

Assessment of Prevalence and Association of Hyperuricemia and Hypertension in Obesity as Potential Screening Tests for Cardiovascular Disease: A Case Control Study

Amruta Bakshi¹, Jayshree Bavikar², Shilpa Asegaonkar³

Associate Professor^{1,2}

Dept of Biochemistry^{1,2,3}, Terna Medical College¹, Nerul,
Navi Mumbai, Govt. Medical College^{2,3}, Aurangabad

Abstract: Assessment of prevalence and association of hyperuricemia and hypertension in obesity as potential screening tests for cardiovascular disease: A case control study. **Introduction:** Obesity is largely emerging as a global epidemic severely affecting Indian subcontinent and its association with cardiovascular disease is well established. Impact of obesity on the development of hypertension and hyperuricemia is beyond doubt, but limited data exist about prevalence and the strength of association of these co morbidities if considered together in obesity. **Materials and Methods:** OPD based case control study including 100 obese cases of and 100 controls evaluated in a stepwise manner. Results were assessed by appropriate statistical software. **Observations & Results:** Significantly high values of BMI (29.5+5.6 vs 22.3+3.9 kg/m²), WHR (0.98+0.07 vs 0.83+0.09), SBP (139.4+25.5 vs 114.4+17.9 mm Hg) and SUA (6.12+1.5 vs 4.3+1.2 mg/dl) in cases compared to controls. Obese hyperuricemics were more aged (45.4+10.7 vs 40.9+9.8yrs), had higher SBP (141.1+22.1 vs 125.5+14.6), DBP (89.2+8.7 vs 83.8+8.1), BMI (28.7+3.9 vs 26.5+5.7) and WHR (1.08+0.23 vs 0.87+0.16) than their obese normouricemic counterparts. Prevalence of Prehypertension, hypertension and central obesity was much higher in hyperuricemic group than normouricemic group. **Conclusion:** This study essentially emphasizes on strong association of hyperuricemia and hypertension in obesity and their better predictive potential for cardiovascular risk compared to their independent value. Urgent need to cautiously observe and monitor the complex association of these co morbidities in obesity and targeted interventions to high risk group is urgently warranted.

Keywords: Obesity, Hypertension, Uric Acid, Cardiovascular Disease

Introduction:

Obesity may be defined as a disease of extensive fat accumulation to the extent that health and wellbeing are affected. Obesity is largely emerging as a global epidemic, severely affecting Indian subcontinent. Obesity has long been recognized to be associated with a variety of adverse health consequences; viz type 2 diabetes mellitus, hypertension, dyslipidemia as well as elevated serum uric acid levels which cluster together to significantly raise the cardiovascular risk.^(1,2)

Obesity is one of the most important risk factors for the development of hypertension. Framingham Heart Study has revealed that, among hypertensives, approximately 78% males & 65% females are obese. The complex pathophysiology of obesity related hypertension is attributed to renin-angiotensin-aldosterone system activation, increased sympathetic nervous system activity, dysregulated adipokines secretion, insulin resistance and endothelial dysfunction which highly aggravate in obesity.⁽³⁾

Over recent years, there has been renewed debate about the nature of association between obesity and raised serum

uric acid (SUA) level with more recent studies clearly establishing a link between the two.^(4,5) In obesity, hyperinsulinemia secondary to insulin resistance may enhance the reabsorption of uric acid leading to hyperuricemia. Hyperuricemia then enhances the cardiovascular risk associated with obesity through diverse mechanisms.⁽⁶⁾

A strong association of uric acid (UA) with the occurrence and development of hypertension is known for quite a long time. Hyperuricemia through several mechanisms like inflammation, endothelial dysfunction⁽⁷⁾ and vascular smooth muscle cell proliferation in the renal microcirculation plays a pathological role in development of hypertension.^(8,6) Apart from strong association of hyperuricemia with hypertension, interestingly, asymptomatic hyperuricemia predicts future development of hypertension, irrespective of any contributing factors.⁽⁴⁾ Attempts to lower UA have subsequently resulted in significant improvement in hypertension with a positive impact on clinical outcomes.⁽³⁾

It is evident from the literature that, most studies have separately considered the association of obesity with

hyperuricemia and hypertension. Conflicting data exist about the association of hyperuricemia and hypertension in obese individuals and its subsequent impact on cardiovascular risk. This raises the question of whether and how the two co morbidities interact in obesity and whether they increase the cardiovascular risk. So this study was aimed at evaluating the prevalence as well as association of hyperuricemia and hypertension in obesity to screen high risk patients for the future development of cardiovascular risk, with a hope that these patients can be targeted for timely interventions and subsequent morbidity and mortality can be largely prevented.

