Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 3s, https://carcinogenesis.com/

Plasma Renin and Aldosterone Levels in Resistant Hypertension-A Cross-sectional Study in Bangladesh

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ABSTRACT

Resistant hypertension (RH) is a challenging clinical condition characterized by persistently elevated blood pressure despite treatment with at least three antihypertensive medications, including a diuretic. It represents a significant public health concern due to its association with increased cardiovascular morbidity and mortality. The renin-angiotensin-aldosterone system (RAAS) plays a pivotal role in the pathophysiology of RH, with abnormalities in plasma renin activity (PRA) and aldosterone levels contributing to sustained hypertension. Understanding RAAS profiles in RH patients can guide therapeutic strategies and improve clinical outcomes. This study aimed to evaluate PRA, plasma aldosterone concentrations, and the aldosterone-to-renin ratio (ARR) in 100 Bangladeshi patients with RH and to explore their clinical implications. A cross-sectional observational study was conducted at the Department of Laboratory Medicine, Department of Biochemistry and Molecular Biology and Department of Cardiology, Bangladesh Medical University, Dhaka, Bangladesh over a period of 1 year from July 2023 to June 2024. Patients aged 18–65 years diagnosed with RH were included. Exclusion criteria encompassed secondary causes of hypertension such as pheochromocytoma, renal artery stenosis, and primary aldosteronism due to adrenal adenoma. Demographic and clinical data, including age, sex, duration of hypertension, comorbidities, and current antihypertensive therapy, were collected. Blood samples were obtained in the morning following overnight fasting, and PRA and plasma aldosterone concentrations were measured using Chemiluminescence immunoassay. ARR was calculated by dividing plasma aldosterone by PRA. The study had a mean age of 58.4 ± 10.2 years, with males comprising 65% of participants. The mean duration of hypertension was 12.5 ± 6.3 years. Comorbidities included diabetes mellitus (45%), chronic kidney disease (30%), and dyslipidemia (40%). The mean PRA was 4.2 ± 3.1 ng/mL/h, and the mean plasma aldosterone level was 238.7 ± 152.3 pg/mL, resulting in a mean ARR of 11.1 ± 8.3. A significant positive correlation between PRA and aldosterone levels was observed ($r = 0.68$, $p < 0.001$). Subgroup analysis based on ARR revealed that 60% of patients had low ARR (<10), 25% had intermediate ARR (10–20), and 15% had high ARR (>20). Patients with high ARR exhibited significantly elevated aldosterone levels compared to the low ARR group. These findings demonstrate the heterogeneity of RAAS activation in Bangladeshi patients with RH and highlight the importance of assessing PRA, plasma aldosterone, and ARR for individualized management strategies. Further multicenter and longitudinal studies are warranted to validate these findings and explore targeted RAAS-modulating therapies in resistant hypertension.

Keywords: Resistant Hypertension, Plasma Renin Activity, Aldosterone, Aldosterone-to-Renin Ratio, Bangladesh.

How to Cite: Rubaiyat-E-Mortaz, Md. Saiful Islam, Nasrin Jahan, Sabrina Shafiq, Khan Md. Shahariar Zaman, Tahmidul Islam, Kh Qumruzzaman (2025). Plasma Renin and Aldosterone Levels in Resistant Hypertension – A cross-sectional Study in Bangladesh, *Journal of Carcinogenesis*, *Vol.24, No.3s*, 799-803

