CLINICAL PRACTICE ARTICLE

Frequency of Primary Hyperaldosteronism in Young Hypertensives in a Tertiary Care Setting of Rawalpindi

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ABSTRACT

Objective: To determine the frequency of primary hyperaldosteronism in young hypertensives in hospital settings of Rawalpindi.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Chemical Pathology and Endocrinology, Armed Forces Institute of Pathology (AFIP), Rawalpindi, from June 2016 to May 2017.

Methodology: Two hundred and fifty patients with hypertension (blood pressure of more than 140/90 mm Hg) of both genders, with age between 17-40 years were recruited in the study. Patients on anti-hypertensive medications, renal function derangement, pregnant females and those labelled with secondary hypertension were excluded. Blood samples were taken for the analyses of plasma renin, aldosterone, electrolytes, and blood gases. Parametric quantitative variables were presented as mean ± SD.

Results: Eight cases, out of a total 80 subjects fulfilling the inclusion criteria, were diagnosed with primary hyperaldosteronism and 72 with essential hypertension. Mean age of patients having primary hyperaldosteronism was 29.25 ±7.1 years. The mean diastolic blood pressure of all patients was 90.3 ±6.5 mm of Hg, while mean systolic blood pressure was 142.7 ±10.5 mm of Hg.

Conclusion: Frequency of primary hyperaldosteronism was found to be 10%, emphasising on the fact that it is not very uncommon in young hypertensives.

Key Words: *Renin angiotensin aldosterone disorders, Primary hyperaldosteronism, Essential hypertension.*

INTRODUCTION

Hypertension is a major health problem worldwide and one of the leading risk factors for cardiovascular diseases.[1] In developed countries, it comprises of the bulk portion of the non-communicable diseases.[2,3] In the younger population, the prevalence of hypertension is 20% in men and 15% in women.[4] Extensive work has been done on this subject and a lot of data has been collected, but still the relationship between kidneys and hypertension remains an enigma. It has been termed as the villain victim relationship, with hypertension being both a cause and a consequence of kidney disease.[5]

Renin-Angiotensin-Aldosterone System (RAAS) has an important role in maintaining hemodynamic stability by regulating the water and electrolyte balance, arterial blood pressure and systemic vascular resistance.[6] In case of hypotension, renin is released from kidneys while liver release angiotensinogen in blood, resulting in formation of angiotensin I, which forms angiotensin II, ultimately leading to the secretion of aldosterone from adrenal glands. Aldosterone, in turn, causes sodium reabsorption and potassium excretion from kidneys, returning the blood pressure to normal.[7,8] Chronic activation of RAAS by any pathological mechanism results in excessive vasoconstriction, resulting in the development of hypertension.[9] RAAS disorders, which present with hypertension, include primary hyperaldosteronism, Liddle syndrome, Gordon syndrome, and apparent mineralocorticoid excess syndrome.[10-14]

Conn described PHA for the first time in 1954. The cardinal signs are hypertension and hypokalemia and metabolic alkalosis; but potassium levels can be found normal in some cases. The most common causes include aldosterone producing adenomas, and bilateral adrenal hyperplasia. Less common forms can be familial hyperaldosteronism types I, II, III, adrenocortical carcinomas (pure aldosterone producing), adrenal hyperplasia, ectopic tumors producing aldosterone. PHA is the leading hormonal cause of hypertension with a prevalence of almost 5% in Asian population,[15] and 4.6% to 16.6% among Greeks.[10] Extended screening is required for the patients of PHA because early diagnosis facilitates an effective treatment. Plasma aldosterone concentration to plasma renin activity ratio (PAC/PRA) has been employed as the most common screening test. This ratio has been lately challenged due to the special pre-analytical prerequisites of PRA and lack of inter-

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laboratory reproducibility, it is not well recommended. In place of PRA, plasma active renin concentration (ARC) has been used to overcome these limitations.[16] Confirmation of the diagnosis is done by saline infusion test, fludrocortisone suppression test, oral salt loading, and captopril challenge test.

It is a major risk factor for death, and predicts cardio-vascular incidents that can occur in future.[4] So far no data is available about the frequency of PHA in Pakistani hypertensives. The aim of this study was to determine the frequency of PHA in young population of Pakistan who present with hypertension.

METHODOLOGY

After seeking permission from the Institution Review Board (IRB), this study was conducted from June 2016 to May 2017 at AFIP, Rawalpindi. Study design was cross-sectional. Sample size was calculated from given prevalence rate from formula of sample size estimation (n= z2p(1-p)/d2).[17] Two hundred and fifty patients with hypertension (blood pressure of more than 140/90 mm Hg) of both genders, with age between 17-40 years were recruited in the study. Patients on anti-hypertensive medications, renal function derangement, pregnant females and those labelled with secondary hypertension were excluded. After taking consent from the subjects, sampling was done by nonprobability consecutive sampling technique.

