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HYPERTENSION PHENOTYPES AND KIDNEY INJURY IN YOUNG ADULTS: AN INTERNAL MEDICINE NEPHROLOGY INTERFACE

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ABSTRACT

Background: Hypertension in young adults is increasingly recognized as a precursor of chronic kidney disease, but its impact may vary depending on blood pressure phenotype.

Objective: To determine the distribution of hypertension phenotypes in young adults and to evaluate their association with early indicators of kidney injury.

Methods: A cross-sectional study was conducted at the Department of Nephrology, Mufti Mehmood Teaching Hospital, Dera Ismail Khan, Pakistan, from January to June 2024. Seventy-two young adults aged 18–35 years were enrolled. Demographic and clinical details were recorded, and participants were classified into normotension, isolated systolic hypertension (ISH), isolated diastolic hypertension (IDH), systolic–diastolic hypertension (SDH), masked hypertension, and white-coat hypertension. Renal function was assessed using serum creatinine, estimated glomerular filtration rate (eGFR), and urine albumin-to-creatinine ratio (UACR). Kidney injury was defined as microalbuminuria (UACR ≥ 30 mg/g) or eGFR < 90 ml/min/1.73m².

Results: SDH was the most common phenotype (31.9%), followed by IDH (19.4%) and ISH (16.7%). SDH was strongly associated with kidney injury, with 52.2% of affected individuals showing either microalbuminuria or reduced eGFR ($p = 0.004$). Normotensive participants had preserved renal function, while masked and white-coat hypertension showed intermediate risk.

Conclusion: Hypertension phenotypes in young adults differ in their renal implications, with SDH carrying the highest risk for early kidney injury. Phenotype-specific risk stratification and timely renal monitoring may help reduce the long-term burden of chronic kidney disease in this population.

Keywords: Hypertension phenotypes, systolic diastolic hypertension, isolated diastolic hypertension, isolated systolic hypertension, kidney injury, microalbuminuria, eGFR, young adults, internal medicine, and nephrology.

INTRODUCTION

Hypertension is a major public health concern and a leading modifiable risk factor for cardiovascular and renal disease worldwide. While traditionally considered a disorder of middle age, its occurrence in younger adults is increasingly recognized and carries important long-term health implications. Early-onset hypertension not only increases lifetime cardiovascular risk but also contributes to the development of kidney injury at a stage when preventive interventions may have the greatest impact [1-3].

The classification of hypertension into distinct phenotypes such as isolated systolic hypertension (ISH), isolated diastolic hypertension (IDH), combined systolic–diastolic hypertension (SDH), masked hypertension, and white-coat hypertension provides a more refined understanding of blood pressure patterns [4, 5]. These phenotypes differ in their underlying pathophysiology and clinical consequences. For instance, IDH in young adults has been linked to future cardiovascular risk, while ISH is often associated with arterial stiffness and vascular remodeling. SDH, by contrast, has been shown to exert greater hemodynamic stress on the kidneys, leading to microvascular injury and albuminuria [6, 7].

Kidney injury in young adults with hypertension is particularly concerning, as subtle changes such as microalbuminuria or mild reduction in estimated glomerular filtration rate (eGFR) often go unnoticed until more advanced disease develops [8, 9]. Evidence suggests that even low-grade renal abnormalities are predictive of chronic kidney disease progression and cardiovascular events later in life. Identifying the phenotype most strongly associated with early renal compromise may therefore enable more precise risk stratification and targeted interventions at the internal medicine nephrology interface [10].

Limited regional data exist on the relationship between hypertension phenotypes and kidney injury in young adults, particularly in South Asia, where the burden of hypertension and chronic kidney disease is rising at an alarming pace. Understanding these associations is essential for early detection strategies and for reducing the future burden of renal and cardiovascular morbidity. This study aimed to evaluate the distribution of hypertension phenotypes among young adults and to assess their relationship with early markers of kidney injury.

METHODOLOGY

This study was designed as a cross-sectional observational analysis carried out at the Department of Nephrology, Mufti Mehmood Teaching Hospital, Dera Ismail Khan, Pakistan. The study was conducted over a six-month period, from January 2024 to June 2024. The hospital is a tertiary care referral center that caters to a large population of both urban and rural areas, which provided access to a diverse group of young adult patients with varying clinical presentations of hypertension. The study protocol was reviewed and approved by the Institutional Ethical Review Committee of Mufti Mehmood Teaching Hospital, Dera Ismail Khan. Written informed consent was obtained from all participants before inclusion. Data confidentiality was ensured by anonymizing patient identifiers.

