Association between serum uric acid levels with essential hypertension and its metabolic variables in Hospital Universiti Sains Malaysia

Zulkarnain Mustapha, MSc^{1,3}, Wan Mohd Saifuhisam Wan Zain, MPath^{1,3}, Najib Majdi Yaacob, DrPH^{2,3}, Aniza Mohammed Jelani, MPath^{1,3}

¹Department of Chemical Pathology, School of Medical Sciences, Universiti Sains Malaysia Health Campus, Kelantan, Malaysia, ²Unit of Biostatistics and Research Methodology, School of Medical Sciences, Universiti Sains, Malaysia Malaysia Health Campus, Kelantan, Malaysia, ³Hospital Universiti Sains Malaysia, Kelantan, Malaysia

ABSTRACT

Introduction: Hyperuricaemia is common in essential hypertension with varying results in different populations. This study sought to ascertain the association between serum uric acid levels and essential hypertension in Hospital Universiti Sains Malaysia (HUSM).

Materials and Methods: A case-control study design involving 132 subjects (88 subjects of hypertension patients for case group and 44 subjects for control group) aged 18 to 40 years old of both genders was conducted at HUSM primary care clinic and physician clinic from May 2020 to May 2021. Blood samples were collected from each of the case and control subjects and analysed for serum uric acid, urea, creatinine, total cholesterol, triglycerides, LDL and HDL on chemical analyser Architect c8000. The data were analysed by using SPSS Statistics 26.0 version.

Results: The proportion of subjects with hyperuricaemia in the case group was 48.9%. A significant difference in the uric acid levels between the case group (390.64±92.65µmol/L) and control group (352.09±86.07µmol/L), (p<0.05) was observed. There was no significant difference in the serum uric acid mean ± SD based on the duration of hypertension (<5 years and ≥5 years), (p=0.331) and stages of hypertension (p>0.05). In case group, significant correlations were established between uric acid and triglycerides (r=0.255, p<0.05), uric acid and HDL (r= -0.223, p<0.05), uric acid and urea (r=0.299, p<0.05), uric acid and creatinine (r=0.486, p<0.01). No correlation among uric acid and total cholesterol levels (p>0.05), uric acid and LDL (p>0.05). Serum uric acid was a vital variable in developing hypertension (p<0.05) but not when adapted for age and body mass index (BMI) (p>0.05).

Conclusion: Serum uric acid was significantly elevated in essential hypertension. The significant associations were established between uric acid and triglycerides, HDL, urea and creatinine in essential hypertension. Serum uric acid was a vital variable to develop hypertension, but the association was weakened by other co-founders as age and BMI. A large-scale population-based study is required to truly conclude the association between serum uric acid levels and essential hypertension in our population.

13. on

KEYWORDS:

INTRODUCTION Hyperuricaemia is common in individuals diagnosed with essential hypertension.^{1.3} It is defined as the concentration of serum uric acid above uric acid solubility which is approximately 420 μ mol/l in men and 360 μ mol/l in women.4 Approximately 25% of hypertensive individuals experience hyperuricaemia and the percentage escalates to 75% of those individuals with malignant or severe hypertension.^{5.7}

Uric acid, hypertension, case-control, chemical pathology

A 1 mg/dl (59.48 µmol/L) elevation in serum uric acid concentration is related to a notable rise in the risk of developing new onset hypertension⁸ and a 48% increase in the risk for coronary artery disease.⁹ Hyperuricemia observed in individuals with hypertension signifies an initial involvement of the renal vasculature, which is linked to hypertension.⁶ Serum uric acid shows a direct association with the duration and severity of hypertension.^{5,10} Elevated serum urea, creatinine, total cholesterol, triglycerides, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were significantly noted in hypertensive patients with hyperuricaemia.⁹

Mechanisms involved in the occurrence of hypertension in hyperuricaemia are; 1) Uric acid influences the activation of renin-angiotensin system causing vasoconstriction;¹¹ 2) Uric acid causes vascular smooth muscle proliferation and endothelial cells dysfunction.¹²

Besides hypertension and gout, other diseases associated with hyperuricaemia are metabolic syndrome, kidney diseases, stroke and coronary heart disease.¹³ The mechanisms involved are the combination of inflammation, endothelial cells dysfunction, oxidative stress and others.¹³ Serum uric acid may affect antihypertensive treatment in the management of hypertension.⁸ In hypertensive individuals with hyperuricaemia, uric acid lowering therapy may decrease blood pressure levels.¹⁴

