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Original article

Analyzing Serum Uric Acid Levels in Essential Hypertension with Focus on Age and BMI: A Study from a Tertiary Care Center in India"

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Abstract

This study outlines a comprehensive approach to exploring the interplay between serum uric acid levels, age, and BMI in hypertensive patients, aiming to provide actionable insights and contribute to the broader scientific understanding of these relationships.

To fulfill this objective, a study at tertiary-care teaching hospital, Northern India (June 2017 - December 2018) involved 145 hypertensive patients and 145 matched controls, using a case-control, cross-sectional design. Participants were randomly selected and included those over 12 years old with hypertension per JNC 7/8 criteria, excluding individuals with severe hypertension, recent myocardial infarction, major infections, chronic diseases, or those on specific drugs affecting uric acid. Smokers and heavy drinkers were also excluded. Data collection included informed consent, venipuncture, history, physical exams, and tests such as blood pressure, serum uric acid, BMI, and various blood tests. Statistical analysis was performed with mean, standard deviation, t-tests, and Pearson's correlation, with significance set at $p < 0.05$.

The study reveals a balanced age distribution with most participants over 40 years, and consistent blood pressure categories across cases and controls, with cases showing higher rates of hypertension. Cases also exhibit significantly higher average blood pressure levels. Weight categories are similarly distributed between cases and controls, with a trend towards higher SUA levels in individuals with higher BMI. A strong positive correlation is observed between SUA levels and both systolic and diastolic blood pressure. Males show a slightly higher prevalence of hypertension compared to females, reflecting a greater overall burden of the condition.

The study concludes that elevated SUA levels are significantly correlated with higher blood pressure, both systolic and diastolic. The analysis reveals that hypertensive cases exhibit higher average blood pressure levels and a trend towards increased SUA levels with higher BMI. Additionally, males show a slightly greater prevalence of hypertension compared to females. These findings underscore the importance of monitoring SUA levels and BMI in managing hypertension and suggest that interventions targeting these factors could be beneficial in reducing cardiovascular risk.

Keywords: ***Serum Uric Acid (SUA), Essential Hypertension, Age Distribution, Body Mass Index (BMI), Hypertension Stages***

1. Introduction

Hypertension poses a significant global and national health challenge, being a leading cause of mortality. In India, its prevalence varies from 20-30% among urban adults and 10-15% among rural adults [1]. Elevated blood pressure is consistently and independently associated with an increased risk of cardiovascular events. Hypertensive individuals face a doubled risk of coronary artery disease, a fourfold risk of congestive heart failure, and a sevenfold risk of cerebrovascular diseases and stroke compared to those with normal blood pressure [2]. Hypertension is a physiological condition influenced by factors such as age, sex, and body mass index (BMI) [3]. It exhibits a strong and continuous positive correlation with the risk of various severe health outcomes, including stroke, myocardial infarction, heart failure, renal disease, and overall mortality. Essential hypertension refers to high blood pressure with no identifiable cause. Practically, it is defined by the blood pressure level at which treatment significantly benefits the patient, varying based on individual cardiovascular risk.

Uric acid, a byproduct of purine metabolism (adenosine and guanosine), is present in the body as a result of purine catabolism [4]. Approximately 10% of the Indian population experiences hyperuricemia at least once in their lifetime. In human blood plasma, the reference range for serum uric acid (SUA) is typically 3.4-7.0 mg/dL (200-430 µmol/L) for men and 2.4-6.1 mg/dL (140-360 µmol/L) for women [5]. Uric acid is thought to activate the renin-angiotensin system, potentially causing damage to pre-renal blood vessels. Hyperuricemia may contribute to hypertension through mechanisms such as endothelial dysfunction, impaired oxidative metabolism (possibly due to reactive oxygen species), increased granulocyte adherence, and enhanced platelet aggregation [6]. Elevated uric acid levels stimulate vascular smooth muscle cell proliferation through mechanisms involving mitogen-activated protein kinase, cyclooxygenase-2, and platelet-derived growth factor. This elevation is linked with increased severity of heart failure. Hypertension and hyperuricemia together heighten the risk of coronary artery disease and cerebrovascular disease by 3 to 5 times [7]. Elevated serum uric acid is associated with dyslipidemia, hypertension, insulin resistance, menopause, aging, and a sedentary lifestyle. Higher serum uric acid levels correlate with increased systolic and diastolic blood pressure, greater body mass index, and elevated triglycerides and total cholesterol [8].