A total of 72 young adults aged between 18 and 35 years were enrolled. Participants were recruited from both inpatient and outpatient nephrology services during the study period. Individuals with previously known secondary causes of hypertension, congenital renal anomalies, chronic kidney disease stage 4 or above, and systemic illnesses likely to influence renal function (such as systemic lupus erythematosus or vasculitis) were excluded to maintain homogeneity of the study group. Pregnant women and patients on nephrotoxic medications were also excluded.

After obtaining informed consent, demographic and clinical information was collected through structured interviews and review of medical records. Demographic variables included age, gender, body mass index (BMI), and family history of hypertension. Lifestyle factors such as smoking status were also documented. Clinical data included history of diabetes mellitus, dyslipidemia, and the use of antihypertensive medications.

Blood pressure was measured using a standardized protocol, with at least two readings taken at five-minute intervals in a seated position. Hypertension phenotypes were defined according to the mean systolic and diastolic blood pressure values, categorized into normotension, isolated systolic

hypertension (ISH), isolated diastolic hypertension (IDH), combined systolic–diastolic hypertension (SDH), masked hypertension, and white-coat hypertension.

Venous blood samples were collected for the measurement of serum creatinine, fasting glucose, and lipid profile. Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI equation. Urine samples were analyzed for proteinuria, and the urine albumin-to-creatinine ratio (UACR) was determined from spot urine specimens. Kidney injury was defined as either the presence of microalbuminuria (UACR ≥ 30 mg/g) or a reduction in eGFR below 90 ml/min/1.73m².

All measurements were performed in the hospital's central diagnostic laboratory, which is accredited and follows standardized quality control procedures. Blood pressure was measured with calibrated sphygmomanometers by trained staff to reduce inter-observer variability. Laboratory values were cross-checked by duplicate assays for accuracy.

Data were entered and analyzed using SPSS version 26. Continuous variables such as age, BMI, serum creatinine, eGFR, and UACR were expressed as mean ± standard deviation (SD). Categorical variables, including gender, hypertension phenotypes, and presence of kidney injury, were presented as frequencies and percentages. Group comparisons were performed using Chi-square test for categorical variables and one-way ANOVA for continuous variables. A p-value < 0.05 was considered statistically significant.

RESULTS

Among the 72 young adults included in this study, the mean age was 28.4 ± 4.7 years, with a slightly higher representation of males (56.9%) compared to females (43.1%). The mean BMI was 26.2 ± 3.9 kg/m², with nearly two-thirds of the participants classified as overweight (38.9%) or obese (31.9%). A positive family history of hypertension was present in more than half of the subjects (51.4%). Comorbid conditions included diabetes mellitus in 15.3% and dyslipidemia in 22.2%. Smoking was reported in 19.4% of participants, reflecting the presence of modifiable cardiovascular risk factors in this relatively young cohort.

Table 1. Demographic and Baseline Characteristics of Study Participants (n = 72)

Variable	Mean ± SD / n (%)
Age (years)	28.4 ± 4.7
Gender (Male/Female)	41 (56.9%) / 31 (43.1%)
Body Mass Index (kg/m²)	26.2 ± 3.9
Normal weight	21 (29.2%)
Overweight	28 (38.9%)
Obese	23 (31.9%)
Family history of HTN	37 (51.4%)
Diabetes mellitus	11 (15.3%)
Dyslipidemia	16 (22.2%)
Smoking	14 (19.4%)

Analysis of hypertension subtypes revealed that combined systolic–diastolic hypertension (SDH) was the most common phenotype, present in nearly one-third of the study population (31.9%). Isolated diastolic hypertension (19.4%) and isolated systolic hypertension (16.7%) were also frequently observed. Normotensive individuals accounted for 20.8% of the participants, while less common categories included masked hypertension (6.9%) and white-coat hypertension (4.2%). These findings highlight the heterogeneous nature of hypertension phenotypes in young adults.

