



RESEARCH ARTICLE

A STUDY OF ASSOCIATION BETWEEN METABOLIC SYNDROME AND NEPHROLITHIASIS

*Chengalvarayan Gopal, Ramesh Arumugam and Suresh Kumar, N.

Assistant Professor, Rajiv Gandhi Government General Hospital, Chennai

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ABSTRACT

Introduction: Introduction: Metabolic syndrome is a complex of medical disorders; when they occur together have clinical significance like increased risk of developing cardiovascular disease, cerebrovascular accidents, diabetes mellitus (type two) and atherosclerosis. There are different definitions for defining metabolic syndrome and they all include the main components – obesity or waist circumference, hypertension, hyperlipidemia and hyperglycemia. The associations of metabolic syndrome with nephrolithiasis were showed by many studies in a defined population. The exact patho-physiology of this association was not clear, but shown to be associated with metabolic syndrome patient's urinary constituents like decrease in urinary PH, increased urinary calcium and uric acid excretion and decreased excretion of urinary citrate which is an important inhibitor of nephrolithiasis. We investigate this association in patient population in our institute with nephrolithiasis and compare with individuals without nephrolithiasis.

Materials and Methods: The study was conducted in institute of urology, Madras Medical College, Chennai. The study was prospective study conducted from March 2012 to February 2013. Patients with unilateral or bilateral renal calculus was included as cases and individuals without renal calculus was included as controls.

Results and Observations: The Mean age group of control (Group 2) was 35.62 + 10.99 years. The mean age group of cases (Group 1) was 38.25+9.67 years. In Group 1 (cases) there were 47 females and 53 males. In Group 2 (controls) there were 48 females and 52 males. The components of metabolic syndrome were waist circumference, blood pressure, fasting blood sugar, serum triglycerides and serum high density lipoprotein. Each component of the metabolic syndrome was compared between cases (Group 1) and control (Group 2)

Conclusion

- Metabolic syndrome is significantly associated with nephrolithiasis
- Of the components of metabolic syndrome a statistically significant association with nephrolithiasis is noted for increased waist circumference and hypertension.
- In the present study the other three components of metabolic syndrome namely diabetes mellitus, increased serum triglycerides and decreased serum HDL were found to be statistically insignificant with regard to nephrolithiasis

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INTRODUCTION

Urinary stone disease is a common disease affecting mankind and it was described since historical times. The life time risk of developing stone disease was 1% to 15 % (Asplin *et al.*, 1996). It varies between races, geographical area of living, age (Stamatelou *et al.*, 1994), gender, occupation etc... Generally there is increased prevalence of stone disease in western countries when compared to south Asian countries, but due to westernization of culture in these countries there is increased incidence of nephrolithiasis. Nephrolithiasis were polycrystalline aggregates containing various proportions of

crystal and organic matrix components. The common nephrolithiasis calculus were calcium oxalate stones, calcium phosphate stones, uric acid stones, calcium magnesium ammonium phosphate stone (triple phosphate stone or struvite stone) and cystine stone. Because of profound morbidity due to the disease and during treatment, loss of renal function with end stage renal disease in some neglected cases and increased cost of expenditure for diagnosis and treatment, there was shift of focus from treatment to prevention of nephrolithiasis. The development of nephrolithiasis was most likely a multi factorial process and it is not fully addressed by current theories. Metabolic syndrome (Anderson *et al.*, 2001) is a complex of medical disorders; when they occur together have clinical significance like increased risk of developing cardiovascular disease, cerebrovascular accidents, diabetes mellitus (type two)

*Corresponding author: Chengalvarayan Gopal,

Assistant professor, Rajiv Gandhi Government General Hospital, Chennai

and atherosclerosis. There are different definitions for defining metabolic syndrome and they all include the main components – obesity or waist circumference, hypertension, hyperlipidemia and hyperglycemia. The associations of metabolic syndrome with nephrolithiasis were showed by many studies in a defined population. The exact patho -physiology of this association was not clear, but shown to be associated with metabolic syndrome patient's urinary constituents like decrease in urinary PH, increased urinary calcium and uric acid excretion and decreased excretion of urinary citrate which is an important inhibitor of nephrolithiasis (Sakhae and Maalouf, 2008). We investigate this association in patient population in our institute with nephrolithiasis and compare with individuals without nephrolithiasis.