Evidence from both Asian and Western studies indicates that hyperuricemia increases the risk of developing hypertension and vice versa [9]. However, the current understanding of this relationship in our local community, particularly in northern India, remains limited due to a scarcity of relevant studies. This research aims to address this gap by investigating serum uric acid levels in individuals with essential hypertension, focusing on age and body mass index (BMI).

2. Material and Methods

The study was conducted at a tertiary care hospital in Bihar, over an 18-month period from June 2017 to December 2018. It focused on hypertensive patients according to the Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7/8) [10]. The research included 145 hypertensive patients and 145 age- and sex-matched controls, selected from relatives of patients with conditions unrelated to hypertension. Simple random sampling was used to select participants. The study utilized a case-control, observational, cross-sectional design at a single center.

The study aimed to investigate hypertension by including patients over 12 years old diagnosed with hypertension on at least three separate occasions according to JNC 7/8 guidelines. Normal controls matched by age and sex were also included. Exclusion criteria were comprehensive, removing patients with secondary hypertension, accelerated or malignant hypertension (systolic BP > 180 mmHg or diastolic BP > 110 mmHg), recent myocardial infarction, cerebrovascular events, recent stent placement, serious infections, significant weight loss, cardiac arrhythmias, active malignancies, recent pregnancy-induced hypertension, chronic renal or liver disease, chronic psychiatric illness, diabetes mellitus, familial hypercholesterolemia or dyslipidemia, and those on specific drugs known to affect uric acid levels (either increasing or decreasing). Additionally, smokers with more than 10 cigarettes per day and individuals consuming more than two alcoholic drinks per day were excluded.

In the study, participants were fully briefed about the study and gave informed consent before undergoing venipuncture. Their detailed history, including personal and family background, was recorded along with a thorough physical examination. Blood pressure measurements were taken using a dial sphygmomanometer, with the cuff correctly positioned at heart level and measurements averaged from two readings. Hypertension was defined by JNC 7/8 criteria as systolic BP >140 mmHg and diastolic BP >90 mmHg. A 12-hour fasting venous blood sample was collected for serum uric acid measurement using an autoanalyzer. Body Mass Index (BMI) was calculated and categorized into normal, overweight, and various classes of obesity. Additional tests included a complete hemogram, fasting blood sugar, liver function tests, blood urea and creatinine levels, urinalysis, chest X-ray, abdominal ultrasound, serum electrolytes, and lipid profile.

Data will be summarized using mean and standard deviation. Statistical analysis will be conducted using tests such as the t-test and Pearson's correlation coefficient with SPSS or other suitable software. Statistical significance will be set at a p-value of less than 0.05.

3. Results

The age distribution among the 296 participants (47.65 ±10.94 years), split evenly between cases and controls, reveals a similar pattern for both groups. Most participants are over 40 years old. Specifically, the largest age group is 40-49 years, comprising 31.8% of both cases and controls. The 50-59 years group follows closely, making up 27.0% of the total. The youngest group (20-29 years) constitutes 5.1% of the total, while the oldest group (70-79 years) is the smallest at 1.7%. Both cases and controls show consistent distributions across age groups, reflecting a balanced representation of older age categories in the study (**Table 1**).

Table 1: The distribution of cases and controls across different age groups and the overall distribution.

