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Association and Sensitivity of Serum Uric Acid Levels with Certain Anthropometric Parameters in Overweight and Obese Subjects

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ABSTRACT

Introduction: Metabolic syndrome is a significant medical morbidity progressing to cardiovascular complications both in developing and developed world. Uric acid is produced during metabolism of nucleotide and adenosine triphosphate (ATP) and contains the final product of human purine metabolism. It acts both as an antioxidant and pro-inflammatory marker and has positive association with visceral fat in overweight subjects.
Methodology: The study included 124 urban obese and overweight Indian subjects above 18 years of age from general population of city of north India, who were free of any known underlying disease. Uric acid concentrations were measured by the uricase method. Anthropometric measurements and information on lifestyle factors and disease history were collected by in-person meeting.
Results: Body mass index (BMI), waist-to-hip ratio (WHR), weight and sagittal abdominal diameter (SAD) were positively correlated with the serum uric acid level and result was highly significant.
Conclusion: In present study, we found that serum uric acid level increases as body fat content increases. Statistical data shows remarkable results for significant correlation of uric acid level with BMI, WHR and SAD. Hypertrophy occurs as a result of Inflammatory processes and oxidative stress when the supply of energy starts to exceed the storage capacity of adipocytes, as a result adipokines such as interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor-necrosis factor alpha (TNF-α) are released more frequently which lead to low-grade chronic inflammation, that starts in adipose tissue and finally reaches the circulation and other organs. Antioxidants system including enzymes like superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase and non enzymatic substrates like as ferritin, transferrin, bilirubin, ceruloplasmin, carrier of albumin low molecular weight, like uric acid and lipoic acid controls oxidative stress. This shows uric acid levels are much lean towards visceral obesity than overall body fat content. Earlier studies also shows visceral adiposity is key factor for increasing oxidative stress and uric acid level.

Keywords: Uric acid, Hyperuricemia, obesity, overweight, metabolic syndrome, inflammatory markers

INTRODUCTION

Metabolic syndrome is a significant medical morbidity progressing to cardiovascular complications both in developing and developed world. Risk factors affecting the cardiovascular system like hypertension, insulin resistance, central obesity, and atherogenic dyslipidemia (high LDL-cholesterol, high triglycerides, and low HDL-cholesterol) have a role in metabolic syndrome (MetS), which is also known as syndrome X or insulin resistance syndrome [1]

Hypertrophy occurs as a result of inflammatory processes and oxidative stress when the supply of energy starts to exceed the storage capacity of adipocytes. [2] As a result adipokines such as interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor-necrosis factor alpha (TNF-α) are released in excess which lead to low-grade chronic inflammation, that starts in adipose tissue and finally reaches the circulation and other organs [3,4]

Increased fat mass leads to decreased supply of oxygen eventually leading to tissue necrosis. Phagocytosis takes place which removes these dead cells and causes infiltration of inflammatory mediators and release of reactive oxygen species like nitric oxide and hydrogen peroxide causing oxidative stress. [5,6] This causes a negative effect on MetS. [7]

Uric acid on the basis of various mechanisms related to chronic inflammation, was known as an inert metabolic end-product of purine metabolism, it is involved in pathogenesis of chronic diseases, like hypertension, metabolic syndrome, diabetes, non-alcoholic fatty liver disease, and chronic kidney disease. Many experimental and clinical studies have been done to support the role of uric acid as a causal factor contributing in these conditions. [8]

Uric acid works as an antioxidant proving the fact that it improves endothelial function [9]. But it is expected that uric acid is an antioxidant in the extracellular environment. Although there are many studies suggesting that in the intracellular environment it is a pro oxidant [10,11] in the process of inactivating peroxynitrite uric acid liberates two urate based radicals [12,13] therefore without any radical generation uric acid shows its effects.

Due to an imbalance between synthesis and degradation of reactive oxygen species (ROS) there occurs oxidative stress .In the process of oxidation of fatty acid or glucose for ATP or heat production in the mitochondria there is generation of ROS which is essential for normal transduction of signal in cells [14]. Although if the production occurs in excess it leads to oxidative stress, when there is increased supply of fatty acid and glucose to mitochondria as in case of obesity which is associated with hyperlipidemia and hyperglycemia. It causes oxidative stress. Induction of oxidative stress occurs by fatty acids like oleic acid [15-17], and glucose [18–19]. ROS is also generated by hypoxia [20]. In hyperglycemia, oxidants like advanced glycation end products (AGE) or lipoxidation end products are in vivo [21].

