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## Uric acid and other Risk factors in Hypertension in province of Al-Najaf.

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### ABSTRACT

Study the role and relationship of uric Acid and other risk factors in hypertension. This study was executed on 654 patients and were divided into two groups, the first group included [(302 patients; male 174, female 128) with high uric acid], the 2<sup>nd</sup> group included [(352 patients; 157 male, 195 female) with normal or low uric acid], all of them are suffering from hypertension and control group that they were consist of [ (200 patients; 120 male, 80 female)] during 3 years (from January 1<sup>st</sup> 2013 to August 15<sup>th</sup> 2015). This study included the relation between uric acid and other risk factor (age, weight, obesity, gender, job, and residence) and different diseases. These data were analyzed statically with SPSS 8.0 statistical package (ANOVA- analysis of variance - two ways analyze; Mean  $\pm$  SE). (P) values less than or equal to 0.05 has been evaluated as statistical significant. Among many risk factors of hypertension uric acid possess the same average effect on the gender (male and female) of individual outpatients [( F<sub>calculated</sub> = 0.036, F<sub>tabulated</sub> = 1.68), ( P $\leq$ 0.05)]. The number of female patients with hypertension due to elevated uric acid enrolled undercounts in corresponding with male (male = 21.75 $\pm$ 9.36, female = 16.00 $\pm$ 5.02), (P $\leq$ 0.05) and both of them have the high effect in comparison with another risk factors, whereas the obesity of male and female have highest average effect with significant differences of hypertensive cases, in which superiority of female more than male (male = 14.00 $\pm$ 6.35, female = 9.25 $\pm$ 3.08). The higher average was recorded in the age about (31- 40), and (41-50) years in male (42, 70) more than female (10, 30). The other risk factor (Gout) has minimum effect in the patients suffering from hypertension (male = 2.00 $\pm$ 0.95, female = 1.50 $\pm$ 0.37) with significant differences (P $\leq$ 0.05). Also, there are no significant differences in the second study in which all risk factors have the same average effect in patients suffering from hypertension [( F<sub>calculated</sub> = 0.029, F<sub>tabulated</sub> = 1.68), (P $\leq$ 0.05)]. The female predominantly more than male in age about (41-50), (51-60) years (46,40) (26,30) respectively. The male patients that residence in urban of the province of Al-Najaf possessed large count of hypertension in comparison with female [(male = 12.5 $\pm$ 5.96; 9.25 $\pm$ 3.77, female = 10.00 $\pm$ 3 $\pm$ 3.62; 6.00 $\pm$ 1.54), (P $\leq$ 0.05)], while the patients are suffering from Gout enrolled undercount of hypertension outcome with significant differences [(male = 2.00 $\pm$ 0.47, female = 1.5 $\pm$ 0.36), (P $\leq$ 0.05)]. There is clear effect of uric acid in inducing of hypertension. Uric acid has correlation with other risk factor in individual outpatients that suffering from hypertension. Blood pressure possibly can be higher without increasing of uric acid serum.

