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Association between Metabolic Syndrome and Urolithiasis- Descriptive Study

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Abstract

The prevalence of kidney stones has been on the rise over the last 2 decades worldwide. Many studies have indicated a possible association between metabolic syndrome and kidney stone disease. Several hypotheses have been proposed to explain the pathophysiology of urolithiasis resulting from metabolic syndrome, amongst which are the insulin resistance and Randall's plaque hypothesis. Newer terminologies like Metabesity and Diabesity have been mentioned in recent literature. Many studies have found factors contributing to urolithiasis in patients suffering from metabolic syndrome, out of which obesity, overweight, and sedentary lifestyles have been identified as major etiological factors. This study is done to assess the association of urolithiasis and metabolic syndrome.

Keywords: Metabolic Syndrome; Urolithiasis; Metabesity; Diabesity

Abbreviations: WHO: World Health Organization; BPH: Benign Prostatic Hyperplasia; VLDL: Very-Low-Density Lipoproteins; HDL-C: High-Density Lipoprotein Cholesterol; EGIR: European Group for the Study of Insulin Resistance; NCEP-ATP-3: National Cholesterol Education Program Adult Treatment Panel- III; IDF: International Diabetes Foundation; AHA: American Heart Association; NHLBI: National Heart, Lung, and Blood Institute; BMI: Body Mass Index; WC: Waist Circumference; SHT: Systemic Hypertension; TG: Triglycerides; HDL: High Density Lipoprotein; DM: Diabetes Mellitus.

Introduction

Urolithiasis is one of the most common disorders of the urinary tract. A large number of people are suffering from urolithiasis all over the globe [1]. It is most common between third to sixth decades of life. Men are more commonly affected than women [2]. In India, 12% of the population is expected to have urinary stones [3]. Recurrent stone formation is a common problem with all types of stones and therefore preventive measures are an important part of the care of patients with urolithiasis. Etiopathogenesis of stones is multifactorial. Recent studies have suggested that obesity is a significant contributing factor to urolithiasis. World Health Organization (WHO) estimation is that 1.7 billion people are overweight and obese worldwide [4]. An increased incidence of urolithiasis of greater than 75% is seen in overweight and obese patients compared to their normal counterparts [5].

Metabolic syndrome is a worrying entity which is not only prevalent in the developed countries but also in

developing countries like India. Its correlation with the cardiovascular diseases has been well established [6]. However, some studies [7,8] have indicated a significant correlation between metabolic syndrome and urolithiasis. As urolithiasis, metabolic syndrome or Syndrome X is also multifactorial. Several epidemiological studies [9-11] have focused on the search for a pathophysiological relationship between the different components of this syndrome (obesity, hypertension, diabetes, dyslipidaemia) and urological problems. Most established aspects of the metabolic syndrome are linked to benign prostatic hyperplasia (BPH) and prostate cancer. Fasting plasma insulin, in particular, has been linked to BPH and incident, aggressive and lethal prostate cancer [12-15]. The metabolic syndrome has also been shown to be associated with non-prostatic urological conditions such as male hypogonadism, nephrolithiasis, overactive bladder and erectile dysfunction, although data on these conditions are still sparse and not definite.

Reaven coined the term 'syndrome X' for this conglomeration of various metabolic abnormalities [16,17], including glucose intolerance, hypertension, increased very-low-density lipoproteins (VLDL), triglycerides, and decreased high-density lipoprotein cholesterol (HDL-C), with insulin resistance being the basic underlying pathophysiologic problem. Over the last two decades, various organizations like World Health Organization (WHO 1998), European Group for the Study of Insulin Resistance (EGIR) (1999), National Cholesterol Education Program Adult Treatment Panel- III (NCEP-ATP-3) (2001), International Diabetes Foundation (IDF) (2005) and American Heart Association /National Heart, Lung, and Blood Institute (AHA/NHLBI) (2005) have proposed different definitions, using varying terminologies for metabolic syndrome [18-22].

New addition to the glossary of terms is the concept of diabesity. Diabesity is a combination of diabetes and obesity. Recently, Dr. Alexander Fleming who is an endocrinologist added a different dimension to the definition of metabolic syndrome by introducing the concept of metabesity (2013). According to Dr. Fleming, metabesity describes all relevant conditions (diabetes mellitus, obesity, metabolic syndrome, cardiovascular disease, dyslipidaemia≥, cancer promoting factors and accelerated aging) which impose a serious burden on healthcare, and economic state [23].