Age Group (years)	Case Frequency (%)	Control Frequency (%)	Total Frequency (%)
20-29	4 (2.7)	11 (7.4)	15 (5.1)
30-39	31 (20.9)	27 (13.2)	58 (19.6)
40-49	47 (31.8)	47 (31.8)	94 (31.8)
50-59	39 (26.4)	41 (27.7)	80 (27.0)
60-69	25 (16.9)	19 (12.0)	44 (14.9)
70-79	2 (1.4)	3 (2.0)	5 (1.7)
Total	**148 (100)**	**148 (100)**	**296 (100)**

The distribution of blood pressure categories among cases and controls, highlighting key differences and overall trends. In the "Normal" blood pressure category, both cases and controls are equally represented, each with 51 individuals, making up 34.5% and 17.2% of their respective groups. The total proportion of individuals with normal blood pressure is 34.4%. For "Pre-hypertension," both cases and controls have 97 individuals each, accounting for 65.5% of the cases and 32.8% of the controls, which combined represents 65.5% of the overall population. In the "Stage 1 Hypertension" category, both groups have 87 individuals each, with cases representing 58.8% and controls 29.4%, making up 58.8% of the total population. Finally, the "Stage 2 Hypertension" category includes 61 individuals from both cases and controls, with cases at 41.2% and controls at 20.6%, together accounting for 41.2% of the total (**Table 2**). Overall, the data shows a higher prevalence of elevated blood pressure levels among cases compared to controls, with a significant portion of the population classified as having pre-hypertension or hypertension.

Table 2: Blood Pressure Distribution in case and control groups.

Blood Pressure Category	Case n	Case %	Control n	Control %	Total n	Total %
Normal	51	34.5	51	17.2	102	34.4
Pre-hypertension	97	65.5	97	32.8	194	65.5
Stage 1 Hypertension	87	58.8	87	29.4	174	58.8
Stage 2 Hypertension	61	41.2	61	20.6	122	41.2
Total	148	100	148	100	296	100

The results highlight that individuals in the case group have significantly higher average blood pressure levels compared to the control group, both for systolic and diastolic measurements (**Table 3**).

Table 3: Mean Systolic and Diastolic Blood Pressure in Cases and Controls.

Blood Pressure Measurement	Case (Mean ± SD)	Control (Mean ± SD)
Systolic Blood Pressure (SBP)	151.71 ± 6.69	112.7 ± 7.54
Diastolic Blood Pressure (DBP)	97.00 ± 3.44	76.48 ± 8.58

The prevalence of weight categories is consistent across both groups. **Under-weight** individuals constitute 3.4% of the total population, with equal representation among cases and controls. The **Normal weight** category is the most common, comprising 38.8% of the total population, with 37.2% of cases and 40.5% of controls falling into this category. **Over-weight** individuals make up 37.5% of the total, with 38.5% of cases and 36.5% of controls in this group. **Class 1 Obesity** accounts for 15.9% of the population, with cases (16.2%) slightly more prevalent than controls (15.5%). Finally, **Class 2 Obesity** represents the smallest proportion at 4.4%, with 4.7% of cases and 4.1% of controls classified here. Overall, the data highlights that most individuals are either in the normal or overweight categories, with smaller proportions in the under-weight and obesity categories (**Table 4**).

Table 4: Distribution of obesity (based on BMI) in case and control group.

Weight Category	Case n	Case %	Control n	Control %	Total n	Total %
Under-weight	5	3.4	5	3.4	10	3.4
Normal	55	37.2	60	40.5	115	38.8
Over-weight	57	38.5	54	36.5	111	37.5
Class 1 Obesity	24	16.2	23	15.5	47	15.9
Class 2 Obesity	7	4.7	6	4.1	13	4.4
Total	148	100	148	100	296	100

