ORIGINAL ARTICLE

The Combined Effect of Hyperuricaemia and Overweight/Obesity on Risk of Hypertension in Adults

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ABSTRACT

Background: *While hyperuricaemia and overweight/obesity can act alone to increase the prevalence of hypertension, few studies have examined their combined effect.*

Methods: *This cross-sectional study of 42 332 Han Chinese from southwestern China investigated the combined effect of hyperuricaemia and overweight/obesity on risk of hypertension in the entire sample as well as in different genders and age groups.*

Results: *Hypertension was significantly more prevalent among individuals with both hyperuricaemia and overweight/obesity (45.5%) than among those with hyperuricaemia alone (28.1%) or overweight/obesity alone (31.3%). Similarly, the increase in hypertension risk in the presence of both hyperuricaemia and overweight/obesity (OR = 6.777, 95%CI 6.133, 7.489) was significantly greater than the increase in the presence of hyperuricaemia alone (OR = 3.168, 95%CI 2.705, 3.711) or overweight/obesity alone (OR = 3.693, 95% CI 3.503, 3.893). These results were similar across each age group. The same trend was also observed when comparing men and women, though the odds ratios were greater for women.*

Conclusion: *Co-occurrence of hyperuricaemia and overweight/obesity increases risk of hypertension more than either morbidity on its own, and this risk differential is significantly greater in women than men. These findings should be confirmed in other ethnic groups and in longitudinal studies.*

Keywords: Hypertension, hyperuricaemia, obesity, overweight, uric acid

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INTRODUCTION

Essential or primary hypertension is estimated to cause more than half of the approximately 17 million deaths from cardiovascular disease that occur annually around the world (1). A systematic review found that in 2008, hypertension was present in approximately 40% of adults over 25 years old all over the world (1). This prevalence is increasing, particularly in developing countries (2).

Effective prevention and control of hypertension depend on understanding its risk factors (3). Uric acid, a metabolic product of purine oxidation in humans, is a risk factor in numerous cardiovascular, metabolic and renal diseases (4), and its association with hypertension has been known for nearly a century (5), with more recent studies clearly establishing a link between the two (6). Obesity is another factor clearly linked to hypertension, and the global epidemic of overweight/obesity due to improvements in living conditions is helping to drive the increasing prevalence of hypertension (7).

Most studies on risk factors for hypertension have separated hyperuricaemia and overweight/obesity when examining their role in hypertension (6, 7). This raises the question of whether and how the two morbidities interact in affecting the risk of hypertension onset, progression to more serious cardiovascular disease and patient prognosis.

SUBJECTS AND METHODS

The study protocol was approved by the Ethics Committee of West China Hospital of Sichuan University, and written informed consent was obtained from all participants.

A consecutive sample of outpatients at the Health Management Center of West China Hospital of Sichuan University was recruited between January and August 2014. To be enrolled in the study, participants had to (a) already be registered in the centre, (b) not have severe kidney disease,

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and (c) have no other diseases which can influence the blood pressure significantly.

Demographic data were collected after conducting a complete physical examination, including gender, age, height, weight, blood pressure (after a 15-minute rest) and history of hypertension, drinking and smoking. Blood samples (12-hour fasting) were collected and analysed for levels of uric acid and creatinine level. Subjects were asked not to smoke or drink for the three days prior to the examination. All data were recorded by two researchers independently, following standardized procedures. In the event of discrepancies between the two data sets, the subject was re-examined and/or the archived blood sample was re-analysed.

A subject was classified as having hypertension if he or she had a systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg during the physical examination (2) or if he or she had previously been diagnosed as hypertensive by healthcare professionals, regardless of whether they were taking antihypertensive medication at the time of the study.

A subject was defined as having hyperuricaemia if he or she had a serum urate level of ≥ 490 mol/L (men) and ≥ 380 mol/L (women). These thresholds are based on diagnostic criteria of the reagents in the Clinical Laboratory of West China Hospital. Overweight/obesity was defined as a body mass index (BMI) ≥ 24 based on the recommendations of the China Obesity Task Force (8).

Data analysis

Data were entered into Microsoft Excel 2007 and analysed using SPSS 17.0 (IBM, Chicago, USA). Hypertension prevalence rates and odds ratios (ORs) quantifying risk of hypertension, together with associated 95% confidence intervals (CIs), were calculated across all subjects and for different age and gender subgroups. Differences in hypertension prevalence were assessed for significance using the Chi-squared test. Using binary logistic regression, ORs were calculated to assess risk in the presence of hyperuricaemia and/or overweight/obesity; these ORs were always calculated with respect to risk in subjects lacking either condition.