American Heart Association

Metabolic syndrome occurs when a person has three or more of the following measurements:

a. Abdominal obesity (Waist circumference >40 inches in men, and > 35 inches in women).
b. Triglyceride level of ≥150 milligrams per dl of blood.
c. HDL cholesterol of less than <40 mg/dL in men or <50 mg/dL in women.
d. Systolic blood pressure (top number) of ≥130 mm Hg, or diastolic blood pressure (bottom number) of ≥ 85 mm Hg.
e. Fasting glucose of ≥100 mg/dl.

Objectives: This is a prospective descriptive study. The objectives of this study are to:

a. analyse the correlation between various components of metabolic syndrome and urolithiasis
b. analyse relation between certain lifestyle factors like smoking, alcoholism and urolithiasis

Patients and Methods

All patients who attended the urology OPD in MGMCRI, Pondicherry between Jan 2017 and July 2018 were enrolled in this study. The diagnosis of metabolic syndrome was based on AHA criteria. Blood pressure was measured with mercury sphygmomanometer. Subjects whose reading was higher than 130 mmHg (systolic) or 85 mmHg (diastolic) (average of 3 values at 1 min interval) and those who reported to be under antihypertensive drugs were considered hypertensive. Participants whose fasting glucose was equal to or above 100 mg/dl and those who reported oral use of hypoglycaemic agents and/or insulin were considered diabetic. Body weight was measured by electronic weighing machine. The body mass index (BMI) was calculated as the ratio of weight (in kilograms) and squared height -BMI = Weight (kg)/ Height $(m)^2$ (Table 1).

Under 18.5	Underweight
18.5–24.9	Healthy weight range
25.0–29.9	Overweight
30.0–34.9	Obesity I
35.0–39.9	Obesity II
40.0 (and above)	Obesity III

Table 1: Showing Overweight & Obesity.

Waist circumference was assessed on three occasions using an inextensible tape-measure, at the midpoint of the distance between the iliac crest and the last costal margin, with the patient upright and at expiration. Biochemical serum parameters were obtained after 8h of fasting. Standard serum parameters included glucose, total cholesterol, Low-density lipoprotein-cholesterol, HDL-C, triglycerides.

Statistical Analysis

The study is about observing the association between various parameters of metabolic syndrome and Urolithiasis. The parameters related to metabolic syndrome are Waist Circumference (WC), Systemic Hypertension (SHT), Triglycerides (TG), High density Lipoprotein (HDL), Body Mass Index (BMI) and Diabetes mellitus (DM). All these were coded as nominal variables. Association was observed using statistical test -Chi-Square test and all the results were compared at 0.05 level. Multiple Bar diagrams are depicted to show the distribution of cases with respect to categories of metabolic syndrome and Urolithiasis. The entire analysis is carried out using IBM SPSS 19.0 version.

Results

Total of 241 patients who agreed to take part in the study were enrolled.
159 patients were males (65.9%) and 82(34.1%) patients were females.
Age of the patients ranged from 18-85 years.
38 (M=27, F=11) (15.7%) of the 241 patients had urolithiasis (Table 2 & 3, Graph 2 & 3).

Gender		Male	Female
Urolithiasis	Yes	27	11
	No	132	71

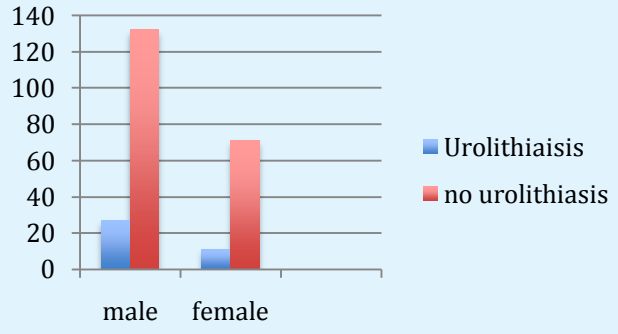

Table 2 & Graph 2: Showing Gender distribution.

