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Hyperuricemia in newly diagnosed Hypertension: A Study of Prevalence and Implications

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ABSTRACT

Introduction: Hyperuricemia, defined as increased serum uric acid levels and hypertension, characterized by elevated blood pressure. Hyperuricemia is more common in males; hypertension is prevalent in both genders. Uric acid, a purine metabolite, is considered as a risk factor for hypertension. Studies suggest a direct link between hyperuricemia and hypertension, with mechanisms including nitric oxide reduction and renin-angiotensin system activation. The prevalence of hyperuricemia is 30.1% with males being more commonly affected while the prevalence of hypertension is 35.1% In Pakistan.

Aims & Objectives: Our study aims to determine the frequency of hyperuricemia among newly diagnosed hypertensive patients as an early predictor of adverse outcomes.

Methodology: Nonprobability consecutive sampling was employed over a six-month duration with a sample size of 86 patients. Inclusion criteria encompass newly diagnosed hypertensive patients aged 35-70 years, while exclusion criteria include various comorbidities. Data collection was conducted via structured forms after obtaining informed consent from patients at FMH medical.

Results & Findings: 47.2 +_ 8.1 years was the mean age of our study group was. The average age ranged between 38 and 45 years. Among the total 86 patients (newly diagnosed hypertensive),57 participants (66.3%) had hyperuricemia, while 29 participants (33.7%) did not have high uric acid levels. The minimum uric acid level was 4.60mg/dl and maximum was 10.70mg /dl with a mean of 7.3mg/dl and standard deviation of 1.57.

Conclusions: Hyperuricemia has an established association with increased blood pressure. Furthermore, as both variables increase cardiometabolic risks independently, early identification and prompt management of these two along with other risk factors is essential to reduce the morbidity and mortality outcomes overall.

KEYWORDS: Hyperuricemia, hypertension, serum uric acid, cardiometabolic risk, newly diagnosed hypertensive patients.

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INTRODUCTION

Hyperuricemia is high uric acid level in the blood and is defined as a serum urate concentration exceeding 420 mmol/L in men and 360 mmol/L in women [1]. Obesity is classified as a BMI ≥ 28 kg/m², while abdominal adiposity is defined as a waist circumference of ≥85 cm in men and ≥80 cm in women [2]. Hypertension is defined as a systolic blood pressure greater than 130 mm Hg and a diastolic blood pressure greater than 80 mmHg [3]. Hyperuricemia is more prevalent in males (7.9%) than in females (4.9%) [4] comparable to hypertension that is also more common in males 34.6% than in women 30.8% [5] When compared between different ethnic groups, African American ethnicity demonstrates a marked decrease in the risk of hyperuricemia when contrasted with Caucasian ethnicity [6] while hypertension is more common in blacks than in whites [7]. Hypertension is the major disease globally and affects one-third of the world population and is the common cause of morbidity and mortality [8]. Although etiology of hyperuricemia in hypertension remains unknown in most cases, uric acid, a purine metabolite, is the risk factor for hypertension independent of traditional risk factors like age, family history, obesity, unhealthy diet and dyslipidemias [9]. Hypertension significantly increases the risks of coronary heart disease, stroke, peripheral artery disease, and other forms of cardiovascular disease (CVD) [10]. Hyperuricemia, a growing global metabolic issue linked to hypertension for over 130 years, significantly increases the risk of developing hypertension. A meta-analysis confirms this risk rises with higher uric acid levels and remains consistent across subgroups, establishing hyperuricemia as an independent risk factor [11]. It has been observed that each 0.5mg/dl increase in uric acid levels result in a 10mmHg rise in blood pressure, but it is yet to check whether all hypertensive patients have preexisting hyperuricemia or not [12]. Studies have identified mechanisms linking uric acid to hypertension, including reduced nitric oxide, renin-angiotensin system activation, vascular injury, and smooth muscle proliferation. Hyperuricemia initially causes renal vasoconstriction through endothelial dysfunction and renin-angiotensin activation, followed by microvascular disease from smooth muscle proliferation, inflammation, oxidative stress [13-]. Although the incidence of hyperuricemia is increasing, overall, the prevalence among Pakistani population is 30.1% with male population being more affected (39.9%) compared to females (17.9%) [15] Whereas prevalence of hypertension is nearly 35.1% [16]. Some Studies have also been conducted to find the association of hyperuricemia and

hypertension in Pakistani population and statically significant associations have been established [17]. The rationale of our study is to find the frequency of hyperuricemia among newly diagnosed hypertensive patients as an early predictor of worse outcome, as better control of hypertension can minimize cardiovascular risk.