MATERIALS AND METHODS

The study was conducted in tertiary care centre for a period of one year from March 2012 to February 2013. The study design was prospective case control study. Ethical committee clearance was taken from institute ethics committee prior to the start of the study. Patients with unilateral or bilateral renal calculus was included as cases (Group 1) and individuals without renal calculus (Group 2) was included as controls. Patients with congenital renal abnormalities, acute or chronic renal failure patients, patients with metabolic bone disorder or taking treatment for osteoporosis, patients with gout, patients with major debilitating disease like cancer, patients with complication of calculus disease like calculus pyelonephritis, pyonephrosis, pregnancy, patients with contracted kidney are excluded from the study. Sample size was about 100 cases in group 1 and 100 cases in group 2 patients.

Methodology

The presence of metabolic syndrome was defined by presence of 3 or more positive points in the below criterias:

- 1) **Waist-** circumference ≥ 90 cms in males and ≥ 80 cms in females (Alberti *et al.*, 2009)
- 2) **Serum-** triglycerides > 150 mg/100ml or on treatment for lipid disorders
- 3) **Serum-**cholesterol < 40 mgs/100ml in males and < 50 mg/100ml in females or on treatment for high cholesterol.
- 4) **Systolic-** blood pressure ≥ 130 mm of Hg or
- 5) **Diastolic-** blood pressure ≥ 85 mm of Hg or on any anti hypertensive drug
- 6) **Fasting-**serum- glucose ≥ 100 mg/100ml or on any drug treatment for diabetes mellitus.

Metabolic syndrome presence in nephrolithiasis group (cases) was compared with metabolic syndrome in normal individuals (controls). Again each component of metabolic syndrome was compared with cases and control.

Statistical method

For discrete data-proportion is computed and the mean and standard deviation are computed for the continuous data. The chi square test was applied to compare the proportions between the groups to assess the statistical significance. All analyses were two tailed and $p < 0.05$ was considered significant. SPSS version 16.0 was used for data analysis.

RESULTS AND OBSERVATIONS

The Mean age group of control (Group 2) was 35.62 ± 10.99 years. The mean age group of cases (Group 1) was 38.25 ± 9.67 years. Age group between cases and control was comparable and was statistically insignificant (P value > 0.05). In Group 1 (cases) there were 47 females and 53 males. In Group 2 (controls) there were 48 females and 52 males. The gender difference between two groups was comparable and was statistically insignificant (P -value > 0.05).

Table 1. Metabolic Syndrome

		Metabolic Syndrome group			
		Yes	No	Total	
Group	Case	Count	42	58	100
		% within Group	42.0%	58.0%	100.0%
	Control	Count	26	74	100
		% within Group	26.0%	74.0%	100.0%
Total		Count	68	132	200
		% within Group	34.0%	66.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2sided)	Exact Sig. (2-sided)(Pvalue)	Exact Sig. (1sided)
Pearson Chi-Square	5.704a	1	.017		
Continuity Correction b	5.013	1	.025		
Likelihood Ratio	5.744	1	.017		
Fisher's Exact Test				0.025	0.012
Linear-by-Linear Association	5.676	1	.017		
N of Valid Cases b	200				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 34.00.

b. Computed only for a 2x2 table

Table 2. Distribution of basic characteristics and abnormalities of metabolic syndrome components by Case and control

Variable	Case (N=100)	Control (N=100)	P-value
Mean Age	38.2±9.67	35.6±10.9	0.074
Mean Stone size	1.58±0.51	-	-
SEX			
Male(%)	53	52	1.000
Female(%)	47	48	
Abnormalities			
WC(%)	52	31	0.004
BP(%)	47	23	0.001
FBS(%)	33	21	0.079
TGL(%)	34	28	0.445
HDL(%)	29	25	0.633
Metabolic syndrome(%)	42	26	0.025

P-value<0.05 was significant. TGL-Triglycerides, HDL- High density lipoprotein, WC-Waist Circumference, BP- Blood Pressure, FBS- Fasting Blood Sugar.

Inter group comparison

By AHA/NHLBI criteria for metabolic syndrome with Ethnic specific cut off for waist circumference, the number of patients with metabolic syndrome in Group 1 (Cases) was 42(42%) and in Group 2(Control) it was 26(26%). The metabolic syndrome in two groups were compared by chi square test for test for significance. The proportion of metabolic syndrome was significantly (P-value <0.05) higher (42% Vs 26%) in Cases when compared to Control as given in Table 1. So patients with metabolic syndrome has higher chances of getting nephrolithiasis. The components of metabolic syndrome were waist circumference, blood pressure, fasting blood sugar, serum triglycerides and serum high density lipoprotein. Each component of the metabolic syndrome was compared between cases (Group 1) and control (Group 2). The proportion of each component of metabolic syndrome was given in Table 2. Of the components of metabolic syndrome a statistically significant association with nephrolithiasis is noted for increased waist circumference and hypertension.