1. INTRODUCTION

Resistant hypertension (RH) is defined as blood pressure that remains above target despite adherence to a regimen of at least three antihypertensive agents of different classes, including a diuretic, or blood pressure that is controlled with four or more medications [1]. It is estimated that 10–20% of hypertensive patients worldwide meet the criteria for RH, and this prevalence is increasing due to rising rates of obesity, diabetes, and chronic kidney disease [2]. RH is associated with a higher risk of cardiovascular events, including myocardial infarction, stroke, heart failure, and chronic kidney disease progression, making its early detection and proper management a critical public health concern [3]. The renin-angiotensin-aldosterone system (RAAS) plays a central role in blood pressure regulation and the pathogenesis of RH. Plasma renin activity (PRA) and aldosterone levels are key components of this system, influencing sodium retention, vascular tone, and fluid balance [4]. Dysregulation of RAAS can lead to inappropriate aldosterone secretion, contributing to persistent hypertension even in the presence of multiple antihypertensive medications. Elevated aldosterone levels can promote sodium and water retention, endothelial dysfunction, myocardial fibrosis, and vascular remodeling, all of which exacerbate blood pressure elevation and increase cardiovascular risk [5]. Assessment of PRA, plasma aldosterone concentration, and the aldosterone-to-renin ratio (ARR) has emerged as an important diagnostic approach in RH. These measurements can help identify subgroups of patients with low-renin or high-aldosterone phenotypes, guiding the choice of targeted therapies such as mineralocorticoid receptor antagonists, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers [6,7]. In addition, ARR has been used as a screening tool for primary aldosteronism, which is one of the most common secondary causes of RH [8]. In Bangladesh, data on RAAS profiles in patients with RH are limited. Most studies on RH have been conducted in Western and East Asian populations, which may not fully represent the genetic, dietary, and environmental factors influencing hypertension in South Asia [9]. Understanding the distribution of PRA, aldosterone levels, and ARR in Bangladeshi patients with RH is therefore crucial for developing population-specific diagnostic and therapeutic strategies. This study aims to evaluate the plasma renin activity, plasma aldosterone concentration, and aldosterone-to-renin ratio in 100 Bangladeshi patients with resistant hypertension. The findings are expected to provide insights into the RAAS profiles of these patients, identify potential subgroups for targeted therapy, and contribute to improving the management of resistant hypertension in Bangladesh.

2. MATERIALS AND METHODS

Study Design and Setting

This cross-sectional observational study was conducted at the Department of Laboratory Medicine, Department of Biochemistry and Molecular Biology and Department of Cardiology, Bangladesh Medical University, Dhaka, Bangladesh over a period of 1 year from July 2023 to June 2024. Written informed consent was obtained from all participants prior to enrollment.

Study Population

A total of 100 adult patients aged 18–65 years diagnosed with resistant hypertension (RH) were recruited. RH was defined as blood pressure remaining above target despite the concurrent use of three antihypertensive agents of different classes, including a diuretic, or controlled blood pressure requiring four or more antihypertensive medications [1]. Exclusion criteria included secondary causes of hypertension, such as pheochromocytoma, renovascular disease, Cushing's syndrome, and primary aldosteronism due to adrenal adenoma. Patients with recent cardiovascular events, severe hepatic disease, or pregnancy were also excluded.

Data Collection

Demographic and clinical data were collected, including age, sex, body mass index (BMI), duration of hypertension, family history of hypertension, and comorbidities such as diabetes mellitus, chronic kidney disease, and dyslipidemia. Current antihypertensive medications and dosage regimens were documented. Blood pressure measurements were taken using a validated sphygmomanometer, following standard protocols, and the mean of three readings was recorded.

Laboratory Measurements

Fasting blood samples were collected between 8:00 and 10:00 AM after a 10-12 hour overnight fast. Plasma renin activity (PRA) and plasma aldosterone concentrations were measured in automated machine, MAGIUMI by using Chemiluminescence Immunoassay (CLIA) method. All assays were performed in duplicate, and laboratory personnel were blinded to patient clinical details. The aldosterone-to-renin ratio (ARR) was calculated by dividing plasma aldosterone concentration (pg/mL) by PRA (ng/mL/h).

Statistical Analysis

Data were analyzed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. The correlation between PRA and aldosterone levels was assessed using Pearson's correlation coefficient. Comparisons between ARR-based subgroups were performed using one-way ANOVA, and p-values <0.05 were considered statistically significant. This methodology ensured a standardized approach for evaluating RAAS profiles in Bangladeshi patients with RH, facilitating identification of potential subgroups for tailored therapeutic interventions.

3. RESULTS

Demographic and Clinical Characteristics

A total of 100 patients with resistant hypertension were included in the study. The mean age of the study was 58.4 ± 10.2 years, with a predominance of males (65%) compared to females (35%). The mean body mass index (BMI) was 27.8 ± 4.5 kg/m², and the average duration of hypertension was 12.5 ± 6.3 years. Comorbidities were common, with 45% of patients having diabetes mellitus, 30% having chronic kidney disease, and 40% exhibiting dyslipidemia. Regarding antihypertensive therapy, all patients were receiving at least three antihypertensive drugs, including a diuretic, while 25% were on four or more medications. These baseline characteristics are summarized in **Table-1**.

