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ARTERIAL HYPERTENSION IN WOMEN OF FERTILE AGE: PREDICTIVE VALUE OF ENDOTHELIN-1 AND LIFESTYLE RISK FACTORS

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Abstract

Introduction: Arterial hypertension (AH) remains one of the most prevalent cardiovascular conditions, with rising incidence among women of reproductive age due to metabolic and lifestyle changes.

Objective: To evaluate risk factors for AH and develop individualized prevention strategies using a stratified patient group model.

Methods: A prospective clinical study was conducted involving 172 women aged 20–49, stratified into five groups based on risk factors and clinical parameters. Anthropometric, biochemical, and hemodynamic variables were analyzed.

Results: Endothelin-1 (ET-1) was identified as a significant predictive biomarker for early hypertension, showing a strong correlation with glucose levels and BMI. Regression and ROC analysis confirmed the diagnostic value of ET-1 (AUC = 0.96).

Conclusion: Targeted monitoring of ET-1 and lifestyle modifications can significantly improve early detection and prevention of AH in women of reproductive age.

Keywords: Arterial hypertension, women, prevention, endothelin-1, cardiovascular risk, reproductive age, ROC analysis

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1. Introduction

Arterial hypertension (AH) remains one of the most prevalent and critical public health challenges worldwide. According to the World Health Organization, approximately 30% of the adult population suffers from elevated blood pressure, contributing significantly to cardiovascular morbidity, stroke, and renal failure. Despite increased awareness and therapeutic advancements, the prevalence of hypertension continues to rise, particularly among women of reproductive age.

The increasing incidence of AH in women aged 20 to 49 is attributed to multiple interrelated factors including obesity, insulin resistance, endothelial dysfunction, and lifestyle-related stress. This demographic is particularly vulnerable due to the dual burden of cardiovascular risks and the potential impact of hypertension on reproductive health. Early development of hypertension in this population may impair fertility, complicate pregnancy outcomes, and elevate long-term cardiovascular risk.

Recent studies underscore the pivotal role of endothelial dysfunction in the pathogenesis of hypertension. Among the endothelial markers, endothelin-1 (ET-1), a potent vasoconstrictor, has gained prominence for its diagnostic and prognostic relevance. Elevated ET-1 levels have been consistently linked to increased vascular resistance and early vascular impairment in hypertensive patients. Moreover, metabolic factors such as elevated body mass index (BMI) and serum glucose further potentiate the hypertensive state by influencing vascular tone and promoting inflammatory responses.

Despite the availability of effective antihypertensive therapies, the early identification and stratification of at-risk individuals—particularly young women without overt hypertension—remain insufficiently addressed in clinical practice. Therefore, a personalized prevention model integrating vascular biomarkers such as ET-1, alongside metabolic and hemodynamic parameters, may enhance the early detection and prevention of AH in women of childbearing age.

The present study aims to assess the predictive role of ET-1 and other clinical variables in a stratified cohort of 172 women and to formulate practical strategies for personalized prevention of arterial hypertension in this population.

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2. Materials and Methods

This prospective study was conducted from 2023 to 2025 in three family polyclinics in Bukhara (Clinics No. 1, 3, and 4). A total of **172 women aged 20–49 years** were enrolled and stratified into **five clinical groups** based on age, risk factors, and clinical data:

Group 1 – 16 participants, Group 2 – 20, Group 3 – 26, Group 4 – 48, Group 5 – 62.

Inclusion criteria included reproductive-age women without a prior diagnosis of arterial hypertension and who provided informed consent.

Exclusion criteria were pregnancy, serious somatic diseases (e.g., diabetes, chronic kidney disease), and current use of antihypertensive drugs.

All participants underwent anthropometric measurements (height, weight, BMI), blood pressure assessment (three readings per arm), and laboratory tests (CBC, urinalysis, lipid profile, glucose, creatinine). **Endothelin-1 (ET-1)** levels were measured via ELISA. Additional assessments included **24-hour ambulatory blood pressure monitoring (ABPM)** and **electrocardiography (ECG)**.