**Keywords:** Uric acid, Risk factors, Hypertension, urate, hyperuricemia, Alcohol, Obesity, renal diseases, purine.

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## INTRODUCTION

Hypertension is one of the important public health challenges worldwide because of its high frequency and concomitant risks of cardiovascular and kidney disease[1]. Non pharmacological approaches to the treatment of Hypertension have included a reduction of salt intake and increases in dietary potassium and calcium consumption, weight loss, and increased physical activity. Although the small reductions in blood pressure from these non-pharmacological measures could theoretically have important beneficial public health consequences [2]. Uric acid (UA), the end product of purine metabolism, possesses both antioxidant and pro-oxidant properties, depending on its chemical microenvironment. Hypertension is an increasingly important medical and public health issue worldwide, affecting approximately one billion individuals[3]. As a major risk factor for cardiovascular and renal morbidity and mortality. Hypertension is one of the leading contributors to global disease burden, with its current prevalence in many developing countries, particularly in urban societies already as high as those seen in developed countries[4]. Hyperuricemia predisposes to disease through the formation of urate crystals that cause gout, but it is also associated with hypertension and diabetes, all risk factors for atherosclerosis [5]. It has been identified as a leading risk factor for mortality and ranked third as a cause of disability adjusted life-years[6]. Inefficient urate excretion, which accounts for 90 percent of cases of hyperuricemia, occurs in renal insufficiency of any cause and with certain medications. Despite extensive research into the etiology and contributing causes of essential hypertension, the pathogenesis of the condition is still not explained. An elevation in serum uric acid has been associated with an increased risk for the development of hypertension and 25% to 50% of hypertensive individuals are hyperuricemic [7]. Hyperuricemia also confers increased risk for cardiovascular mortality, especially in women [8]. Despite the clinical and epidemiological evidence, many authorities do not consider an elevated uric acid to be a true cardiovascular risk factor, because patients with hyperuricemia often have other well established risk factors for cardiovascular disease, such as hypertension, renal disease, obesity, dyslipidemia, and insulin resistance [9]. The build-up of serum uric acid in the body can lead to an increase in uric acid crystals in various organs, which can result in gout or the formation of kidney stones[10]. Human studies also show that fructose loading leads to increased serum uric acid levels acutely, and that chronic increased fructose consumption leads to chronically increased serum uric acid and increases in BP[4]. There is evidence of an association between elevated serum uric acid levels, also known as hyperuricaemia, and risk of renal and cardiovascular disease[11]. Alcoholic and high-purine foods consumption, low water consumption and poorly exercising are contributing factors responsible for hyperuricaemia. Its normal level in the body is <7 mg/dl in men and <6 mg/dl in women, based on the limits of solubility of the monosodium urate in serum at a temperature of 36.8 oC [12]. Development of progressive renal damage as a result of any of the two most frequent causes of end-stage renal disease, hypertension and diabetes mellitus, contributes to further increases in uric acid levels and its potential deleterious cardiorenal consequences [13]. Despite extensive research into the etiology and contributing causes of essential hypertension, the pathogenesis of the condition is still not explained. Nonpharmacological approaches to the treatment of hypertension have included a reduction of salt intake and increases in dietary potassium and calcium consumption, weight loss, and increased physical activity. Although the small reductions in blood pressure from the nonpharmacological measures could theoretically have important beneficial public health consequences, it has not been shown that these approaches can serve as primary measures to retard or prevent the onset of hypertension in the general population[2].

The aim of this study assess is the evaluation and the role uric acid and other risk factors and correlation between them in Hypertension.

## MATERIALS AND METHODS

This study was executed on 654 patients and were divided into two groups, the first group included [(302 patients; male 174, female 128) with high uric acid], the 2<sup>nd</sup> group included [(352 patients; 157 male, 195 female) with normal or low uric acid], all of them are suffering from hypertension and control group that they were consist of [ (200 patients; 120 male, 80 female)] during 3 years (from January 1<sup>st</sup> 2013 to August 15<sup>th</sup> 2015). This study included the relation between uric acid and other risk factor (age, weight, obesity, gender, job, and residence) and different diseases.

These data were analyzed statically with SPSS 8.0 statistical package (ANOVA- analysis of variance - two ways analyze; Mean  $\pm$  SE). (P) values less than or equal to 0.05 has been evaluated as statistical significant[14]. The statistical formulations that are used in this study as follow:

[(Mean =  $\sum x_i / n$ , (SD =  $\sqrt{\sum (x_i - \text{mean})^2 / (n-1)}$ , (SE =  $\sqrt{\text{VSD} / n}$ ), ( $F_{\text{calculated}} = \text{ms}(\text{factors}) / \text{ms}(\text{error})$ )]  
( $\sum$ ; summation, n; number of patients, SD = standard deviation, xi = patient, SE= standard error, ms = mean square,)