This article was accepted: 17 June 2024 Corresponding Author: Wan Mohd Saifuhisam Bin Wan Zain Email: wansaifu1985@usm.my

The specific objectives of this study were as followed; 1) To ascertain the proportion of hyperuricaemia among essential hypertension patients in a case-control study design in Hospital Universiti Sains Malaysia (HUSM); 2) To investigate the association between serum uric acid levels and stage as well as duration of hypertension; 3) To investigate the relationship between serum uric acid levels with routine laboratory tests specifically serum urea, creatinine, total cholesterol, triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL); 4) To analyse the risk of essential hypertension occurrence based on serum uric acid.

To the best of our knowledge, there has been no similar study conducted in Malaysia before. Studies on other populations and countries have revealed varying results1 possible due to other confounding factors for examples dietary and lifestyle. Thus, the aim of our study is to ascertain the association between serum uric acid levels and essential hypertension in local study population.

Our hypothesis was there was an association between serum uric acid levels and essential hypertension in our study population.

MATERIALS AND METHODS

Study Design and Participants

A matched case-control design based on age was used in this study. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Setting

This study was conducted on essential hypertension patients at primary care and physician clinics at HUSM, Kubang Kerian Kelantan Malaysia from May 2020 to May 2021 for case group. Volunteers (non-hypertensive subjects) were recruited for control group during similar period of time.

Study Participants

For case group, essential hypertension patients of male and female aged between 18 and 40 years old were randomly chosen from the list of hypertension patients attending the clinics and who had fulfilled the inclusion and exclusion criteria. The age 18 to 40 years was chosen as previous study had shown the link between serum uric acid and blood pressure in this age group.¹ The inclusion criterion is individual diagnosed with essential hypertension. The exclusion criteria are secondary hypertension including renal parenchymal disease, endocrine disorders, renovascular disease, coarctation of the aorta, iatrogenic treatment with steroids and other causes of secondary hypertension. Other exclusion criteria are diabetes, pregnancy, ischaemic heart disease, congestive cardiac failure, gout, obesity, history of alcohol intake, renal insufficiency, glomerulonephritis, pyelonephritis, hereditary nephropathy, patients on drugs including levodopa, ethambutol, pyrazinamide, nicotinic acid, cytotoxic drug, low dose aspirin, thiazide diuretics, allopurinol and other drugs that can affect serum uric acid level.

The volunteers for control group were recruited randomly from the list of individuals attending clinics for regular medical check-up. The inclusion criterion is individual without medical illness aged between 18 and 40 years of male and female to match with hypertensive group. The exclusion criteria are primary and secondary hypertension in addition to other exclusion criteria similar to the hypertensive group.

The sample size was determined by G-power software version 3.1.6 with 5% of type I error, 80% of type II error, 2:1 ratio between case and control group and 10% of anticipated incomplete data (n=88 for case group, n=44 for control group).

Observational Data

The demographic data of case and control groups consisted of age, gender, gender, ethnicity, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate and smoking status.

Sample Collection and Laboratory Analysis

Fasting venous blood samples (5 ml) were taken from each subject of case and control groups. The serum was taken after centrifugation and was analysed for uric acid, urea, creatinine, total cholesterol, triglycerides, LDL and HDL on chemical analyser Architect c8000.

Data Analysis

The data were analysed by using SPSS Statistics 26.0 version. Numerical data were presented as the mean and standard deviation (SD) and categorical data were presented as frequencies (n) and percentage (%). The normality testing was performed prior to performing statistical analysis to confirm that the data exhibit Gaussian distribution. Independent t-test was used for comparing the mean of serum uric acid levels between case and control groups. An independent t-test was used to compare the mean of serum uric acid levels between case and control groups as well as the mean of serum uric acid levels between the duration of hypertension (< 5 years and \geq 5 years). The 5 years cut-off was selected based on the previous study.16. One way analysis of variance (ANOVA) test was used for comparing mean of serum uric acid levels between stages of hypertension (Stage 1 for mild (SBP 140-159mmHg and/or DBP 90-99mmHq), Stage 2 for moderate (SBP 160-179mmHq and/or 100-109mmHg), Stage 3 for severe (SBP≥180mmHg and/or DBP>110mmHg) based on Clinical Practice Guidelines Management of Hypertension 5th edition by Malaysia Ministry of Health. Pearson correlation was used for analysing the correlation between serum uric acid levels with serum creatinine, serum total cholesterol and serum HDL as the data were parametric. Spearman correlation was used for analysing the correlation between serum uric acid level with serum urea, serum triglycerides and serum LDL as the data were nonparametric. Baseline routine laboratory tests of both case and control groups were analysed initially. Data showed normal serum urea, creatinine, triglycerides, no major risk factor for heart disease based on HDL level and just mildly elevated for total cholesterol and LDL. Simple and multiple logistic regression analysis were used to analyse the risk of essential hypertension occurrence based on serum uric acid.