Presence of chronic and low grade inflammation in obesity is also seen in many chronic illnesses like type 2 diabetes, hypertension, atherosclerosis, fatty liver, cancer, asthma, and sleep apnea. As Inflammation is a physiological process in which there is increased number of white blood cells or the levels of pro-inflammatory cytokines are in high number in the circulation or tissue. Generally, inflammation is important for organ remodelling, tissue repairing, wound healing and immunity against various infections. Therefore it is a type of defence protective reaction in the body which controls the harmful insults and helps in starting the healing process. Exaggerated inflammatory response can cause various side effects like tissue injury and organ dysfunction. In Obesity there is inflammation which begins in adipose tissue and liver along with infiltration of macrophages and increased expression of pro-inflammatory cytokines. There occurs systemic inflammation when these pro-inflammatory cytokines enter the blood stream. So there are both beneficial and detrimental effects of inflammation in obesity [22].

MATERIAL & METHODS

The study was conducted in department of physiology, King Georges Medical University, Lucknow over a period one year, after getting approval institutional ethics committee, Research Cell, KGMU, Lucknow. All subjects are included from North Indian general population who are

obese or overweight. They are not on any regular medication and are not suffering from any underlying disease. Detailed history of diet, occupation, family and lifestyle was taken. Standard protocols were followed for measuring anthropometric parameters. Patients suffering from type 1 diabetes, any known endocrinal, renal or nutritional disorder, any known anatomical deformity which can interfere with anthropometric data, pregnancy, known subjects with gout were excluded from study. Jelliffe technique was used for weight and height measurement. BMI was calculated by using formula weight in kilograms divided by square of height in meters widest. Hip circumference was measured at the widest circumference over great trochanter. According to WHO's recommendation, waist circumference was measured with inelastic and flexible measuring tape with the subject in standing position. Sagittal abdominal diameter was measured midway between lowest rib and iliac crest in supine position with bent knees. Skin fold thickness was measured using Harpenden skinfold calliper. [23,25] Neck circumference was measured just below the laryngeal prominence [24]. Waist hip ratio and waist to height ratio was also calculated. Enzymatic colorimetric method is used for estimation of uric acid. [26]

RESULT

All participants of the study subjects who are obese and overweight. Pearson correlation was done by using Microsoft excel for statistical analysis. Body mass index (BMI), waist-to-hip ratio (WHR), waist to height ratio (WHtR), waist circumference (WC), neck circumference (NC), weight , age, sagittal abdominal diameter (SAD), skin fold thickness (SFT) were positively correlated with the serum uric acid level. Correlation of weight, BMI, SAD, WHR was statistically significant with P value < 0.05. Physical activity, height and hip circumference were inversely correlated with serum uric acid levels. (Table 1 and Figure 1)

Table 1. Pearson's Correlation between Serum Uric Acid with other parameters

Parameter	R- Value	p- Value
S. Uric Acid vs Age	0.068	0.46
S. Uric Acid vs Height	-0.029	0.75
S. Uric Acid vs Weight	0.308	0.0005
S. Uric Acid vs BMI	0.39	0.00005
S. Uric Acid vs N.C	0.059	0.510
S. Uric Acid vs W.C.	0.099	0.28
S. Uric Acid vs H.C.	-0.07	0.44
S. Uric Acid vs SAD	0.275	0.002
S. Uric Acid vs SFT	0.085	0.3460
S. Uric Acid vs WHR	0.332	0.00016
S. Uric Acid vs WHtR	0.1117	0.2166