Three milliliters venous blood was taken in EDTA vacutainers for plasma aldosterone and renin. Heparinized syringe was used to collect arterial blood sample for blood gases, pH and electrolytes (sodium, bicarbonate and potassium). Arterial blood was analysed on COBAS b221 by potentiometry; and bicarbonate levels were calculated by Henderson Hassel Balch equation. Plasma renin was done by sandwich chemiluminescence immunoassay on Diasorin Liason® and plasma aldosterone by ELISA (enzyme linked immunosorbent assay) on Biorad PhD™ system. Sample for aldosterone and renin was collected from patient in morning in seated ambulatory position. All patients were on unrestricted salt intake. Hypokalemia found was corrected with oral potassium supplements. Saline infusion test was performed on patients having a positive screening test for primary hyperaldosteronism by intravenous administration of two liters of 0.9% isotonic saline over four hours (from 8 AM to 12 PM), while the patient was comfortably seated to check for aldosterone suppression. Aldosterone concentration, after four hours, below 139 pmol/L was considered as a normal response, whereas values above 277 pmol/L were consistent with primary aldosteronism.[20] Aldosterone to renin ratio (ARR) was computed after measuring plasma aldosterone and plasma active renin concentration (ARC). This was used as a screening test for primary hyperaldosteronism. An ARR of more than 130 pmol/mIU was consistent with suspicion of primary hyperaldosteronism, while ARR below 100 pmol/mIU was suggestive of essential hypertension.[21]

Statistical Package for Social Sciences (SPSS) version 24 was used for data analysis. Mean and standard deviations were calculated for all the parametric quantitative variables while frequencies with percentages were used for qualitative variables.

RESULTS

Out of 250 patients, 188 (75.2%) patients gave consent for the study, out of which only 80 (42.5%) were selected as they fulfilled the inclusion criteria. Out of these 80 patients, 68 (85%) were males and 12 (15%) were females. Mean diastolic blood pressure of all patients was 90.3 ±6.5 mm of Hg while mean systolic blood pressure was 142.7 ±10.5 mm of Hg. Mean age of all the patients was 30.8 ±7.1 years (Table I).

Among the studied subjects, eight (10%) patients screened positive for primary hyperaldosteronism, and all were males. Seventy-two (90%) patients were reported with essential hypertension, out of whom 60 (83.3%) were males and 12 (16.6%) were females (Figure 1). All eight patients with ARR >130 pmol/mIU were subjected to saline infusion test for confirmation of primary hyperaldosteronism, and all showed failure of suppression of aldosterone after saline infusion, thus confirming the diagnosis (Table II).

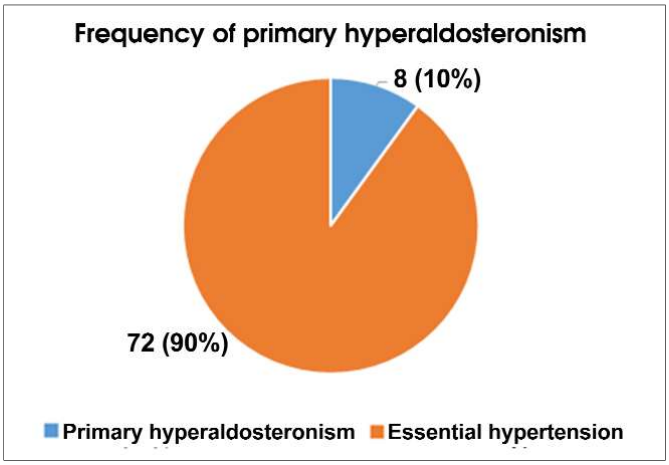

Figure 1: Pie chart showing frequency of primary hyperaldosteronism cases in a study population of 80 subjects.

Table I: Descriptive analysis of different study factors.

	Age	Diastolic BP	Systolic BP	Serum Potassium	Serum Sodium
All cases (Mean+SD) years	30.8 ±7.1	90 ±6.5	142.7 ±10.5	4.23 ±0.6	137.8 ±6.5
With primary hyperaldosteronism (Mean+SD) mmHg	29.25 ±7.1	92.5 ±4.6	143.12 ±11.6	3.73 ±0.4	140.6 ±6.3
With essential hypertension (Mean+SD) mmHg	30.97 + 7.1	90.06 ±6.6	142.70 ±10.5	4.29 ±0.6	137.5 ±6.5

Table II: Frequency with percentages of patients with positive screening test (ARR) for primary hyperaldosteronism.

Number of patients	ARR >130pmol/mIU	Failure to saline infusion suppression test
80	8 (10%)	8 (10%)

DISCUSSION

Primary (insuppressible) secretion of aldosterone is an underdiagnosed cause of hypertension. PHA is characterised by hypertension, hypokalemia and metabolic alkalosis, uninhibited secretion of aldosterone and a very low renin concentration. It is screened by PAC/PRC and screened cases are finally diagnosed following the confirmatory tests like the saline infusion test.[18]

Primary hyperaldosteronism cases found in 10% cases. All these positive patients were males. A very similar finding has been reported by a study conducted in Italy by Rossi *et al*., which is 11.2% without gender differences and same study population characteristics (*e.g.* age).[14] A Greek study, conducted by Douma *et al*. in Aristotle University, reported a frequency of 11.3% of primary hyperaldosteronism,[19] which is consistent with the present findings.

Roberto *et al*. documented a prevalence of 5.9% in Italy after confirmation by saline infusion test.[20] This difference can be explained by the fact that different ethnic groups and races have different expression of diseases; therefore, emphasizing on the fact that each population should be studied separately for the prevalence of a particular disease.[21]

Douma *et al*. reported a mean age for primary hyperaldosteronism of 56.7 $\pm$12.3 years and that for essential hypertension was 56.3 $\pm$12.3 years,[19] while in this study the mean age of patients having essential hypertension was 30.97 $\pm$7.1 years and of those with primary hyperaldosteronism was 29.25 $\pm$7.1 years. This difference can be explained by the fact that our study was based on young hypertensive population, while age was not a criterion in their inclusion.

Although these results project will serve as a preliminary data for future information and studies, but lack of genetic testing, single center study and a small sample size are the limitations. Therefore, the authors would recommend a metacentric study with an advanced study design and a bigger sample size for more authentic results.

CONCLUSION

Primary hyperaldosteronism is common in young hypertensive population. It should always be considered in young population who present with hypertension. Screening of the patients first with ARR and then confirmation by saline infusion test should be the protocol.

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