Material And Methods:

Study population: This randomized OPD based case control Study was carried out in department of Biochemistry during period from January to June 2011. Research protocol was approved by institutional ethics committee.

Study comprised of 100 apparently healthy overweight and obese individuals ($BMI > 25 \text{ kg/meter}^2$) as cases and 100 age & sex matched normal weight ($BMI: 18.5 - 24.99 \text{ kg/meter}^2$) healthy controls between age group of 15 to 60 years. Written and informed consent was obtained from all participants. Patients with existing renal disease, cardiovascular disease, taking medications that influence uric acid levels like uricosuric drugs, antihypertensive drugs were excluded from the study.

Study protocol: Study was conducted as per prescribed proforma including history, clinical examination and laboratory investigations. Detailed history mainly consisted of demographic data, personal habits as well as any past history of medical ailments.

Clinical examination consisted of systolic and diastolic blood pressure (mm of Hg), weight (Kg), Height (meters), Body Mass Index (BMI), Waist circumference (WC), Hip circumference (HC), and Waist/Hip ratio (WHR). Body weight was taken on a calibrated scale to the nearest 0.1 kg. Height was taken with a wall-mounted stadiometer to the nearest 0.5 cm. Body mass index (BMI) was calculated as body weight (kg) to the squared height (m^2). Waist circumference (WC) was measured at the mean point between the lowest rib margin and iliac crest with the participant standing and at the maximum point of normal expiration. Hip circumference was measured at the level of greatest protuberance of buttocks without compression of skin. Blood pressure was taken in sitting position after resting the participant for 5 minutes. 3 readings were taken 5 minutes apart and average was recorded. Normal Blood pressure was interpreted at $SBP < 120$ and $DBP < 80$ mm of Hg. Prehypertension was defined as SBP of 120 to 139

and/or DBP of 80 to 89 mm of Hg. Hypertension was defined as $SBP > 140$ and/or $DBP > 90$ mm of Hg.⁽⁹⁾ Central obesity was defined as WC > 40 inches for men & > 35 inches for women. WHR of > 0.9 for men and > 0.85 for women was considered as abnormal.⁽¹⁰⁾

Blood samples were collected from all participants under strict aseptic precautions in plane vacutainers for uric acid estimation. Serum was separated after 1 hour by centrifugation at 3000 rpm for 10 minutes. Serum uric acid was estimated by Uricase end point method using kits from TECO diagnostics, USA

Statistical analysis: The results were analyzed using windows SPSS programme (version 10.0). The results were interpreted as mean + S.D. for quantitative parameters and as number / percentage for qualitative data. $P < 0.05$ was considered statistically significant. Correlation coefficients (r value) were calculated between uric acid, SBP, DBP and anthropometric measures to find out the strength of association.

Results:

100 cases of overweight and obese individuals & 100 age and sex matched healthy controls were enrolled for the study. Finding in case and control group are shown in tabular form along with their statistical significance, comparison of characteristics in cases in accordance with uric acid levels as well as correlation coefficients of uric acid with studied parameters.

From table 1, It can be observed that, mean values of age and DBP in cases were higher in cases than controls but the difference was statistically not significant. While the values of SBP, WHR, BMI & SUA were found to be higher in cases than controls and the difference was statistically significant.

From table 2, which recategorises the cases depending on uric acid levels, it can be observed that, the cases with $UA > 7 \text{ mg/dl}$ were comparatively aged, with high SBP, DBP, WHR & BMI than those with $UA < 7 \text{ mg/dl}$ and the difference is statistically significant.

From table 3, it's observed that, the prevalence of hyperuricemia, prehypertension, hypertension & raised WHR was higher in cases as compared to controls.

Table 4 shows that, the number/ percentage of Prehypertension, hypertension as well as raised WHR was significantly higher in obese hyperuricemic group as compared to obese normouricemic group.

From table 5, it can be observed that; Uric acid shows

positive correlation with age, SBP, DBP, BMI and WHR. SUA shows strongest positive correlation with SBP and WHR.

