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Determinants, Clinical Patterns, and Treatment Disparities of Hypertensive Heart Disease: A Retrospective Cross-Sectional Comparative Study of 600 Patients in Makassar, Indonesia, and Kuala Terengganu, Malaysia

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Abstract

Introduction: Hypertensive heart disease (HHD) is a major contributor to cardiovascular morbidity and mortality in Southeast Asia, yet comparative evidence between neighboring populations with different healthcare systems remains limited.

Aim: To compare the prevalence of HHD and identify its independent determinants among hypertensive patients in Makassar, Indonesia, and Kuala Terengganu, Malaysia.

Material and Methods: A retrospective cross-sectional study included 600 adults with hypertension (300 from Makassar and 300 from Kuala Terengganu) treated at five tertiary hospitals between January 2021 and December 2024. HHD was defined as hypertension-related left ventricular hypertrophy, heart failure, or atrial fibrillation. Independent variables included age, sex, body mass index, smoking, diabetes mellitus, hypertension duration, and access to guideline-directed medical therapy. Multivariable logistic regression was performed to identify predictors.

Results: HHD prevalence was significantly higher in Makassar than Kuala Terengganu (41.7% vs. 33.0%; p=0.027). Older age (aOR 1.04; 95% CI 1.02–1.07), longer hypertension duration (aOR 1.08; 95% CI 1.05–1.11), diabetes mellitus (aOR 1.82; 95% CI 1.27–2.61), obesity (aOR 1.59; 95% CI 1.12–2.26), and absence of guideline-directed therapy (aOR 2.11; 95% CI 1.43–3.12) were independent predictors. Male sex predicted HHD only in Makassar, whereas smoking was significant only in Kuala Terengganu.

Conclusion: HHD burden remains substantial in both cities despite differences in healthcare access. Universal cardiometabolic risk factors coexist with region-specific determinants, highlighting the need for context-adapted hypertension prevention and management strategies across Southeast Asia.

Keywords: Hypertensive heart disease; cross-sectional study; retrospective; comparative epidemiology; hypertension determinants; cardiovascular risk score

1.Introduction

1.1 Burden of Hypertensive Heart Disease

Hypertension is the single most important modifiable risk factor for cardiovascular disease globally, contributing to approximately 54% of all stroke-related deaths and 47% of all ischemic heart disease deaths. In Southeast Asia, hypertension prevalence exceeds 35% among adults aged 25 years and older, yet blood pressure control rates remain below 30% in most countries, with profound consequences for end-organ damage. Chronic, uncontrolled hypertension induces progressive structural and functional remodeling of the heart—collectively termed hypertensive heart disease (HHD)—manifesting as left ventricular hypertrophy (LVH), heart failure with reduced or preserved ejection fraction (HFrEF/HFpEF), atrial fibrillation, and increased susceptibility to acute coronary syndromes.

In Indonesia, hypertension accounts for 27% of total cardiovascular mortality, with South Sulawesi and other eastern regions reporting some of the highest prevalence and poorest control rates nationwide. In Malaysia, hypertension is responsible for 23% of all non-communicable disease deaths, with the East Coast states exhibiting distinct epidemiological profiles compared to peninsular urban centers. Despite shared tropical climates, predominantly Muslim populations, and comparable demographic transitions, Makassar and Kuala Terengganu differ substantially in socioeconomic structure, health insurance coverage, healthcare financing models, and clinical practice pathways—factors that may critically shape HHD patterns and outcomes.

Patho physiologically, HHD develops through a continuum of pressure overload, neurohormonal activation, inflammation, and interstitial fibrosis. Initially, LVH represents an adaptive response to increased afterload; over time, however, maladaptive remodeling progresses to diastolic dysfunction, impaired coronary microcirculation, chamber dilation, systolic failure, and arrhythmogenicity. Asian populations, including Indonesians and Malays, demonstrate heightened susceptibility to hypertensive end-organ damage at similar blood pressure levels compared to Western cohorts, likely due to greater salt sensitivity, higher sodium intake, and metabolic vulnerability at lower body mass thresholds.

1.2 Research Gap and Novelty

Most existing literature on HHD in Southeast Asia consists of single-center or national studies, with limited use of standardized comparative designs that disentangle biological, lifestyle, and health-system determinants. Direct cross-border comparisons using identical definitions and methodology are virtually non-existent, despite the potential to identify shared and context-specific priorities for intervention. This work introduces four key innovations suitable for journal submission:

- First retrospective cross-sectional comparative study of HHD between Makassar and Kuala Terengganu using identical inclusion criteria, variable definitions, and diagnostic standards;
- Structured analytical framework explicitly testing seven predefined predictors against one primary outcome, enabling robust statistical comparison and adjustment for confounding;
- Development of a locally derived and validated risk index that outperforms widely used Western-derived scores in both populations;
- Integrated analysis linking clinical determinants to health-system performance, identifying actionable disparities within and between settings.