Variable	G	p-value	
	Case (n = 88)	= 132 Control (n = 44)	-
Age (years) ^a	36.22 (4.13)	34.07 (3.69)	0.004
Gender⁵			
Male	52 (59.1)	26 (59.1)	1.000
Female	36 (40.9)	18 (40.9)	
Ethnic ^b			
Malay	79 (89.8)	43 (97.7)	0.271
Non-Malay	9 (10.2)	1 (2.3)	
BMI (kg/m ²) ^a	25.28 (2.10)	23.54 (2.24)	<0.001
Systolic blood pressure (mmHq) ^a	152.11 (12.05)	114.82 (11.04)	<0.001
Diastolic blood pressure (mmHg) ^a	95.72 (10.17)	73.84 (8.71)	<0.001
Heart rate (beats/min) ^a	81.25 (10.71)	73.73 (8.33)	<0.001
Stage of hypertension ^b			
Stage 1	34 (38.6)		
Stage 2	46 (52.3)	-	-
Stage 3	8 (9.1)		
Duration of hypertension ^b			
< 5 years	54 (61.4)	-	-
≥ 5 years	34 (38.6)		
Smoking ^b			
Yes	15 (17)	1 (2.3)	0.014
No	73 (83)	43 (97.7)	
Hyperuricaemia ^b	43 (48.9)	11 (25)	0.07

Table I: Baseline characteristics of the study subjects.

^aMean (SD) ^bno (%)

Table II: Comparison of mean serum uric acid levels between case and control groups.

Variable Mean (SD)		Mean difference	t statistic	р	Reference Interval	
	Case group (df)	Control group value*	(95% CI)			(µmol/L)
Serum uric acid (µmol/L)	390.64 (92.65)	352.09 (86.07)	38.55 (5.48, 71.61)	2.306 (130)	0.023	Male: 210-420 Female:150-350

*Independent t test

Table III: Comparison of mean serum uric acid levels between stages and duration of essential hypertension.

Variable (s)	Serum uric acid (µmol/L) Mean (SD)	F statistic (df)/ t statistic (df)	p-value
Stages of essential hypertension			
Stage 1 (mild)	378.20 (80.31)	2.042 (2, 85)	0.136ª
Stage 2 (moderate)	389.37 (99.10)		
Stage 3 (severe)	450.75 (90.77)		
Duration essential hypertension			
<5 years	398.30 (86.17)	0.977 (86)	0.331 ^b
≥5 years	378.47 (102.24)		

^aOne-way ANOVA

^b Independent sample t test

Table IV: Crude and adjusted logistic regression of hypertension variables between case and control.

Variable (s)	Crude odd ratio (95% Cl)	p-value	Adjusted OR (95% CI)*	p-value
Serum uric acid	1.005 (1.001, 1.009)	0.025	1.004 (0.999, 1.009)	0.082
BMI	1.408 (1.183, 1.676)	< 0.001	1.400 (1.162, 1.688)	<0.001
Age	1.137 (1.038, 1.246)	0.006	1.138 (1.031, 1.257)	0.010
Gender	1.000 (0.479, 2.088)	1.000		

