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CLINICOAETIOLOGICAL PROFILE OF PATIENTS PRESENTING WITH MODERATE TO SEVERE HYPERTENSION IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Hypertension affects over 1.2 billion individuals worldwide and has become the most critical and expensive public health problem. It is a multifactorial disease involving environmental and genetic factors together with risk conferring behaviours. Most cases of hypertension are idiopathic, where it is also known as essential hypertension. It has long been suggested that an increase in salt intake increases the risk of developing hypertension. Hypertension is also associated with atherosclerosis, coronary and cerebrovascular disease, diabetes and can lead to myocardial infarction, stroke, renal failure, and consequent death if not detected early and treated appropriately. Hypertension can occur due to many underlying causes, when it is known as secondary hypertension, mainly due to Cushing's disease, phaeochromocytoma, hyperthyroidism, renovascular disease, raised intracranial pressure, aortic coarctation and renal parenchymal disease **(1).** It is a major contributor to the most common causes of morbidity and mortality in adult populations.

KEYWORDS- Essential hypertension, Dyslipidemia, Secondary hypertension

ABBREVIATIONS-

Tumour Necrosis Factor Alpha	TNF α
American Heart Association	AHA
American Medical Association	AMA
Very Low Density Lipoprotein	VLDL
Dietary Approaches to Stop Hypertension	DASH
High Density Lipoprotein	HDL
Interleukin 6	IL-6
Joint National Committee	JNC
Low Density Lipoprotein	LDL
Left Ventricle Hypertrophy	LVH
Non Steroidal Anti Inflammatory Drug	NSAID
Obstructive Sleep Apnea	OSA
Body Mass Index	BMI

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Systolic Blood Pressure	SBP
Diastolic Blood Pressure	DBP
Chronic Kidney Disease	CKD

Hypertension is one of the most significant modifiable risk factors for cardiovascular disease and one of the main causes of morbidity and mortality globally. In the 2017, the Global Burden of Disease Study performed a systematic analysis, in which it was found that high systolic blood pressure (SBP) was the leading risk factor for mortality and disability-adjusted life years **(2)**

The risk of cardiovascular illnesses is doubled by hypertension, these include coronary artery disease, congestive cardiac failure (CHF), stroke, chronic kidney disease, and peripheral artery disease. It generally accompanies other cardiovascular disease risk factors, and the impact of all associated factors raises the likelihood of developing cardiovascular disease. **(3)**

Guidelines for BP measurement

The following are 7 strategies recommended by the AHA/AMA for accurate attainment of BP: 1) no conversation, 2) empty bladder, 3) use correct cuff size, 4) place BP cuff on bare arm, 5) support arm at heart level, 6) keep legs uncrossed, and 7) support back and feet **(4).**

Secondary Hypertension

Clinical clues that should raise suspicion for a secondary cause of hypertension include snoring/daytime sleepiness, abrupt onset of hypertension, hypertension onset < 30 years of age, accelerated/malignant hypertension, abrupt loss of BP control in a patient with prior BP control, use of BP raising substances such as NSAIDs/amphetamines/immunosuppressive agents, resistant (taking 3 or 4 antihypertensive drugs, including a diuretic and BP above goal or taking > 4 drugs, including a diuretic and BP below goal) or refractory hypertension (taking > 5 drugs, including a diuretic, and BP above goal), unprovoked (not taking a diuretic) or excessive hypokalaemia, and/or the onset of diastolic hypertension in older patients (> 65 years).

Risk factors for hypertension

The prevalence of hypertension increases with age in both males and females **(5)**. Although men's blood pressure is greater at younger ages than women's, women's blood pressure rises more quickly over the course of a decade. Women have a higher mean blood pressure and prevalence of hypertension as compared to men. Race and ethnicity also have an important role in the development of hypertension **(6)**.

High sodium intake

In 2010, the PURE study estimated that on an average, 3,950 mg of sodium were consumed globally per day, which is substantially more than the recommended daily consumption of less than 2,300 mg **(7)**. Observational epidemiological studies and randomised clinical trials have proven that there is a causal link between high sodium intake and high blood pressure. The majority of observational studies were crosssectional and found a substantial link between dietary salt intake and hypertension **(8)**.

Low dietary potassium

The best available measure of potassium intake is the 24-hour urinary potassium excretion. Like sodium, 24-hour urine potassium excretion varies greatly by region, with Europe and South America having the highest amounts and Asia and Africa having the lowest values **(9).** An inverse association of dietary potassium intake has been found with blood pressure levels and hypertension.

