copper sulphate in a glycine-NaOH buffer. The resultant nitrite was diazotised with sulphanilamide and combined with N-(1-naphthyl) ethylenediamine to produce a stable azo dye that was detected at 540 nm. Concentrations were calculated using a sodium nitrite standard curve, with findings in µmol/L.[12]

Statistical Analysis

Microsoft Excel was utilised to enter the data. The SPSS program (version 20) was used to analyse the data.

- The Shapiro-Wilk and Kolmogorov-Smirnov tests were used to determine if the continuous data were normal. As applicable, descriptive statistics were provided, such as the mean, standard deviation, counts, and percentages.

The following statistical tests were applied:

- For continuously distributed data with a normal distribution, Pearson's correlation was applied.
- When dealing with variables that were not normally distributed, Spearman's rho correlation was utilised.

Numerous groups were compared using analysis of variance (ANOVA)

- The Kruskal-Wallis H test was utilised for non-parametric data analysis.
- When overall significance ($p < 0.05$) was discovered, post-hoc pairwise comparisons were done using Tukey's HSD test (for ANOVA) or Dunn's test (for Kruskal-Wallis).
- A p-value of less than 0.05 was considered statistically significant. It was a two-tailed test.

3. Result:

Factors related to demographics and anthropometry

Demographic and anthropometric comparisons between the four study groups are summarised in Table -1.

Table 1: Anthropometric and Hemodynamic Parameters across Study Groups

Parameter	OHTN (n=23)	NOHTN (n=23)	OC (n=23)	NOC (n=23)	p-value
Age (years)	51.63 ± 9.62	56.22 ± 10.08	47.74 ± 10.35	46.93 ± 8.04	0.073 (NS)
BMI (kg/m²)	29.48 ± 3.59	21.10 ± 2.11	29.40 ± 3.20	21.09 ± 2.27	<0.001**
Waist Circumference (m)	1.06 ± 0.19	0.87 ± 0.1	0.99 ± 0.07	0.86 ± 0.19	<0.001**
Hip Circumference (m)	1.13 ± 0.196	0.96 ± 0.076	1.07 ± 0.09	0.93 ± 0.06	0.021*
Waist-to-Hip Ratio	0.91 ± 0.209	0.90 ± 0.06	0.86 ± 0.106	0.87 ± 0.07	0.038*
Systolic BP (mmHg)	144.6 ± 5.67	145.35 ± 6.02	113.04 ± 4.705	114.33 ± 5.040	<0.001**
Diastolic BP (mmHg)	91.5 ± 3.83	92.09 ± 3.41	82.61 ± 6.88	78.33 ± 6.47	<0.001**

Abbreviations: The study uses OHTN to denote Obese Hypertensive individuals and NOHTN for Non-Obese Hypertensive individuals, while OC represents Obese Control subjects, NOC stands for Non-Obese Control participants, BMI indicates Body Mass Index, and BP stands for Blood Pressure.

Note: Data are provided as mean ± SD for normally distributed variables and median (IQR) for non-normal variables. P-values indicate comparisons between the four research groups using one-way ANOVA (for normal data) or the Kruskal-Wallis test (for non-normal data). Tukey's HSD was used to do post-hoc pairwise comparisons (for ANOVA) or Dunn's test (for Kruskal-Wallis) when overall $p < 0.05$. The significance thresholds are as follows: $p < 0.05$ (*) statistically significant, $p < 0.01$ (**) highly significant, $p < 0.001$ (***) very highly significant, and $p > 0.05$ (ns).

The mean age across groups was 51 ± 14 years. The OHTN group demonstrated a markedly higher body mass index (BMI) compared to the NOHTN group ($p < 0.001$). Both hypertensive groups showed significantly higher systolic blood pressure (SBP) and diastolic blood pressure (DBP) values than the control groups.