Age Group	Number of Cases	Number with Urolithiasis
<20	5	1
20-40	64	8
40-60	131	21
60-80	37	7
>80	4	1

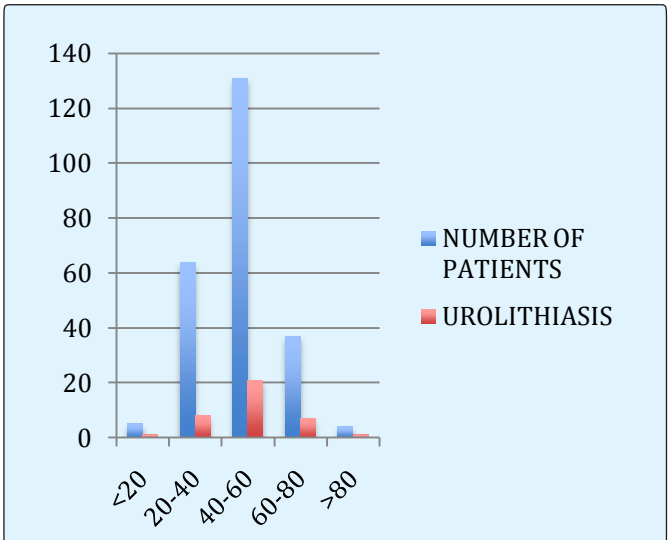

Table 3 & Graph 3: Showing age group and number of patients with Urolithiasis.

Triglycerides & Urolithiasis

69 patients had Triglycerides >150 out of which 19 patients had urolithiasis (27.5%).
172 patients had Triglycerides <150 Out of which 19 patients had urolithiasis (11.04%) (Table 4 & Graph 4).

TG		>150	<150
Urolithiasis	Yes	19	19
	No	50	153

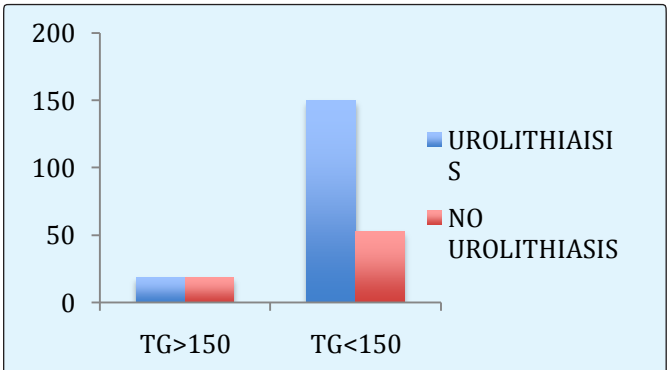

Table 4 & Graph 4: Depicting Triglycerides level and number of patients with Urolithiasis.

Diabetes Mellitus and Urolithiasis

57 patients were Diabetics and Out of these 8 patients had urolithiasis (14%).
184 patients were non-diabetics and 30 of them had urolithiasis (19%) (Table 5 & Graph 5).

Diabetes		Yes	No
Urolithiasis	Yes	8	30
	No	49	154

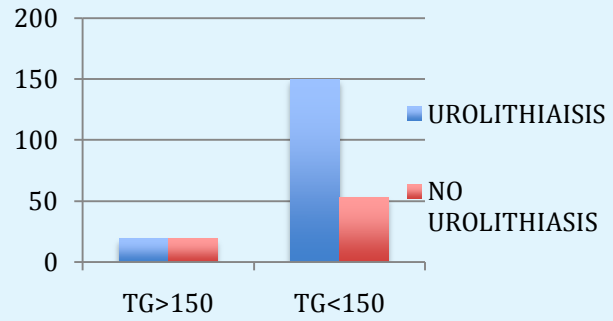

Table 5 & Graph 5: Showing incidence of diabetes and urolithiasis.

Systemic Hypertension and Urolithiasis

54 patients were found to be hypertensive of which 9 patients had urolithiasis (16%). 187 patients were normotensive of which 29 had urolithiasis (17%) (Table 6 & Graph 6).

Hypertension		Yes	No
Urolithiasis	Yes	9	29
	No	45	158

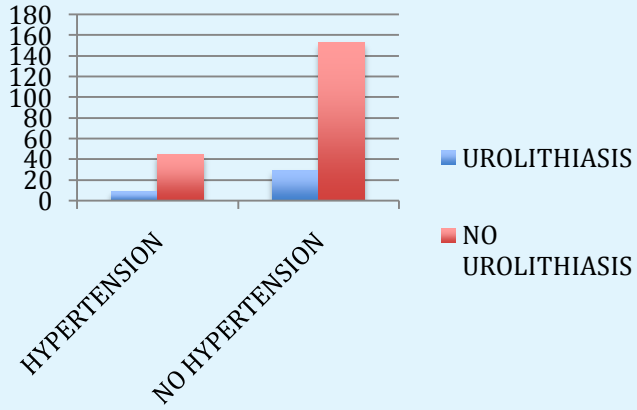

Table 6 & Graph 6: Showing incidence of Systemic Hypertension and Urolithiasis.

