A CORRELATIVE STUDY SHOWING THE RELATIONSHIP OF SALIVARY URIC ACID LEVEL WITH THE METABOLIC SYNDROME COMPONENTS & ITS SEVERITY

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ABSTRACT

Introduction: Uric acid, the metabolic product of Purine nucleotide, increased in the metabolic syndrome condition which is a major risk factor for cardiovascular disease and diabetes. The metabolic syndrome comprises components of some complex interrelated factors such as dysglycemia, raised blood pressure, elevated triglyceride levels, low – high density lipoprotein cholesterol levels, and obesity. As uric acid level in serum & saliva increases in metabolic syndrome, testing of salivary uric acid may be a useful noninvasive approach for monitoring cardio metabolic risk.

Objective: To find out the correlation, if any, between salivary uric acid and the components of metabolic syndrome and its severity.

Materials and methods: Among the patients came to hospital for metabolic syndrome clinic, the volunteers without any known condition that affect salivation were recruited as subjects (195) for the study. The subjects were divided into three groups based on the number of components of the metabolic syndrome as group I (having 3components), group II (having more than 3 components) and group III (having 1 or 2 components) and their height, weight, blood pressure, waist circumference, was measured and blood test with lipid profile and fasting blood glucose were obtained. Saliva samples were collected and salivary uric acid levels were determined in all the subjects.

Result & Discussion: Salivary uric acid was significantly elevated in subjects with more number of metabolic abnormalities (Group II), $p = < 0.0001$. Significant correlations were seen when comparing the Salivary uric acid level with either of the WC ($r = 0.343$, $p = <0.0001$), systolic BP ($r = 0.272$, $p = < 0.0001$), diastolic BP ($r = 0.362$, $p = <0.0001$), FBG ($r = 0.224$, $p = 0.0016$), Total Cholesterol ($r = 0.145$, $p = 0.042$), Triglycerides ($r = 0.276$, $p = <0.0001$), HDL – C ($r = -0.407$, $p = <0.0001$), LDL – C ($r = 0.173$, $p = 0.0156$) levels.

Conclusion: Salivary uric acid can be used as a non – invasive biomarker for monitoring the metabolic syndrome.

Key words: Salivary uric acid, biomarker, metabolic syndrome.

INTRODUCTION

Uric acid is a final enzymatic product from purine degradation, contributes to the antioxidant capacity of both blood and saliva. However, the enzyme responsible for its production also generates free radicals, hence several studies indicted uric acid as pro – inflammatory and pro – oxidant agent (Maria Soukup et al 2012). There is a growing body of evidence to show that hyperuricemia or elevated serum uric acid levels, even within the normal range, are associated with metabolic syndrome and its components (Yongfeng Tian et al 2015, Chen Li Ying et al 2007).

The metabolic syndrome include the complex interrelated factors such as dysglycemia, raised blood pressure, elevated triglyceride levels, low – high density lipoprotein cholesterol levels, and obesity (K.G.M.M. Alberti et al 2009). The factors of metabolic syndrome (MS) form the major risk factors for cardiovascular disease (CVD) and diabetes. It has been widely demonstrated that metabolic syndrome is associated with 2 to 3 fold increase in CVD risk and nearly 7 fold for incidence of type 2 diabetes mellitus (DM). Metabolic syndrome and hyperuricemia are important risk factors for cardiovascular disease (Wen-Ko Chion et al 2010, A.N. Al – Isa et al 2013) and the cardiovascular disease is the leading cause of death and disability worldwide (Falcone C et al 2014).

As uric acid level in serum & saliva increases in metabolic syndrome, the testing of salivary uric acid level may be a useful noninvasive approach for monitoring cardio metabolic risk. Regardless of whether it plays a causative role or not, it is an indicator of metabolic disturbances, and hence uric acid level in saliva may be a useful biomarker for identifying high risk patients and monitoring the response to lifestyle interventions (Maria Soukup et al 2012).

OBJECTIVE
To find out the correlation, if any, between the salivary uric acid level and the various components and severity of metabolic syndrome.

MATERIALS AND METHODS
The study was carried out on 195 volunteers who were come to hospital and were diagnosed metabolic syndrome patients and treated were recruited for the present study. The diagnostic criteria for metabolic syndrome were according to National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria (≥3 of 5 risk factors). The patients included in this study were divided into three groups on the basis of metabolic syndrome criteria, each comprising of 65 subjects.
Group I: Subjects with any three components of metabolic syndrome (normal MS group)
Group II: Subjects with more than three components of metabolic syndrome (severe MS group)
Group III: Subjects with less than three components of metabolic syndrome (control group)
Exclusion criteria: Subjects with conditions known to affect salivation, uric acid, or inflammatory biomarkers including gout, renal insufficiency, autoimmune disease, active infection, pregnancy were excluded (Maria Soukup et al 2012).