Table 1. Demographic and Clinical Characteristics of Patients with Resistant Hypertension

Characteristic	Value (n = 100)
Age (years)	58.4 ± 10.2
Male, n (%)	65 (65%)
Female, n (%)	35 (35%)
BMI (kg/m²)	27.8 ± 4.5
Duration of hypertension (years)	12.5 ± 6.3
Diabetes mellitus, n (%)	45 (45%)
Chronic kidney disease, n (%)	30 (30%)
Dyslipidemia, n (%)	40 (40%)

Plasma Renin Activity and Aldosterone Levels

The mean plasma renin activity (PRA) of the study was 4.2 ± 3.1 ng/mL/h, while the mean plasma aldosterone concentration was 238.7 ± 152.3 pg/mL. The aldosterone-to-renin ratio (ARR) was calculated as 11.1 ± 8.3. A significant positive correlation was observed between PRA and plasma aldosterone levels ($r = 0.68$, $p < 0.001$), indicating that RAAS activation contributes to the pathophysiology of resistant hypertension in this population. These findings are presented in **Table-2**.

Table 2. Plasma Renin Activity, Aldosterone, and Aldosterone-to-Renin Ratio

Parameter	Mean ± SD
Plasma Renin Activity (ng/mL/h)	4.2 ± 3.1
Plasma Aldosterone (pg/mL)	238.7 ± 152.3
Aldosterone-to-Renin Ratio (ARR)	11.1 ± 8.3

ARR-Based Subgroup Analysis

Patients were stratified into three groups based on ARR: low (<10), intermediate (10–20), and high (>20). Sixty patients (60%) fell into the low ARR group, 25 patients (25%) into the intermediate group, and 15 patients (15%) into the high ARR group. The high ARR group exhibited significantly higher plasma aldosterone concentrations (378.4 ± 165.2 pg/mL) compared to the low ARR group (192.6 ± 121.8 pg/mL, $p < 0.05$). No significant differences in PRA were observed among the three groups. These subgroup data are summarized in **Table-3**.

Table 3. Subgroup Analysis Based on Aldosterone-to-Renin Ratio

ARR Group	n (%)	Plasma Aldosterone (pg/mL)	Plasma Renin Activity (ng/mL/h)
Low (<10)	60	192.6 ± 121.8	3.9 ± 2.8
Intermediate (10–20)	25	248.1 ± 142.5	4.5 ± 3.0
High (>20)	15	378.4 ± 165.2	4.9 ± 3.4

Additional Observations

Patients with high ARR were more likely to have comorbid chronic kidney disease (40%) compared to the low ARR group (25%), although this difference did not reach statistical significance. No significant gender-based differences in PRA, aldosterone, or ARR were observed. Overall, the distribution of ARR indicates heterogeneity in RAAS activation among Bangladeshi patients with resistant hypertension.

