Relationship between Genetic Polymorphisms and Clinical Parameters in Mexican Postmenopausal Women: A Study on Cardiovascular Health

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Background and rationale

Cardiovascular disease (CVD) is a leading cause of illness and death among postmenopausal women, particularly in areas with high rates of obesity and hypertension (González et al., 2020). The hormonal changes that accompany menopause can adversely affect cardiovascular health (Miller et al., 2019). In Mexico, the prevalence of overweight and obesity is alarmingly high, further elevating the risk of CVD in this population (Salinas et al., 2021).

Genetic factors significantly contribute to the development of CVD, with certain polymorphisms linked to hypertension and lipid metabolism (Wang et al., 2018). Notably, polymorphisms in the angiotensin-converting enzyme (ACE) gene, angiotensinogen gene, and estrogen receptor alpha gene are of particular interest due to their roles in the renin-angiotensin system and estrogen signaling pathways (Khan et al., 2020). Understanding how these genetic variations correlate with clinical indicators can provide valuable insights into individual susceptibility to cardiovascular diseases.

This study aims to investigate the connection between these genetic polymorphisms and biochemical markers related to cardiovascular health in overweight postmenopausal women in Mexico.

By analyzing the interplay between genetic markers (ACE I/D, angiotensinogen M235T, and XbaI at the estrogen receptor alpha) and clinical parameters such as lipid profiles and blood pressure, (Hernández et al., 2022) we seek to address a significant gap in the existing literature.

The findings from this research could enhance our understanding of personal risk factors for CVD, aiding in the creation of targeted prevention and intervention strategies tailored to the specific genetic and biochemical traits of this group. Ultimately, this research aspires to improve cardiovascular health management for postmenopausal women, emphasizing the importance of personalized approaches that meet their distinct health needs.

Objectives

This study aimed to evaluate the biochemical parameters and genetic polymorphisms associated with cardiovascular health in overweight postmenopausal women:

- Evaluate Biochemical Parameters: Assess cardiovascular biochemical parameters in postmenopausal women.
- Identify Genetic Polymorphisms: Identify ACE I/D, angiotensinogen M235T, and XbaI polymorphisms.
- Analyze Clinical and anthropometric Profiles: focusing on mean arterial systolic blood pressure and BMI, body fat, waist-to-height ratio and adiposity index.
- Correlate Data: Investigate correlations between genetic polymorphisms and biochemical parameters.
- Assess Cardiovascular Risk: Determine the prevalence of cardiovascular risk factors, including borderline HDL levels.
- Enhance Risk Assessment: Provide insights to improve cardiovascular risk assessment, highlighting the protective effect of the angiotensinogen M235T variant.

Methods

Study Design

This is a clinical, observational, transversal, and prospective study.

Participants

The study included postmenopausal women aged 45 years and older, confirmed by 12 consecutive months without menstruation. Inclusion criteria required no history of cardiovascular disease or metabolic disorders. Exclusion criteria included recent hormone replacement therapy (within 6 months) and severe comorbidities like uncontrolled hypertension or diabetes. Participants were stratified into normotensive and hypertensive groups based on medical history.

Methods

Data Collection

Clinical Data

Demographic and clinical data were collected through structured interviews and medical history assessments, recorded in a case report form. Blood pressure was measured using a calibrated sphygmomanometer, following the guidelines of the Seventh Report of the Joint National Committee on High Blood Pressure.

Anthropometric Indices

Height and weight were measured to calculate Body Mass Index (BMI = weight in kg/height in m^2). Waist and hip circumferences were measured to determine waist-to-hip ratio and assess body fat distribution.

Biochemical Assessments

Blood samples were analyzed for serum levels of total cholesterol, HDL, LDL, triglycerides, and glucose using standard spectrophotometry protocols.

Genetic Polymorphism Analysis

Genetic polymorphisms analyzed included:

•I/D polymorphism of the Angiotensin-Converting Enzyme (ACE) gene
•M235T polymorphism of the angiotensinogen gene
•XbaI polymorphisms of the estrogen receptor gene (ESR1)

DNA was extracted using a phenol-chloroform method, and polymorphisms were identified through polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) analysis.

Statistical Analysis

Statistical analyses were performed using SPSS and R software, with significance set at $p < 0.05$. Descriptive statistics were calculated for demographic, clinical, and biochemical variables. Logistic regression models assessed associations between genetic polymorphisms and blood pressure levels, adjusting for confounding variables such as age, BMI, and comorbidities. Correlation analyses examined relationships between anthropometric indices and biochemical parameters.