DISCUSSION

Nephrolithiasis is a common disorder affecting the urinary tract. The morbidity produced by nephrolithiasis to the patients and the huge amount spend on the diagnosis, treatment and follow up leads to search for preventive strategies of nephrolithiasis. Gupta *et al.* (2009) on their population based study in north India showed that there is low prevalence of metabolic syndrome during adolescence age and very rapid increase in metabolic syndrome prevalence above age of 30. He called for urgent interventions to prevent epidemic of metabolic syndrome. Sedentary life habit, increased intake of animal proteins and salted food and lack of exercise leads to obesity, hypertension, type two diabetes mellitus and dyslipidemia. Sakhae *et al.* (2002) first described the association of diabetes mellitus with uric acid calculus formation in 2002. He suggested decreased ammonia formation in the kidney due to insulin resistance was the cause of acidic urine and uric acid calculus formation. There were many international studies describing the association of metabolic syndrome with nephrolithiasis. Till date no study was available comparing this association in our part of the

country. This study was conducted to evaluate the association of metabolic syndrome in nephrolithiasis patient population in our part of country. In this study patients with nephrolithiasis (Cases) was compared with persons without nephrolithiasis (Control) for the presence of metabolic syndrome. We also compared the association of individual component of metabolic syndrome between cases and controls. The present study demonstrated highly significant (Pvalue<0.05) association of metabolic syndrome in nephrolithiasis patients when compared to control group (42% Vs 26%). Jeong *et al.* (2011) in their cross sectional study of 34,895 persons who underwent general health screening observed nephrolithiasis in 2.4% and metabolic syndrome in 13.7% of the screened population. He demonstrated significant association of metabolic syndrome in nephrolithiasis group with OR of 1.25. Kim *et al.* (2013) demonstrated significant association of metabolic syndrome in the patients having renal calculus (15.9% Vs 11%) when compared to individuals without renal calculus. Rendina *et al.* (2008) in their study of data's of inpatients in southern Italy showed significant association of metabolic syndrome in renal calculus patients. He observed metabolic syndrome in 31% of the inpatient population. The present study also shows significant association in patient population. The present study shows significant association between components of metabolic syndrome with nephrolithiasis when compared with control. The metabolic component hypertension has statistically (P-value<0.05) significant association with nephrolithiasis (47% Vs 23%) when compared with control. This association was also observed by Kim *et al.* (2013) with a odd ratio of 1.08 for males and 1.24 for females. Jeong *et al.* (2011) observed statistic significance association between nephrolithiasis and increased waist circumference. In this study we demonstrated statistic significant (P-value<0.05) association of increased waist circumference (52% Vs 31%) between nephrolithiasis (cases) and control groups.

Though there was no statistic significant association shown for increased fasting blood sugar, increased serum triglycerides and decreased HDL between cases and control, the proportions of these components were high in nephrolithiasis group when compared to control. Taylor *et al.* (2005) demonstrated increased incidence of nephrolithiasis in diabetes mellitus patients and was probably due to insulin resistance. Kohjimoto *et al.* (2013) observed increased in metabolic syndrome traits with severity of renal calculus disease. We also observed increasing trends of components of metabolic syndrome in nephrolithiasis group. The present study has significant clinical implication in public health care in the prevention of formation of nephrolithiasis. Since metabolic syndrome prevalence is increasing in our community, it is very important to formulate policies to prevent and treat this syndrome. For the treatment of metabolic syndrome there were no randomized control trials oriented guidelines available. The initial treatments of metabolic syndrome were changes in lifestyle and diet modifications. Sedentary life style habits should be discouraged even from childhood. More activities should be included in the daily schedule like regular walking, minimum of thirty minutes exercise. Diets rich in fat or animal protein or salted foods should be restricted. Diets rich in vegetables, fruits, grains, legumes and low or no fat were encouraged. Controlled weight reduction is advised in order to prevent increased risk of developing calculus by marked weight reduction programs like bariatric surgery. Pharmacological treatment for hypertension, diabetes and dyslipidemia can be

taken for control of metabolic syndrome. The limitations of this study were stone composition in metabolic syndrome positive cases was not analysed, the change in urinary constituents in metabolic syndrome positive patients was not correlated, the duration of metabolic syndrome was not correlated with occurrence of nephrolithiasis and was not a longitudinal study, so causal relationship is not established.

Conclusion

- Metabolic syndrome is significantly associated with nephrolithiasis
- Of the components of metabolic syndrome a statistically significant association with nephrolithiasis is noted for increased waist circumference and hypertension.
- In the present study the other three components of metabolic syndrome namely diabetes mellitus, increased serum triglycerides and decreased serum HDL were found to be statistically insignificant with regard to nephrolithiasis.

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