The study was carried out in the department of Physiology, A C S Medical College and Hospital, Chennai. The participants were from A C S Medical College and Hospital, Saveetha Medical College and Hospital, Chennai. The study commenced after getting the approval from the Institutional Human Ethical Committee (IHEC), Saveetha University, Chennai. Age & sex matched subjects were recruited for the study. The data were collected from the participants after giving detailed explanation about the procedure and their cooperation and willingness was obtained with written informed consent. A detailed clinical history and information regarding oral health status of all the subjects were taken. Relevant past history, family history, any drug history, personal history like smoking, alcoholism etc were taken.
The following parameters were studied using the method as mentioned.

 - ➢ Waist circumference (WC) -- was measured at the end of normal expiration, between the lower rib margin and the iliac crest.
 - ➢ Systolic and Diastolic Blood Pressure was recorded by Sphygmomanometer.
 - ➢ The blood samples were collected from all the subjects after overnight fast to study -- Fasting Blood Glucose(FBS), Total Cholesterol(TC), Triglycerides(TG), High Density Lipoprotein – cholesterol (HDL - C), Low Density Lipoprotein – cholesterol (LDL - C).
 - ➢ Saliva samples to study uric acid level were collected from all the subjects in fasting conditions during morning in a sterile container for the measurement of salivary uric acid. Measurement of salivary uric acid was done with semi automated biochemical analyzer by enzymatic colorimetric method.

STATISTICAL ANALYSIS
Statistical analyses were performed using SAS 9.2 version. All the variables of Table 1 were analyzed between the groups with ANOVA. Correlations were investigated by calculating Pearson's correlation coefficient for all the subjects. It was used to investigate correlations between salivary uric acid and the components of metabolic syndrome. Statistical significance was considered if the p – value is less than 0.05.

RESULTS

The results of the present study (Table 1, Figure 1) showed the following data. The mean age of the study group was 49.32 ± 8.462 which showed no significant difference among the study groups. It showed that Salivary uric acid levels were significantly elevated in subjects with more number of metabolic abnormalities (Group II), $p = < 0.0001$. Significant positive correlations were seen when the Salivary uric acid is compared with WC ($r = 0.343$, $p = <0.0001$), systolic BP ($r = 0.272$, $p = < 0.0001$), diastolic BP ($r = 0.362$, $p = <0.0001$), FBG ($r = 0.224$, $p = 0.0016$), Total Cholesterol ($r = 0.145$, $p = 0.042$), Triglycerides ($r = 0.276$, $p = <0.0001$), LDL – C ($r = 0.173$, $p = 0.0156$) whereas the Salivary uric acid levels were negatively correlated with HDL ($r = -0.407$, $p = <0.0001$) levels.

Table 1: Comparison of different components of metabolic syndrome in study groups
(Values expressed as mean ± SD)

Variable	Total (195)	Group I (65)	Group II (65)	Group III (65)	P - value
Age	49.32 ± 8.462	49.72 ± 8.06	49.92 ± 7.39	48.30 ± 9.77	0.496 NS
Waist circumference (WC)	96.87 ± 9.821	97.44 ± 8.76	102.36 ± 9.06	90.8 ± 8.05	<0.0001***
Systolic BP (mmHg)	134.86 ± 10.34	136.2 ± 7.41	138.76 ± 9.78	129.6 ± 11.30	<0.0001***
Diastolic BP (mmHg)	83.99 ± 7.329	83.87 ± 6.93	88.09 ± 6.35	80.01 ± 6.41	<0.001**
Fasting Blood Glucose (mg/dl)	133.67 ± 32.731	136.89 ± 37.68	141.10 ± 26.66	123.01 ± 30.57	<0.0039**
Total Cholesterol (mg/dl)	158.96 ± 24.787	161.84 ± 21.19	164.26 ± 27.12	150.77 ± 23.9	<0.0038**
Triglycerides(mg/dl)	151.05 ± 40.718	145.95 ± 36.62	174.35 ± 48.34	132.85 ± 20.79	<0.0001***
HDL – C (mg/dl)	46.03 ± 5.892	47.44 ± 5.04	41.59 ± 5.61	49.06 ± 4.12	<0.0001***
LDL – C (mg/dl)	77.48 ± 20.679	78.30 ± 16.76	79.73 ± 22.11	74.40 ± 22.59	0.3151 NS
Salivary uric acid (mg/dl)	3.91 ± 1.203	3.59 ± 0.86	5.04 ± 1.00	3.06 ± 0.70	<0.0001***