Anthropometric and Hemodynamic Parameters:

The OHTN group had a significantly higher BMI than the NOHTN group ($p < 0.001$). Both hypertension groups (OHTN and NOHTN) exhibited higher systolic and diastolic blood pressures than the control groups, with the OHTN group seeing the most significant mean increase ($p < 0.001$).

Oxidative Stress Markers

Table 2 demonstrates that hypertensive groups had considerably higher MDA values, indicating increased lipid peroxidation. Lower GSH levels were found in these groups, indicating poor antioxidant defence, with the lowest level in the OHTN group. NO levels were dramatically lowered in hypertension patients, particularly in the NOHTN group, indicating severe endothelial dysfunction.

Table 2: Oxidative Stress Markers across StudyGroups

Parameter	OHTN (n=23)	NOHTN (n=23)	OC (n=23)	NOC (n=23)	p-value
MDA (µmol/L)	3.99 ± 1.30	4.13 ± 1.01	2.32 ± 0.75	2.305 ± 0.56	<0.001***
GSH (mg/dL)	24.30 ± 9.12	26.63 ± 10.19	29.33 ± 9.43	24.67 ± 6.62	<0.001***
NO (µmol/L)	33.23 ± 9.98	32.72 ± 11.71	44.71 ± 10.22	39.30 ± 9.52	<0.001***

Note: Data are provided as mean ± SD for normally distributed variables & median (IQR) for non-normal variables. P-values indicate comparisons between the four research groups using one-way ANOVA (for normal data) or the Kruskal-Wallis test (for non-normal data). (For ANOVA) or Dunn's test (for Kruskal-Wallis) when overall $p < 0.05$. The significance thresholds are as follows: $p < 0.05$ (*), $p < 0.01$ (**), $p < 0.001$ (***), $p < 0.001$ (***), & $p > 0.05$ (ns).

Levels of TIMP-1 and MMP-9

Table 3 demonstrates that OHTN has the most significant MMP-9 expression, followed by NOHTN. The control groups showed considerably lower levels ($p < 0.001$). TIMP-1 concentrations followed a similar pattern, with higher levels in hypertensive groups, particularly OHTN. As measured by the MMP-9/TIMP-1 ratio, the extracellular matrix remodelling imbalance was highest in OHTN & lowest in NOHTN.

Table 3: MMP-9 & TIMP-1 Levels across Study Groups

Parameter	OHTN (n=23)	NOHTN (n=23)	OC (n=23)	NOC (n=23)	p-value
MMP-9 (ng/mL)	977.66 ± 308.32	866.79 ± 299.46	820 ± 280.76	725.03 ± 257.94	< 0.001***
TIMP-1 (ng/mL)	1185.07 ± 366.73	1236 ± 346.37	1138.96 ± 227.61	985.72 ± 227.719	< 0.001***
MMP-9/TIMP-1 Ratio	0.877 ± 0.35	0.745 ± 0.35	0.71 ± 0.19	0.75 ± 0.28	<0.001***

Note: Data are provided as mean ± SD for normally distributed variables & median (IQR) for non-normal variables. P-values indicate comparisons between the four research groups using one-way ANOVA (for normal data) or the Kruskal-Wallis test (for non-normal data). Post-hoc pairwise comparisons were done using Tukey's HSD. (For ANOVA) or Dunn's test (for Kruskal-Wallis) when overall $p < 0.05$. The significance thresholds are as follows: $p < 0.05$ (*) statistically significant, $p < 0.01$ (**) highly significant, $p < 0.001$ (***) very highly significant, and $p > 0.05$ (ns) not significant.