MATERIAL AND METHODS

The study design is described as a descriptive case series, utilizing nonprobability consecutive sampling over duration of six months from the approval of the synopsis. With a sample size of 86 patients selected based on a 5% level of significance, 95% confidence level. Inclusion criteria encompass newly diagnosed hypertensive patients of both genders aged 35-70 years. Exclusion criteria include patients with comorbidities such as diabetes mellitus, chronic liver disease, chronic lung disease, ischemic heart disease, pregnancy, malignant disorders, and autoimmune disorders. Data was collected in a structured Performa after informed consent from medical OPD and admitted patients of FMH. Blood samples will be drawn by phlebotomists and sent to FMH laboratory Data will be analyzed on SPSS version 22 and variables (age, blood pressure values) will be presented as mean +/- S.D. Gender and uric acid levels will be presented as frequency and percentage. Data will be stratified for age, gender, BMI, duration of hypertension and medication of hypertension. Post-stratification chi-square test will be applied and $P < 0.05$ will be considered significant.

RESULTS

During the study period, 86 patients were evaluated. The mean age of our study group was 47.2 +_ 8.1 years. The average age ranged between 38 and 45 years. Among these, 16 (18.6%) participants were males and 70 (81.4%) were females (Fig 1). Most of these participants were overweight with 64 people (74.4%) having BMI more than 25 and only 22 (25.6%) were in normal range of BMI (18.5-24.9) (Fig 2). Regarding duration of hypertension, most people (25.6%) had elapsed 8 months since the diagnosis of hypertension, 20.9% had elapsed 6 months from the diagnosis of hypertension, 16.3% had 2 months, 15.1% had 10 months, 11.6% had 12 months and 10.5% had elapsed 4 months since the time of diagnosis of hypertension (Fig 3). Of those, 62 participants (72.1%) were on some kind of anti-hypertensive medication while 24 participants (27.9%) were not taking any blood pressure lowering medications for one reason or another (Fig 4). Among total 86 patients that were evaluated, 57 participants (66.3%) had hyperuricemia established while 29 participants (33.7%) did not have high uric acid levels (Fig 5). The minimum uric acid level was 4.60mg/dl and maximum was 10.70mg/dl with a mean of 7.3mg/dl and standard deviation of 1.57 (table 1). These results confirmed the relationship of hypertension and hyperuricemia as majority of the people (66.3%) had high uric acid levels.