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Alcohol consumption

Several observational epidemiological studies have revealed that excessive alcohol use is a risk factor for high blood pressure **(10)**. According to the Atherosclerosis Risk in Communities Study, drinking alcohol and the risk of developing hypertension have a J-shaped relationship **(10)**. Alcohol intake was positively and linearly linked with blood pressure in a large prospective cohort study of more than 500,000 Chinese people **(11)**.

Lack of physical activity

According to a study that looked at trends in physical inactivity from 2001 to 2016, the prevalence of insufficient physical activity, defined as less than 150 minutes per week of moderate-intensity activity or 75 minutes per week of vigorous-intensity activity, or any equivalent combination of the two, was higher in women (31.7%) than in men (23.4%) **(12)**.

PATHOGENESIS

Increased peripheral arterial resistance is the hallmark of essential hypertension. he active component of arteriolar resistance depends on the contraction of vascular smooth muscle cells. Structural changes in the wallto-lumen ratio are termed vascular remodelling**.** Histopathological studies of gluteal arterioles mounted on wire myographs have shown that resistance vessels of hypertensive patients have a reduced lumen, an increased media-tolumen ratio, but a normal medial cross-sectional area**.** Experimental evidence favours the notion that these morphological alterations arise as an adaptation to the increased blood pressure through changes in the neurohumoral milieu, and that they amplify rather than cause increase of blood pressure **(13).**

Inflammatory Markers in Hypertension

Whilst there is a distinction between primary inflammatory markers and vascular markers that may be indirectly involved in the inflammatory process (inflammatory sensitive markers), the boundaries are somewhat blurred. Nevertheless, there is an increasing evidence base to support a relationship between elevation in vascular inflammatory markers and hypertension **(14).**

Highly sensitive C-Reactive Protein (CRP)

Highly sensitive CRP has evolved as the most robust and reproduceable marker of vascular inflammation and is considered the prototypic downstream marker of inflammation **(15).**

Interleukin 6 and Interleukin-1b

IL-6 is a pleiotropic cytokine produced by T-cells, macrophages, and endothelial cells that has many diverse physiological roles, including mediation of both proinflammatory responses and cyto-protective functions**.** IL-6 stimulates the synthesis of several acute-phase reaction proteins, including CRP, Serum amyloid-A and fibrinogen, and counter regulates TNF-a and IL-1 b **(16).**

Tumour Necrosis Factor Alpha (TNF-a)

TNF-a is a 185 amino acid glycoprotein peptide hormone that is synthesized mainly by monocytes and macrophages. TNF-a plays a significant role in the initial activation of the immune system **(17)**

SECONDARY HYPERTENSION

About 5-10% of hypertensive patients have an underlying cause. The main causes of secondary hypertension are parenchymal renal disease, primary aldosteronism and renovascular hypertension. The identification of these patients is important because it enables the etiological management of the underlying disease and in some cases leads to blood pressure control without antihypertensive medications **(18)**.

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MATERIAL AND METHODS

This open label, hospital based, prospective, cross-sectional, observational study was carried out in the medicine OPD, nephrology OPD/ward, emergency department, and patients admitted in the medicine wards, coronary care unit and critical care ward of Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh. A total of 164 patients were enrolled for the study. This study was conducted from December 2020 to October 2022.

Inclusion criteria:

a. All patients with newly diagnosed hypertension stages 1 and 2 as per Joint National Committee 8 (JNC 8) criteria.

b. Patients diagnosed with hypertension stages 1 and 2 as per Joint National Committee 8 (JNC 8) criteria who have been started on antihypertensive therapy for less than 8 weeks duration.

Exclusion criteria:

a. Patients on antihypertensive therapy for more than 8 weeks of duration.

b. Congestive cardiac failure

c. Chronic kidney disease on haemodialysis

d. Malignancy

e. Moribund patients

f. Stroke

g. Pregnant patients

h. Patients on oral contraceptive pills or steroid therapy

i. Haemodynamically unstable patients (till stabilized)

j. Patients not giving voluntary consent for the study.

The study was approved by the Institutional Ethics Committee and the study was conducted as oer the standards of Good Clinical Practice.