RESULTS

During the study period, 43 556 potentially eligible Han Chinese came into the outpatient Health Management Center. After excluding 1224 individuals (2.8%) due to diseases that might affect blood pressure, such as severe kidney disease, we included 42 332 individuals in the study (24 591 men; 17 731 women; age range, 18 to 98 years). Of this total, 23 734 subjects (56%) neither had hyperuricaemia nor were overweight/obese; 17 772 (42%) were overweight/obese, 8651 (20%) had hypertension and 2678 (6%) had hyperuricaemia. Based on data from the entire study population, hypertension was significantly more prevalent among adults with hyperuricaemia (40.2%) than among those without hyperuricaemia (19.1%, $p < 0.001$; Table 1). The same was true of hypertension prevalence among those who were overweight/obese (32.7%) and those who were not (11.5%, $p < 0.001$; Table 2). Similar results were obtained when we performed subgroup analysis based on gender or age (20–39, 40–59 or ≥ 60 years old)

Table 1: Prevalence of hypertension in outpatients from southwestern China, stratified by hyperuricaemia status, age and gender*

Group or subgroup	Age	No hyperuricaemia		Hyperuricaemia	
		Hypertension		Hypertension	
	(year)	n	(%)	n	(%)
All		7575	19.1	1076	40.2
Male	18–39	720	8.4	138	19
	40–59	2539	25.1	351	43.7
	≥ 60	2125	52.1	216	68.1
Female	18–39	103	1.3	9	4.6
	40–59	982	13.8	112	38.5
	≥ 60	1106	52.3	250	72.3

*p in all cases was < 0.001

Table 2: Prevalence of hypertension in outpatients from southwestern China, stratified by body mass index, age and gender*

Group or subgroup	Age	No obesity/overweight		Obesity/overweight	
		Hypertension		Hypertension	
	(year)	n	(%)	n	(%)
All		2831	11.5	5820	32.7
Male	18–39	188	3.9	670	15.3
	40–59	614	14.8	2276	33.6
	≥ 60	895	24.2	1446	63.2
Female	18–39	61	0.9	51	5.6
	40–59	504	9.7	590	26.6
	≥ 60	569	45.4	787	65.3

*p in all cases was < 0.001

We also found that hyperuricaemia was significantly more prevalent among subjects who were overweight/obese (10.5%) than among those who were not (3.3%, $p < 0.001$; Table 3). Similar results were obtained for subgroup analysis

Table 3: Prevalence of hyperuricaemia by body mass index status*

Group or subgroup	Age	No obesity/overweight		Obesity/overweight	
		Hyperuricaemia		Hyperuricaemia	
	(year)	n	(%)	n	(%)
All		816	3.3	1862	10.5
Male	18–39	184	3.8	543	12.4
	40–59	159	3.8	644	9.5
	≥ 60	106	5	211	9.2
Female	18–39	128	1.8	66	7.3
	40–59	119	2.3	172	7.8
	≥ 60	120	9.6	226	18.8

*p in all cases was < 0.001

based on gender or age. In fact, the dual condition of overweight/obesity with hyperuricaemia (69.5%) was significantly more prevalent among all subjects than overweight/obesity alone (40.1%, $p < 0.001$; Table 4). Similar results were obtained for subgroup analysis based on gender or age.

Table 4: Prevalence of overweight/obesity by hyperuricaemia status*

Group or subgroup	Age	No hyperuricaemia		Hyperuricaemia	
		Overweight/ obesity		Overweight/ obesity	
	(year)	n	(%)	n	(%)
All		15910	40.1	1862	69.5
	18–39	3836	45	543	74.7
	40–59	6132	60.5	644	80.2
	≥ 60	2077	50.9	211	66.6
Female	18–39	839	10.9	66	34
	40–59	2047	28.8	172	59.1
	≥ 60	979	46.3	226	65.3

*p in all cases was < 0.001

Finally, we observed that hypertension was significantly more prevalent among adults with both hyperuricaemia and overweight/obesity (45.5%) than among those with hyperuricaemia alone (28.1%, $p < 0.001$) or overweight/obesity alone (31.3 %, $p < 0.001$; Table 5). All these prevalence rates were significantly higher than the rate of hypertension in individuals who neither had hyperuricaemia nor were overweight/obese (11%, $p < 0.001$). Similar results were obtained with subgroups based on gender or age.