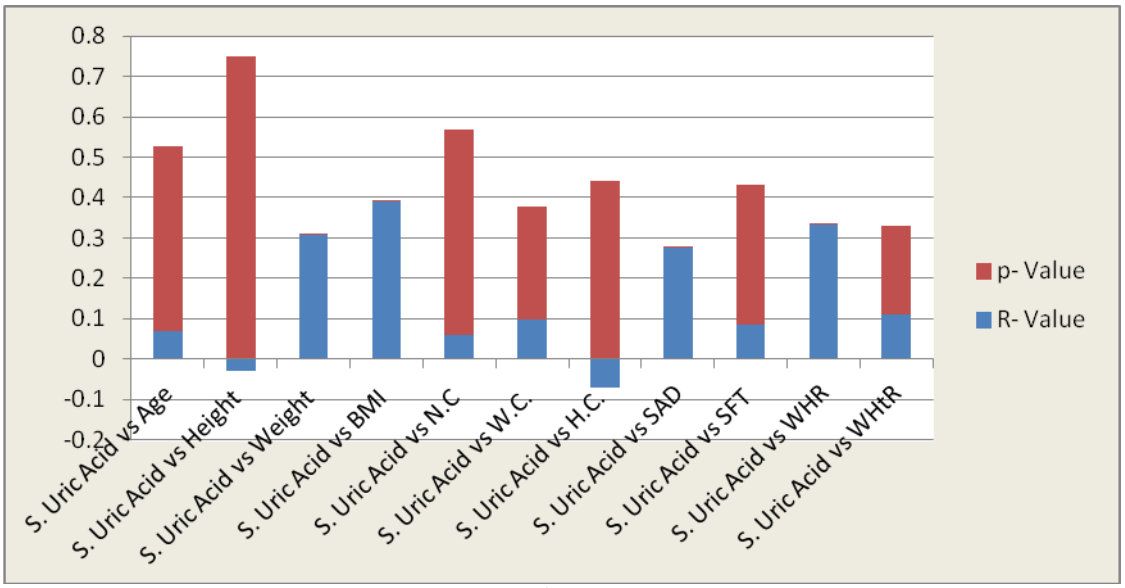

Figure 1. Graph Showing Mean Values of Anthropometric & Biochemical Parameters

DISCUSSION

In present study, we found that serum uric acid level increases as body fat content increases. Statistical data shows remarkable results for significant correlation of uric acid level with BMI, WHR and SAD.

The present study demonstrated that that obesity is an important risk factor of hyperuricemia among North Indian population, and found the increase of visceral adiposity was positively associated with hyperuricemia risk. Compared to other types of obesity, visceral adiposity had a better discriminatory ability in identifying the risk of hyperuricemia by using parameters like BMI, waist to hip ratio, sagittal abdominal diameter. Additionally, our findings highlight that greater visceral adiposity was significantly and independently associated with hyperuricemia in our subjects. It is not possible in routine clinics to measure all anthropometric parameters because it is very time taking procedure. So, we focus only on those anthropometric parameters like SAD, WHR and BMI to check for hyperuricemia.

The oxidative stress is related with aconitase inhibition in the Krebs cycle that prompts citrate collection and the induction of ATP citrate lyase bringing about raised fat synthesis, just as a hindrance of enoyl CoA hydratase results in disturbed beta fatty acid oxidation that is additionally potentiated by the hindrance of AMPK-initiated protein kinase [27,28,29].

The role of SUA on a cellular level is not quite clear. Mouse models have shown that adipose tissues can produce and secrete uric acid and secretion is enhanced in obesity [30]. Uric acid is also involved in the production of key pro-inflammatory adipokines in adipose tissues [31]. Especially VAT secretes pro-inflammatory adipocytokines and cytokine-like factors such as tumor necrosis factor α and interleukin-6, thereby contributing to chronic low-grade inflammation. This might be mainly due to accelerated hypertrophic lipogenesis without appropriate angiogenesis, thus resulting in hypoxia, apoptotic and necrotic adipocytes, inflammation and an overbalance of unfavorably polarized M1-macrophages [32]. Several pathways potentially link hyperuricemia to hepatic lipogenesis: First, increased intra-cellular uric acid levels affect hepatocyte mitochondrial function. Thus, they promote an increased accumulation of reactive oxygen species and induce stress on the endoplasmatic reticulum which results in lipogenesis [33,34]. Second, increased uric acid levels upregulate fructokinase, an enzyme responsible for dietary fructose metabolism. Overexpression of fructokinase modulates the lipogenic effects of fructose by inducing increased triglyceride accumulation in hepatocytes [35]. Third, uric acid leads to downregulation of adenosine monophosphate activated kinase (AMPK). Lower expression of AMPK leads to reduced lipolysis, i.e. lower depletion of hepatocytes, lower fat oxidation and higher lipogenesis [36]. However, the directionality of this effect is not straightforward, as fatty liver has also been found to be a predictor of incident hyperuricemia. [37,38]

CONCLUSION

In present study, we found that serum uric acid level increases as body fat content increases. Statistical data shows remarkable results for significant correlation of uric acid level with BMI, WHR and SAD. Hypertrophy occurs as a result of Inflammatory processes and oxidative stress when the supply of energy starts to exceed the storage capacity of adipocytes, as a result adipokines such as interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor-necrosis factor alpha (TNF-α) are released more frequently which lead to low-grade chronic inflammation, that starts in adipose tissue and finally reaches the circulation and other organs. Antioxidants system including enzymes like superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase and non enzymatic substrates like

as ferritin, transferrin, bilirubin, ceruloplasmin, carrier of albumin low molecular weight, like uric acid and lipoic acid controls oxidative stress. This shows uric acid levels lean more towards visceral obesity than overall body fat content. Earlier studies also shows visceral adiposity is key factor for increasing oxidative stress and uric acid level.

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