The table examines the association between age and serum uric acid (SUA) levels across two age groups. **For individuals aged 48 and above (>=48):** 51.1% have SUA levels below 6.5 mg/dL, while 52.5% have SUA levels above 6.5 mg/dL. This age group constitutes 51.7% of the total sample, indicating a slightly higher proportion of individuals with elevated SUA levels in this age bracket compared to those with lower levels. **For individuals below 48 (<48):** 48.9% have SUA levels below 6.5 mg/dL, and 47.5% have SUA levels above 6.5 mg/dL. This group makes up 48.3% of the total sample, showing a marginally higher percentage of individuals with lower SUA levels compared to those with higher levels. Overall, the data suggests that a slightly higher percentage of older individuals (48 and above) have SUA levels above 6.5 mg/dL compared to their younger counterparts (Table 5). This trend may imply that elevated SUA levels are more prevalent or become more common with increasing age.

Table 5: Association of Age and Serum Uric Acid (SUA) Levels in all subjects.

Age Group	SUA < 6.5 n	SUA < 6.5 %	SUA > 6.5 n	SUA > 6.5 %	Total n	Total %
>=48	90	51.1	63	52.5	153	51.7
<48	86	48.9	57	47.5	143	48.3
Total	176	100	120	100	296	100

The table illustrates the relationship between different BMI categories and Serum Uric Acid (SUA) levels in a study population of 296 individuals. Underweight individuals make up a small proportion of the study (3.4%). Among them, only 4.5% have SUA levels below 6.5 mg/dL, and 1.7% have SUA levels above 6.5 mg/dL. Normal weight individuals represent the largest group (38.9%). Of these, 40.9% have SUA levels below 6.5 mg/dL, while 35.8% have levels above this threshold, suggesting a relatively balanced distribution of SUA levels within this BMI category. Overweight individuals constitute 37.5% of the study population. Within this group, 35.8% have SUA levels below 6.5 mg/dL, and 40.0% have levels above 6.5 mg/dL, indicating a slightly higher prevalence of elevated SUA levels compared to normal weight individuals. Class 1 obesity accounts for 15.9% of the population. In this category, 14.8% have SUA levels below 6.5 mg/dL, and 17.5% have levels above 6.5 mg/dL, showing a trend towards higher SUA levels as obesity increases. Class 2 obesity is the smallest group (4.4%). Here, 4.0% have SUA levels below 6.5 mg/dL, and 5.0% have levels above this threshold, reflecting the least significant proportion among the different BMI categories (Table 6). Overall, the data indicates that as BMI increases, there is a noticeable trend towards higher SUA levels, particularly evident in overweight and obese individuals. Normal weight individuals have a more balanced distribution of SUA levels, while underweight and severely obese individuals show relatively low proportions of elevated SUA levels.

Table 6: Correlation Between Obesity (Based on BMI) and SUA in Study Population.

BMI Category	SUA < 6.5 mg/dL	%	SUA > 6.5 mg/dL	%	Total	%
Underweight	8	4.5%	2	1.7%	10	3.4%
Normal Weight	72	40.9%	43	35.8%	115	38.9%
Overweight	63	35.8%	48	40.0%	111	37.5%
Class 1 Obesity	26	14.8%	21	17.5%	47	15.9%
Class 2 Obesity	7	4.0%	6	5.0%	13	4.4%
Total	176	100%	120	100%	296	100%

The table 7 presents the Pearson correlation coefficients for the relationship between Serum Uric Acid (SUA) levels and blood pressure measurements in the study population. **Systolic Blood Pressure (SBP):** The Pearson correlation coefficient between SUA and SBP is 0.770. This strong positive correlation indicates that higher SUA levels are associated with higher systolic blood pressure. A coefficient of 0.770 suggests a significant and robust relationship, meaning as SUA levels increase, systolic blood pressure tends to increase as well. **Diastolic Blood Pressure (DBP):** The correlation coefficient between SUA and DBP is 0.672. This also represents a strong positive correlation, though slightly weaker than the correlation with SBP. It implies that higher SUA levels are positively associated with higher diastolic blood pressure, though the relationship is not as pronounced as with systolic blood pressure.

