RESEARCH PAPER

Target Organ Damage in Young Hypertensive Females With and Without Metabolic Syndrome: A Comprehensive Cross-Sectional Study

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ABSTRACT

Background: Arterial hypertension is frequently accompanied by a cluster of metabolic abnormalities—specifically abdominal obesity, dyslipidemia, elevated plasma glucose, and insulin resistance—collectively termed the metabolic syndrome (MS). The presence of MS significantly increases the risk of subsequent cardiovascular events. This study aimed to comprehensively evaluate and compare markers of preclinical target organ damage, namely albuminuria, hypertensive retinopathy, and left ventricular hypertrophy (LVH), in a cohort of young hypertensive female patients with and without MS. **Methods:** An observational comparative cross-sectional study was conducted among 400 young female patients (aged 18–40 years) with a 5–10 year history of essential hypertension. MS was identified using the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) criteria. Target organ damage was evaluated utilizing echocardiography for LVH, fundoscopy for retinopathy, and urine spot testing for albuminuria.**Results:** The study cohort comprised 170 patients with MS and 230 patients without MS. Echocardiographic evidence of LVH was significantly higher in the MS group (60.6%) compared to the non-MS group (33.0%) (p=0.0005). Albuminuria was detected in 61.8% of patients with MS versus 31.3% of those without MS (p=0.0005). Furthermore, hypertensive retinopathy was significantly more prevalent in the MS cohort (68.2%) compared to the non-MS cohort (23.9%) (p=0.0005). Significant elevations in waist circumference, triglycerides, fasting plasma glucose, and blood pressure were also recorded in the MS group, alongside notable reductions in high-density lipoprotein (HDL) levels.**Conclusion:** Metabolic syndrome profoundly amplifies hypertension-related cardiac, renal, and retinal structural changes, extending its impact well beyond the contributions of its individual components. Rigorous follow-up and timely, aggressive therapeutic interventions are critical to halt the progression of extensive target organ damage in this vulnerable demographic.

Keywords: Metabolic Syndrome; Essential Hypertension; Target Organ Damage; Left Ventricular Hypertrophy (LVH); Albuminuria; Hypertensive Retinopathy; Endothelial Dysfunction; Cardiovascular Risk.

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1. INTRODUCTION

Arterial hypertension rarely exists in clinical isolation; it is frequently associated with an array of metabolic

abnormalities, including abdominal obesity, dyslipidemia, elevated plasma glucose, and insulin resistance. These clustering features constitute the metabolic syndrome (MS), a condition historically identified as syndrome X, the deadly quartet, or the insulin resistance syndrome.

Various organizations, including the World Health Organization (WHO), the American Association of Clinical Endocrinologists, and the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III), have proposed diagnostic criteria for MS. Among these, the NCEP-ATPIII criteria remain the simplest and most practical for clinical application. According to this definition, MS is diagnosed when three or more specific metabolic abnormalities—impaired glucose metabolism, elevated blood pressure, hypertriglyceridemia, low HDL cholesterol, and central obesity—are present in a single individual.

The adverse prognostic implications of MS, as defined by NCEP-ATPIII, have been widely documented across diverse populations, including in men and women without a prior history of cardiovascular disease, as well as in established hypertensive cohorts. It is widely posited that the amplified cardiovascular risk conferred by MS in hypertensive subjects is largely mediated through accelerated, preclinical end-organ damage.

Our study was specifically designed to evaluate the precise influence of MS—defined by NCEP-ATPIII criteria—on cardiac, renal, and retinal markers of target organ damage in a substantial cohort of non-diabetic, young to middle-aged female patients with essential hypertension, who otherwise possessed no clinical or laboratory evidence of overt cardiovascular or renal disease. Because these markers of preclinical target organ damage are established independent predictors of cardiovascular events, our findings may help elucidate the enhanced cardiovascular risk inextricably linked to MS.

2. PATHOPHYSIOLOGY AND REVIEW OF LITERATURE

To thoroughly grasp the compounded risk MS presents to hypertensive patients, it is necessary to examine the underlying mechanisms driving damage across distinct organ systems.

