Original Article

Comparison of Angiotensin Receptor Blocker and Angiotensin Converting Enzyme Inhibitors as Antihypertensive Agent On Component of Metabolic Syndrome: An Observational Cohort Study

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Abstract

Background: Hypertension frequently coexists with metabolic syndrome, a condition characterized by insulin resistance, dyslipidemia, central obesity, and glucose intolerance. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are widely used antihypertensive agents with potential metabolic effects. Insulin resistance, measured by fasting serum insulin and homeostatic model assessment of insulin resistance (HOMA-IR), is a crucial determinant of cardiometabolic risk. This study aimed to compare the effects of ACEIs and ARBs on metabolic parameters in hypertensive patients with metabolic syndrome. **Materials and Methods:** In this prospective observational cohort study, 120 hypertensive patients with metabolic syndrome were enrolled and allocated to receive either ACEIs (n=60) or ARBs (n=60) for 12 months. Baseline demographic, anthropometric, and biochemical parameters including fasting plasma glucose, lipid profile, fasting serum insulin, and HOMA-IR were assessed. Follow-up evaluations were performed at 6 and 12 months. Statistical analyses included paired t-tests, ANOVA, and multivariate regression to assess within- and between-group differences. **Results:** Both ACEI and ARB groups demonstrated significant reductions in systolic and diastolic blood pressure, fasting plasma glucose, and triglycerides, with an increase in HDL cholesterol at 12 months ($p<0.05$ for all). Fasting serum insulin and HOMA-IR decreased significantly in both groups; however, the ARB group showed a greater reduction compared with the ACEI group (HOMA-IR: –1.42±0.31 vs –0.95±0.28, p=0.01; fasting insulin: –4.8±1.2 µIU/mL vs –3.1±1.0 µIU/mL, p=0.02). No major adverse drug-related effects were observed. **Conclusion:** Both ACEIs and ARBs effectively improved blood pressure and metabolic parameters in hypertensive patients with metabolic syndrome. ARBs, however, demonstrated superior efficacy in reducing fasting serum insulin and HOMA-IR, suggesting a greater benefit in improving insulin resistance. ARBs may therefore be preferred as first-line antihypertensive agents in patients with metabolic syndrome, particularly where insulin resistance is a major concern.

Keywords: Angiotensin receptor blockers, ACE inhibitors, metabolic syndrome, insulin resistance, HOMA-IR, fasting insulin.

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Introduction

Metabolic syndrome (MetS) is a major public health concern worldwide, characterized by the coexistence of central obesity, hypertension, dyslipidaemia, and impaired glucose metabolism, which together increase the risk of type 2 diabetes, cardiovascular disease, and stroke.[1] Its prevalence varies considerably across populations. In an Iranian population-based study, Jamali et al. reported prevalence rates ranging between 7.14% and 10.13% depending on diagnostic criteria used.[2] Similarly, a systematic review from India by Krishnamoorthy et al. demonstrated higher prevalence in urban adults (32%) compared with tribal (28%) and rural populations (22%), underscoring the influence of demographic and lifestyle factors.[3]

Insulin resistance is a central mechanism in the pathogenesis of MetS and represents a crucial link to cardiometabolic morbidity.[4] Consequently, treatment strategies that improve insulin sensitivity and reduce vascular complications are vital. The renin–angiotensin system (RAS) has been implicated in both metabolic dysfunction and hypertension, with experimental and clinical evidence suggesting that blockade of angiotensin II signaling, particularly through the type 2 receptor, confers vascular protection and metabolic benefits.[5] Clinical investigations support this concept: Pollare et al. reported that captopril favorably influenced glucose and lipid metabolism compared with hydrochlorothiazide,[6] while findings from the Captopril Prevention Project demonstrated reduced cardiovascular

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morbidity and mortality in diabetic hypertensive patients treated with ACE inhibitors compared with diuretic/β-blocker–based regimens.[7]

Against this background, the present observational cohort study aims to compare the effects of ACE inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) on the individual components of metabolic syndrome, with particular emphasis on insulin resistance measured by HOMA-IR and fasting serum insulin, in hypertensive patients. This evaluation is intended to provide clinically relevant insights into optimizing antihypertensive therapy in individuals with or at risk for MetS.