Table 2. Distribution of Hypertension Phenotypes

Hypertension Phenotype	Frequency (n)	Percentage (%)
Normotensive	15	20.8
Isolated Systolic HTN (ISH)	12	16.7
Isolated Diastolic HTN (IDH)	14	19.4
Systolic–Diastolic HTN (SDH)	23	31.9
Masked HTN	5	6.9
White-coat HTN	3	4.2

Comparison of kidney function indices across the hypertension phenotypes showed significant variation. Participants with SDH had the highest mean serum creatinine (1.15 ± 0.26 mg/dL) and the lowest mean eGFR (88.7 ± 12.6 ml/min/1.73m²), indicating early signs of renal compromise. Albuminuria, measured by UACR, was also most pronounced in the SDH group (32.7 ± 9.6 mg/g). In contrast, normotensive individuals demonstrated preserved renal function with lower creatinine and higher eGFR values. Statistical analysis revealed significant differences in creatinine ($p = 0.012$), eGFR ($p = 0.001$), and UACR ($p < 0.001$) across groups.

Table 3. Renal Function Parameters across Hypertension Phenotypes

Parameter	Normotensive (n=15)	ISH (n=12)	IDH (n=14)	SDH (n=23)	Masked/White-coat (n=8)	p-value
Serum Creatinine (mg/dL)	0.89 ± 0.14	0.96 ± 0.19	1.01 ± 0.22	1.15 ± 0.26	0.92 ± 0.17	0.012*
eGFR (ml/min/1.73m²)	104.2 ± 9.1	99.5 ± 11.2	95.4 ± 10.8	88.7 ± 12.6	101.6 ± 9.7	0.001**
UACR (mg/g)	13.5 ± 5.2	18.9 ± 6.1	21.4 ± 7.3	32.7 ± 9.6	15.8 ± 5.9	<0.001**

* Significant at $p < 0.05$; **Highly significant at $p < 0.01$

The prevalence of kidney injury markers varied considerably by hypertension phenotype. Microalbuminuria was present in 39.1% of individuals with SDH compared to only 6.7% of normotensive participants. A reduced eGFR (<90 ml/min/1.73m²) was also most common in the SDH group (34.8%), while none of the normotensive individuals demonstrated such decline. When combining all indicators of kidney injury, over half of the SDH group (52.2%) showed evidence of renal impairment. Statistical analysis confirmed significant associations between hypertension subtype and kidney injury (p-values ranging from 0.015 to 0.004).

Table 4. Association of Hypertension Phenotypes with Kidney Injury

Kidney Injury Marker	Normotensive (n=15)	ISH (n=12)	IDH (n=14)	SDH (n=23)	Masked/White-coat (n=8)	p-value
Microalbuminuria present	1 (6.7%)	2 (16.7%)	3 (21.4%)	9 (39.1%)	1 (12.5%)	0.028*
eGFR < 90 ml/min/1.73m²	0 (0%)	1 (8.3%)	2 (14.3%)	8 (34.8%)	1 (12.5%)	0.015*
Any kidney injury	1 (6.7%)	3 (25%)	4 (28.6%)	12 (52.2%)	2 (25%)	0.004**