STATISTICAL ANALYSIS

All categorical variables were presented in the form of number and percentage (%). Quantitative data was presented as the mean ± SD and as median with 25th and 75th centiles (interquartile range). The following statistical tests were applied for the results: a. The association of the variables which were quantitative in nature were analyzed using independent t test (for two groups) and ANOVA test (for more than two groups). b. The association of the variables which were qualitative in nature were analyzed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used. The data entry was done in the Microsoft Excel spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, Ver 26.0. For statistical significance, p value of less than 0.05 was considered statistically significant.

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RESULTS

A total of 164 patients presenting with moderate to severe hypertension were enrolled in our study.

The characteristics were analysed and were evaluated for underlying secondary causes of hypertension.

Age group (years)	Moderate Hypertension	Severe Hypertension
<30	**1**	**3**
30-39	**12**	**6**
40-49	**29**	**29**
50-59	**19**	**11**
60-69	**13**	**10**
70-79	**11**	**3**
>80	**3**	**0**

TABLE 1

56.7% patients were males and 43.3% patients were females. In majority (56%) of patients, lifestyle was sedentary. Mean value of age (years) of study subjects was 58.53 ± 5.67 with median (25th-75th percentile) of 50 (45-52.75)

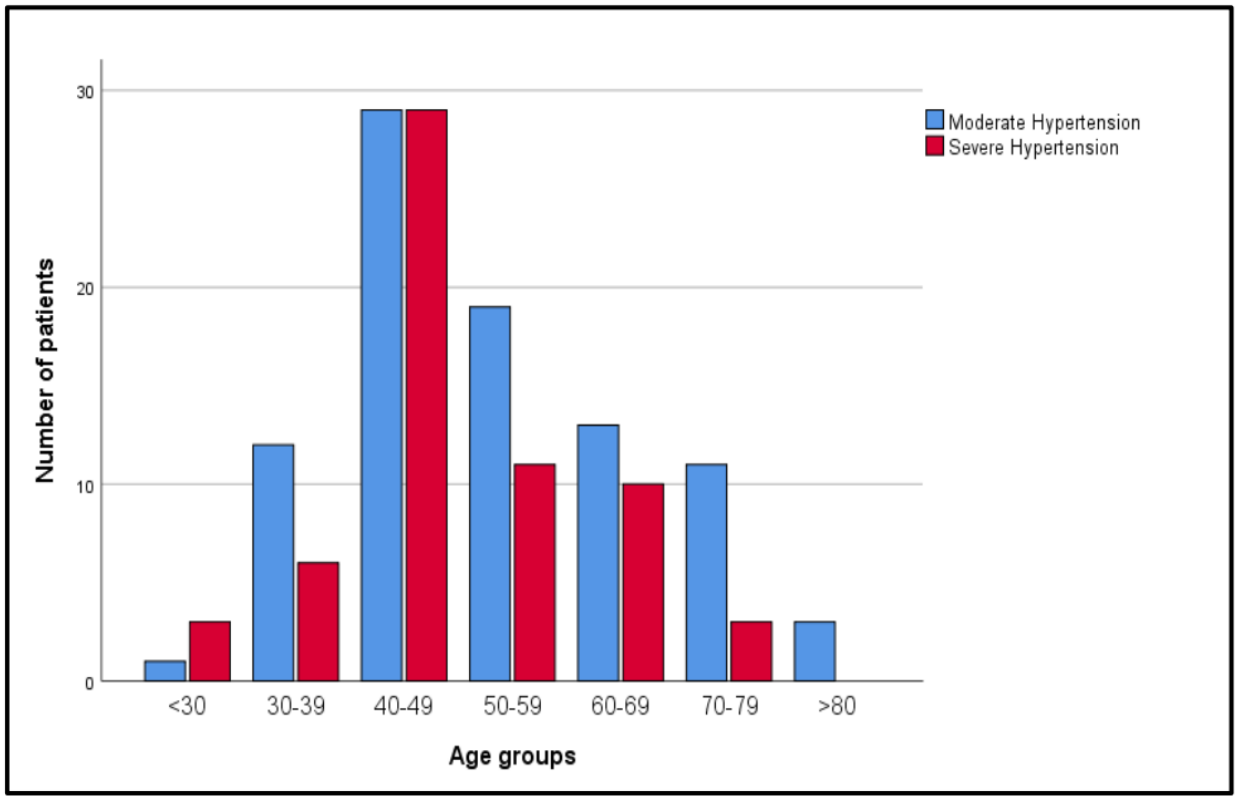

FIGURE 1

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The maximum age of patients in our study was found to be 90 years, and the minimum age was 16 years. The mean age of our study population was 51.53 ± 12.7 years. In similar studies conducted in India**,** the mean age was 59.2 ± 13 years **(19).**

Majority of the patients were young (between 40-49 years) (40%) followed by 24% in older age groups and only 4% were in extremes of age.