Table No.1: Demographic and clinical characteristics in studied groups

Quantitative data (Mean + SD) and qualitative data (number/percentage)

Sr. no.	Parameter	Cases (100)	Controls (100)	P value
1	Age (Years)	41.6 + 6.7	40.1 + 3.2	0.15
2	Sex (Male/ Females)	53/47	59/41	NA
3	Body mass index (BMI)	29.5 + 5.6	22.3 + 3.9	<0.05 *
4	Waist hip ratio (WHR)	0.98 + 0.07	0.83+ 0.09	< 0.01 **
5	SBP (mm of Hg)	139.4 + 25.5	114.4 + 17.9	< 0.05 *
6	DBP (mm of Hg)	88.9 + 9.8	79.0 + 6.7	P = 0.08
7	Sr. uric acid (mg / dl)	6.12 + 1.5	4.3 + 1.2	<0.05 *

* : significant P value, ** : Highly significant P value

Table No. 2: Demographic and clinical parameters in cases according to uric

Sr. no.	Parameter	Overall N = 100	Uric acid (>7 mg/dl) N= 49	Uric acid (<7 mg/dl) N = 51	P Value
1	Sr. Uric acid	6.12 + 1.5	7.7 + 1.9	4.1 + 1.6	<0.01 **
2	Age	41.6 + 6.7	45.4 + 10.7	40.9 + 9.8	<0.05*
3	Sex (M / F)	53/47	28/21	25/26	NA
4	SBP	139.4 + 25.5	141.1+ 22.1	125.5 + 14.6	P< 0.05*
5	DBP	88.9 + 9.8	89.2 + 8.7	83.8 + 8.1	P< 0.05*
6	WHR	0.98 + 0.07	1.08 + 0.23	0.87 + 0.16	<0.01 **
7	BMI	29.5 + 5.6	28.7 + 3.9	26.5 + 5.7	<0.05 *

Table No. 3: Hyperuricemia, Prehypertension, hypertension & raised WHR in

Parameter	Cases (n=100)	Controls (n=100)
Hyperuricemia (SUA> 7mg/dl)	49	12
Prehypertension: (mm of Hg) (SBP:120-139 &/or DBP: 80-89)	41	06
Hypertension: (mm of Hg) (SBP > 140 &/or DBP > 90)	34	08
Raised WHR (>0.9: men & >0.85: women)	68	11

Discussion:

Obesity, with increasing worldwide prevalence in the population, not only causes severe harm to individual health but also imposes a considerable burden on healthcare system. A strong association between obesity and cardiovascular disease through a highly complex interaction of various clinico-metabolic derangements has to be addressed on a high priority.

Table No. 4: Prevalence of Prehypertension, hypertension & raised WHR

Parameter	Cases (n= 100)	Uric acid (>7 mg/dl) N= 49	Uric acid (<7 mg/dl) N = 51
Prehypertension: (mm of Hg) (SBP: 120-139 &/or DBP: 80-89)	41	24 (48.9%)	17 (33.3%)
Hypertension: (mm of Hg) (SBP > 140 &/or DBP > 90)	34	21 (42.9%)	13 (25.5%)
Raised WHR (>0.9: men & >0.85: women)	68	42 (85.7%)	26 (50.9%)

Table No.5: Correlation coefficients of demographic and clinical parameters

Sr. no.	Parameter	R value
1	Age	+ 0.34
2	Body mass index (BMI)	+ 0.47
3	Waist hip ratio (WHR)	+ 0.54
4	SBP	+ 0.59
5	DBP	+ 0.41

In our study we observed high BMI, SBP and SUA levels in cases compared to controls and the difference was significant. Raised WHR was highly significant in cases compared to controls. Prevalence of hyperuricemia, Prehypertension and hypertension was higher in cases than controls. Rise in SUA with age is observed in previous studies and is mainly attributed to age related changes in renal function which adversely affect renal clearance of uric acid. In agreement with previous studies, positive association of SUA with BMI and in particular WHR may be because of a state of chronic low grade inflammation, hyperinsulinemia and subsequent reduction in renal excretion of uric acid associated with adiposity.^[11] Hyperinsulinemia in particular is associated with abdominal adiposity as evident from raised WHR and this is in turn strongly linked to SUA and Hypertension event with normal BMI.⁽⁶⁾

When Obese individuals were further divided based on UA values, hyperuricemic individuals were comparatively more aged and had higher SBP, DBP, BMI and WHR than their obese normouricemic counterparts. The difference of age and DBP also became more significant in hyperuricemic groups. Prevalence of Prehypertension, hypertension and central obesity was much higher in hyperuricemic group as compared to normouricemic group. The underlying mechanisms to justify our findings are discussed hereunder.