Data analysis was performed using Excel 2010 and Statistica 8.0. Statistical methods included descriptive statistics, ANOVA, Pearson/Spearman correlations, linear regression, and **ROC analysis** to evaluate the predictive value of ET-1 for hypertension (SBP ≥140 mmHg).

3. Results

A total of 172 women of reproductive age were enrolled and stratified into five clinical groups based on age, metabolic risk factors, and vascular indicators. **Tables 1 and 2** summarizes key clinical and laboratory characteristics, including body mass index (BMI), fasting glucose, total cholesterol, endothelin-1 (ET-1), and 24-hour systolic blood pressure (SBP) as assessed by ambulatory blood pressure monitoring (ABPM).

Table 1.

Metabolic Parameters by Clinical Group

This table presents the mean values of body mass index (BMI), fasting glucose, and total cholesterol for five stratified clinical groups. An upward trend in glucose indicates metabolic deterioration across groups.

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Group	BMI (kg/m²)	Glucose (mmol/L)	Cholesterol (mmol/L)
Group 1	33.05	5.20	6.48
Group 2	31.73	5.60	6.30
Group 3	32.13	6.10	6.34
Group 4	32.80	6.40	6.37
Group 5	33.10	6.80	6.40

Table 2.
Vascular Biomarkers and 24-Hour BP by Clinical Group
This table summarizes mean values of endothelin-1 (ET-1) and 24-hour systolic blood pressure (SBP). A progressive rise in both indicators reflects increasing vascular burden across the stratified groups.

Group	ET-1 (pg/mL)	SBP 24h (mmHg)
Group 1	4.39	126.20
Group 2	5.17	130.50
Group 3	5.67	134.80
Group 4	6.30	139.10
Group 5	7.20	142.60

While BMI values were consistently elevated across all groups (ranging from 31.7 to 33.1 kg/m²), there were no statistically significant differences between them, suggesting that excess weight was a baseline risk factor common to the entire cohort. Serum cholesterol values remained within a narrow range (6.30–6.48 mmol/L), but were elevated above clinical norms across all groups, further reinforcing the background presence of metabolic imbalance.

More pronounced differentiation was observed in fasting glucose and ET-1 levels. A progressive and statistically significant increase in glucose was noted from Group 1 (5.2 mmol/L) to Group 5 (6.8 mmol/L), with ANOVA confirming these intergroup differences ($F = 14.66$, $p < 0.000003$). ET-1 levels followed a similar trend, rising from 4.39 pg/mL in Group 1 to 7.20 pg/mL in Group 5 ($F =$

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18.18, $p < 0.0000003$), as illustrated in **Figure 1**. These values suggest progressive endothelial dysfunction consistent with elevated cardiovascular risk and early-stage hypertensive transformation.