BMI and Urolithiasis

BMI		Underweight <18.5	Normal 18.5-24.9	Pre-obese 25-29.9	Obesity 1 30-34.9	Obesity 2 35-39.9	Obesity 3 ≥40
Urolithiasis	Yes	0	9	18	6	4	1
	No	7	59	96	28	10	3

Total no of patients with BM I<18.5 were 7 out of which none had urolithiasis.
Total no of patients with BMI 18.5-24.9 were75 of which 9 (13.2%) had urolithiasis.
Out of 75 patients who were well within the Normal BMI range 9 patients had urolithiasis-12%.
Total no of patients with BMI 25-29.9 were 114 out of which 18 (15.7%) had urolithiasis
Total no of patients with BMI 30-34.9 were 34 out of which 6(17.6%) had urolithiasis.
Total no of patients with BMI 35-39.9 were 14 out of which 4(28.5%) had urolithiasis.
Total no of patients with BMI ≥ 40 were 4 out of which 1(25%) had urolithiasis.
Out of 166 patients who had high BMI 29 had urolithiasis (17.5%) (Table 7 & Graph 7)**.**

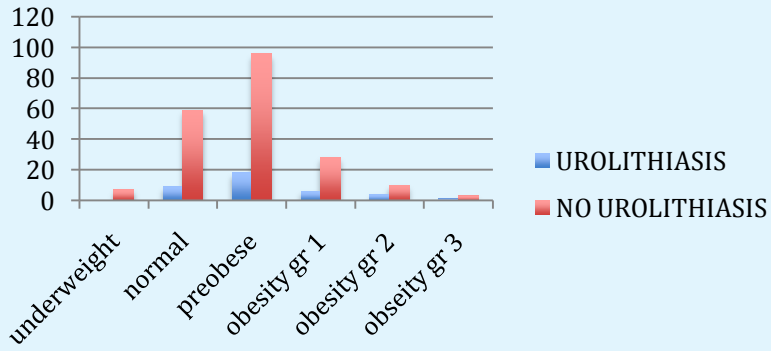

Table 7 & Graph 7: Showing BMI levels and incidence of Urolthiasis.

HDL and Urolithiasis

		Men		Women	
HDL		< 40mg/dl	> 40mg/dl.	<50mg/dl	>50mg/dl
Urolithiasis	Yes	4	23	5	6
	No	11	121	27	44

Out of 15 male patients with HDL<40, 4(26.7%) had urolithiasis

Out of 144 male patients with HDL>40, 23(15.9%) had urolithiasis

Out of 32 female patients with HDL<50, 5(15.6%) had urolithiasis

Out of 50 female patients with HDL>50, 6(12%) had urolithiasis (Table 8 & Graph 8).

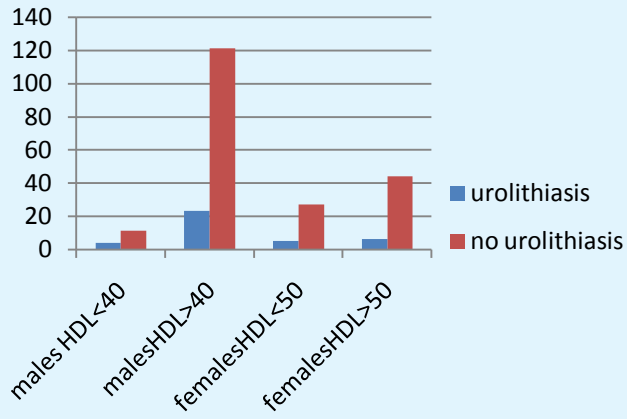

Table 8 & Graph 8: Showing levels of HDL and number of patients with Urolithiasis.

Confounding Variables

Smoking and Urolithiasis

Smokers		Yes	No
Urolithiasis	Yes	14	24
	No	24	179

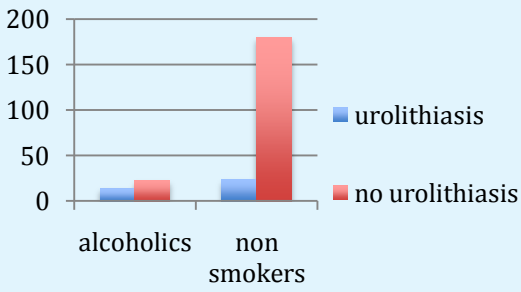

Table 9 & Graph 9: Showing the Number of Smokers and number of patients with Urolithiasis.