## RESULTS AND DISCUSSION

The results show in the first group that all risk factors and uric acid possess the same average effect on the gender (male and female) patients in which without significant differences [(  $F_{\text{calculated}} = 0.036$ ,  $F_{\text{tabulated}} = 1.68$ ), (  $P \leq 0.05$ )], in this study we investigate the causes that are leading to hypertension and the relationship extent among factors especially uric acid and other risk factors (gender, age, residence, job, weight, obesity, diabetes mellitus and Gout), and it has agreement with [15] in which confirm that Hyperuricemia is a level of uric acid in the blood that is abnormally high. The number of female of patients of hypertension cases due to uric acid enrolled undercounts in corresponding with male (male =  $21.75 \pm 9.36$ , female =  $16.00 \pm 5.02$ ), ( $P \leq 0.05$ ) and both of them have the high effect in comparison with another risk factors, this study is agreement with previous study of [16] were proved that Men have a greater risk of developing hyperuricemia than women in all age groups, although the sex ratio tends to equalize with advancing age. Also, the male of obesity have highest average effect and by significant differences of hypertensive cases of patients (male =  $14.00 \pm 6.35$ , female =  $9.25 \pm 3.08$ ), these differences between male and female in production and excretion of urate may be due to differences in effectiveness between male and female about this study are due to different pharmacokinetics and pharmacodynamics [17]. The higher average was recorded in the age factor about (31-40), and (41-50) years in male (42),(70) more than female (10),(30) respectively. The other risk factor (Gout) has minimum effect in the patients suffering from hypertension (male =  $2.00 \pm 0.95$ , female =  $1.50 \pm 0.37$ ) and with significant differences ( $P < 0.05$ ) (table 1), and these results explain that the amount of urate in the body is affected by the balance of its production and excretion, also conditions associated with urate overproduction and reduced renal excretion also causes hyperuricemia, the relationship between hypertension and age in this study were in agreement with study trial of [18] which are confirm that there are elderly patients have had more variable results; raising the possibility that uric acid may be more significant to hypertension in the young, also there are a two-phase mechanism for the development of hyperuricemic hypertension. Initially, uric acid induces vasoconstriction by activation of the renin-angiotensin system and reduction of circulating nitric oxide, which can be reversed by lowering uric acid. Over time, uric acid uptake into vascular smooth muscle cells causes cellular proliferation and secondary arteriosclerosis that impairs pressure natriuresis, causing sodium-sensitive hypertension. The correlation between hyperuricemia and diabetes mellitus have been found in this study in (male and female) ( $3.25 \pm 1.47$ ;  $3.00 \pm 1.35$ ) respectively, also effective of obesity and diabetes mellitus on the level elevation of uric acid in blood ( hyperuricemia ) and it is agreement with previous study of [19] which is ensure that excessive intake of sugar, and in particular fructose, may be an important cause of type 2 diabetes. Excessive intake of fructose as more than 50 g/d based on population studies suggesting that obesity rates are greater than 10% when mean intake increases beyond this amount. Fructose intake is associated with the metabolic syndrome, thus supporting this latter condition as a disease entity. Furthermore, fructose appears to cause insulin resistance through classic (adiposity based). Fructose is also highly lipogenic, stimulates triglyceride synthesis, and increases fat deposition in the liver, likely mediated in part by increasing fatty acyl coenzyme A and diacylglycerol and one of the more striking aspects of fructose is its ability to stimulate uric acid production, As ATP is consumed, AMP accumulates and stimulates AMP deaminase, resulting in uric acid production [20]. Serum uric acid can increase rapidly after ingestion of fructose, resulting in increases as high as 2 mg/dl within 1 h , Although initially the rise in uric acid is transient, studies in which high fructose (or sucrose) diets have been administered have found that even fasting uric acid levels will increase after several weeks [21].