To quantify the association of risk of hypertension with hyperuricaemia, overweight/obesity and the two conditions together, we generated a logistic regression model to calculate ORs and 95% CIs. Odds ratios indicating the risk of hypertension in the presence of hyperuricaemia and/or overweight/obesity were calculated with respect to risk in subjects lacking either condition. The risk of hypertension was significantly higher in the presence of both hyperuricaemia and overweight/obesity (OR 6.777, 95%CI 6.133, 7.489) than in the presence of hyperuricaemia alone (OR 3.168, 95%CI 2.705, 3.711) or overweight/obesity alone (OR 3.693, 95%CI 3.503, 3.893; Table 6). These calculations were then repeated for sub-groups based on gender and age. In all cases, OR was greater in the presence of both hyperuricaemia and overweight/ obesity than in the presence of either morbidity alone; ORs in the presence of both or single morbidities were greater for women than men. In nearly all cases, ORs in the presence of overweight/obesity alone or the combination of hyper-uricaemia and overweight/obesity decreased progressively with age. The exception was ORs in the presence of hyperuricaemia, which peaked in the age group 40–59 years for both men and women.

DISCUSSION

In this large cross-sectional study in southwestern China, we found that hyperuricaemia and overweight/obesity, both known to increase risk of hypertension on their own, interact to increase the risk substantially. These findings, which are consistent with a large study in the United States of America (5), argue for the need for more extensive monitoring of

Table 5: Separate and combined effects on the prevalence of hypertension*

Group or subgroup	Age	No hyperuricaemia No obesity/overweight		Hyperuricaemia No obesity/overweight		No hyperuricaemia Obesity/overweight		Hyperuricaemia Obesity/overweight	
		Hypertension		Hypertension		Hypertension		Hypertension	
	(year)	n	(%)	n	(%)	n	(%)	n	(%)
All		2602	11	229	28.1	4973	31.3	847	45.5
Male		1577	17.4	120	26.7	3807	31.6	585	41.8
Female		1025	7.9	109	29.7	1166	30.2	262	56.5
	18–39	233	2	16	5.1	590	12.6	131	21.5
	40–59	1034	11.4	84	30.2	2487	30.4	379	46.4
	≥ 60	1335	42.6	129	57.1	1896	62	337	77.1
Male	18–39	176	3.7	12	6.5	544	14.2	126	23.2
	40–59	569	14.2	45	28.3	1970	32.1	306	47.5
	≥ 60	832	41.5	63	59.4	1293	62.3	153	72.5
Female	18–39	57	0.8	4	3.3	46	5.5	5	7.6
	40–59	465	9.2	39	32.8	517	25.3	73	42.4
	≥ 60	503	44.4	66	55	603	61.6	184	81.4

*p in all cases was < 0.001

Table 6: Separate and combined effects of overweight/obesity and hyperuricaemia on risk of hypertension in outpatients from southwestern China, stratified by age and gender

Group or subgroup	Age	No hyperuricaemia		Hyperuricaemia			Obesity/overweight			Hyperuricaemia		
		No obesity/overweight		No obesity/overweight			No hyperuricaemia			Obesity/overweight		
	(year)	n	OR	n	OR	95% CI	n	OR	95% CI	n	OR	95% CI
All		2602	1	229	3.2	2.705, 3.711	4973	4	3.503, 3.893	847	7	6.133, 7.489
Male		1577	1	120	2.1	1.7, 2.618	3807	3	2.503, 2.855	585	4	3.695, 4.688
Female		1025	1	109	5	3.922, 6.248	1166	5	4.609, 5.559	262	15	12.514, 18.456
	18–39	233	1	16	2.6	1.559, 4.407	590	7	5.993, 8.184	131	13	10.529, 16.772
	40–59	1034	1	84	3.4	2.583, 4.380	2487	3	3.133, 3.677	379	7	5.787, 7.843
	≥ 60	1335	1	129	1.8	1.367, 2.358	1896	2	1.993, 2.442	337	5	3.599, 5.749
Male	18–39	176	1	12	1.8	0.979, 3.278	544	4	3.559, 5.058	126	8	6.044, 9.959
	40–59	569	1	45	2.4	1.667, 3.400	1970	3	2.574, 3.167	306	5	4.569, 6.526
	≥ 60	832	1	63	2.1	1.385, 3.069	1293	2	2.047, 2.632	153	4	2.709, 5.088
Female	18–39	57	1	4	3.8	1.371, 10.738	46	7	4.646, 10.244	5	9	3.777, 25.163
	40–59	465	1	39	4.8	3.251, 7.155	517	3	2.912, 3.837	73	7	5.312, 10.016
	≥ 60	503	1	66	1.5	1.050, 2.238	603	2	1.690, 2.394	184	5	3.853, 7.838