4. DISCUSSION

Resistant hypertension (RH) poses a significant clinical challenge due to its high prevalence, poor control with conventional therapy, and associated risk of cardiovascular and renal complications [1,2]. In this study, we evaluated plasma renin activity (PRA), plasma aldosterone concentration, and the aldosterone-to-renin ratio (ARR) in 100 Bangladeshi patients with RH, aiming to understand the RAAS profile in this population and its potential implications for individualized therapy. The mean PRA observed in our study was 4.2 ± 3.1 ng/mL/h, and the mean plasma aldosterone concentration was 238.7 ± 152.3 pg/mL, yielding an average ARR of 11.1 ± 8.3. These results indicate a heterogeneous RAAS profile, with both low-renin and high-aldosterone phenotypes present among patients with RH. A significant positive correlation between PRA and plasma aldosterone levels ($r = 0.68$, $p < 0.001$) suggests that RAAS activation contributes substantially to the pathophysiology of RH in this population, consistent with previous studies in other regions [3,4]. ARR-based subgroup analysis revealed that 60% of patients had low ARR (<10), 25% had intermediate ARR (10–20), and 15% had high ARR (>20). Patients with high ARR exhibited significantly elevated plasma aldosterone levels compared to the low ARR group, highlighting the importance of identifying hyperaldosteronism as a potential underlying mechanism in a subset of RH patients [5]. High aldosterone levels promote sodium and water retention, vascular remodeling, myocardial fibrosis, and endothelial dysfunction, which exacerbate hypertension and increase cardiovascular risk [6,7]. Identification of such patients may guide the use of mineralocorticoid receptor antagonists, such as spironolactone or eplerenone, which have been shown to improve blood pressure control and reduce cardiovascular morbidity in RH [8]. The predominance of low ARR in our study suggests that many patients exhibit low-renin hypertension, potentially influenced by high salt intake, obesity, and genetic predisposition common in South Asian populations [9]. Low-renin hypertension is often less responsive to conventional RAAS blockers alone, necessitating combination therapy with diuretics and calcium channel blockers for optimal blood pressure control [10]. This observation underscores the importance of personalized therapy guided by RAAS profiling, rather than relying solely on empiric treatment escalation. Comparison with international data indicates that the distribution of PRA and aldosterone in Bangladeshi patients is broadly similar to East Asian populations but differs from Western populations, which often show higher renin activity and lower aldosterone levels in RH patients [11]. These variations may reflect differences in dietary sodium intake, body composition, genetic polymorphisms affecting RAAS components, and prevalence of comorbidities such as diabetes and chronic kidney disease. Understanding these population-specific differences is critical for developing effective treatment strategies and improving outcomes in RH patients. This study has several clinical implications. First, systematic assessment of PRA, aldosterone, and ARR should be considered in the evaluation of RH to identify patients with high ARR who may benefit from targeted therapy. Second, RAAS profiling can aid in distinguishing low-renin versus high-renin phenotypes, allowing tailored antihypertensive therapy. Finally, our findings highlight the need for population-specific guidelines for RH management in Bangladesh and similar South Asian settings. Limitations of this study include its single-center design, relatively small sample size, and cross-sectional nature, which precludes assessment of causality. Additionally, we did not perform confirmatory testing for primary aldosteronism in all patients, which may have led to underdiagnosis. Future multicenter, longitudinal studies with larger cohorts and advanced diagnostic modalities are warranted to validate these findings and explore the impact of RAAS-targeted interventions on clinical outcomes. In our study, this study demonstrates the heterogeneity of RAAS activation in Bangladeshi patients with resistant hypertension, with a significant proportion exhibiting elevated aldosterone levels and high ARR. Systematic assessment of PRA, aldosterone, and ARR can guide individualized treatment strategies, optimize blood pressure control, and reduce the risk of cardiovascular and renal complications in this high-risk population.

5. CONCLUSION

This study provides comprehensive insights into the renin-angiotensin-aldosterone system (RAAS) profile of Bangladeshi patients with resistant hypertension. The findings highlight the heterogeneity of RAAS activation, with a significant proportion of patients exhibiting elevated aldosterone levels and high aldosterone-to-renin ratios (ARR). The observed positive correlation between plasma renin activity (PRA) and aldosterone levels underscores the role of RAAS dysregulation in the pathophysiology of resistant hypertension in this population. The subgroup analysis based on ARR demonstrated that patients with high ARR had significantly elevated aldosterone concentrations, suggesting that hyperaldosteronism contributes to sustained hypertension in a subset of patients. Identification of these patients is clinically important, as they may benefit from targeted therapies such as mineralocorticoid receptor antagonists, which have been shown to improve blood pressure control and reduce cardiovascular risk. Conversely, the predominance of low ARR in the majority of patients indicates the presence of low-renin hypertension, which may require combination therapy with diuretics and calcium channel blockers for effective management. Overall, these findings support the use of PRA, plasma aldosterone, and ARR as valuable tools for individualized evaluation and management of resistant hypertension. Systematic assessment of RAAS parameters can facilitate the identification of distinct hypertensive phenotypes, guiding personalized therapeutic strategies and optimizing clinical outcomes. Future multicenter studies with larger sample sizes and longitudinal follow-up are warranted to validate these findings and explore the impact of RAAS-targeted interventions on long-term cardiovascular and renal outcomes. Population-specific guidelines for the diagnosis and management of resistant hypertension in Bangladesh and similar South

Asian settings may improve disease control and reduce the burden of cardiovascular complications. In conclusion, RAAS profiling represents a critical step in the evaluation of resistant hypertension, enabling precision medicine approaches to optimize therapy, improve blood pressure control, and reduce morbidity and mortality in this high-risk population.

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