# Artikel Asli/Original Articles

# Dietary and Lifestyle Factors and its Risk to Kidney Stone Disease: A Case Control Study at UKM Medical Centre (Faktor Diet dan Gaya Hidup dan Risikonya terhadap Penyakit Batu Karang Ginjal: Satu Kajian Kes Kawalan di Pusat Perubatan UKM)

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# ABSTRACT

Nutrition has been widely recognized to have certain levels of influence on the risk of kidney stone formation. Thus, this case-control study was conducted to determine the association of dietary intake and lifestyles factors with kidney stone disease. Sociodemographic data, dietary intake, supplements intake, smoking and alcohol habit, medical history, physical activity and anthropometric data were obtained using interviewer-administered pre-tested questionnaires among 81 patients who had been diagnosed with kidney stone disease and 81 patients without kidney stone disease at Universiti Kebangsaan Malaysia Medical Centre. The results indicated that body mass index and hip circumference were higher among cases as compared to controls in both men and women (p < 0.05). Energy, macronutrients and micronutrients intake were higher for case subjects compared to control subjects for all significant parameters (p < 0.05). Results showed positive association of kidney stone with consumption of nuts ( $\geq 1$  time/week) for men and women while consumption of eggs (1-3 times/month) and beans (1-6 times/week) showed positive association for women. Analysis of multivariate found the risk factor among women was diabetes mellitus [Adjusted OR = 27.6 (95% CI = 1.43-53.3)] (p < 0.05). Whilst, plain water intake of at least 6 glasses [Adjusted OR = 0.001 (95% CI = 0.000-0.08)] (p < 0.05) and 8 glasses per day [Adjusted OR = 0.001 (95% CI = 0.000-0.02)] (p < 0.05) reduced the risk among women. The risk factors for men were smoking habits [Adjusted OR = 16.2 (95% CI = 1.29-203)] (p < 0.05), consumption of carbonated drink 1-3 times per month [Adjusted OR = 6.25 (95% CI = 1.04-40.7)] (p < 0.05) and 1-6 times per week [Adjusted OR = 6.25 (95% CI = 1.04-40.7)] 12.5 (95% CI = 1.41-111)] (p < 0.05). Unhealthy dietary and lifestyles factors increased the risk of kidney stone disease and various risk factors were found for different sexes.

Keywords: Kidney stone disease; nephrolithiasis; risk factor; dietary; beverages

# ABSTRAK

Pemakanan telah dikenal pasti mempengaruhi risiko pembentukan penyakit batu karang ginjal. Oleh itu, kajian keskawalan telah dijalankan untuk mengkaji peranan diet dan gaya hidup dalam pembentukan penyakit batu karang ginjal. Data sosiodemografi, pengambilan makanan, pengambilan makanan tambahan, tabiat merokok dan pengambilan alkohol, sejarah perubatan, aktiviti fizikal, dan data antropometri telah diperolehi dengan menggunakan borang soal selidik dalam kalangan 81 pesakit yang menghidap penyakit batu karang ginjal dan 81 pesakit tanpa penyakit batu karang ginjal di Pusat Perubatan Universiti Kebangsaan Malaysia. Keputusan menunjukkan bahawa indeks jisim tubuh dan lilitan pinggul adalah lebih tinggi dalam kalangan subjek kes berbanding kawalan bagi lelaki dan wanita (p < 0.05). Pengambilan tenaga, makronutrien dan mikronutrien adalah lebih tinggi bagi subjek kes berbanding subjek kawalan untuk semua parameter (p < 0.05). Hasil kajian menunjukkan perkaitan positif penyakit batu karang ginjal dengan pengambilan kacang (≥1 masa/minggu) untuk lelaki dan wanita manakala pengambilan telur (1-3 kali/bulan) dan kekacang (1-6 kali/ minggu) menunjukkan perkaitan positif untuk wanita. Analisis multivariat mendapati faktor risiko dalam kalangan wanita adalah penyakit diabetes mellitus [Adjusted OR = 27.6 (95% CI = 1.43-53.3)] (p < 0.05). Sementara itu, pengambilan air kosong sekurang-kurangnya 6 gelas [Adjusted OR = 0.001 (95% CI = 0.000-0.08)] (p < 0.05) dan 8 gelas sehari [Adjusted OR = 0.001 (95% CI = 0.000-0.02)] (p < 0.05) mengurangkan risiko dalam kalangan wanita. Faktor-faktor risiko untuk lelaki adalah tabiat merokok [Adjusted OR = 16.2 (95% CI = 1.29-20.3)] (p < 0.05), pengambilan minuman berkarbonat 1-3 kali sebulan [Adjusted OR = 6.25 (95% CI = 1.04 - 40.7)] (p < 0.05) dan 1-6 kali seminggu [Adjusted OR = 12.5 (95% CI = 1.41-111) (p < 0.05). Pemakanan dan gaya hidup yang tidak sihat meningkatkan risiko penyakit batu karang ginjal dan pelbagai faktor risiko telah dijumpai untuk jantina yang berbeza.