1.3 Study Objectives

- To compare the prevalence and clinical spectrum of HHD between patients in Makassar and Kuala Terengganu;
- To quantify the independent association of age, sex, body mass index, smoking status, diabetes mellitus, duration of hypertension, and access to guideline-directed medical therapy with HHD in the combined cohort and separately by region;
- To identify region-specific effect modifiers and construct a comparative risk prediction model;
- To contrast blood pressure control rates and treatment patterns across settings.

2. Methods

2.1 Study Design and Setting

A retrospective cross-sectional study was conducted across five tertiary referral hospitals: three in Makassar (Andi Makkasau General Hospital, Nene Mallomo Hospital, and Arifin Nukman Hospital) and two in Kuala Terengganu (Hospital Sultanah Nur Zahirah and Universiti Sultan Zainal Abidin Medical Centre). Records were retrieved for patients diagnosed between 1 January 2021 and 31 December 2024. The protocol was approved by the Health Research Ethics Committee, Faculty of Medicine, Hasanuddin University (No. 089/UN4.6.4.5.31/PP36/2025) and the Medical Research Ethics Committee, Universiti Sultan Zainal Abidin (No. UniSZA/2025/008). All data were fully de-identified before analysis, with strict adherence to the Declaration of Helsinki and institutional data protection regulations.

2.2 Participants

The total sample comprised 600 patients (300 per region), selected via systematic random sampling from eligible records to ensure balanced representation and minimize selection bias.

- **Inclusion criteria:** Age ≥ 18 years; established diagnosis of hypertension (≥ 140/90 mmHg on repeated measurements or on antihypertensive medication for ≥ 6 months); complete records for all study variables; minimum 12 months of follow-up; and documented echocardiographic or clinical assessment of cardiac structure and function.
- **Exclusion criteria:** Secondary hypertension due to renal, endocrine, renovascular, or iatrogenic causes; primary cardiomyopathy; congenital heart disease; significant valvular heart disease; acute coronary syndromes within three months before assessment; and incomplete or missing key data.

2.3 Variable Definitions

All variables were defined a priori to ensure consistency across sites.

Tabel

Variable Type	Variable Name	Definition
Dependent Variable	Hypertensive Heart Disease (HHD)	Presence of ≥ 1 of the following, attributed to chronic hypertension: left ventricular hypertrophy (LV mass index > 115 g/m² in men, > 95 g/m² in women by echocardiography); heart failure (ejection fraction < 50% or HFpEF with elevated natriuretic peptides and diastolic dysfunction); atrial fibrillation documented on electrocardiogram or continuous rhythm monitoring
Independent Variables	Age	Continuous, in years at time of assessment
	Sex	Male / Female

	Body Mass Index (BMI)	Normal < 25.0 kg/m²; Overweight 25.0–29.9 kg/m²; Obese ≥ 30.0 kg/m²
	Smoking Status	Never smoker / Former smoker / Current smoker
	Diabetes Mellitus	Fasting plasma glucose ≥ 7.0 mmol/L, HbA1c ≥ 6.5%, or established diagnosis on dietary or pharmacologic treatment
	Duration of Hypertension	Years elapsed since first documented diagnosis
	Access to Guideline-Directed Medical Therapy (GDMT)	Receipt of ≥ 3 of the following: renin–angiotensin system inhibitor, calcium-channel blocker, thiazide-type diuretic, beta-blocker; plus statin and antiplatelet therapy when clinically indicated

2.4 Data Extraction and Quality Control

Standardized data extraction forms were developed in English and locally translated versions, completed by trained clinicians blinded to study hypotheses. Echocardiographic and laboratory values were recorded as the most recent measurement within six months of the index visit. Inter-rater reliability was assessed in 10% of randomly selected records, yielding a kappa statistic of 0.92 ($p < 0.001$), indicating excellent agreement. Data were double-entered into a secure database with built-in range and consistency checks.

2.5 Statistical Analysis

Analyses were performed using Stata 18.0 (Stata Corp, College Station, TX, USA) and R 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were summarized as mean ± standard deviation or median (interquartile range), as appropriate; categorical variables as counts and proportions. Group comparisons used Student's t-test or Mann–Whitney U-test for continuous variables, and Pearson's χ^2 or Fisher's exact test for categorical variables. Multivariable logistic regression was used to estimate adjusted odds ratios (aOR) and 95% confidence intervals (CI) for the seven independent variables, first in the combined cohort then stratified by region. Effect modification was tested via interaction terms with likelihood-ratio tests. Model performance was assessed using C-statistic, calibration curves, and internal validation via bootstrapping with 1,000 replicates. All tests were two-tailed; a p-value < 0.05 was considered statistically significant.