2.1 The Metabolic Syndrome and Insulin Resistance

Obesity, particularly abdominal or visceral obesity, is deeply associated with resistance to the effects of insulin on peripheral glucose and fatty acid utilization. Insulin resistance, accompanied by hyperinsulinemia, hyperglycemia, and adipocyte-derived cytokines (adipokines), actively promotes vascular endothelial dysfunction, abnormal lipid profiles, and vascular inflammation, all of which act as catalysts for atherosclerotic cardiovascular disease. While definitions of MS have evolved—with the International Diabetes Federation (IDF) attempting to harmonize criteria by removing waist circumference as a strict prerequisite in 2009—the clustering of these metabolic risk factors undeniably identifies patients at elevated risk for macrovascular complications.

2.2 Left Ventricular Hypertrophy (LVH)

Left ventricular hypertrophy (LVH) is a compensatory structural process that initially develops in response to wall stress or significant hemodynamic pressure/volumetric burden. The increased mass of myocardial fibers serves to maintain contractile forces against an elevated afterload, a classic consequence of essential hypertension. However, this compensatory benefit is eventually offset by a profound increase in the stiffness of the hypertrophied walls, leading to increased diastolic ventricular pressures. A critical pathophysiological component of LVH is the concomitant development of myocardial fibrosis, which is linked directly to the renin-angiotensin-aldosterone system (RAAS). Angiotensin II has been shown to produce a profound profibrotic effect in the myocardial tissue of hypertensive patients.

2.3 Albuminuria and Endothelial Dysfunction

Albuminuria is defined by a urinary albumin-to-creatinine ratio (ACR) of 30 mg/g or greater. The normal rate of albumin excretion is less than 30 mg/day (20 mcg/min); persistent albumin excretion between 30 and 300 mg/day is classified as moderately increased albuminuria. Microalbuminuria clusters heavily with the metabolic syndrome, and both conditions independently predict cardiovascular disease mortality. Emerging evidence points to oxidation and inflammation as vital mediators, with systemic endothelial dysfunction—exacerbated by dyslipidemia—serving as a primary driver. Because endothelial dysfunction uniquely manifests as microalbuminuria in the kidneys, this relationship explains the strong association between MS, chronic inflammation, and renal impairment.

2.4 Hypertensive Retinopathy

Hypertensive retinopathy shares the pathophysiology of damaged retinal vascular endothelium. Unlike diabetic retinopathy, where metabolic damage is the primary instigator, vascular endothelial damage in hypertensive retinopathy is primarily mechanically induced by increased blood flow and pressure. However, MS introduces additional pathological layers. Dysfunctional adipose tissue increases systemic oxidative stress and cytokine production, further contributing to the pathogenesis of retinopathy.

3. MATERIALS AND METHODS

3.1 Study Design and Setting

An observational comparative cross-sectional study was executed among patients attending the Medicine Outpatient Department (OPD) at Sree Balaji Medical College, Chennai. The sample size calculation mandated a

minimum of 300 participants; the final study successfully enrolled and assessed 400 subjects.

3.2 Study Population and Selection Criteria

The study population was exclusively drawn from young females presenting with a known hypertension duration of more than 5 years.

- **Inclusion Criteria:** Young female patients aged 18 to 40 years. A confirmed diagnosis of essential hypertension, as defined by the American College of Cardiology/American Heart Association (ACC/AHA), for a duration ranging from 5 to 10 years.
- **Exclusion Criteria:** Male patients; females under 18 or over 40 years of age. Patients with known diabetes mellitus, or those displaying fasting glycemia greater than or equal to 126 mg/dL. Individuals with known cardiovascular or cerebrovascular diseases. Patients with renal diseases (defined as serum creatinine > 1.5 mg/dL) or overt proteinuria. Patients diagnosed with secondary hypertension, or those currently on lipid-lowering therapies.