Results

A total of 87 Mexican postmenopausal women participated in the study, consisting of 60 normotensive and 27 hypertensive individuals (Figure 1).

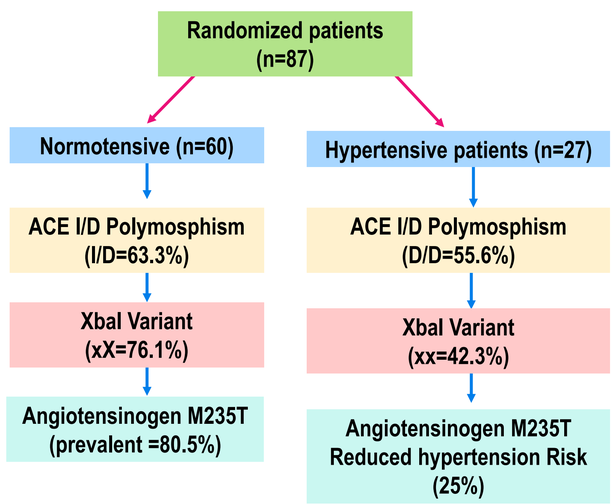

Figure 1. Flow of participants through the study stages, including eligibility, randomization, and genetic polymorphisms distribution.

The mean arterial systolic blood pressure was 116.7 mmHg (95% CI: 114.54–118.99), with the majority classified as overweight, exhibiting a mean Body Mass Index (BMI) of 28.7 (95% CI: 27.95–29.60). HDL levels were found to be borderline, with 50% of participants showing values indicative of increased cardiovascular risk.

Significant correlations were observed between BMI and body fat percentage (r=0.54), waist-to-height ratio (r=0.55), and adiposity index (r=0.84). Additionally, triglycerides exhibited an inversely proportional relationship with LDL levels (r=-0.27), while the atherogenic index correlated positively with the Heard scale (r=0.46).

- **Genetic polymorphisms**

Regarding genetic polymorphisms, all genotypes were identified in the sample studied (Figure 2), in normotensive women, the ACE I/D polymorphism was predominantly I/D (n=38, 63.3%). In contrast, among hypertensive women, the D/D genotype was more common (n=15, 55.6%).

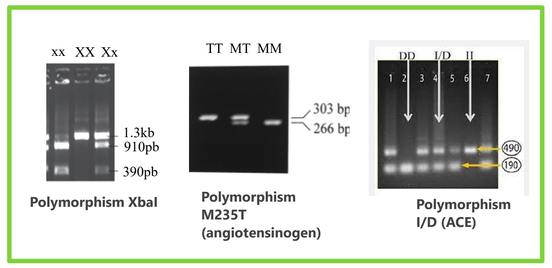

Figure 2. Representative Image of agarose gel of the polymorphism identified.

The XbaI variant was prevalent in normotensive women (xX, n=35, 76.1%) and hypertensive women (xx, n=11, 42.3%). The angiotensinogen M235T variant was also more frequent in normotensive women (n=33, 80.5%) and was associated with a 25% reduction in hypertension risk (Table 1).

Table 1. Frequency of polymorphisms and alleles of polymorphisms, according to blood pressure (normotensive/hypertensive)

	Normotensive n=60 (%)	Hypertensive n=27 (%)	OR	95% CI	P
Polymorphism I/D (ACE)					
I/I	4 (6.67)	2 (3.33)			
I/D	38 (63.3)	10 (20.8)	0.52	0.08, 3.29	0.493
D/D	18 (30)	15 (45.5)	1.66	0.26, 10.39	0.584
Polymorphism M235T (angiotensinogen)					
TT	15 (25)	14 (48.3)			
MT	33 (55)	8 (19.5)	0.26	0.09, 0.75	0.013*
MM	12 (20)	5 (29.4)	0.44	0.12, 1.59	0.214
Polymorphism XbaI (alpha estrogen receptor)					
xx	15 (5.77)	11 (4.23)			
xX	35 (76.1)	11 (23.9)	0.42	0.15, 1.20	0.107
XX	10 (66.7)	5 (33.3)	0.68	0.18, 2.56	0.571

These findings highlight the complex interplay between genetic factors and cardiovascular health in this population, emphasizing the need for further investigation into personalized risk assessment and management strategies for postmenopausal women.

Conclusions

This study indicates that genetic polymorphisms and obesity metrics are associated with cardiovascular health in postmenopausal women, emphasizing the importance of integrating biochemical parameters and genetic predispositions in cardiovascular risk assessment.

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