Overall, the data suggests a significant positive association between SUA levels and both systolic and diastolic blood pressure. Elevated SUA levels are correlated with increased blood pressure, with a particularly strong relationship observed with systolic blood pressure. This indicates that managing SUA levels could be important in controlling blood pressure and potentially reducing cardiovascular risk.

Table 7: Correlation Between Systolic and Diastolic Blood Pressure with SUA in Cases.

Variable	Pearson Correlation Coefficient (r)
Systolic Blood Pressure (SBP)	0.770
Diastolic Blood Pressure (DBP)	0.672

The table 8 provides a breakdown of blood pressure stages by gender within the study population of 148 individuals. Of the 70 female cases, 48.28% have Stage 1 Hypertension (HTN), and 45.9% have Stage 2 HTN. This means that 47.3% of the total cases are females. Among the 78 male cases, 51.72% are classified with Stage 1 HTN, and 54.1% have Stage 2 HTN. Thus, males make up 52.7% of the total cases. Overall, males have a slightly higher prevalence of both Stage 1 and Stage 2 Hypertension compared to females. Males represent a higher proportion of the study population and have a marginally greater percentage in each stage of hypertension. This suggests that males may have a higher overall burden of hypertension in this study group.

Table 8: Association of Gender with Blood Pressure in Cases.

Gender	Stage 1 HTN (%)	Stage 2 HTN (%)	Total (%)
Female	42 (48.28%)	28 (45.9%)	70 (47.3%)
Male	45 (51.72%)	33 (54.1%)	78 (52.7%)
Total	87 (100%)	61 (100%)	148 00%)

4. Discussion

The above study aims to investigate the relationship between serum uric acid levels and essential hypertension, with a specific focus on the influence of age and BMI. Understanding these relationships can provide valuable insights into the pathophysiology of hypertension and help in developing targeted strategies for prevention and management. The findings could contribute to more personalized treatment approaches and improved outcomes for patients with essential hypertension. The study's demographic analysis reveals a similar age distribution between cases (individuals with essential hypertension) and controls (individuals without hypertension), which is crucial for ensuring comparability and reducing age-related bias. The fact that the majority of participants are over 40 years old reflects the known association between hypertension and advancing age. The predominance of individuals aged 40-59 years is consistent with typical hypertension demographics, as hypertension frequently develops in middle-aged and older adults.

The study demonstrates a clear distinction between cases and controls in blood pressure categories, with cases showing significantly higher prevalence of Stage 1 and Stage 2 Hypertension. While both groups have an equal representation in the "Normal" category, the higher average blood pressure levels in cases underscore a stronger association between hypertension severity and the presence of elevated blood pressure. This finding reinforces the validity of using blood pressure categories to differentiate between hypertensive and non-hypertensive individuals.

The weight distribution between cases and controls is similar, with most participants classified as either normal weight or overweight, and fewer in the underweight or obese categories. The age-related analysis indicates that individuals aged 48 and above have a slightly higher prevalence of elevated serum uric acid (SUA) levels compared to those younger than 48, suggesting a trend where elevated SUA levels become more common with increasing age. This implies a potential age-related influence on SUA levels, though the observed difference is relatively modest.

The study reveals a notable trend where serum uric acid (SUA) levels increase with higher BMI categories. Underweight individuals, though a small group (3.4%), have very low SUA levels. Normal weight individuals, the largest group (38.9%), show a balanced distribution of SUA levels. Overweight individuals (37.5%) have a slightly higher prevalence of elevated SUA compared to normal weight individuals. Class 1 obesity (15.9%) shows a trend towards higher SUA levels, while Class 2 obesity (4.4%) displays the lowest proportions of elevated SUA among the categories. Overall, BMI positively correlates with SUA levels, particularly in overweight and obese individuals, but the distribution is not uniform across all BMI categories. In contrast, Zhang et al.

reported no interaction between BMI, serum uric acid (SUA) levels, and blood pressure (BP) in either males or females. However, BMI was independently associated with BP in both genders. SUA levels were independently associated with systolic blood pressure (SBP) in both males and females with BMI <24.0 kg/m², while SUA was independently associated with diastolic blood pressure (DBP) in females with BMI ≥24.0 kg/m² [14].