3.3 Clinical and Laboratory Assessment

Comprehensive medical histories were recorded, detailing previous diagnoses, drug intake (anti-hypertensives, anti-diabetic agents, hypercholesterolemia medications), and lifestyle habits including smoking and alcohol consumption. Clinical examinations were conducted to record body weight, height, and waist circumference. Blood pressure was documented by a physician, recorded as the calculated average of three consecutive measurements obtained using a mercury sphygmomanometer after the patient had been resting in a supine position for 5 minutes.

Fasting blood samples were extracted to evaluate routine blood chemistry, fasting lipid profiles (inclusive of HDL and triglycerides), and blood sugar levels (fasting and post-prandial).

3.4 Definition of Metabolic Syndrome

Patients were evaluated for MS utilizing the NCEP ATP III criteria, which defines the syndrome as the presence of any three of the following five physiological traits:

- **Abdominal Obesity:** Waist circumference $\ge$ 88 cm (35 in) in females.
- **Hypertriglyceridemia:** Serum triglycerides $\ge$ 150 mg/dL (1.7 mmol/L) or current drug treatment for elevated triglycerides.
- **Low HDL Cholesterol:** Serum high-density lipoprotein (HDL) cholesterol < 50 mg/dL (1.3 mmol/L) in females or drug treatment for low HDL.
- **Elevated Blood Pressure:** Blood pressure $\ge$ 130/85 mmHg or active drug treatment for hypertension.
- **Elevated Fasting Plasma Glucose (FPG):** FPG $\ge$ 100 mg/dL (5.6 mmol/L) or drug treatment for elevated blood glucose.

3.5 Target Organ Damage Screening Methods

The participants were divided into two distinct groups: young hypertensive females with MS, and those without MS. Both groups were subjected to rigorous screening for end-organ damage:

- **Left Ventricular Hypertrophy (Cardiac Damage):** A comprehensive 2D Echocardiography study was conducted to ascertain the presence and extent of left ventricular hypertrophy.
- **Albuminuria (Renal Damage):** Urine spot protein-to-creatinine ratio (PCR) and urine albumin levels were analyzed to detect microalbuminuria.
- **Retinopathy (Retinal Damage):** Fundus examinations were performed to identify retinal changes. Retinopathy was systematically graded utilizing the Mitchell-Wong simplification of the Keith-Wagener-Barret system:
    - *Grade 1 (Mild Retinopathy):* Characterized by generalized and focal arteriolar narrowing, AV nicking, and/or arteriolar wall opacity (copper wiring).
    - *Grade 2 (Moderate Retinopathy):* Defined by the presence of hemorrhage, microaneurysms, cotton wool spots, and/or hard exudates.
    - *Grade 3 (Malignant/Severe Retinopathy):* Includes all features of moderate retinopathy combined with optic disc swelling.

3.6 Statistical Analysis

All collated data were meticulously analyzed utilizing IBM SPSS Statistics for Windows, Version 23.0 (Armonk, NY: IBM Corp). Descriptive statistical techniques, including frequency and percentage analyses, were applied to categorical variables, whereas the mean and standard deviation (S.D.) were computed for continuous variables. To ascertain statistical significance between the bivariate samples in independent groups, the Independent sample t-test was deployed. For qualitative categorical data, the Pearson's Chi-Square test was utilized. Across all statistical instruments, a probability (p) value of < 0.05 was adopted as the threshold for statistical significance.

4. RESULTS

4.1 Baseline Demographic Distribution

The study cohort consisted of 400 female patients. Age distribution was highly skewed toward the upper parameters of the inclusion criteria: patients up to 25 years constituted 1.5% (n=6), 26–30 years made up 12.3% (n=49), 31–35 years represented 40.8% (n=163), and the 36–40 years demographic accounted for 45.5% (n=182) of the study population. Pearson's Chi-Square testing revealed a highly statistically significant association between increasing age within this bracket and the presence of metabolic syndrome (X^2=17.781, p=0.0005).