**Table (1): numbers of patients suffering from Hypertension via measuring of uric acids (> 7 mg/dl) in male, (> 6 mg/dl) in female.**

Age yrs	Uric acid		Job				Address				Weight (kg.)				Clinical cases								Total	
	No. of outpatients		Employed		Non-employed		Urban		Rural		High		Normal or Low		Obesity		Diabetes mellitus		Renal failure		Gout			
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female		
1-10	4	12	0	0	4	12	2	8	2	4	0	4	4	4	8	0	4	2	2	2	4	0	2	16
11-20	4	12	2	6	2	6	2	6	2	6	0	8	4	4	0	8	0	2	2	0	2	2	2	16
21-30	24	14	8	6	16	8	10	6	14	8	14	8	10	6	14	8	2	2	4	2	4	2	2	38
31-40	42	10	16	6	26	4	32	6	10	4	24	4	18	6	24	4	8	2	6	2	4	2	2	52
41-50	70	30	48	12	22	18	40	20	30	10	48	18	22	12	48	18	10	6	6	4	6	2	2	100
51-60	14	40	4	26	10	14	6	28	8	12	12	24	2	16	12	24	2	10	0	4	0	2	2	54
61-70	12	8	4	2	8	6	6	4	6	4	10	6	2	2	10	6	2	0	0	2	0	0	0	20
71-80	4	2	0	0	4	2	2	2	2	0	4	2	0	0	4	2	0	0	0	0	0	0	0	6
Total	174	128	82	58	92	70	100	80	74	48	112	74	62	54	112	74	26	24	20	18	16	12	12	n = 2
	21.75±9.36tA	16.00±5.02Bb	10.25±6.44F5	7.25±3.41Jl	11.5±3.57Em	8.75±2.17Hl	12.5±5.96Dd	10.00±3.62Gn	9.25±3.77Ho	6.00±1.54Lg	14.00±6.35Cr	9.25±3.08Hi	7.75±3.26Kk	6.75±2.09Mh	14.00±6.35Cr	9.25±3.08Hi	3.25±1.47Of	3.00±1.35Ne	2.50±1.02Rd	2.25±0.66Ob	2.00±0.95Pc	1.50±0.37Sa	1.50±0.37	
	302		302				302				302				302									

- Different capital refer to significant differences between groups horizontally (P<0.05). The values represent Mean±SE

There are no significant differences in the second study in which all risk factors have the same average effect in patients suffering from hypertension [( F<sub>calculated</sub> = 0.029, F<sub>tabulated</sub> = 1.68), (P<0.05)]. The female predominantly more than male in age factor about (41-50), (51-60) years (46),(40) (26),(30) respectively. The male and female of patients that live in urban of Al-Najaf province possessed large count of hypertension in comparison with another factors [(male = 12.12±3.4, female = 17.25±5.66), (P<0.05)], while the patients suffering from Gout enrolled undercount of hypertension outcome with significant differences [(male = 2.00±0.47, female = 1.5±0.36), (P<0.05)] (table 2), In spite of other results that included hypertension cases in individual outpatients without higher average of uric acid may be due to exercise, salts intake, high fatty food, agitation or paroxysmal, anxiety, drug abuse, social problems, elderly, smoking, alcohol, and heredity. The high average of uric acid serum In Gout, renal failure and diabetes mellitus may be occur in development status of diseases, and This study agree with the previous study of[22] in which they proved the possibility of existence of an association between uric acid levels and other risk factors for hypertension.

**Table (2): numbers of patients suffering from Hypertension via measuring of uric acids (< 7mg/dl) in male, (< 6mg/dl) in female.**