Correlation between Extracellular Matrix Biomarkers and Oxidative Stress Markers

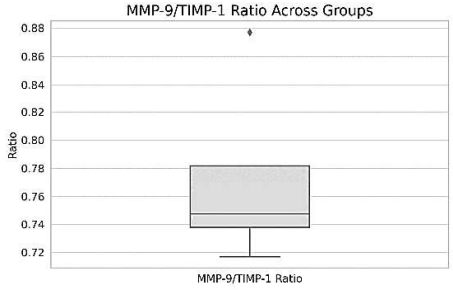

Figure 1: MMP-9/TIMP-1 Ratio across Groups

Correlation between MMP-9 and Oxidative Stress Markers:

Table 4 demonstrates a substantial association between MMP-9 and oxidative stress indicators, including a positive correlation with MDA ($r = 0.56$, $p < 0.05$) and negative correlations with NO ($r = -0.42$, $p < 0.05$) and GSH ($r = -0.49$, $p < 0.05$). This shows that greater MMP-9 levels are associated with increased oxidative stress and endothelial dysfunction.

Table 4: Correlation Analysis between MMP-9 and Oxidative Stress Markers

Correlation	Pearson's r	p-value	Interpretation
MMP-9 vs MDA	0.56	<0.05*	A positive correlation (higher MMP-9 linked to increased lipid peroxidation)
MMP-9 vs NO	-0.42	<0.05*	Negative correlation (higher MMP-9 associated with endothelial dysfunction)
MMP-9 vs GSH	-0.49	<0.05*	Negative correlation (higher oxidative stress reduces GSH)

Note: Data are provided as mean ± SD for normally distributed variables and median (IQR) for non-normal variables. P-values indicate comparisons between the four research groups using one-way ANOVA (for normal data) or the Kruskal-Wallis test (for non-normal data). Post-hoc comparisons among pairs were done using Tukey's HSD. (For ANOVA) or Dunn's test (for Kruskal-Wallis) when overall $p < 0.05$. The significance thresholds are as follows: $p < 0.05$ (*) statistically significant, $p < 0.01$ (**) highly significant, $p < 0.001$ (***) very highly significant, and $p > 0.05$ (ns).

TIMP-1 correlations:

Table 5 displays modest and non-significant relationships between TIMP-1 and oxidative stress markers. TIMP-1 levels, unlike MMP-9, were not significantly affected by oxidative stress in this research sample.

Table 5. Correlation Analysis between TIMP-1 and Oxidative Stress Markers

Correlation	Pearson's r	p-value	Interpretation
TIMP-1 vs MDA	0.072	>0.05 (NS)	Weak positive, not significant
TIMP-1 vs GSH	–0.147	>0.05 (NS)	Weak negative, not significant
TIMP-1 vs NO	0.066	>0.05 (NS)	Weak positive, not significant

Note: Data are provided as mean ± SD for normally distributed variables and median (IQR) for non-normal variables. P-values indicate comparisons between the four research groups using one-way ANOVA (for normal data) or the Kruskal-Wallis test (for non-normal data). Post-hoc comparisons among pairs were done using Tukey's HSD. (For ANOVA) or Dunn's test (for Kruskal-Wallis) when overall $p < 0.05$. The significance thresholds are as follows: $p < 0.05$ (*) statistically significant, $p < 0.01$ (**) highly significant, $p < 0.001$ (***) very highly significant, and $p > 0.05$ (ns).