The mean age of males included in study was lower than females i.e., 38.41 years in males as compared to 40.71 years in females. This is similar to previous studies done in India and World **(20)**. Male sex is one of the most consistently confirmed risk factors for hypertension. **(21)**

Majority of study population had sedentary lifestyle in our study (56%) as compared to active lifestyle (44%) as seen in other similar studies such **(22)**.

In the present study, it was found that the majority (53.33%) of patients had Normal BMI followed by Obese (24%), Overweight (12%) and Underweight 10.67%. Mean value of body mass index (kg/m²) of study subjects was 22.59 ± 3.34 with median (25th-75th percentile) of 22.04 (20.429-24.34). This was comparable to previous studies in patients with essential hypertension **(23).**

Dyslipidaemia in our study was seen in 85.33% of patients which was similar to but was higher than few other studies **(24)**. This is due to different reference range taken for dyslipidaemia. Dyslipidaemia appears to be the cause of essential hypertension in young South Asians.

Phosphate levels

In our study, it was observed that the mean phosphate levels were high (6.2 mg/dl) in patients with secondary hypertension. This is higher than previous studies. This is because in our study, majority of patients with secondary hypertension had renal parenchymal disease in which the phosphate levels increase due to decreased excretion from the circulation **(25).**

LDL was high in 53.33% patients with a mean value of 68.46 ± 23.70 with a positive skew deviation. The reason for this is that patients with secondary hypertension had normal LDL levels and resulted in a positive skew deviation. The mean was comparable to similar studies done in India **(26)**

HDL Levels

HDL was low in 76% patients which was similar to other such studies and mean HDL was 39.42 ± 4.74 which was similar in **(27).**

Triglyceride Levels

In majority (52%) of patients, Triglyceride(mg/dL) was High and mean value of Triglyceride (mg/dL) of study subjects was 135.22 ± 39.96 as seen in **(28)**

Total Cholesterol Levels

Total cholesterol (mg/dL) was High in 53.33% patients and mean value of total cholesterol (mg/dL) was 134.93 ± 27.38. Similar findings were seen in **(29).**

IL-6

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Our study suggested that the mean IL-6 level was elevated in all patients and was found to be 70.91 ± 7.69 pg/ml, with a range of 59 to 86. There was no significance between IL-6 levels among patients with moderate and with severe hypertension ($p > 0.05$). This was comparable to previous studies **(30)**

TNF- α

In our study, it was observed that mean TNF-α level was elevated in all patients and was found to be 123.73 ± 14.29 pg/ml, with a range of 102 to 159. There was no significance between TNF-α levels among patients with moderate and with severe hypertension ($p > 0.05$). A similar result was found in previous studies **(31)**

Aetiology of secondary hypertension

In our study, it was observed that 49% of patients with secondary hypertension had underlying renal parenchymal disease, 27% of them had hypothyroidism, 8% of patients had hyperthyroidism, 5% of patients had Cushing's syndrome and Takayasu arteritis each, and 3% of them had phaeochromocytoma, renal artery stenosis was found in 3% of the patients. These results were similar to previous studies done for evaluation of secondary hypertension **(32)**