Age(yrs)	Uric acid		Job				Address				Weight (kg.)				Clinical cases								Total												
	No. of outpatients														Employed		Non-employed		Urban		Rural			High		Normal or Low		Obesity		Diabetes mellitus		Renal failure		Arthritis	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female													
1-10	5	4	3	2	2	2	4	2	1	2	0	0	5	4	0	0	1	4	3	0	1	0	9												
11-20	13	17	8	6	5	11	6	10	7	7	0	2	13	15	0	2	3	6	7	6	3	3	30												
21-30	18	28	10	11	8	17	10	20	8	8	10	20	8	8	10	20	6	5	1	2	1	1	46												
31-40	22	33	9	13	13	20	12	25	10	8	13	23	9	10	13	23	5	6	2	2	2	2	55												
41-50	26	46	16	26	10	20	14	35	12	11	16	29	10	17	16	29	6	9	3	6	1	2	72												
51-60	30	44	12	30	18	14	18	37	12	7	14	30	16	14	14	30	10	9	3	3	3	2	74												
61-70	35	20	25	8	10	12	28	8	7	12	13	9	22	11	13	9	14	5	4	4	4	2	55												
71-80	8	3	6	2	2	1	5	1	3	2	4	1	4	2	4	1	2	1	1	1	1	0	11												
Total	157	195	89	98	68	97	97	138	60	57	70	114	87	71	70	114	47	45	24	24	16	12	352												
	19.62±1.39 Bf		24.3±5.80At		11.1±2.72Go		12.2±4.2 Eq		8.5±2.19 Kk		12.12±2.64Fn		12.12±3.4 Fp		17.25±5.66Cs		7.5±1.57 Lh		7.12±1.45Mg		8.75±2.57 Jm		14.25±5.08Dr		10.87±2.38Hl		8.87±2.14 Jj		8.75±2.57 Jm		14.25±5.08Dr		10.87±2.38Hl		8.87±2.14 Jj
352			352				352				352				352																				

- Different capital refer to significant differences between groups horizontally (P<0.05). The values represent Mean ± SE

In table (3), the results were shown that there are differences in effects average among many factors (gender, obesity and non-obesity) according to different ages of patients, in which there were found superiority of male have higher average of normal value of uric acid more than female [(15±4.81, 10±3.29),respectively and in obesity group (8.5±2.93, 6.25±2.19), in non-obesity group (6.5±2.13, 3.75±1.64) (P<0.05)], whereas the many people individuals that have uric acid normal value have the same average of effects on the different ages except in (31-40) years and (41-50) years (70),(42), respectively higher average of individual numbers of uric acid normal value recorded and they are followed by [(42,30), in obesity group (22),(20) and non-obesity group (20),(10)], respectively in (male and female) and also, the results were shown superiority of male in comparison with female. [Alcoholic and high-purine foods consumption, low water consumption and poorly exercising are contributing factors responsible for hyperuricemia], also Hyperuricemia predisposes to disease through the formation of urate crystals that cause gout, but it is also associated with hypertension and diabetes, all risk factors for atherosclerosis[5,10].

**Table (3): numbers of patients doesn't suffer from Hypertension with low or normal uric acids (control group).**

Age (yrs.)	Individual No.	Gender		obesity		Non-obesity	
		male	Female	male	female	male	female
1-10	2	2	0	0	0	2	0
11-20	16	8	8	2	4	6	4
21-30	28	22	6	12	4	10	2
31-40	72	42	30	22	20	20	10
41-50	42	24	18	20	12	4	6
51-60	22	12	10	8	6	4	4
61-70	10	6	4	2	2	4	2
Over 71	8	4	4	2	2	2	2
Total	200 25±66.83	120	80	68	50	52	30
		15±4.81 Af	10±3.29 Be	8.5±2.93 Cd	6.25±2.19 Ec	6.5±2.13 Db	3.75±1.64 Fa
		200		118		82	
		200					

- Different capital refer to significant differences between groups horizontally ( $P \leq 0.05$ ). The values represent Mean  $\pm$  SE

### CONCLUSIONS

1. There is clear effect of uric acid in inducing of hypertension.
2. Uric acid has correlation with other risk factor in individual outpatients that suffering from hypertension.
3. Male has affected predominantly more than female in (31- 40), and (41-50) years, and vice versa in (41-50), (51-60) years.
4. Blood pressure possibly can be higher without increasing of uric acid serum.

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