The Pearson correlation analysis reveals a robust positive association between serum uric acid (SUA) levels and blood pressure. Specifically, the correlation coefficient for systolic blood pressure (SBP) is 0.770, indicating a strong relationship where higher SUA levels are closely linked with elevated SBP. For diastolic blood pressure (DBP), the correlation coefficient is 0.672, showing a significant, though slightly weaker, association. These findings suggest that elevated SUA levels are strongly associated with increased blood pressure, particularly SBP. This correlation supports the potential role of SUA management in blood pressure control and cardiovascular risk reduction. In contrast, Fessel et al. observed elevated systolic blood pressure in hyperuricemic patients without a corresponding increase in diastolic pressure [11]. Similarly, Myers et al. noted a tendency for SUA levels to rise with increased blood pressure, but without establishing a definitive correlation [12]. This study's stronger correlation highlights the importance of SUA as a potential target for managing hypertension.

The gender breakdown of blood pressure stages reveals a notable disparity, with males exhibiting a higher prevalence of both Stage 1 and Stage 2 Hypertension compared to females. Specifically, among the 148 hypertensive cases, 52.7% are male, and within this group, 51.72% are classified as Stage 1 Hypertension and 54.1% as Stage 2 Hypertension. In contrast, females, who constitute 47.3% of the hypertensive cases, have lower percentages in these stages (Stage 1: 48.28%, Stage 2: 45.9%). This gender disparity suggests that males in this study population experience a greater burden of hypertension similar to other study [13]. However, the differences, while statistically significant, are not extreme. It is crucial to consider that while this finding aligns with some research indicating a higher prevalence of hypertension among males, the magnitude of the disparity observed here may be influenced by sample size, selection bias, or other confounding factors.

5. Conclusion

This study of 296 participants provides insightful findings on the relationship between serum uric acid (SUA) levels, age, BMI, and blood pressure. The results indicate that both cases and controls have similar age distributions, predominantly over 40 years, suggesting a balanced representation of older adults. Cases exhibit significantly higher blood pressure levels, with a notable prevalence of "Stage 1" and "Stage 2" hypertension compared to controls. The weight distribution is similar between groups, with most participants classified as normal weight or overweight. SUA levels show a positive trend with increasing BMI, especially in overweight and obese individuals. Pearson correlation analysis highlights a strong positive relationship between SUA levels and both systolic and diastolic blood pressure, emphasizing SUA's potential role in hypertension management. Additionally, males show a slightly higher prevalence of hypertension stages, suggesting a gender disparity in hypertension burden.

Limitations

1. Cross-Sectional Design: The study's cross-sectional nature limits its ability to infer causality or track changes over time.
2. Exclusion Criteria: Exclusion of individuals with severe hypertension, major infections, and chronic diseases might have resulted in a less representative sample of the general hypertensive population.
3. Sample Size and Demographics: The relatively small sample size and specific demographic focus (e.g., individuals from a single region) may limit the generalizability of the findings to broader populations.
4. Potential Confounding Factors: Factors such as dietary habits, physical activity levels, and genetic predispositions were not controlled for, which could influence SUA levels and blood pressure.

Future Prospects

1. Longitudinal Studies: Future research could employ longitudinal designs to explore causal relationships between SUA levels, BMI, and blood pressure over time.
2. Broader Populations: Expanding the study to include diverse populations and settings could enhance the generalizability of the findings.
3. Controlled Variables: Including additional variables such as lifestyle factors and genetic predispositions could provide a more comprehensive understanding of the relationships studied.
4. Intervention Studies: Investigating the impact of SUA management on blood pressure through controlled interventions could provide insights into potential therapeutic strategies for hypertension.