Table 1: Uric Acid Levels

	Minimum	Maximum	Mean	S.D
Serum Uric Acid level	4.60	10.7	7.3	1.5

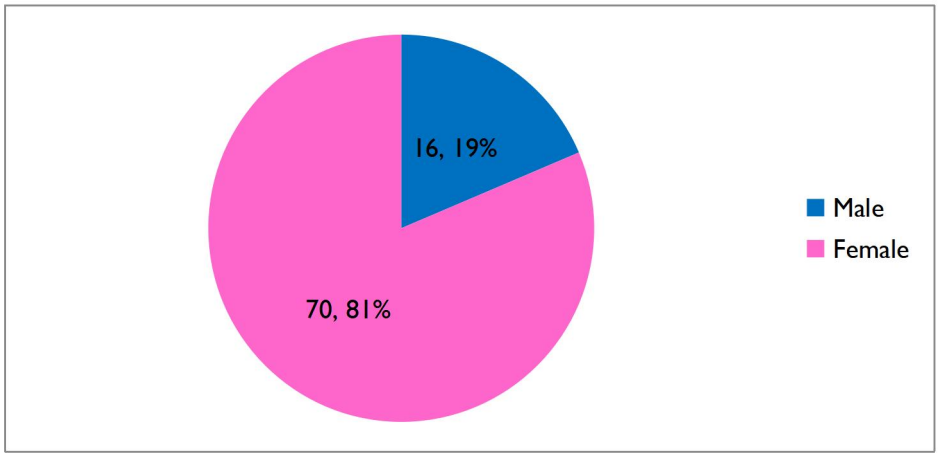

Figure 1: Gender Distribution

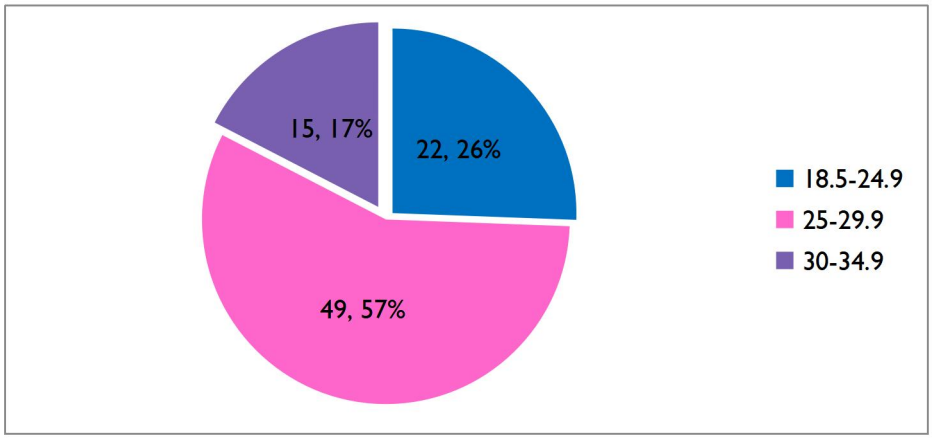

Figure 2: BMI Distribution

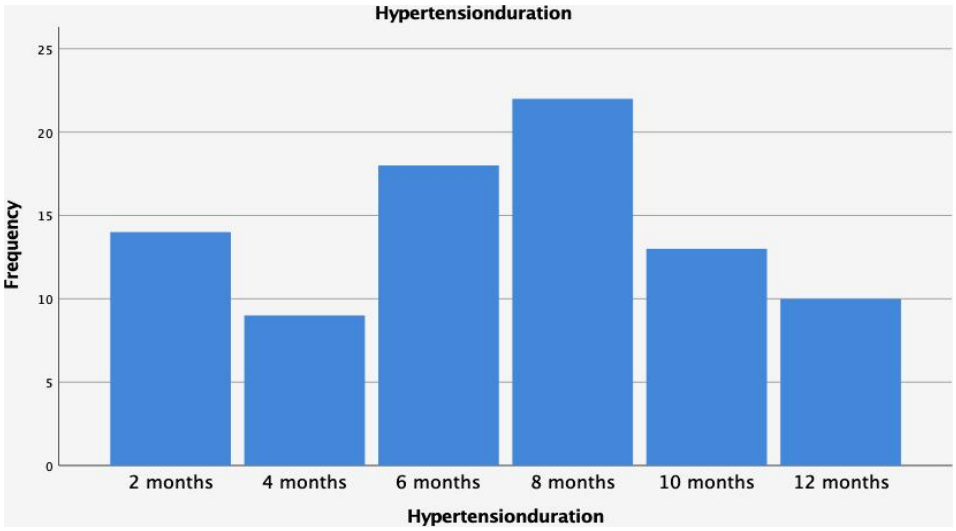

Figure 3: Duration of Diagnosis of Hypertension

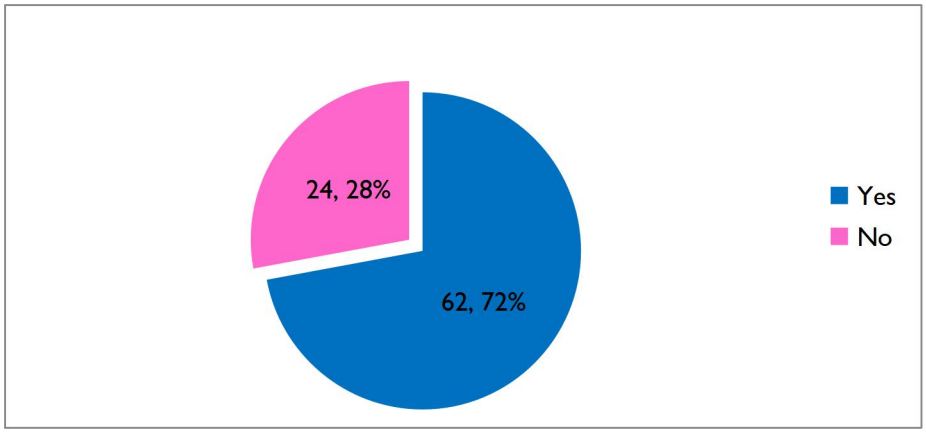

Figure 4: Frequency of patient taking Anti-Hypertensive