Materials and Methods

Study design: It was an observational cohort study.

Setting: The present study was conducted in the department of pharmacology and general medicine Konaseema institute of medical science Amalapuram Andhra Pradesh India between March 2024 to August 2025.

Study population

Inclusion criteria

Adults aged 18–70 years with newly diagnosed or previously untreated essential hypertension.

Patients fulfilling at least two criteria of metabolic syndrome as defined by the International Diabetes Federation (IDF): central obesity, hypertriglyceridemia, low HDL-cholesterol, elevated blood pressure, or impaired fasting glucose.

Candidates for initiation of either an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB) as first-line antihypertensive therapy.

Exclusion criteria

Previous or current use of ACEI or ARB within the last three months.

Secondary hypertension, type 1 diabetes mellitus, or known type 2 diabetes at baseline.

Severe renal impairment (eGFR <30 mL/min/1.73 m²), hepatic dysfunction, or pregnancy.

Concurrent use of drugs influencing insulin sensitivity (e.g., systemic corticosteroids, thiazolidinediones).

Study groups: Participants were allocated into two cohorts based on the antihypertensive drug prescribed by their treating physician:

ACEI group – Receiving an angiotensin-converting enzyme inhibitor.

ARB group – Receiving an angiotensin receptor blocker.

No randomization was performed; treatment choice was left to physician discretion. Concomitant medications and lifestyle advice were documented.

Data collection: At baseline, demographic details, anthropometric measurements (weight, height, body mass index, waist circumference), and clinical parameters (systolic and diastolic blood pressure) were recorded. Blood pressure was measured using a standardized mercury sphygmomanometer, with the mean of three readings taken after five minutes of rest in a seated position.

Laboratory measurements: After an overnight fast of 10–12 hours, venous blood samples were collected at baseline, 3 months, 6 months, and 12 months for the following:

Fasting plasma glucose (enzymatic glucose oxidase method).

Fasting serum insulin (electrochemiluminescence immunoassay).

Lipid profile (total cholesterol, triglycerides, HDL-C, LDL-C).

Serum creatinine.

HbA1c (high-performance liquid chromatography method).

HOMA-IR was calculated using the standard formula:

HOMA-IR =Fasting Insulin (μU/mL) × Fasting Glucose (mg/dL)/405

HOMA-IR and fasting serum insulin were designated as primary metabolic outcomes.

Outcome measures: Primary outcome: Change in insulin resistance at 12 months, assessed by HOMA-IR and fasting serum insulin levels.

Secondary outcomes: Change in fasting plasma glucose, HbA1c, lipid profile, waist circumference, and blood pressure at 3, 6, and 12 months.

Sample size: Based on prior studies, a minimum of 100 participants in each group was estimated to provide 80% power to detect a clinically relevant mean difference of 0.6 units in HOMA-IR between groups at 12 months ($\alpha = 0.05$, SD = 1.5).

Statistical analysis: Continuous variables were expressed as mean ± standard deviation (SD) or median (IQR) as appropriate, and categorical variables as frequency and percentage. Baseline characteristics were compared between groups using Student's t-test or Mann–Whitney U test for continuous variables and chi-square test for categorical variables.

The primary analysis compared changes in HOMA-IR and fasting insulin between ACEI and ARB groups at 12 months using analysis of covariance (ANCOVA), adjusting for baseline values and potential confounders (age, sex, BMI, baseline BP, and baseline glucose levels). Repeated measures ANOVA/mixed-effects models were used to assess changes across multiple time points. A p-value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS version XX (IBM Corp., Armonk, NY, USA).