4.2 Left Ventricular Hypertrophy (LVH)

Echocardiographic assessments yielded a stark and significant disparity in cardiac remodeling between the two groups. Echocardiographic LVH was confirmed in 60.6% (103 out of 170) of the patients presenting with MS. Conversely, only 33.0% (76 out of 230) of the non-MS hypertensive patients exhibited LVH. This disparity returned a highly statistically significant difference upon Chi-Square analysis (X^2=29.996, p=0.0005).

4.3 Renal Target Organ Damage: Albuminuria

Urine albumin analysis underscored significant renal impairment correlated with MS. Albuminuria was positively identified in 61.8% (105 patients) of the MS cohort, compared to a mere 31.3% (72 patients) in the non-MS cohort. This finding was highly significant (X^2=36.764, p=0.0005). Routine dipstick analysis corroborated these findings, demonstrating higher severity grades in the MS group: 37.6% tested 1+ and 13.5% tested 2+ for protein, while in the non-MS group, 14.8% tested 1+ and only 1.7% tested 2+. The dipstick variance between the two groups was highly significant (X^2=58.319, p=0.0005).

4.4 Hypertensive Retinopathy

Retinal fundus examinations revealed that hypertensive retinopathy was significantly more widespread and severe in patients afflicted with MS. Overall, retinopathy was present in 68.2% (116/170) of the MS group, in stark contrast to 23.9% (55/230) of the non-MS group. This overall difference was highly statistically significant (X^2=78.460, p=0.0005).

When analyzing by severity grade using the Mitchell-Wong classification:

- **Grade 1:** Found in 33.5% of the MS group vs. 20.0% of the non-MS group.
- **Grade 2:** Found in 25.3% of the MS group vs. 3.9% of the non-MS group.
- **Grade 3:** Found in 9.4% of the MS group vs. 0.0% of the non-MS group. The comparison of specific retinopathy grading between the cohorts was highly significant (X^2=96.512, p=0.0005).

4.5 Clinical and Anthropometric Profiles

Independent sample t-tests confirmed that the MS group exhibited significantly deteriorated clinical markers across all measured physiological parameters:

- **Waist Circumference:** The MS group averaged 92.2 cm, significantly higher than the 83.5 cm average in the non-MS group (t=23.723, p=0.0005).
- **Serum Triglycerides:** Highly elevated in the MS group, averaging 173.8 mg/dL, compared to 125.0 mg/dL in the non-MS group (t=22.138, p=0.0005).
- **HDL Cholesterol:** Significantly suppressed in the MS group, averaging 42.1 mg/dL, versus 56.8 mg/dL in the non-MS group (t=35.361, p=0.0005).
- **Systolic Blood Pressure (SBP):** Averaged 146.3 mmHg in the MS group versus 138.6 mmHg in the non-MS group (t=7.225, p=0.0005).
- **Diastolic Blood Pressure (DBP):** Averaged 87.3 mmHg in the MS group versus 85.1 mmHg in the non-MS group (t=2.950, p=0.003).
- **Fasting Plasma Glucose (FPG):** Substantially higher in the MS group, averaging 146.1 mg/dL compared to 85.2 mg/dL in the non-MS group (t=31.535, p=0.0005).

5. DISCUSSION

The primary objective of the present study was the robust evaluation of the association between MS (defined strictly by NCEP-ATPIII criteria) and critical indices of preclinical cardiac, renal, and retinal damage. Our findings uniformly assert that MS drastically accelerates target organ deterioration beyond the predictable impacts of essential hypertension.

Regarding echocardiographic parameters, hypertensive patients exhibiting MS characteristics demonstrated a substantially increased prevalence of left ventricular hypertrophy (60.6% vs 33.0%). This robust association parallels findings from the Strong Heart Study, a seminal longitudinal investigation involving American Indian communities. In a subset of 1436 non-diabetic participants without prevalent cardiovascular disease, researchers found that subjects with MS possessed significantly greater left ventricular dimensions, increased LV mass, and a higher overall prevalence of LV hypertrophy compared to unaffected cohorts.