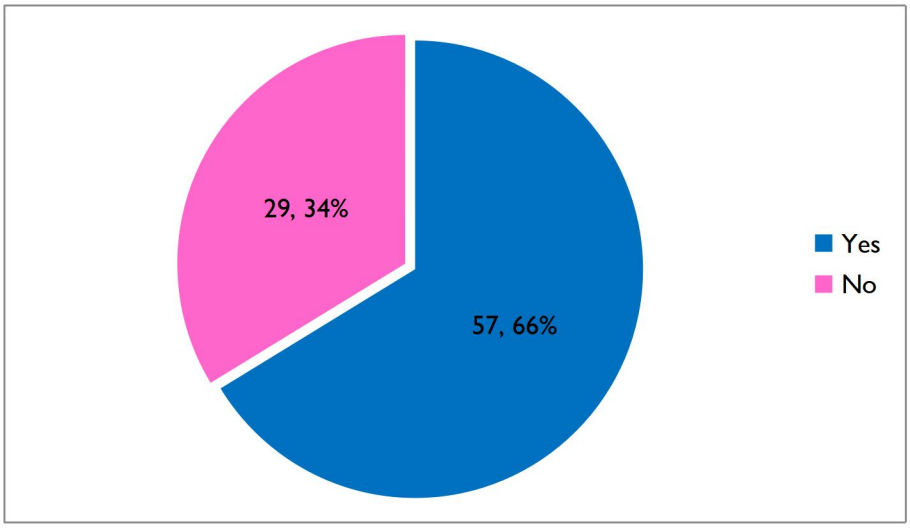

Figure 5: Frequency of Hyperuricemia in Hypertensive people

DISCUSSION

Among a total of 86 patients that were evaluated, 57 participants (66.3%) had hyperuricemia, while 29 participants (33.7%) did not have high uric acid levels. These results confirmed the relationship of hypertension and hyperuricemia as majority of the people (66.3%) had high uric acid levels.