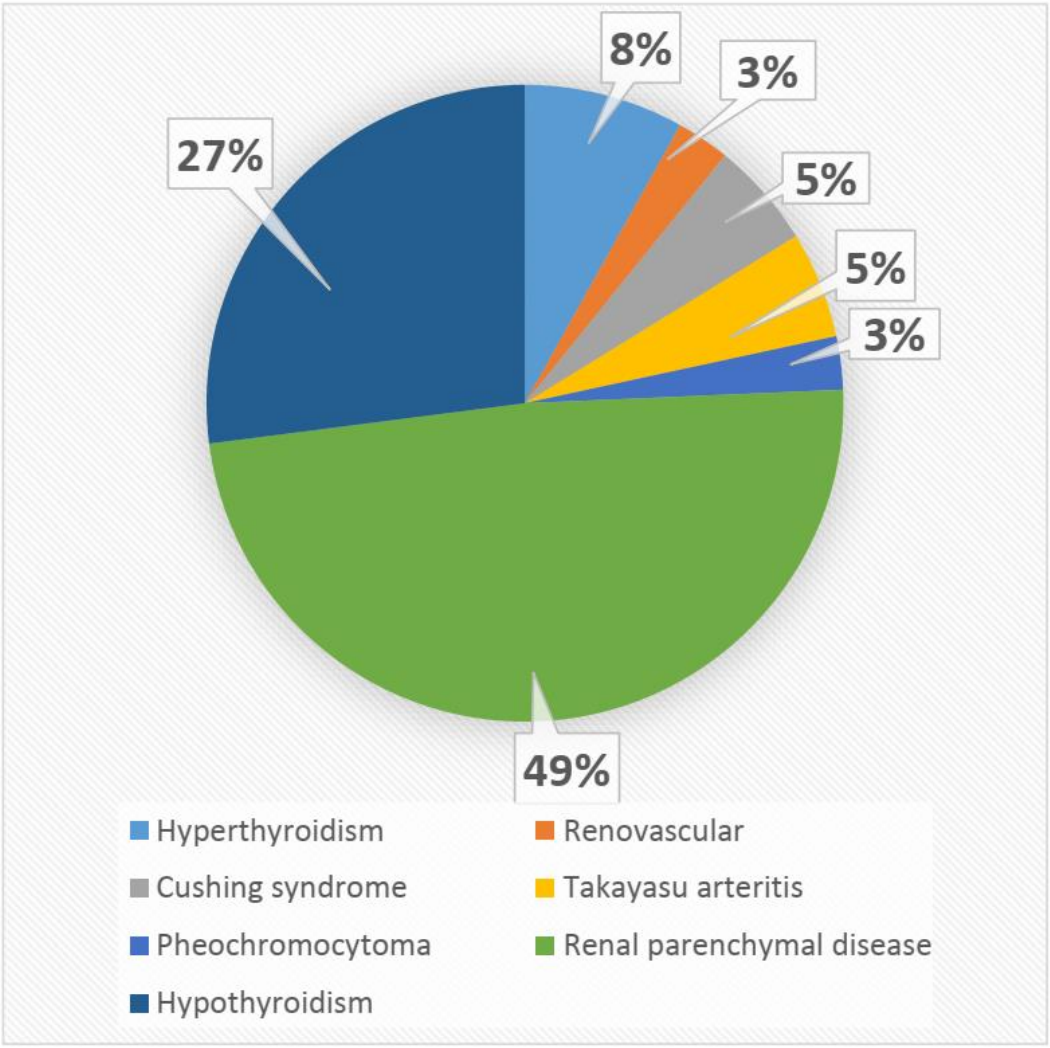

FIGURE 2

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Our study revealed that the mean age of the patients was 59.53 years and most common age group affected was 40 to 49 years showing aggravated risk with increasing age. Males were affected predominantly in young patients with hypertension and at an earlier age than females. Dyslipidaemia (85.33%) was the most prevalent risk factor in young patients, followed by Smoking (74.67%), Obesity (36%), Family history (24%), Hypothyroidism (17.33%) and Diabetes Mellitus (10.67%). LDL was raised in majority (85.33%) of the patients and this was more than other similar studies due to reference range used in our study was as per Asian population. HDL was low in 76% patients; Triglyceride was high in 52% patients and Total Cholesterol was high in 53.33% patients. The most common cause of secondary hypertension included renal parenchymal diseases (29%) and the second most common cause was found to be hypothyroidism (6%). Inflammatory markers, Interleukin-6 (70.91 ± 7.7) and Tumour Necrosis Factor- α (102 ± 14.3) were found to be raised in all patients presenting with untreated hypertension, irrespective of the severity.

LIMITATIONS OF THE STUDY

The limitations of our study include the following:

- Inherent to the nature of observational study design, chances of potential residual confounders always persist.
- This was a single centre study, and the sample size was small. Therefore, the results require further validation from larger multicentre prospective studies.
- As there was no follow-up, so short-term and long-term morbidity and mortality was uncertain.
- All causes of secondary hypertension could not be assessed as it was not affordable for most of the study population.
- Genetic framework could not be assessed due to financial constraints.

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CONFLICTS OF INTEREST

None