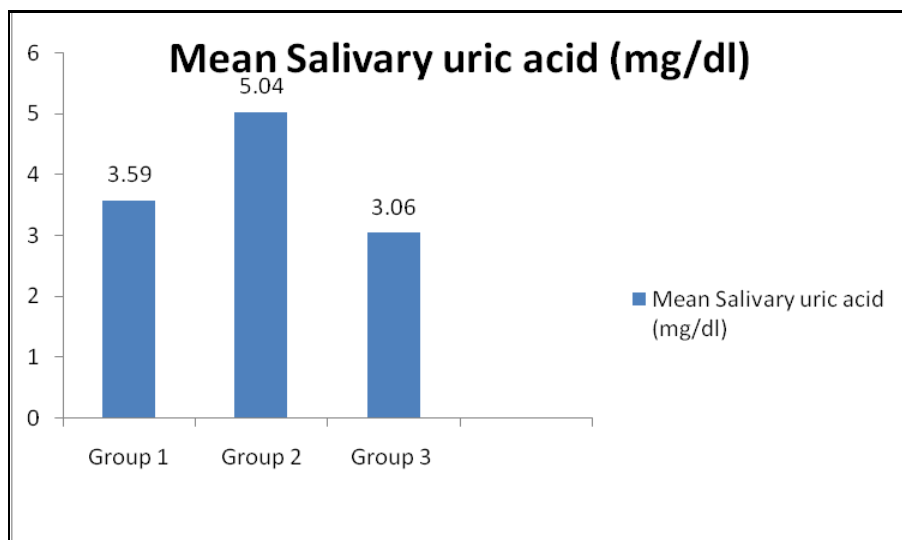NS – Not significant; ** Significant; *** Highly significant.

Figure 1: Mean salivary uric acid level (mg/dl) in different study groups.

DISCUSSION

Metabolic syndrome, a major risk factor associated with cardiovascular disease is an increasingly common medical problem not only in developed countries, but also in the developing countries. Since metabolic syndrome involves complex interrelated components, it is essential to identify a common bio-marker (preferably the one that could have determined by non – invasive technique) which would enable the society to participate in screening program and can monitor the progression of the disease and prevent the further complications.

This study attempted to identify salivary uric acid as one such bio-marker for metabolic syndrome as recently, the association between metabolic syndrome and elevated serum uric acid level were reported in literature (Ju – Mi Leeet al 2012, Shi – Dou Lin et al 2006). In 2006, Shi – Dou Lin et al reported that mean serum uric acid level increased as the number of metabolic factors increased and abnormal TG had the most influence on serum uric acid. Further, the work of Ju – Mi Lee et al in 2012 showed that the number of metabolic abnormalities increased gradually with increasing serum uric acid levels. Because a linear relationship exists between serum and salivary uric acid (SUA) concentration, this study was carried out by estimating the salivary uric acid level in different metabolic syndrome groups. The result of the present study indicates that the mean salivary uric acid level is proportionately increased with the increase in the components of metabolic syndrome. In the present work, the group II (severe MS) with more than 3 components of metabolic syndrome showed highly significant increase in SUA level ($p = <0.0001$) than the group I (having 3 components) and group III (with 1 or 2 components). Even when compared SUA level between the groups I and II, group II and III and group I and III, it showed significant results. So, the present study clearly indicates that salivary uric acid level increases with the severity of the disease and clearly supports the previous study of Ju – Mi Lee et al and also reiterates that not only serum uric acid level but also salivary uric acid level correlate with severity of the metabolic syndrome component.

The present study also revealed that each and every components of metabolic syndrome significantly correlated with the salivary uric acid level. Here, except, the HDL level which showed negative correlation, all the other components (WC, BP, FBS, Cholesterol, TG) had positive correlation with salivary uric acid level.

Hyperuricemia is commonly observed in metabolic syndrome (Zohreh Soltani et al 2013) and it plays a role in the development of metabolic syndrome (Ju – Mi Lee et al 2012, Shi – Dou Lin et al 2006). The proposed mechanisms related to these findings may include effect of uric acid on endothelial dysfunction (Shi – Dou Lin et al 2006, Zohreh Soltani et al 2013) and overproduction of reactive oxygen species (ROS) (Zohreh Soltani et al 2013). As, uric acid have been shown to inhibit endothelial NO bioavailability and because insulin requires endothelial NO to stimulate skeletal muscle glucose uptake, hyperuricemia may also have a causal role in the pathogenesis of insulin resistance (Adriana Iliesin et al 2010). One other mechanism linking hyperinsulinemia with hyperuricemia may be explained by a decreased renal excretion of uric acid (A.N. Al – Isa et al 2013). It was well established that hyperuricemia induces intracellular ROS production in adipose cells. Since oxidative stress in adipocytes has been considered as a major factor of insulin resistance, hyperuricemia – induced oxidative stress in adipose tissue might play a key role in these dysregulations (Zohreh Soltani et al 2013). As the salivary uric acid having positive correlation with serum uric acid, one can assume that the above observations clearly support the findings of the present study also.

Since measurement of salivary uric acid is non – invasive, relatively cheap and less time – consuming, it can be used for screening of metabolic syndrome population thereby reduces the cardiovascular risk too.

Present study has got some limitations as the oral health status was self reported and detailed information regarding their emotional status were not collected which could otherwise affect either salivation or uric acid level. However, exploration of the present result in this approach are needed which will be of use for all the clinicians and they can incorporate into their day – to – day practice.

CONCLUSION

The result of the present study clearly established that the salivary uric acid levels have significant correlation with the different components of the metabolic syndrome and also it increases proportionate with the severity of metabolic syndrome. So we could conclude that salivary uric acid can be used as a non – invasive biomarker for monitoring the metabolic syndrome. Larger follow – up studies are needed to prove the result of present study.

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