Arterial hypertension, a leading cardiovascular risk factor, causes 10.4 million deaths annually and affects 30% globally. Most cases are primary hypertension with no identifiable cause. Hyperuricemia and heat shock protein 70 (HSP70) are linked to innate immune activation and inflammatory processes in hypertension [18]. Our results are consistent with the findings from the global prevalence of hypertension in adults aged 25 years and above is approximately 26.4%, projected to rise to 60% by 2025, totaling 1.5 billion individuals. In Japan, a study estimated 43 million people with high blood pressure, with male and female prevalences of 60% and 45%, respectively [19-20]. In our study of 86 participants, hyperuricemia was observed in 66.3% of hypertensive individuals, with a mean serum uric acid level of 7.3 ± 1.57 mg/dL. In contrast a study conducted in Pakistan, where 84% of hyperuricemia patients were hypertensive, compared to only 41% of individuals without hyperuricemia. The odds ratio of 7.55 in their population is comparable to the strong association observed in our cohort [8]. Poudel et al. observed significantly higher mean serum uric acid levels and a higher prevalence of hyperuricemia in the hypertensive group compared to those without hypertension (28.8% vs. 13.7%), with an odds ratio of 2.55[21]. Hypertensive men were 1.79 times more likely, and hypertensive women almost six times more likely, to have hyperuricemia [20]. Evidence suggests a strong link between hyperuricemia and primary hypertension in children and adolescents. An 8-week double-blind study showed allopurinol significantly reduced clinical and ambulatory blood pressure (BP) in hypertensive adolescents by lowering systemic vascular resistance and plasma renin activity. Achieving serum urate levels below 5.0 mg/dL normalized BP in 19 of 22 subjects, compared to just 1 of 30 in the placebo group [22]. Studies involving American teenagers demonstrated a direct correlation between serum uric acid levels and systolic and diastolic blood pressures. This finding was later confirmed in adults, showing a 2.21-fold increased risk of developing hypertension.our study included adult population [23]. In a study of 5,889 Japanese individuals aged 30–85 years, elevated uric acid levels were associated with higher incidences of dyslipidemia (23.1% vs. 15.5%, $p<0.001$), CKD (19.0% vs. 10.7%, $p<0.001$), and obesity (8.9% vs. 3.0%, $p<0.001$).In another study,in Brazil found elevated uric acid levels linked to increased fat mass and lipid alterations in 149 adults aged 20–55 years. Silva et al. observed hyperuricemia in 80 patients with metabolic syndrome, including men with abdominal obesity, women with obesity, low HDL levels, and hypertension ($p<0.05$). Hyperuricemia is also associated with primary hypertension in children, despite its higher prevalence in older adults. This age range align with the range in our study [24-25]. The kidneys excrete about 70% of daily uric acid, while 30% is eliminated through intestinal bacterial uricolysis. Different Studies indicate a bidirectional relationship between hyperuricemia and hypertension [26]. Hypertension is a major risk factor for cardiovascular mortality and morbidity, while hyperuricemia is linked to increased risks of cardiovascular disease, gout, renal dysfunction, and metabolic syndrome. Recent research has emphasized the connection between hypertension and hyperuricemia [27-28]. Lowering uric acid levels of serum have been shown to reduce blood pressure in patients with hyperuricemia [29- 30]. Various mechanisms contribute to elevated blood pressure in individuals with high uric acid levels [31]. Hyperuricemia is independently associated with hypertension, with serum uric acid (SUA) identified as a predictor of a non-dipping blood pressure (BP) profile in essential hypertension, which increases cardiovascular, cerebrovascular and renal disease risk. Studies show allopurinol improves vascular endothelial function, likely by reducing oxidative stress, benefiting elderly heart failure patients, heavy smokers, and type 2 diabetics. While SUA is a risk factor for hypertension, definitive evidence supporting UA-lowering therapies to treat or prevent hypertension or reduce disease risk remains limited. Xanthine oxidase inhibitors may offer greater benefits than uricosuric agents due to their dual effects on SUA and oxidative stress [32]. Another study found allopurinol and probenecid reduced BP in obese prehypertensive adolescents, with added benefits of weight reduction in the allopurinol group. A third study showed allopurinol enhanced the effects of ACE inhibitors [33]. Regular monitoring of blood pressure in patients with hyperuricemia or gout, and monitoring of uric acid levels in hypertensive patients, can help manage uric acid levels and reduce the risk of hypertension and other cardiovascular diseases.

CONCLUSION

So, with all the above discussion, keeping in view different studies conducted in the past, globally and locally, we can draw an inference that hyperuricemia has an established association with increased blood pressure. Furthermore, both these variables increase the cardiometabolic risks independently. Other Risk factors like dyslipidemia, NAFLD, Diabetes can also cluster in such population and impart increased burden of morbidity and mortality. So, evaluation of all these independent variables in newly diagnosed hypertensive is essential for future risk stratification and managing all these variables can improve morbidity and mortality outcome.

Limitations of the study:

This study is subject to limitations, including recall bias, as participants may inaccurately recall past events. Conducted at Fatima Memorial Hospital in Lahore, its single-center design limits generalizability. The use of non-probability consecutive sampling may introduce selection bias, as participants were included based on availability rather than random selection, potentially limiting the representativeness of the findings. Additionally, some variables, such as the duration of hypertension, rely on subjective responses, introducing potential inaccuracies. Observer error is another concern; blood pressure readings recorded for a short duration may not accurately reflect the true readings, leading to possible misinterpretation of the data. Although our study had some confounders, most important being the unknown status of type of anti-hypertensives, patients were on.

Conflict of interest:

The authors report no conflicts of interest in this work as approved by IRB (Ref. No: FMH-04-2021-IRB-896-M). Participants' confidentiality and anonymity was strictly maintained in this research. No AI tool has been employed.

Author Contributions

- Concept & Design of the study: Dr. Muhammad Kamran Rauf & Fatima Shahid
- Drafting: Dr. Fatima Shahid & Dr. Muhammad Bilal Basit
- Data analysis: Dr. Anum Tanveer & Dr. Abdul Rehman Khan
- Critical Review: Dr. Sidra Anwar & Muhammad Kamran Rauf

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the study's integrity.

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