*Constant= -13.717

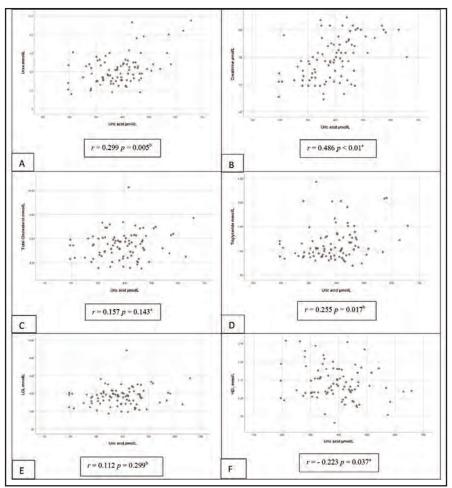
*Backward LR method was applied

*No interaction

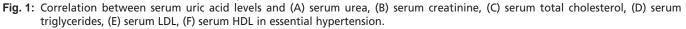
*Hosmer Lemeshow test, p-value= 0.236

*Classification table 72.0% correctly classified

*Area under Receiver Operating Characteristics (ROC) curve was 77.1%



^aPearson correlation ^bSpearman correlation



Ethical Considerations

This study was given approval by the Human Research Ethics Committee USM (HREC). Reference code: USM/JEPeM/19120845

RESULTS

A comparison of the following variables, age, gender, ethnicity, BMI, systolic blood pressure, diastolic blood pressure, heart rate, smoking status and no of hyperuricaemic subject between the case and control groups is presented in Table I. A total 132 subjects were involved in this study in which 88 were hypertensive subjects for case group and 44 subjects for control group. There were significant differences in the mean±SD between the case and control groups in terms of age, BMI, blood pressure and heart rate. The mean (SD) for age for case and control groups were 36.22 (4.13) years old and 34.07 (3.69) years old, respectively (p<0.05). The mean (standard deviation) for BMI for case and control groups were 25.28 (2.10) kg/m² and 23.54 (2.24) kg/m², respectively (p<0.001). The mean (SD) for systolic blood pressure for case and control groups were 152.11 (12.05) mmHg and 114.82 (11.04) mmHg, respectively (p < 0.001). The mean (SD) for diastolic blood pressure for case and control groups were 95.72 (10.17) mmHg and 73.84

(8.71) mmHg, respectively (p<0.001). The mean (SD) for heart rate for case and control groups were 81.25 (10.71) beats/min and 73.73 (8.33) beats/min, respectively (p < 0.001). There was no significant difference between the case and control group in terms of ethnicity and gender. A significant difference between the percentage of smoker and non-smoker in case group and control group was seen. Most of the participants were non-smokers (n=116, 87.9% which [n = 73] in case group and [n = 43] in control group, p<0.05).

The proportion of hyperuricaemia for case and control groups were 48.9% and 25%, respectively with no significant difference (p>0.05).

A comparison of mean of serum uric acid levels among case group and control group are shown in Table II. There were significant differences in the mean \pm SD between the case and control groups for serum uric acid. Mean (SD) for serum uric acid in case and control groups were 390.64 (92.65) µmol/L and 352.09 (86.07) µmol/L, respectively (p=0.023). A comparison of mean of serum uric acid levels corresponding to stages and duration of essential hypertension are shown in Table III. No significant difference between the mean (SD) for serum uric acid levels and stages 1, 2 and 3 of hypertension 378.20 (80.31) µmol/L, 389.37 (99.10) µmol/L and 450.75

(90.77) µmol/L, respectively (p=0.136). No significant difference between the mean (SD) for duration of hypertension of <5 years and ≥5 years 398.30 (86.17) µmol/L and 378.47 (102.24) µmol/L, respectively (p = 0.331). A correlation between serum uric acid levels and routine laboratory tests in case group are shown in Figure 1. Among the lipid profile, significant positive correlation was found between serum uric acid levels and triglycerides levels (r=0.255, p=0.017), while an inversed correlation was observed between serum uric acid levels and HDL levels (r= -0.223, p=0.037). No significant correlation between serum uric acid levels and total cholesterol levels and LDL in essential hypertension (r=0.157, p=0.143) and (r=0.112, p=0.299) respectively. A significant correlation between serum uric acid levels and serum urea levels (r=0.299, p=0.005) and serum creatinine (r=0.486, p<0.01) was observed in essential hypertension.

To analyse the importance of serum uric acid in the development of hypertension, the association of serum uric acid with the presence of essential hypertension is shown by simple logistic regression and multiple logistic regression in Table IV. For simple logistic regression, serum uric acid was an important variable in developing hypertension at univariate analysis (p=0.025). The crude (unadjusted) odd ratio was 1.005. At univariate analysis, a person with 1 µmol/L higher serum uric acid had 1.005 times the odds to develop hypertension. The BMI was an important variable for developing hypertension at univariate analysis (p<0.001). The crude (unadjusted) odd ratio was 1.408. At univariate analysis, a person with 1 kg/m² higher BMI had 1.408 times the odds to develop hypertension. Age was an important variable for developing hypertension at univariate analysis (p=0.006). The crude (unadjusted) odd ratio was 1.137. At univariate analysis, a person one year older had 1.137 times the odd to develop hypertension. Gender was not an important variable for developing hypertension at univariate analysis (p=1.000).