Kata kunci: Penyakit batu karang ginjal; nefrolitiasis; faktor risiko; pemakanan; gaya hidup

## INTRODUCTION

The prevalence rate of kidney stone disease (KSD) has been reported to have increased in the world (Romero et al. 2010). In 1994, the National Health and Nutrition Examination Survey (NHANES) reported a KSD prevalence of 5.2%. A more recent NHANES data from 2007-2010, revealed an overall prevalence of 8.8%. According to the NHANES in 2012, 10.6% of men and 7.1% of women in the United States have been diagnosed with renal stone disease, compared to just 6.3% of men and 4.1% of women in 1994 (Scales et al. 2012). The risk of KSD was 13% among men and 7% among women (Pearle et al. 2005). Although renal stone can be cured, the subsequent disorder causes painful and recurrent episodes that lead to high medical costs and a lot of procedures (Pak 1991). Kidney stone formation has a high recurrence rate of nearly 30% to 50% after five years due to lack of proper control and management of risk factors (Saxena & Sharma 2010). Several etiological factors have been determined to contribute to KSD including unhealthy lifestyle and dietary factors. Several etiological factors can be adequately modified through diet as urine composition and super-saturation are directly related to diet (Dai et al. 2013). Other factors include epidemiology, biochemical and also genetic factors (Abbagani et al. 2010). Metabolic syndrome and obesity have also been indicated as the cause of KSD (Inci et al. 2012; Jeong et al. 2011). In terms of lifestyle factors, physical activity has been shown to reduce the risk of KSD by 31% (Sorenson et al. 2014). Smoking habits have also been shown to increase the risk of KSD (Tamadon et al. 2013). Numerous dietary factors such as protein, fibre, calcium, oxalate and specific beverages, as reported in previous studies, can alter urinary composition and super-saturation, but the findings were not consistent (Siener 2006). However, the impacts of dietary and lifestyle factors on kidney stone formation among Asians have not been fully investigated yet. Moreover, the dietary and lifestyle factors in Malaysia vary from other countries as well. Thus, the objective of this study is to examine the dietary and lifestyle factors in relation to the risk of kidney stone in certain multi-ethnic Malaysian adult population.

# MATERIALS AND METHODS

# SUBJECTS AND STUDY DESIGN

This study was a case-control study involving 81 patients with KSD from the Urology ward and outpatient clinic at Universiti Kebangsaan Malaysia Medical Centre; where they were recruited through convenience sampling. The centre is one of the main referral centres and it is also a teaching hospital located in Klang Valley, central of Malaysia. The inclusion criteria for cases were patients newly diagnosed with KSD for less than 6 months from June 2014 until November 2014. The diagnostic criteria were

made based on x-ray, ultrasound or scan results as stated in their medical records and aged between 18 to 80 years old. Another 81 patients were chosen as controls, matched with age ( $\pm$ 5 years), sex and ethnicity. The control group was comprised of healthy patients who underwent a routine examination at the urology clinic and did not have KSD based on x-ray, ultrasound and scan tests. The exclusion criteria for both cases and controls included patients with cancer, kidney disease, stroke, uncontrolled diabetes mellitus and hypertension. Patients with mental problems and pregnant women were also excluded from this study. The design of this study was approved by Universiti Kebangsaan Malaysia Medical Centre committee board and informed consent was obtained from all subjects.

#### DATA COLLECTION

Data were collected from subjects by trained interviewer using interviewer-administered questionnaires on sociodemographic, lifestyle and dietary factors. The training of interviewer, initial site survey and preliminary questionnaire testing were completed before data collection. For case subjects, the questionnaires assessed the lifestyle and dietary intake of subjects for the past 6 months before diagnosed with KSD while for control subjects the lifestyle and dietary intake were assessed for the past 6 months before the interview session. The anthropometry data was measured at the end of the session.

### SOCIODEMOGRAPHIC DATA

Sociodemographic data and health profile include education level, occupation, nature of job, monthly income, smoking habits and alcohol consumption, date of kidney stone diagnosis, treatment received, size of kidney stone, alternative treatment used, family history of KSD, past medical history and supplements consumption were obtained through interview or extracted from the medical records.