* Significant at $p < 0.05$; **Highly significant at $p < 0.01$

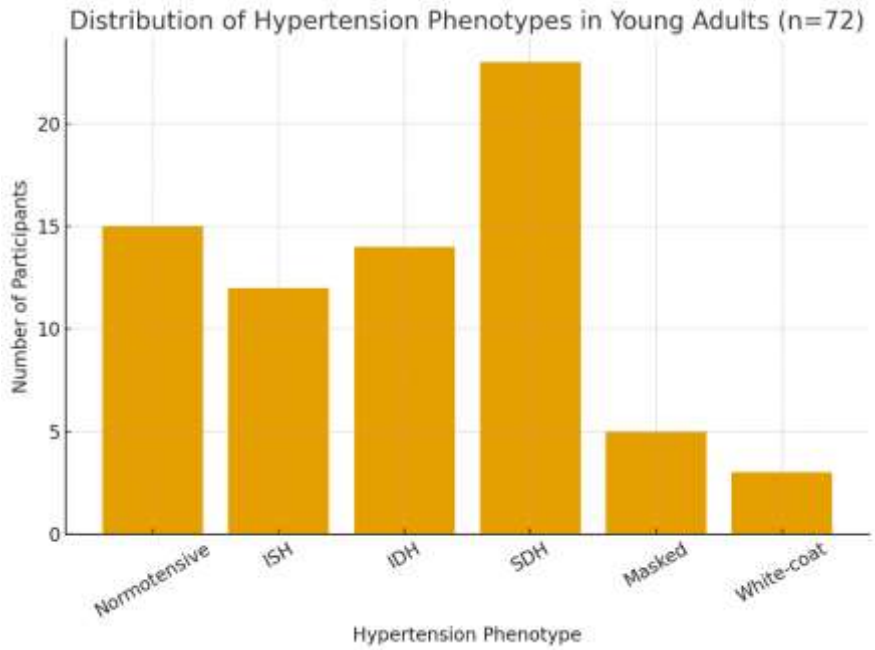

Figure 1: distribution of hypertension phenotypes in your sample of 72 young adults. It visually highlights that systolic diastolic hypertension (SDH) is the most common phenotype, followed by IDH and ISH.

DISCUSSION

Hypertension in young adults is increasingly recognized as an important contributor to early renal injury, particularly in South Asian populations where cardiovascular and metabolic risk factors emerge earlier compared to Western cohorts. In this analysis of young adults, combined systolic diastolic hypertension (SDH) was the most frequent phenotype, accounting for nearly one-third of the participants. This observation was consistent with findings with findings of studies reported that SDH in younger populations is strongly associated with increased cardiovascular risk and renal dysfunction compared with isolated systolic or diastolic forms [11-13].

Renal function assessment demonstrated a clear gradient of impairment across hypertension phenotypes. Individuals with SDH had the highest mean serum creatinine and the lowest mean eGFR, alongside markedly elevated albuminuria levels. These findings align with studies showed that early albuminuria and declining eGFR often precede overt kidney disease and serve as independent predictors of cardiovascular morbidity [14, 15]. The strong association between SDH and renal injury emphasizes that combined blood pressure elevation places a disproportionate burden on the renal microvasculature, leading to glomerular hyperfiltration, endothelial dysfunction, and progressive nephron loss.

Isolated diastolic hypertension (IDH) and isolated systolic hypertension (ISH) were also common phenotypes in the study population. Although less severe than SDH, both forms showed evidence of renal compromise. This finding corresponds with the studies, which highlighted that IDH in younger adults should not be considered benign, as it is linked with subclinical target organ damage including microalbuminuria [16, 17]. Similarly, ISH has been associated with increased arterial stiffness and early glomerular injury in otherwise healthy young individuals, as demonstrated in research [18, 19].

The prevalence of masked hypertension and white-coat hypertension was lower in this cohort but remains clinically significant. Masked hypertension, although representing a smaller proportion, has been strongly linked to kidney damage in population-based studies due to its under-recognition and lack of timely intervention. White-coat hypertension, while traditionally considered less harmful, may still carry risk when persistent [20].

The overall prevalence of kidney injury defined by either microalbuminuria or reduced eGFR was highest in participants with SDH, where more than half demonstrated renal impairment. These results were consistent with findings from the CRIC study which showed that albuminuria and hypertension

interact synergistically to accelerate chronic kidney disease progression [21]. The high burden of renal abnormalities in young adults underscores the importance of early detection, lifestyle modification, and aggressive management strategies to prevent long-term renal and cardiovascular complications. Several clinical implications emerge from these findings. First, hypertension phenotypes should not be viewed as uniform entities; rather, they exhibit distinct associations with renal injury. Second, early screening for microalbuminuria and monitoring of eGFR in hypertensive young adults is essential for timely intervention. Third, aggressive risk factor modification, including weight reduction, smoking cessation, and optimal control of blood pressure, may help mitigate renal damage in this age group.

CONCLUSION

Hypertension phenotypes in young adults display heterogeneous patterns of renal involvement, with combined systolic diastolic hypertension being most strongly associated with kidney injury. Early manifestations of renal dysfunction, including microalbuminuria and reduced eGFR, were significantly more common in this phenotype compared with isolated forms of hypertension. These findings highlight the clinical need for phenotype-specific risk stratification, early renal monitoring, and comprehensive management strategies at the internal medicine nephrology interface to prevent the progression of chronic kidney disease in young populations.

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