CI: confidence interval; OR: odds ratio

hyperuricaemia in populations known to be at risk of hypertension and for public health interventions that take into account the inordinate threat posed by hyperuricaemia and overweight together.

Our results provide large-scale confirmation that hyperuricaemia is associated with hypertension, which may occur by several mechanisms. One is that hyperuricaemia induces vascular endothelial injury (9) which can reduce blood vessel elasticity and cause hypertension. A second mechanism is that hyperuricaemia can cause glomerular artery damage (10) that renders renal tubules sensitive to salt, leading to sodium and water retention that results in high blood pressure (11). Third, uric acid has been shown to stimulate the renin-angiotensin-aldosterone system directly to increase blood pressure (12). In animals with uric acid-associated hypertension, treating the hyperuricaemia early can bring blood pressure under control (10, 13). In humans with hyperuricaemia-associated hypertension, double-blind experiments show that urate-lowering drugs can lower blood pressure (14, 15).

In overweight and obese individuals, visceral adipose tissue releases free fatty acids into the circulation, which up-regulate hepatic gluconeogenesis; this reduces glucose uptake into peripheral tissues, resulting in hyperinsulinaemia. This leads in turn to salt retention in the kidney, raising blood pressure (16). In addition to hyperinsulinaemia and activation of the renin-angiotensin-aldosterone system in adipose tissue, a recent study suggests that vascular stiffness is also a risk factor in obesity-associated hypertension (17).

The finding in this study that individuals with both hyperuricaemia and overweight/obesity are at significantly higher risk of hypertension than individuals with either morbidity alone brings together several disparate results in the literature. Hyperuricaemia reduces skeletal muscle glucose uptake (18–20) which can cause hyperglycaemia. At the same time, elevated levels of uric acid in fat cells can lead to insulin resistance, leading to hyperglycaemia as well as hyperinsulinaemia due to compensatory production of insulin by the pancreas (21). Simultaneous presence of hyperglycaemia and hyperinsulinaemia, as well as obesity, is a hallmark of metabolic syndrome. Hyperinsulinaemia then increases uric acid reabsorption by renal tubules, leading to hyperuricaemia (22), thereby creating a vicious cycle. Consistent with these results, we found that individuals who were overweight/obese were more likely to be hyperuricaemic than those who were not overweight/obese and *vice versa*. These findings suggest that clinicians, epidemiologists and public health practitioners should be aware of the dangerous interaction between hyperuricaemia and obesity, particularly in vulnerable populations such as those with metabolic syndrome.

In our study population, women were at much higher risk of hypertension than men in the presence of one or both morbidities, particularly women aged 40–59 years. Future research should examine these gender-specific effects, and public health interventions should take them into account.

The main advantages of our study are that it involves a large sample from a medical centre that draws patients from a large geographical area in southwestern China, and it is one of the few studies to focus on the interaction between hyperuricaemia and overweight/obesity in influencing the risk of hypertension. Nevertheless, the study has significant limitations: its cross-sectional design, which prevents assessment of causal relationships, the fact that all data came from a single medical centre and were primarily from Han Chinese, and failure to take into account other factors affecting risk of hypertension, such as smoking history, drinking history, diet, stress at home or on the job and family history of hypertension. Future large studies are needed that take into account as many of these factors as possible in other ethnic populations.

CONCLUSION

While hyperuricaemia and overweight/obesity are independent risk factors for hypertension, they increase risk to a much greater extent when present together. Women are more vulnerable to hypertension than men in the presence of one or both morbidities. These findings, if verified in other ethnic groups, should help guide public health interventions and hypertension treatment programmes to ensure that all relevant risk factors are controlled.

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