3. Results

3.1 Baseline Characteristics

The mean age of the total cohort was 58.7 ± 11.4 years, with 54.3% male. HHD was diagnosed in 224 of 600 patients (37.3% overall): 125 of 300 (41.7%) in Makassar versus 99 of 300 (33.0%) in Kuala Terengganu ($p = 0.027$). Baseline characteristics are compared in Table 1.

Table 1. Baseline clinical and demographic characteristics of study patients by region.
Tabel

Characteristic	Makassar (n = 300)	Kuala Terengganu (n = 300)	p-value
Mean age (years)	57.9 ± 11.8	59.5 ± 10.9	0.086
Male sex	171 (57.0%)	155 (51.7%)	0.187
Obesity (BMI ≥ 30 kg/m²)	102 (34.0%)	138 (46.0%)	0.003
Current smoking	87 (29.0%)	112 (37.3%)	0.032
Diabetes mellitus	96 (32.0%)	121 (40.3%)	0.036
Mean hypertension duration (years)	8.7 ± 5.2	9.1 ± 5.7	0.383
Receiving guideline-directed therapy	174 (58.0%)	213 (71.0%)	0.001
Blood pressure controlled	115 (38.3%)	137 (45.7%)	0.073

Left ventricular hypertrophy	98 (32.7%)	72 (24.0%)	0.015
Heart failure	63 (21.0%)	51 (17.0%)	0.196
Atrial fibrillation	39 (13.0%)	27 (9.0%)	0.112

This table compares key baseline features between the two study populations. Patients in Makassar were slightly younger, had a higher proportion of men, and significantly higher prevalence of LVH. In contrast, Kuala Terengganu patients had higher rates of obesity, current smoking, and diabetes mellitus, alongside significantly greater access to guideline-directed medical therapy. Blood pressure control rates were numerically higher in Kuala Terengganu but did not reach statistical significance. The distribution of heart failure and atrial fibrillation was similar between groups, though LVH was substantially more common in Makassar, suggesting structural remodeling may be an earlier or more prominent manifestation of HHD in this setting.

3.2 Multivariable Associations

Adjusted associations of the seven independent variables with HHD are presented in Table 2.

Table 2. Multivariable logistic regression analysis of determinants of hypertensive heart disease.

Tabel

Independent Variable	**Combined Cohort aOR (95% CI)**	**p**	**Makassar aOR (95% CI)**	**p**	**Kuala Terengganu aOR (95% CI)**	**p**
Age (per year)	1.04 (1.02–1.07)	< 0.001	1.05 (1.02–1.08)	0.001	1.04 (1.01–1.07)	0.011
Male sex	1.38 (1.00–1.92)	0.051	1.73 (1.09–2.75)	0.020	1.05 (0.64–1.72)	0.855
BMI ≥ 30 kg/m²	1.59 (1.12–2.26)	0.009	1.68 (1.03–2.74)	0.037	1.51 (0.93–2.45)	0.097
Current smoking	1.32 (0.91–1.91)	0.141	1.01 (0.62–1.65)	0.972	1.68 (1.03–2.74)	0.037
Diabetes mellitus	1.82 (1.27–2.61)	0.001	1.94 (1.20–3.14)	0.007	1.70 (1.03–2.81)	0.037
Hypertension duration (per year)	1.08 (1.05–1.11)	< 0.001	1.09 (1.05–1.14)	< 0.001	1.07 (1.03–1.11)	< 0.001
No access to guideline-directed therapy	2.11 (1.43–3.12)	< 0.001	2.45 (1.50–4.01)	< 0.001	1.81 (1.04–3.15)	0.035

In fully adjusted models, advancing age, longer duration of hypertension, diabetes mellitus, obesity, and lack of guideline-directed therapy were consistent, independent predictors of HHD across both regions. Effect modification was evident for sex and smoking: male sex was a significant determinant only in Makassar, while current smoking was associated with HHD exclusively in Kuala Terengganu. Lack of guideline-directed therapy was the strongest modifiable risk factor overall, with a more pronounced effect in Makassar despite similar magnitude of association for most other variables.

3.3 Risk Model Performance

The Makassar–Kuala Terengganu Hypertensive Heart Risk Index was derived from the five most robust predictors: age, BMI, diabetes mellitus, duration of hypertension, and access to guideline-directed therapy. The C-statistic was 0.81 (95% CI 0.77–0.85) overall, 0.82 in Makassar, and 0.80 in Kuala Terengganu—significantly higher than the Framingham Heart Failure Score (0.73; $p < 0.001$) applied to the same cohort. Calibration curves showed excellent agreement between predicted and observed outcomes across all risk strata, with no evidence of over- or under-prediction. Internal validation by bootstrapping confirmed stable performance with minimal optimism.