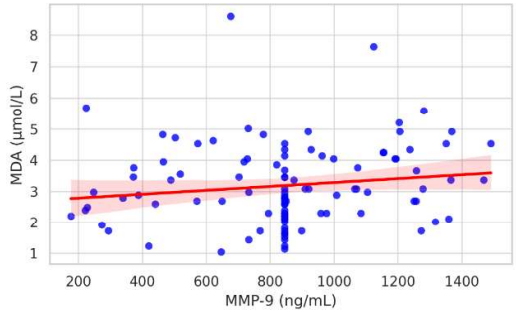

Figure 2: Correlation between MMP-9 and MDA

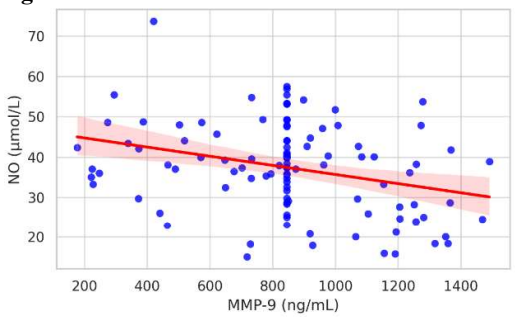

Figure 3: Correlation between MMP-9 and NO

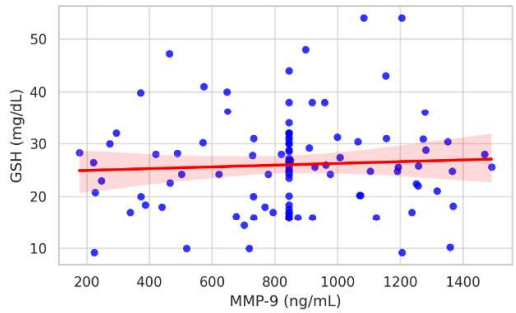

Figure 4: Correlation between MMP-9 and GSH

4. Discussion

This cross-sectional research at a hospital investigated the interaction among hypertension, obesity, oxidative stress, and extracellular matrix (ECM) remodelling markers—namely, MMP-9 and TIMP-1. Our findings indicate that individuals with hypertension had higher levels of MMP-9 and TIMP-1, particularly with remarkable elevation among the obese. Like

previous studies, our findings show that MMP-9 has a role in vascular remodelling via ECM protein breakdown and vascular tone modulation, leading to arterial stiffness and the development of hypertension [4, 13].

Recent research also confirms these correlations. For example, a research study demonstrated that the MMP-9 protein concentrations are considerably higher among patients with hypertensive crises, indicating its possible use as a biomarker for acute blood pressure rise [4]. Moreover, evidence shows that obesity promotes MMP-9 expression, indicative of a synergistic influence on cardiovascular risk among hypertensive patients [13].

TIMP-1, being a natural inhibitor of MMPs, also demonstrated elevated levels in our obese and hypertensive groups. This is likely reflective of a compensatory response to counteract increased MMP activity. However, dysregulation between MMPs and TIMPs can contribute to pathological vascular remodelling and organ damage. Consistent with this, a review drew attention to the pathogenic role of MMP/TIMP dysregulation in organ damage caused by hypertension [8].

Our study also demonstrated increased oxidative stress in hypertensive and obese subjects, shown by decreased amounts of GSH and NO and rising levels of MDA. One indicator of lipid peroxidation is MDA, and GSH is an important intracellular antioxidant. Low NO levels reflect endothelial dysfunction, a characteristic of hypertension. Our observations are based on recent research emphasising the role that oxidative stress plays in the aetiology of vascular dysfunction and hypertension [7, 12].

In this study, MMP-9 showed close correlations with oxidative stress markers, negative correlations with GSH and NO, and positive correlations with MDA. The findings indicate that enhanced MMP-9 levels could be related to endothelial dysfunction, lower antioxidant defence, and enhanced lipid peroxidation in hypertensive patients. The correlations confirm that oxidative stress may affect MMP-9 activity, resulting in ECM remodelling.

In contrast, only weak and statistically non-significant associations were observed with TIMP-1 for MDA, GSH, and NO, indicating that TIMP-1 levels within this cohort were less likely to be directly affected by oxidative stress status. Despite this, its increased status within hypertensive groups could represent a compensatory effect in response to enhanced MMP-9 activity in preference to an action of oxidative stress. This trend is consistent with the earlier literature that suggests that although MMP-9 is very sensitive to oxidative shifts, TIMP-1 regulation can be through other metabolic or inflammatory pathways [7, 12]

Notably, our research design contributes new information by correlating MMP-9, TIMP-1, and significant markers of oxidative stress (MDA, GSH, NO) in hypertensive-obese versus hypertensive-no obese patients, an integrated analysis not commonly described in the previous literature. Unlike earlier research that considered individual parameters or particular comorbidities, our stratified analysis identifies how obesity enhances oxidative stress and ECM remodelling in hypertensive patients. This detailed evaluation in an Indian hospital-based population presents region-specific data and implies that combined biomarker profiling can improve the clinic's risk stratification and early diagnosis [7, 12].