Based on multiple logistic regression, no association was found between serum uric acid and hypertension when adapted for age and BMI (p=0.082). A significant association between BMI and hypertension when adjusted for serum uric acid and age. A person with 1kg/m^2 higher BMI had 1.400 times the odd to develop hypertension (p<0.001). A significant association was observed between age and hypertension when adjusted for serum uric acid and BMI. A person 1 year older had 1.138 times the odd to develop hypertension (p=0.010).

Results of multiple logistic regression does not support serum uric acid as a significant association with essential hypertension.

DISCUSSION

Hyperuricaemia has been linked to hypertension, which is one of the major determinants for cardiovascular, cerebral and renal diseases. The effects of serum uric acid on hypertension were observed in other epidemiological studies. However, studies conducted in different populations have shown variable results.¹ This study had shown that the proportion of hyperuricaemia in the case group was higher (48.9%) compared to control group (25%). The previous studies which stated approximately 20-47% of hypertensive adults had developed hyperuricaemia.^{15,33} The difference in percentage of hyperuricaemia in hypertensive adults in our study compared to previous study were due to our study involved few study subjects and not a general population-based study. The contributing factors for the high prevalence of hyperuricaemia are dietary style, improved life expectancy, increased obesity rate and increased medication use for example antihypertensive of diuretic type.¹⁵ The relationship between serum uric acid and blood pressure differs at different ages in various populations.¹

Our study showed that the serum uric acid level was significantly increased in essential hypertension as there was a notable difference between the mean (SD) of serum uric acid in hypertensive group 390.64 (92.65) µmol/L and control group 352.09 (86.07) µmol/L (p < 0.05). Our results showed an agreement with the results from studies by Divyen et al.,⁵ and Meti K et al.,¹⁶ which the mean (SD) of serum uric acid in hypertensive group were significantly higher compared to control group 367.62 (106.48) µmol/L (p<0.05) and 374.75 (65.43) µmol/L (p<0.01), respectively. However, multiple logistic regression did not support our study findings. Thus, the significant association found in univariate analysis therefore is due to co-founding factors.

The results from most of epidemiological studies of population-based had supported that hyperuricaemia was an important independent predictor for the occurrence of hypertension with a higher relative risk shown in Korean,¹⁷ black and white from the US,¹⁸ native Japanese¹⁹ and Japanese immigrants in the US.²⁰ It was reported that high serum uric acid concentrations were linked to high blood pressure in Korean aged <40 but not ≥40 years old, whereas this association was observed in Japanese aged ≥40 but not <40 years old.¹ Our study only involved participants in age group of 18 to 40 and subjects aged more than 40 were not included in our study. Thus, the association between serum uric acid and essential hypertension with age could not be concluded in our study.

Various studies had reported that serum uric acid showed a direct relation to the duration and the severity of hypertension.^{5,10} However, this study had showed that there was no notable difference between mean (SD) of serum uric acid and stages of essential hypertension (p > 0.05) and also no notable difference between mean (SD) of serum uric acid and duration of essential hypertension in <5 years 398.30 (86.17) μ mol/L and \geq 5 years 378.47 (102.24) μ mol/L (p>0.05). These findings were in accordance with other study by Ansari²¹ which stated there was no notable statistical difference found between serum uric acid level and the severity of hypertension in stage 1 and stage 2 (p>0.05). Nevertheless, the findings were contradicted with Divyen et al.,⁵ study which reported a significant difference between mean (SD) of serum uric acid of stage 1 296.83 (76.62) µmol/L and stage 2 394.98 (104.16) µmol/L (p<0.001) of essential hypertension. Meti K et al.,¹⁶ reported that there was a significant difference between mean (SD) of serum uric acid and the duration of essential hypertension in <5 years 339.06 (77.33) μ mol/L and \geq 5 years 428.29 (65.43) μ mol/L (p<0.001). There were several factors which contributed to the difference results of this study with the other studies. One of the factors was our study and the study by Ansari RN et al.,²¹ involved smaller sample size of 132 participants (88 hypertensive, 44 control) and 100 hypertensive participants respectively compared to the two studies by Divyen et al.,⁵ and Meti et al.,¹⁶ which both studies involved 200 participants (100 hypertensive, 100 control). Another factor was the difference in the age group of participants in which this study involved participants with age group of 18 to 40 years old whereas Divyen et al.,⁵ and Meti K et al.,¹⁶ studies involved participants with age group of 41 to 80, and 40 to 70, respectively. Although our study showed statistically no significant difference between mean (SD) of serum uric acid and stages of hypertension, there was a rising trend of mean (SD) of serum uric as stages or severity of hypertension increased.