According to some studies, significant positive association

of hypertension with hyperuricemia in partially mediated through obesity and share common underlying mechanisms.⁽¹⁾ Studies have shown that, obese hypertensive patients had higher SUA levels when compared with obese nonhypertensive patients. Obesity related hypertension is often accompanied by hyperinsulinemia, insulin resistance and hyperuricemia.⁽³⁾ It is absolutely necessary to study the individual risk factors as well as the possible existence of interaction between them in obesity to screen high risk cases for CVD.⁽⁹⁾

Thus it may be wisely said that, obese individuals with hyperuricemia are at significantly higher risk of hypertension than their normouricemic counterparts. Extensive monitoring of obese individuals for presence hyperuricemia and hypertension together may definitely throw a light on inordinate cardiovascular disease threat posed by hyperuricemia and obesity together than these morbidities being considered alone. Adding more depth to this study, by including the role of inflammatory mediators, metabolic derangements, renal functions, the interplay of oxidants and antioxidant as well as genetic influences will thoroughly explore the complex interplay of diverse mechanisms operational in obesity with a genuine potential to predict associated cardiovascular risk.

Although Cross sectional design and a relatively small sample size of this study carries some limitations to conclude about the precise causality, this study definitely has some strength. The presence of hyperuricemia and hypertension together in obesity should trigger a high level of clinical suspicion and these high risk individuals should be considered for aggressive interventions. These findings, if assessed and verified on a large scale, should help guide public health interventions to ensure that all relevant risk factors are effectively controlled.

Conclusion: The present study essentially highlights the association of hyperuricemia and hypertension in obesity and their better potential to be used as predictors of cardiovascular risk than being considered as independent entity. Urgent need to cautiously observe and monitor the complex association of these co morbidities in obesity and targeted interventions to high risk group may offer a hope that subsequent morbidity and mortality can be largely prevented.

Acknowledgement : Study Participants

References:

1. Omar K. A., Asad A. O., Huda M., Faisal A. Q. Obesity and Serum Uric Acid. Bahrain Medical

Bulletin. 2007; 29(3).

2. Tang L, Kubota M, Nagai A, Mamemoto K, Tokuda M. Hyperuricemia in obese children and adolescents: the relationship with metabolic syndrome. *Pediatr Rep.* 2010;2(1):e12.
3. Zhang J, Zhang Y, Deng W, Chen B. Elevated serum uric acid is associated with angiotensinogen in obese patients with untreated hypertension. *J Clin Hypertens (Greenwich).* 2014;16(8):569-74.
4. Waring W.S., D.J. Web, S.R.J. Maxwell. Uric Acid As a Risk Factor for cardiovascular disease. *Q. J. Med.* 2000; 93: 707-13.
5. W Qin, L Li, Q Wu, Y Wang. The Combined Effect of Hyperuricaemia and Overweight/Obesity on Risk of Hypertension in Adults. *West Indian Med J.* 2016; 3 (1)
6. Zhang W, Sun K, Yang Y, Zhang H, Hu FB, Hui R. Plasma uric acid and hypertension in a Chinese community: prospective study and metaanalysis. *Clin Chem.* 2009;55(11):2026-34.
7. N. S. Neki, Tamilmani A Study of Serum Uric Acid level in Essential Hypertension *JIMSA Jan. - Mar.* 2015 Vol. 28 No. 1
8. Yoo TW, Sung KC, Shin HS, et al. Relationship between serum uric acid concentration and insulin resistance and metabolic syndrome. *Circ J.* 2005; 69(8):928-33.
9. Nguedia Assob JC, Ngowe MN, Nsagha DS, Njunda AL, Waidim Y, et al. The Relationship between Uric Acid and Hypertension in Adults in Fako Division, SW Region Cameroon. *J Nutr Food Sci.* 2014;4:257.
10. Srikanthan K, Feyh A, Visweshwar H, Shapiro JI, Sodhi K. Systematic Review of Metabolic Syndrome Biomarkers: A Panel for Early Detection, Management, and Risk Stratification in the West Virginian Population. *Int J Med Sci.* 2016;13(1):25-38.
11. Tomader T.A. R. Prevalence of Hyperuricemia among Hospitalized Elderly Patients and Its Association with Metabolic Syndrome. *Advances in Aging Research.* 2014;3:329-37.

Corresponding Author:

Dr. Amruta Bakshi,

Associate Professor,

Dept of Biochemistry,

Terna Medical College, Nerul, Navi Mumbai.

Email: dramrutabakshi@rediffmail.com