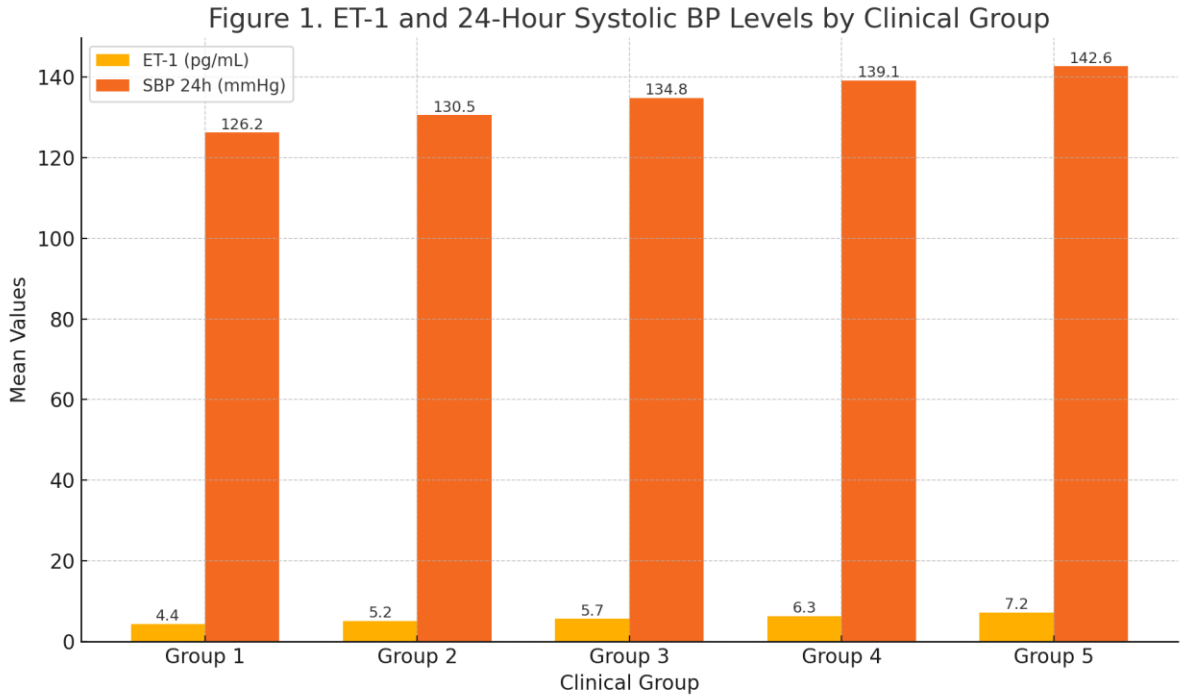

Figure 1.

ABPM data revealed a clear pattern of increasing **24-hour systolic blood pressure** across clinical groups, from a mean of 126.2 mmHg in Group 1 to 142.6 mmHg in Group 5. In addition, patients in Groups 4 and 5 demonstrated **attenuated nocturnal dipping**, indicating loss of physiological blood pressure variability—a hallmark of autonomic imbalance and endothelial impairment. These patterns not only support the cross-sectional trend of increasing vascular burden but also emphasize the value of ABPM in detecting masked or borderline hypertension not captured by isolated clinic measurements.

Correlation analysis revealed a moderate relationship between ET-1 and fasting glucose levels ($r \approx 0.5$), suggesting a metabolic-endothelial interplay. A stronger correlation was observed between BMI and cholesterol ($r \approx 0.9$), reflecting

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typical clustering of metabolic syndrome components. No significant correlations were found between heart rate and other variables.

Linear regression modeling identified ET-1 as the strongest independent predictor of systolic BP, contributing an average increase of **+7.6 mmHg per 1 pg/mL rise**, followed by BMI with **+0.73 mmHg.** Glucose and cholesterol showed weaker and less consistent effects. Logistic regression confirmed ET-1 as the most influential factor in predicting the risk of hypertension (coefficient +2.07), while model accuracy reached **88.2%**, and the ROC curve yielded an **AUC of 0.96**, demonstrating excellent discriminatory power.

These findings support the clinical value of ET-1 as an early **biomarker of preclinical hypertension,** particularly when interpreted in conjunction with ABPM data and metabolic indices. Group-based stratification effectively captured the progressive nature of vascular and metabolic deterioration, suggesting its utility as a preventive screening tool in women of reproductive age.

4. Discussion

This study aimed to evaluate the utility of endothelin-1 (ET-1) and metabolic markers in predicting the risk of arterial hypertension (AH) in women of reproductive age using a five-group stratification model. The results revealed a progressive deterioration of vascular and metabolic health across clinical groups, with **ET-1 emerging as the most powerful predictor** of prehypertensive changes.

The upward trend in **ET-1 levels**, from 4.39 pg/mL in Group 1 to 7.20 pg/mL in Group 5, mirrors the pattern of 24-hour systolic blood pressure (SBP), suggesting a strong pathophysiological link. Endothelin-1, a potent vasoconstrictor produced by endothelial cells, is widely recognized for its role in the development of hypertension. Elevated ET-1 contributes to increased vascular tone, remodeling, and reduced nitric oxide bioavailability. Our findings corroborate earlier studies identifying ET-1 as a **sensitive biomarker of endothelial dysfunction and early vascular impairment** (Wilkinson et al., 2020; Schiffrin, 2018).