There were few studies focusing on the trend of important laboratory parameters with serum uric acid level. Alternation in serum urea, serum creatinine and lipid profiles has been recognised as the independent determinant for essential hypertension. In our study, there was significant correlations between serum uric acid levels and some parameters of renal function (serum urea and serum creatinine). These were shown by positive correlations between serum uric acid levels with serum urea and serum creatinine in essential hypertension (r=0.299, p<0.05), (r=0.486, p<0.01) respectively. Kaewput et al.,²² stated that elevated serum uric acid level was linked to high chronic kidney disease prevalence in hypertensive patients. Aiumtrakul et al.,23 suggested that serum uric acid levels were independently linked to the high incidence of impaired renal function and renal disease progression in a community-based population. Reddy et al.,¹⁰ suggested that uric acid may be an early and more sensitive markers of reduce renal blood flow compared to serum creatinine. The postulated mechanism was uric acid can induce the activation of renin-angiotensin system leading to vasoconstriction, resulting in reduce renal blood flow.¹¹ Even so, the serum uric acid elevation could be the result of hyperinsulinaemia¹⁰ (as the insulin could reduce renal excretion of uric acid) which may influence the mean value of serum uric acid in case group. We did not analyse the serum insulin level in our study but the obese subjects who generally associated with insulin resistance and resultant hyperinsulinaemia were excluded from the study.

There was a significant correlation between serum uric acid levels and serum triglycerides levels in essential hypertension with a fair positive correlation (r=0.255, p<0.05). A significant correlation between serum uric acid levels and serum HDL levels in essential hypertension with poor negative correlation (r= -0.223, p<0.05) was observed. These findings were in agreement with other studies.²⁴⁻²⁷. It is postulated that the synthesis of triglycerides requires nicotinamide adenine dinucleotide phosphate (NADPH) which will lead to an increase of uric acid production.²⁷ Thus, our study had shown that hyperuricaemia was associated with dyslipidaemia²⁸ which can predict the risk for coronary artery disease. The association of serum uric acid with the presence of essential hypertension was shown in our study as a person with 1 µmol/L higher serum uric acid level had 1.005 times the odds to develop hypertension at univariate analysis (p<0.05). De Becker et al.,²⁹ stated that systemic review and meta-analysis recently disclosed that 60 µmol/L rise in uric acid level was related to an increased risk of developing hypertension by 13%. However, in our study no association was observed between serum uric acid and hypertension when adjusted for age and BMI (p>0.05) in multivariate analysis. Age and BMI are the co-founding factors which will influence the effect of serum uric acid towards the risk of developing hypertension. Loh et al.,³⁰ reported that age and BMI had significant associations with hypertension in which the increased in age and BMI will increase the risk to develop hypertension (p < 0.001) in a population-based study in Perak, Malaysia. The individuals aged 30 to 39 years had the adjusted odds of 1.00 and the obese individuals had the higher adjusted odds of 2.34 to develop hypertension.³⁰ Malaysia currently is the country with the highest prevalence of obesity among adult in Southeast Asia in which 50.1% of Malaysia's adult population were reported as being overweight (30.4%) or obese (19.7%) according to 2019 national health and morbidity survey.³¹

There were several limitations to our study. One of the limitations was we did not include the dietary history of the study participants as the possible co-founding factor for the increase serum uric acid level which may influence the mean value of serum uric acid in case group. Approximately one third of the total body uric acid is from dietary purines and the other two thirds are formed endogenously. Nevertheless, the study by Krupp et al³² reported that uric acid was an important predictor of hypertension in Germany's general adult population independent of dietary factors. Our study showed a significant association between serum uric acid and serum triglycerides and HDL levels, but total cholesterol and LDL showed lack of significant association. This could be explained by small study sample. Further larger populationbased studies may increase our understanding regarding serum uric acid, lipid profile and hypertension in our population by increasing representativeness of our population, increasing statistical power and allowing for subgroup analysis. This will generate more robust conclusions.