While the cross-sectional nature of our clinical study restricts us to proposing hypotheses rather than definitively establishing causality regarding MS and cardiac hypertrophy, several biological mechanisms present compelling explanations. Insulin resistance and its accompanying compensatory hyperinsulinemia are recognized as the primary pathophysiological drivers underpinning MS. Trophic, growth-promoting effects of

insulin on myocardial tissue have been thoroughly demonstrated in cell cultures and animal models, effects likely mediated through insulin-like growth factor-1 receptors. Moreover, hyperinsulinemia may influence LV mass indirectly by exacerbating sodium retention, stimulating sympathetic nervous system activation, and increasing endothelin-1 levels. Additionally, biological mediators secreted directly from expanding white adipose tissue in centrally obese individuals—such as leptin and angiotensin II (a notoriously potent myocardial growth factor)—undoubtedly contribute to cardiomyocyte mitogenesis and hypertrophy.

Renal evaluation generated equally alarming data. We observed a dramatically higher prevalence of albuminuria in hypertensive subjects diagnosed with MS (61.8% vs 31.3%). These findings are deeply consistent with cross-sectional evaluations of data derived from the Third National Health and Nutrition Examination Survey (NHANES III). In that study of 5360 US civilian subjects, an identically close association was observed between microalbuminuria and MS (defined by NCEP-ATPIII criteria), with blood pressure and glucose levels acting as the main predictors. The pathophysiological relationship between albumin excretion rates and MS is so deeply entwined that the WHO actively includes microalbuminuria amongst its primary criteria for diagnosing MS. Glomerular hyperfiltration—a functional renal alteration expressed via an increased creatinine clearance rate—is recognized to precede overt glomerulosclerosis and is tightly associated with both obesity and systemic insulin resistance.

Ocular examinations provided a final, critical layer of insight, revealing an increased prevalence of both Grade 1 and Grade 2 hypertensive retinopathy among subjects afflicted with MS. This result is highly consistent with a comprehensive cross-sectional investigation embedded within the Atherosclerosis Risk in Communities Study. In that study of 11,265 participants, researchers observed distinct, unignorable associations between MS and specific retinal anomalies—such as arteriovenous nicking, focal arteriolar narrowing, and generalized arteriolar narrowing—even in cohorts entirely free of clinical diabetes or overt hypertension.

The literature is clear that MS confers a heavily amplified risk of cardiovascular morbidity and mortality. Recently, longitudinal data has confirmed that this adverse prognostic impact deeply affects hypertensive patients. In the Progetto Ipertensione Umbria Monitoraggio Ambulatoriale (PIUMA) study—a prospective observational investigation of Italian adult subjects suffering from essential hypertension—patients presenting with MS (comprising 34% of the cohort) ran a markedly increased risk of developing subsequent fatal cardiac and cerebrovascular events. It is highly probable that the enhanced cardiovascular risk inextricably linked to MS is directly mediated through the exact preclinical cardiovascular and renal changes observed in our study. Preclinical abnormalities, including LV hypertrophy and microalbuminuria, are universally recognized by the scientific community as robust, independent predictors of adverse, endpoint cardiovascular outcomes.

6. CONCLUSION

The prevalence of metabolic syndrome is alarmingly high within modern society, yet it frequently goes entirely unnoticed in routine clinical assessments. This study provides clear, statistically robust evidence that metabolic syndrome fundamentally amplifies hypertension-related cardiac and renal structural changes. This amplification acts over and above the potential, isolated contributions of any single individual risk component of the syndrome.

From the data compiled in this study, it is evident that the clinical prevalence of left ventricular hypertrophy, albuminuria, and hypertensive retinopathy is significantly more widespread and severe in hypertensive patients presenting with metabolic syndrome (as defined by NCEP-ATP III criteria) compared to hypertensive patients without the syndrome. Consequently, highly rigorous, long-term follow-up protocols are critically required for cases presenting with metabolic syndrome. Timely, aggressive therapeutic intervention—spanning lifestyle modifications and targeted pharmacology—is absolutely vital to halt the silent progression of extensive, irreversible damage to these vital physiological systems.

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