The observed **correlation between ET-1 and glucose** ($r \approx 0.5$) further highlights the metabolic–endothelial axis in hypertensive pathogenesis. Hyperglycemia and insulin resistance can enhance ET-1 expression through oxidative stress and

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activation of the renin–angiotensin system. This relationship emphasizes the need to evaluate metabolic parameters even in normotensive patients, especially among women prone to gestational or essential hypertension.

Ambulatory blood pressure monitoring (ABPM) in our study revealed progressive 24-hour SBP elevation across risk groups, validating the use of continuous monitoring over isolated clinic measurements. Importantly, women in Groups 4 and 5 exhibited **blunted nocturnal dipping,** a known marker of autonomic imbalance and future cardiovascular events. These patterns align with previous findings that **non-dipping profiles** are associated with increased risk of stroke, left ventricular hypertrophy, and renal damage (Kario et al., 2019).

Regression and ROC analyses confirmed the diagnostic and predictive value of ET-1, with an **AUC of 0.96** and model accuracy of **88.2%**. Notably, while BMI and glucose showed some association with SBP, their contributions were significantly lower than that of ET-1. This finding supports the growing consensus that **endothelial biomarkers may offer superior predictive power** for early cardiovascular risk detection compared to traditional metabolic indices alone.

From a clinical perspective, the stratification model applied in this study demonstrates clear value in capturing subclinical disease stages. Women in early reproductive age may already exhibit significant vascular abnormalities despite being outside conventional diagnostic criteria for hypertension. **Integrating ET-1 screening and ABPM** into routine checkups for high-risk women may allow clinicians to identify and manage hypertensive risk before irreversible damage occurs.

However, several limitations must be acknowledged. First, the cross-sectional design restricts causality inference. Longitudinal studies are needed to determine whether elevated ET-1 precedes clinical hypertension or co-develops with it. Second, hormonal influences (e.g., menstrual phase, contraceptive use) were not assessed, despite their known effects on endothelial tone. Future studies should include hormonal profiling to refine risk prediction in this population.

In conclusion, our findings support the inclusion of **endothelin-1, ABPM, and stratified metabolic analysis** in early screening programs for women of

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reproductive age. This integrative approach could transform preventive cardiology by enabling proactive, individualized interventions before the onset of clinically evident hypertension.

5. Conclusion

The current study demonstrates that **endothelin-1 (ET-1)** is a highly sensitive and specific biomarker of early vascular dysfunction in women of reproductive age. When combined with **ambulatory blood pressure monitoring (ABPM)** and basic metabolic parameters such as glucose and BMI, ET-1 provides a powerful tool for identifying patients at increased risk for arterial hypertension (AH), even in the absence of overt clinical symptoms.

The five-group stratification model used in this study effectively captured the gradual progression of vascular and metabolic abnormalities, underscoring the need for individualized risk assessment. Importantly, the strong association between elevated ET-1 levels and 24-hour systolic BP supports the hypothesis that endothelial dysregulation precedes and contributes to the development of sustained hypertension.

In light of these findings, routine screening for ET-1—especially in high-risk female populations—may offer an opportunity to initiate preventive strategies **prior to the manifestation of hypertension**, ultimately reducing long-term cardiovascular burden.

6. Recommendations

1. **Routine Screening of High-Risk Women**: Women of reproductive age with elevated BMI or metabolic markers should be screened for endothelial dysfunction, particularly using ET-1 assays.
2. **Incorporation of ABPM into Primary Care**: Ambulatory 24-hour BP monitoring should be integrated into preventive care pathways to identify non-dipping and masked hypertension profiles early.
3. **Risk Stratification Models in Clinical Practice**: Implementing structured risk grouping—based on metabolic and vascular parameters—can facilitate more tailored interventions and monitoring protocols.
4. **Lifestyle Interventions Based on Vascular Risk**: Women with rising ET-1 levels and subclinical BP changes should be counseled on weight management,

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physical activity, and dietary optimization, even if they fall below diagnostic thresholds for hypertension.

5. **Further Research Directions**: Longitudinal studies are needed to evaluate the predictive timeline of ET-1 elevation and assess whether targeted interventions in ET-1–positive individuals delay or prevent the onset of clinical hypertension.

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