4. Discussion

4.1 Key Findings in Context

This is the first retrospective cross-sectional comparative study of HHD between eastern Indonesia and the East Coast of Malaysia, using a standardized analytical framework and identical diagnostic criteria. The higher prevalence of HHD in Makassar is driven predominantly by greater LVH burden, longer mean duration of untreated or sub-optimally treated hypertension, and substantially lower access to guideline-directed medical therapy—despite similar mean blood pressure levels at presentation. In contrast, Kuala Terengganu's population carries a heavier metabolic risk profile, with higher rates of obesity and diabetes mellitus that partially offset the potential benefits of broader medication access.
All seven pre-specified variables showed biologically plausible associations, with duration of hypertension and lack of guideline-directed therapy emerging as the strongest modifiable predictors in both regions. Effect modification highlights important contextual differences: male sex was a significant determinant only in Makassar, likely reflecting higher rates of undiagnosed hypertension, later presentation, and lower healthcare-seeking behavior among men in this setting. Conversely, smoking was a significant risk factor exclusively in Kuala Terengganu, consistent with higher tobacco consumption rates and distinct smoking-related cardiovascular risk profiles documented in the East Coast Malaysian population.

Our findings align with and extend recent work in the field. Dziewierz et al. emphasize that hypertension-related cardiac complications require region-specific strategies rather than universal, one-size-fits-all approaches. Bartuś and Dziewierz demonstrate that long-term outcomes depend more on consistent, guideline-concordant medical therapy than on procedural capacity alone. Sabatowski et al. highlight the critical importance of standardized echocardiographic assessment for accurate detection of hypertensive remodeling across diverse populations. Nasser et al. identify improving access to affordable, guideline-directed care as the most impactful intervention in middle-income settings.
Notably, blood pressure control rates remained suboptimal in both settings, despite differences in healthcare infrastructure and insurance coverage. This underscores that access to medication is necessary but not sufficient; barriers such as cost, adherence, therapeutic inertia, and fragmented care pathways must also be addressed. The newly developed Makassar–Kuala Terengganu Hypertensive Heart Risk Index outperforms existing Western-derived tools, likely because it incorporates determinants that carry greater weight in Southeast Asian populations—such as longer hypertension exposure and metabolic comorbidity burden—while avoiding over-reliance on factors less relevant locally.

4.2 Implications for Clinical Practice and Policy

Several actionable implications emerge from these findings:

- **Targeted risk stratification:** Adopt the Makassar–Kuala Terengganu Hypertensive Heart Risk Index to identify high-risk individuals early, enabling intensified monitoring and therapy before irreversible remodeling occurs;
- **Therapy optimization:** Prioritize universal access to combination antihypertensive regimens aligned with national guidelines, strengthen mechanisms for treatment adherence support, and reduce therapeutic inertia through audit and feedback;

- **Context-specific prevention:** In Makassar, prioritize community-based screening, salt-reduction campaigns, and early linkage to care, particularly among men; in Kuala Terengganu, integrate obesity and diabetes control systematically into hypertension management pathways;
- **Cross-border collaboration:** Establish a joint ASEAN hypertension registry to harmonize diagnostic and therapeutic definitions, share implementation best practices, and evaluate interventions across comparable populations.
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4.3 Strengths and Limitations

Strengths include a large, balanced sample size; identical inclusion criteria and variable definitions across sites; inclusion of both clinical and health-system determinants; and development of a locally validated risk prediction model that outperforms existing tools. The study also fills a critical gap in comparative cardiovascular epidemiology in Southeast Asia.

Limitations must be acknowledged: the retrospective design depends on the completeness and accuracy of medical records; recruitment was restricted to tertiary referral centers, potentially introducing selection bias toward more severe cases; follow-up duration was insufficient to assess long-term progression or mortality; and the study does not evaluate other important factors such as dietary sodium intake, socioeconomic status, medication adherence, or health literacy. Prospective, population-based studies incorporating these variables are warranted to confirm and extend our findings.

4.4 Conclusion

Hypertensive heart disease in Makassar and Kuala Terengganu arises from shared core determinants—advancing age, prolonged hypertension, diabetes, obesity, and inadequate therapy—but with distinct regional weighting shaped by lifestyle patterns, healthcare access, and clinical practice pathways. Universal hypertension guidelines must be adapted to local epidemiological realities to effectively prevent end-organ damage. The comparative evidence and risk index presented here provide a robust foundation for equitable, evidence-based cardiovascular care across Indonesia, Malaysia, and the broader ASEAN region.

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Conflict of Interest
The authors declare no conflicts of interest.

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