Alcoholism and Urolithiasis

Alcohol		Yes	No
Urolithiasis	Yes	14	24
	No	33	170

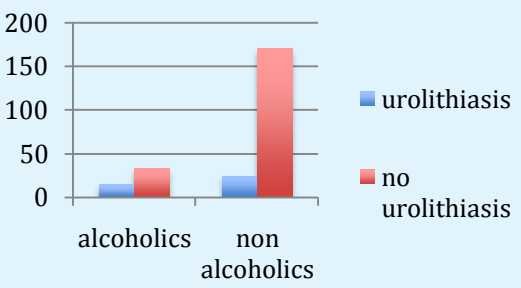

Table 10 & Graph 10: Showing the Number of people consuming alcohol and number of patients with Urolithiasis.

Statistical Analysis

The study is about observing the association between the metabolic syndrome and Urolithiasis. The parameters assessed were WC, SHT, TG, HDL, BMI and DM. All these were coded and were nominal variables. In order to observe the association, the appropriate statistical test is Chi-Square test was used and all the results were compared at 0.05 confidence level. Confounding Variables like smoking and alcoholism were also analysed. The entire analysis is carried out using IBM SPSS 19.0 version.

WC * DIAGNOSIS Cross tabulation		DIAGNOSIS			Total
		other cases		urolithiasis	
WC	<100	Count	130	25	155
		% within WC	83.90%	16.10%	100.00%
		% within DIAGNOSIS	64.00%	65.80%	64.30%
	>100	Count	73	13	86
		% within WC	84.90%	15.10%	100.00%

		% within DIAGNOSIS	36.00%	34.20%	35.70%
Total		Count	203	38	241
		% within WC	84.20%	15.80%	100.00%
		% within DIAGNOSIS	100.00%	100.00%	100.00%

Chi-square=0.043, p-value =0.836^{NS}.
Table 11: Cross Tabulation & Association between WC and Urolithiasis.

In Table 12, the association between Diabetes mellitus (DM) and Diagnosis is observed to be insignificant with p-value is 0.875 (>0.05). This outlines the fact that absence/presence of DM does not support to relate the urolithiasis.

DM * Urolithiasis Cross tabulation			DIAGNOSIS		Total
			other cases	urolithiasis	
DM	no	Count	158	30	188
		% within DM	84.00%	15.90%	100.00%
		% within diagnosis	77.83%	78.90%	78.00%
	yes	Count	45	8	53
		% within DM	84.90%	14.00%	100.00%
		% within DIAGNOSIS	22.16%	21.05%	21.99%
Total		Count	203	38	241
		% within DM	84.20%	15.70%	100.00%
		% within diagnosis	100.00%	100.00%	100.00%

Chi-square = 0.025; p-value = 0.875^{NS}.
Table 12: Cross Tabulation & Association between DM and Urolithiasis.

In Table 13, the results show an insignificant p-value 0.642 (>0.05), giving rise to the fact that even the categories of SHT cannot be used to determine the outcome of the diagnosis.

SHT * DIAGNOSIS Cross tabulation			DIAGNOSIS		Total
			other cases	urolithiasis	
SHT	No	Count	158	29	187
		% within SHT	84.40%	15.50%	100.00%
		% within DIAGNOSIS	77.80%	76.30%	78.60%
	yes	Count	45	9	54
		% within SHT	83.30%	16.70%	100.00%
		% within DIAGNOSIS	22.10%	23.60%	21.40%
Total		Count	203	38	241
		% within SHT	84.20%	15.70%	100.00%
		% within DIAGNOSIS	100.00%	100.00%	100.00%

Chi-square = 0.216; p-value = 0.642^{NS}.
Table 13: Cross Tabulation & Association between SHT and Urolithiasis.

In Table 14, the results show significant p-value 0.008 (<0.05), implies the fact that categories of TG can be used to determine the outcome of the diagnosis. The outcome of TG can be associated with the urolithiasis, and equal percentage of patients is distributed across two categories of TG.