Deregulation of the MMP/TIMP pathway in the hypertensive, particularly obese, patient points toward new therapeutic strategies. Therapies that block MMP action or re-establish TIMP-1 balance may prevent pathological extracellular matrix remodelling, decrease vascular stiffness, and improve endothelial function. In addition, drugs reducing oxidative stress or inflammation may secondarily correct MMP/TIMP function and represent exciting alternatives for controlling hypertension and cardiovascular disease.

Strengths

- This research is new in that it simultaneously assesses MMP-9, TIMP-1, and oxidative stress indices (MDA, GSH, NO) in stratified hypertensive patients with and without obesity, presenting a singular view of the interrelation between ECM remodelling and redox disorder in different hypertensive phenotypes. [2-8, 10-12]

- Comprehensive analysis of oxidative stress markers (MDA, GSH, and NO) and ECM remodelling markers (MMP-9, TIMP-1) gives a complete picture of the pathophysiological processes of hypertension.
- Measurement of MMP-9 and TIMP-1 inclusion provides information about ECM remodelling, one of the main features of hypertensive vascular pathology.
- Obesity status stratification makes it possible to separate the effect of obesity on vascular biomarkers in patients with hypertension.
- Application of standardised ELISA protocols and cross-validated biochemical assays increases the consistency and reproducibility of biomarker measurements.

Limitations:

- The study used a broad age range (mean 51 ± 14 years) but age-matched groups to reduce bias. Biochemical correlations between markers of oxidative and ECM-related states depend more upon metabolic/inflammatory status, which is characterised by specific markers or conditions, than age.
- The cross-sectional design only captures an instant of oxidative/nitrosative stress in hypertension and does not provide causality; this underscores the need for longitudinal and intervention studies, which present an exciting opportunity for future research in the field.
- The study's single-centre design and small sample size (n=106) may limit generalizability, yet significant patterns and correlations were observed.
- An experimental design of laboratory-based type was impossible because of limited resources and clinical environment; however, future mechanistic validation of in vitro and animal studies, which will involve [specific methods or techniques], is on schedule.
- The study period, stringent inclusion and exclusion criteria, and recruitment of eligible patients decided the sample size.

5. Conclusion

This research indicates that high blood MMP-9 levels, raised oxidative stress indices, and lowered antioxidant defences could be involved in the vascular remodelling and induction of hypertension. TIMP-1 was also raised with MMP-9 as a compensatory response to prevent excessive degradation of the ECM. The increase in TIMP-1 could also advance collagen formation and vascular fibrosis through inhibition of MMP-9. Notably, we had high positive correlation between MMP-9 and MDA and high negative correlations with GSH and NO, highlighting the intimate relationship between oxidative stress and ECM remodelling. While TIMP-1 had weak and non-significant correlations with markers of oxidative stress, its elevated levels in patients with hypertension suggest a possible role in the pathophysiology of the disease. These findings collectively elucidate the interactive relationship between oxidative stress and MMP/TIMP imbalance in vascular dysfunction and propose putative avenues for the early diagnosis and therapeutic intervention of hypertensive patients, especially those who are obese.

Acknowledgement:

The Department of Biochemistry and the Management of BLDE (Deemed to be University) Shri B.M. Patil Medical College and Hospital, Vijayapura, are deeply appreciated by the author for their assistance and direction during the study project. Additionally, the author would like to thank all participants and laboratory personnel for their help with data collection and processing

Conflict of Interest:

The authors and contributors of this article state that they have no conflicts of interest.

Funding Information

No funding was obtained for this research project.