CONCLUSIONS

Serum uric acid concentration was significantly raised in essential hypertension. No significant difference of serum uric acid concentration related to duration and severity of essential hypertension was observed. The significant associations were established between serum uric acid and triglycerides, high-density lipoprotein (HDL), urea and creatinine in essential hypertension. Serum uric acid was an important and significant variable for developing hypertension, but this association was weakened with the presence of other significant co-founders for example age and body mass index. The association of serum uric acid and hypertension is well-established already for years in other populations. Researchers are now investigating, which one is the cause, and which is the outcome. Despite the limitations, this study was the pioneer study assessing the association of serum uric acid with essential hypertension in Malaysia. A large-scale population-based study is required to truly conclude the association in our population.

ACKNOWLEDGEMENTS

This work was funded by bridging grant from Universiti Sains Malaysia. The authors would like to thank the laboratory staffs of Chemical Pathology Department Universiti Sains Malaysia for all the support given to this project.

REFERENCES

- 1. Cheng W, Wen S, Wang Y, Qian Z, Tan Y, Li H, et al. The association between serum uric acid and blood pressure in different age groups in a healthy Chinese cohort. Medicine (Baltimore) 2017; 96(50): 8953.
- 2. Lee JJ, Ahn J, Hwang J, Han SW, Lee KN, Kim JB, et al. Relationship between uric acid and blood pressure in different age groups. Clin Hypertens 2015; 21: 14.
- 3. Kuwabara M, Niwa K, Nishi Y, Mizuno A, Asano T, Masuda K, et al. Relationship between serum uric acid levels and hypertension among Japanese individuals not treated for hyperuricemia and hypertension. Hypertens Res 2014; 37(8): 785-9.
- Borghi C, Rosei EA, Bardin T, Dawson J, Dominiczak A, Kielstein JT, et al. Serum uric acid and the risk of cardiovascular and renal disease. J Hypertens 2015; 33(9): 1729-41.
- 5. Divyen K, Aundhakar SC, Sutariya NL, Ratan V, Hardik P. Evaluation of rol of serum uric acid levels in cases of essential hypertension. Int J Contemp Med Res 2018; 5(5): E18-E21.
- Kumar S, Mahto M, Banerjee A, Kiriti R, Ranjan A, Bharti A. A study of serum uric acid levels in essential hypertension. Int J Med Health Res 2018; 4(5): 123-5.
- 7. Meena CL, Meena VK, Bharti A, Nawal R, Meena LP, Kumar N, et al. Association of serum uric acid and microalbuminuria in pre-hypertension: a cross sectional study. Natl J Physiol Pharm Pharmacol 2013; 3(1): 87-91.
- 8. Grassi G. Effects of serum uric acid on blood-pressure lowering treatment. Curr Med Res Opin 2017; 33(S3): 15-9.
- 9. Chowdeswari N, Jaya, N, Rao RBV. Association between serum uric acid levels and hypertension: a retrospective study. Int J Clin Bioche Res 2016; 3(1):129-33.
- 10. Reddy RP, Monigari N, Hande M. Study of serum uric acid in essential hypertension. Int J Scient Res Public 2015; 5(8): 1-12.
- McMullan CJ, Borgi L, Fisher N, Curhan G, Forman J. Effect of uric acid lowering on renin-angiotensin-system activation and ambulatory BP: a randomized controlled trial. Clin J Am Soc Nephrol 2017; 12(5): 807-16.
- Li H, Qian F, Liu H, Zhang Z. Elevated uric acid levels promote vascular smooth muscle cells (VSMC) proliferation via a nod-like receptor protein 3 (NLRP3)-inflammasome-dependent mechanism. Med Sci Monit 2019; 25: 8457-64.
- 13. Wang H, Zhang H, Sun L, Guo W. Roles of hyperuricemia in metabolic syndrome and cardiac-kidney-vascular system diseases. Am J Transl Res 2018; 10(9): 2749-63.
- 14. Qu LH, Jiang H, Chen JH. Effect of uric acid-lowering therapy on blood pressure: systematic review and meta-analysis. Ann Med 2017; 49(2): 142-56.
- 15. Douglas JS, Langlois V, Noone D. Hyperuricemia and hypertension: links and risks. Integr Blood Press Control 2019; 12: 43-62.