TG * DIAGNOSIS Cross tabulation			DIAGNOSIS		Total
			other cases	urolithiasis	
TG	<150	Count	153	19	172
		% within TG	88.95%	11.04%	100.00%
		% within DIAGNOSIS	74.00%	50.00%	71.36%
	>150	Count	50	19	69
		% within TG	72.40%	27.53%	100.00%
		% within DIAGNOSIS	24.63%	50.00%	28.63%
Total		Count	203	38	241
		% within TG	86.30%	13.70%	100.00%
		% within DIAGNOSIS	100.00%	100.00%	100.00%

Chi-square = 7.011; p-value = 0.008^{S}.
Table 14: Cross Tabulation & Association between TG and Urolithiasis.

In Table 15, the results show an insignificant p-value 0.790 (>0.05), giving rise to the fact that even the categories of HDL cannot be used to determine the outcome of the diagnosis.

HDL * DIAGNOSIS Cross tabulation			DIAGNOSIS		Total
			other cases	urolithiasis	
HDL	>40	Count	165	29	194
		% within HDL	85.05%	14.94%	100.00%
		% within DIAGNOSIS	81.20%	76.30%	80.50%
	<40	Count	38	9	47
		% within HDL	85.10%	14.90%	100.00%
		% within DIAGNOSIS	18.70%	23.60%	19.50%
Total		Count	203	38	241
		% within HDL	84.20%	15.70%	100.00%
		% within DIAGNOSIS	100.00%	100.00%	100.00%

Chi-square = 0.071; p-value = 0.790^{NS}.
Table 15: Cross tabulation and Association between HDL and Urolithiasis.

In Table 16 & 17, the results show significant p-value (<0.05), implies the fact that categories of SMOKING and ALCOHOL can be used to determine the outcome of the diagnosis. Of 38 of patients under urolithiasis, majority of patients have the habit of smoking. With this phenomenon, one can associate that people who smoke regularly or occasionally have the likelihood of observing urolithiasis. Similar kind of interpretation can be drawn for the status of alcohol.

SMOKING * Urolithiasis Cross tabulation			DIAGNOSIS		Total
			other cases	urolithiasis	
SMOKING	No	Count	180	24	204
		% within SMOKING	88.20%	11.80%	100.00%
		% within Urolithiasis	87.40%	67.60%	84.50%
	Yes	Count	22	11	33
		% within SMOKING	71.40%	28.60%	100.00%
		% within Urolithiasis	11.70%	27.00%	13.90%
	Occasional	Count	1	3	4
		% within SMOKING	50.00%	50.00%	100.00%
		% within Urolithiasis	0.90%	5.40%	1.60%
Total		Count	204	37	241
		% within SMOKING	85.30%	14.70%	100.00%
		% within Urolithiasis	100.00%	100.00%	100.00%

Chi-square = 10.750; p-value = 0.005^{S}.
Table 16: Cross Tabulation & Association between Smoking and Urolithiasis.

ALCOHOL * DIAGNOSIS Cross tabulation			DIAGNOSIS		Total
			other cases	Urolithiasis	
ALCOHOL	No	Count	170	24	194
		% within ALCOHOL	87.60%	12.30%	100.00%
		% within DIAGNOSIS	83.70%	63.10%	80.40%
	Yes	Count	29	9	38
		% within ALCOHOL	82.90%	17.10%	100.00%
		% within DIAGNOSIS	14.20%	23.60%	15.70%
	Occasional	Count	4	5	9
		% within ALCOHOL	40.00%	60.00%	100.00%
		% within DIAGNOSIS	1.90%	13.10%	4.00%
Total		Count	203	38	241
		% within ALCOHOL	85.30%	14.70%	100.00%
		% within DIAGNOSIS	100.00%	100.00%	100.00%

Chi-square = 17.671; p-value = 0.000[S].

Table 17: Cross Tabulation & Association between Alcoholism and Urolithiasis.

The influence of smoking and alcoholism on urolithiasis has only been scarcely examined [24-26]. Furthermore, there is no consistent evidence about the effects of smoking and alcoholism on urolithiasis. In the present study there was significant relationship between modifiable risk factors, such as smoking and alcoholism on urolithiasis.

Discussion and Conclusion

In this study, the risk factors for urolithiasis were male gender, Hypertriglyceridemia, smoking and alcoholism and they were statistically significant. We found no relationship between Hypertension, Diabetes Mellitus, Waist circumference, Low Density lipoproteins and urolithiasis. We also did not find statistically significant correlation between BMI and urolithiasis, which is in frank contrast with numerous studies from western literature that demonstrated a positive relationship between obesity and urolithiasis. Smoking and Alcoholism seems to have statistical correlation. The study consists of relatively small number of patients. A study with larger numbers is needed to verify the correlation between metabolic syndrome and urolithiasis.

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