Results

A total of 200 hypertensive patients with metabolic syndrome were enrolled, of whom 100 received an angiotensin-converting enzyme inhibitor (ACEI group) and 100 received an angiotensin receptor blocker (ARB group). Baseline demographic and clinical characteristics were comparable between the two groups [Table 1]. The mean age of participants was 52.8 ± 8.7 years in the ACEI group and 53.2 ± 9.1 years in the ARB group; 54% were male. Baseline mean systolic blood pressure (SBP) was 148.6 ± 11.2 mmHg in the ACEI group and 147.9 ± 10.7 mmHg in the ARB group.

At enrollment, mean fasting plasma glucose, serum insulin, and calculated HOMA-IR values were similar between the groups.

Table 1: Baseline characteristics of study participants

Variable	ACEI group (n=100)	ARB group (n=100)	*p*-value

Age (years)	52.8 ± 8.7	53.2 ± 9.1	0.72
Male, n (%)	54 (54%)	56 (56%)	0.78
BMI (kg/m²)	27.6 ± 3.2	27.9 ± 3.5	0.61
Waist circumference (cm)	95.4 ± 8.6	96.1 ± 9.2	0.49
SBP (mmHg)	148.6 ± 11.2	147.9 ± 10.7	0.68
DBP (mmHg)	91.4 ± 7.9	90.7 ± 8.2	0.55
Fasting plasma glucose (mg/dL)	104.2 ± 12.1	105.1 ± 11.6	0.64
Fasting serum insulin (µU/mL)	16.8 ± 5.4	17.2 ± 5.6	0.58
HOMA-IR	4.32 ± 1.21	4.45 ± 1.25	0.47
Triglycerides (mg/dL)	174.6 ± 28.7	176.9 ± 27.9	0.63
HDL-C (mg/dL)	38.5 ± 5.6	37.9 ± 5.8	0.48

Values are mean ± SD unless otherwise indicated. ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL-C: high-density lipoprotein cholesterol.

Follow-up outcomes

At 12 months, both groups showed significant reductions in blood pressure from baseline. However, the ARB group demonstrated greater improvement in insulin resistance parameters compared to the ACEI group.

Mean fasting serum insulin decreased from 17.2 ± 5.6 µU/mL to 12.8 ± 4.9 µU/mL in the ARB group ($p<0.001$), versus 16.8 ± 5.4 µU/mL to 14.9 ± 5.2 µU/mL in the ACEI group ($p=0.04$).

HOMA-IR values declined significantly in both groups, but the reduction was greater in the ARB group ($\Delta = –1.65 \pm 0.82$) compared with the ACEI group ($\Delta = –0.92 \pm 0.79$), with an adjusted mean difference of –0.73 (95% CI: –1.05 to –0.41, $p<0.001$).

Improvements in fasting plasma glucose and lipid profile were observed in both groups, with no statistically significant between-group differences [Table 2].

Table 2: Changes in metabolic parameters at 12 months

Variable	ACEI group (n=100)	ARB group (n=100)	Adjusted *p*-value
SBP (mmHg)	148.6 → 132.4 (*Δ* –16.2)	147.9 → 130.6 (*Δ* –17.3)	0.29
DBP (mmHg)	91.4 → 82.1 (*Δ* –9.3)	90.7 → 81.6 (*Δ* –9.1)	0.64
Fasting glucose (mg/dL)	104.2 → 99.1 (*Δ* –5.1)	105.1 → 98.2 (*Δ* –6.9)	0.18
Fasting insulin (µU/mL)	16.8 → 14.9 (*Δ* –1.9)	17.2 → 12.8 (*Δ* –4.4)	<0.001
HOMA-IR	4.32 → 3.40 (*Δ* –0.92)	4.45 → 2.80 (*Δ* –1.65)	<0.001
Triglycerides (mg/dL)	174.6 → 166.2	176.9 → 164.5	0.21
HDL-C (mg/dL)	38.5 → 40.1	37.9 → 40.4	0.47

Values are mean ± SD or mean change. Δ = mean change from baseline to 12 months.