Ethical Information

The institution's ethical committee of BLDE (Deemed University), Shri B.M. Patil Medical College and Hospital in Vijayapura, granted

Ethical permission before the research began (clearance number: IEC/BLDE/2022/26). Every participant provided Written informed consent. All techniques followed the Declaration of Helsinki. The study met the Joint National Committee (JNC 8) guidelines

REFERENCES:

1. Peng W, Li K, Yan AF, Shi Z, Zhang J, Cheskin LJ, *et al.* Prevalence, Management, and Associated Factors of Obesity, Hypertension, and Diabetes in the Tibetan Population Compared with China. *Int J Environ Res Public Health.* 2022;19(14):8787.
2. Boumiza S, Chahed K, Tabka Z, Jacob MP, Norel X, Ozen G. MMPs and TIMPs levels are correlated with anthropometric parameters, blood pressure, and endothelial function in obesity. *Sci Rep*. 2021;11:12345.
3. Samara TD, Wartono M, Kosasih A, Alvina A. Association of body mass index with matrix metalloproteinase-9, tissue inhibitor of metalloproteinase-1, and interleukin-6 based on blood pressure. *Iran J Basic Med Sci.* 2021;24:678–85.
4. Cabral-Pacheco GA, Garza-Veloz I, Castruita-De la Rosa C, Ramirez-Acuña JM, Perez-Romero BA, Guerrero-Rodriguez JF, *et al.* The roles of matrix metalloproteinases and their inhibitors in human diseases. *Int J Mol Sci*. 2020;21(24):9739.
5. Bisogni V, Cerasari A, Pucci G, Vaudo G. Matrix metalloproteinases and hypertension-mediated organ damage: current insights. *Hypertens Res*. 2021;44:1234–45.
6. Wang C, Luo Z, Carter G, Wellstein A, Jose PA, Tomlinson J, *et al.* NRF2 prevents hypertension, increased ADMA, microvascular oxidative stress, and dysfunction in mice with two weeks of ANG II infusion. *Am J Physiol Heart Circ Physiol.* 2021;320(3):H1234–45.
7. Agrahari P, Jain A, Jain J, *et al.* Oxidative Stress and Antioxidant Dysfunction in Hypertension: Mechanisms and Clinical Insights. *Front Health Inform.* 2024;13(5):1725.
8. Rodrigues SF, Granger DN. Plasma levels of matrix metalloproteinase-9 are elevated in individuals with hypertensive crisis. *Clin Exp Hypertens.* 2020;42(3):248–52.
9. Shrestha R, Upadhyay SK, Khatri B, Bhattarai JR, Kayastha M, Upadhyay MP. BMI, waist-to-height ratio and waist circumference as a screening tool for hypertension in hospital outpatients: a cross-sectional, non-inferiority study. *BMC Cardiovasc Disord.* 2021;21(1):120.
10. D'souza D, Subhas BG, Shetty SR, Balan P. Estimation of serum malondialdehyde in potentially malignant disorders and post-antioxidant treated patients: a biochemical study. *Contemp Clin Dent.* 2012;3(4):448–51.
11. Beutler E, Duron O, Kelly BM. Improved method for the determination of blood glutathione. *J Lab Clin Med.* 1963;61:882–8.
12. YB M, YM H. Serum nitric oxide and malondialdehyde in a hypertensive population in Sokoto, Nigeria. *Int J Res Med Sci.* 2018;6(12):3929–34.
13. Palei ACT, Sandrim VC, Cavalli RC, Tanus-Santos JE. Comparative assessment of matrix metalloproteinase (MMP)-2 and MMP-9, and their inhibitors, tissue inhibitors of metalloproteinase (TIMP)-1 and TIMP-2 in preeclampsia and gestational hypertension. *Clin Biochem.* 2021;88:50–5.
14. Lam BCC, Koh GCH, Chen C, Wong MTK, Fallows SJ. Comparison of body mass index (BMI), body adiposity index (BAI), waist circumference (WC), waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) as predictors of cardiovascular disease risk factors in an adult population in Singapore. *PLoS One.* 2015;10(4):e0122985.