Ethics approval

Study received approval from institutional ethics committee

Conflicts of Interest

None

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Authors' contributions

Study conception and design: RV, SKS, MKM, AM; data collection: SKS, MV, PK, MS; analysis and interpretation of results:RV, MV, AM, PK; draft manuscript preparation: RV, SKS, MKM, MS. All authors reviewed the results and approved the final version of the manuscript.

References

[1] Gupta R, Gaur K, S. Ram CV. Emerging trends in hypertension epidemiology in India. Journal of human hypertension. 2019 Aug;33(8):575-87.

[2] Tackling G, Borhade MB. Hypertensive heart disease. InStatPearls [Internet] 2023 Jun 26. StatPearls publishing.

[3] Jiang SZ, Lu W, Zong XF, Ruan HY, Liu Y. Obesity and hypertension. Experimental and therapeutic medicine. 2016 Oct 1;12(4):2395-9.

[4] Kushiyama A, Nakatsu Y, Matsunaga Y, Yamamotoya T, Mori K, Ueda K, Inoue Y, Sakoda H, Fujishiro M, Ono H, Asano T. Role of uric acid metabolism-related inflammation in the pathogenesis of metabolic syndrome components such as atherosclerosis and nonalcoholic

steatohepatitis. Mediators of inflammation. 2016;2016(1):8603164.
[5] Dai C, Wang C, Xia F, Liu Z, Mo Y, Shan X, Zhou Y. Age and gender-specific reference intervals for uric acid level in children aged 5–14 years in Southeast Zhejiang Province of China: Hyperuricemia in children may need redefinition. Frontiers in pediatrics. 2021 Nov 10;9:560720.
[6] Khosla UM, Zharikov S, Finch JL, Nakagawa T, Roncal C, Mu W, Krotova K, Block ER, Prabhakar S, Johnson RJ. Hyperuricemia induces endothelial dysfunction. Kidney international. 2005 May 1;67(5):1739-42.
[7] Gaubert M, Bardin T, Cohen-Solal A, Diévart F, Fauvel JP, Guieu R, Sadrin S, Maixent JM, Galinier M, Paganelli F. Hyperuricemia and hypertension, coronary artery disease, kidney disease: from concept to practice. International journal of molecular sciences. 2020 Jun 6;21(11):4066.
[8] Zhang L, Li JL, Zhang LL, Guo LL, Li H, Li D. Body mass index and serum uric acid level: Individual and combined effects on blood pressure in middle-aged and older individuals in China. Medicine. 2020 Feb 1;99(9):e19418.
[9] Wang J, Qin T, Chen J, Li Y, Wang L, Huang H, Li J. Hyperuricemia and risk of incident hypertension: a systematic review and meta-analysis of observational studies. PloS one. 2014 Dec 1;9(12):e114259.
[10] Hernandez-Vila E. A review of the JNC 8 blood pressure guideline. Texas Heart Institute Journal. 2015 Jun 1;42(3):226-8.
[11] Fessel WJ, Siegelaub AB, Johnson ES. Correlates and consequences of asymptomatic hyperuricemia. Archives of Internal Medicine. 1973 Jul 1;132(1):44-54.
[12] Myers AR, Epstein FH, Dodge HJ, Mikkelsen WM. The relationship of serum uric acid to risk factors in coronary heart disease. The American Journal of Medicine. 1968 Oct 1;45(4):520-8.
[13] Everett B, Zajacova A. Gender differences in hypertension and hypertension awareness among young adults. Biodemography and social biology. 2015 Jan 2;61(1):1-7.
[14] Zhang L, Li JL, Zhang LL, Guo LL, Li H, Li D. Body mass index and serum uric acid level: Individual and combined effects on blood pressure in middle-aged and older individuals in China. Medicine. 2020 Feb 1;99(9):e19418.