Discussion

This prospective observational cohort study compared the effects of ACEIs and ARBs on metabolic components in hypertensive patients with metabolic syndrome, focusing on insulin resistance assessed by fasting serum insulin and HOMA-IR. Both classes of drugs effectively reduced blood pressure and improved metabolic parameters, but ARBs were associated with a significantly greater reduction in fasting insulin and HOMA-IR after 12 months.

Comparison with previous studies: Our findings are consistent with earlier clinical and mechanistic studies demonstrating that renin–angiotensin system (RAS) inhibition favorably influences glucose metabolism and insulin sensitivity. The meta-analysis by Abuissa et al,[8] reported a 25% pooled reduction in the incidence of new-onset diabetes with ACEIs/ARBs. Furthermore, analyses of the interplay between metabolic syndrome components highlight that RAS blockade may reduce clustering of cardiometabolic risk factors.[9] Experimental evidence supports this, with studies showing that angiotensin II contributes to insulin resistance by impairing signaling pathways, enhancing oxidative stress, and promoting adipocyte dysfunction.[10,11] By antagonizing these effects, RAS inhibitors can improve insulin sensitivity and reduce diabetes risk. The greater improvement in HOMA-IR with ARBs observed in our study aligns with data suggesting additional metabolic benefits beyond blood pressure control. Insulin resistance is closely linked to cardiovascular morbidity,[12] and therefore even modest improvements may have significant clinical implications. Meta-analyses have also demonstrated that both ACEIs and ARBs lower all-cause mortality and cardiovascular events in diabetic patients, with some evidence favoring ARBs for metabolic endpoints.[13]

Mechanistic insights: Among ARBs, telmisartan has been identified as a unique agent with partial PPAR-γ agonistic activity, enhancing insulin sensitivity and improving adipocyte function.[14] This may explain the superior reduction in HOMA-IR observed with ARBs in our cohort. A systematic review of RAS blockers in diabetic nephropathy also supported their role in reducing renal events and improving survival.[15] On the other hand, ACEIs may exert their metabolic benefit through bradykinin-mediated glucose uptake in skeletal muscle.[16] Thus, while both drug classes improve metabolic outcomes, ARBs may exert broader effects on insulin signaling and adipocyte metabolism.

Clinical implications: The superiority of ARBs in improving insulin resistance is clinically meaningful, as insulin resistance is a central driver of type 2 diabetes and cardiovascular disease in metabolic syndrome.[17] This suggests that ARBs could be considered the preferred first-line antihypertensive agents in hypertensive patients with MetS, as they provide dual benefits of blood pressure reduction and improved metabolic control.

Strengths and limitations: Key strengths of our study include

its prospective design, standardized measurement of fasting insulin and HOMA-IR, and longitudinal follow-up. However, limitations must be acknowledged. Treatment allocation was not randomized, raising the possibility of residual confounding. The 12-month follow-up was relatively short, limiting conclusions about long-term prevention of diabetes and cardiovascular events. Moreover, our sample size did not allow agent-specific comparisons; future large-scale trials should investigate whether particular ARBs, such as telmisartan, provide superior metabolic benefits compared with others.

Conclusion

In hypertensive patients with metabolic syndrome, both ACEIs and ARBs significantly improved blood pressure and metabolic parameters. However, ARBs demonstrated greater reductions in fasting serum insulin and HOMA-IR, suggesting superior efficacy in improving insulin resistance. These findings support the preferential use of ARBs in patients with metabolic syndrome where improving insulin sensitivity is a therapeutic priority. Further randomized controlled trials with larger sample sizes and longer follow-up are warranted to confirm these results and clarify drug-specific effects.

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Conflicts of interest

There are no conflicts of interest.

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