- 16. Meti K, Gaddeppanavar J, Karinagannanavar A, Shashikantha, Girish I. Estimation of serum uric acid level in essential hypertension and its correlation with severity and duration of hypertension. Int J App Res 2015; 1(9): 844-8.
- 17. Yoo TW, Sung KC, Shin HS, Kim BJ, Kim BS, Kang JH, et al. Relationship between serum uric acid concentration and insulin resistance and metabolic syndrome. Circ J 2005; 69(8): 928-33.
- Philip BM, Bleyer AJ, Erlinger TP, Evans GW, Nieto FJ, Wagenknecht LE, et al. Serum uric acid predicts incident hypertension in a biethnic cohort: the atherosclerosis risk in communities study. Hypertension 2006; 48(6): 1037-42.
- 19. Nagahama K, Inoue T, Iseki K, Touma T, Kinjo K, Ohya Y. Hyperuricemia as a predictor of hypertension in a screened cohort in Okinawa, Japan. Hypertens Res 2004; 27(11): 835-41.
- 20. Imazu M, Yamamoto H, Toyofuku M, Sumii K, Okubo M, Egusa G, et al. Hyperinsulinemia for the development of hypertension: data from the Hawaii-Los Angeles-Hiroshima Study. Hypertens Res 2001; 24(5): 531-6.
- Ansari RN. Gandhi RV, Saiyed MN, Jain KD. Study of prevalence and impact of hyperuricemia in a patient of hypertension. Int J Adv Med 2017; 4(2): 367-9.
- 22. Kaewput W, Thongprayoon C, Rangsin R, Ruangkanchanasetr P, Bathini T, Mao, MA, et al. Association between serum uric acid and chronic kidney disease in patients with hypertension: A multicenter nationwide cross-sectional study. J Evid Based Med 2019;12(4): 235-42.
- 23. Aiumtrakul N, Wiputhanuphongs P, Supasyndh O, Satirapoj B. Hyperuricemia and impaired renal function: a prospective cohort study. Kidney Dis 2020. 2021; 7(3): 210-18.
- 24. Son M, Seo J, Yang S. Association between dyslipidemia and serum uric acid levels in Korean adults: Korea National Health and Nutrition Examination Survey 2016-2017. PLoS ONE 2020; 15(2): e0228684.
- 25. Ali N, Rahman S, Islam S, Haque T, Molla NH, Sumon AH, et al. The relationship between serum uric acid and lipid profile in Bangladeshi adults. BMC Cardiovasc Disord 2019; 19(1): 42.
- Peng TC, Wang C-C, Kao T-W, Chan JY-H, Yang Y-H, Chang, Y-W, et al. Relationship between hyperuricemia and lipid profiles in US adults. Biomed Res Int. 2015: 127596.
- 27. Sarmah D, Sharma, B. A correlative study of uric acid with lipid profile. Asian J Med Sci 2013; 4 (2): 8-14.
- Kumar S, Banerjee A, Mahto M, Ranjan, A. Evaluation of relationship between hyperuricemia and lipid profile. Inte J Med Health Res 2018; 4(6): 89-91.
- 29. De Becker B, Borghi C, Burnier M, van de Borne P. Uric acid and hypertension: a focused review and practical recommendations. J Hypertens 2019; 37(5): 878-83.
- Loh KW, Rani F, Chan TC, Loh HY, Ng CW, Moy FM. The association between risk factors and hypertension in Perak, Malaysia. Med J Malaysia. 2013; 68(4): 291-6.
- 31. National Institutes of Health (NIH) Ministry of Health Malaysia (MOH). National health and morbidity survey; 2019.
- Krupp D, Esche J, Mensink GBM, Neuhauser HK, Remer T. Dietindependent relevance of serum uric acid for blood pressure in a representative population sample. J Clin Hypertens (Greenwich) 2017; 19(10): 1042-50.
- Borghi C, Agnoletti D, Cicero AFG, Lurbe E, Virdis A. Uric Acid and hypertension: a review of evidence and future perspectives for the management of cardiovascular risk. Hypertension 2022; 79(9): 1927-36.