### PHYSICAL ACTIVITY

An international physical activity questionnaire (IPAQ) was used to assess the physical activity levels among subjects including walking activity, sedentary intensity activity and also high-intensity activity.

### DIETARY AND BEVERAGES INTAKE

Food consumption was assessed using a validated diet history questionnaire (Suzana et al. 2000). Case subjects were asked about their dietary intake before being diagnosed with KSD. Subjects were asked about the foods and drinks they regularly consumed for the past seven days, serving size and cooking method. Individual daily fluid intake was estimated as millilitre volume or glasses intake of plain water per day. In addition, the frequency of beverages consumption (i.e. tea, coffee, chocolate drink, malt drink, fruit juice, soda drink and cordial) was also assessed either less than once per month, 1-3 times per month, 1-6 times per week, once or more per week, or more than that per week.

## ANTHROPOMETRY MEASUREMENT

Height and weight were measured using the Leicester stadiometer and TANITA weighing scale to the nearest 0.01 m and 0.01 kg, respectively, using the standardized procedure proposed by (Lee & Nieman 2007) in order to determine and to calculate the body mass index (BMI). The fat percentage was assessed using the BIA Omron Hand-Held.

# STATISTICAL ANALYSES

Statistical Product and Service Solutions software 21.0 (SPSS Version 21.0) was used to carry out the analysis. The analysis was performed on men and women subjects separately because it is suggested that different hormone levels between men and women could result in different risks of developing kidney stones. In addition, men and women may have different behaviours and lifestyles, associated with kidney stone formation. The differences in proportions were tested using the chi-square test. The unconditional logistic regression was used to obtain odd ratios (OR) and 95% confidence intervals (95% CI) to estimate the association between dietary and lifestyle factors with risk of kidney stones. Only the variables that have proportional differences between case and control groups were regarded as confounders in this study and were adjusted for the multivariate analysis, i.e. binary logistic regression, enter method, at p < 0.05.

## RESULTS

### SOCIODEMOGRAPHIC DATA

A total of 81 cases and 81 controls were considered in this study which comprised of 55.6% men and 44.4% women. A majority of the subjects were Malays, followed by the Chinese and Indians (Table 1). The mean age  $\pm$  SD for cases and controls were  $55.6 \pm 12.5$  years and  $58.4 \pm 12.5$  years for men, while  $58 \pm 10.3$  years and  $57.8 \pm 9.7$  years for women, (p > 0.05) respectively. The highest percentage for men was in the age range of 60-69 years (26.7%) and 50-59 years for women (38.9%). A univariate analysis indicated that low education levels (i.e. primary schooled and never schooled) and diabetes mellitus increased the risk of KSD by approximately three folds in women (p < 0.05 for both parameters). In addition, a family history of stone disease increased the risk of KSD by three folds in men (p < 0.05). Supplement and herbs intake increased the risk of KSD by three folds in women (p < 0.05). However, there were no significant differences in the types of supplements and

herbs consumed with the risk of KSD in both men and women (Table 2 and 3).

Most of the patients were diagnosed with KSD in the year 2014 and the recurrence of KSD occurred after  $14.2 \pm 12.3$  years for men and  $10.4 \pm 8.6$  years for women. Besides that, one-fourth of the cases have sought for alternative medicine including the recitation of holy verses, usage of ointment, Chinese and Indian medicines and also the service of traditional healers (bomoh) to treat KSD. More than half of the cases have food beliefs related to treatment of KSD including barley water, white radish and watermelon (table not shown).

### SUPPLEMENTS AND HERBS INTAKE

There were no significant differences in terms of types of supplements intake towards the risk of KSD; even though supplement intake was a risk factor for KSD as shown in Table 2. It is because this study only compared the types of supplements based on the highest consumption among case and control subjects. The same trend was shown by women subjects in which their types of supplement intake did not show any relationship with KSD (Table 3).

# ANTHROPOMETRY DATA

As shown in Table 4, BMI and hip circumference were significantly higher in cases as compared to controls in both men and women; and the waist circumference was significantly higher in women cases compared to controls (p < 0.05 for all parameters). Thus, most of the cases fall into the overweight and obesity categories as shown in Figure 1 and Figure 2.

With respect to food intake, the cases had a significantly higher intake of energy, carbohydrate, protein and fat as compared to controls (p < 0.05 for all parameters) (Table 5). Furthermore, among the men patients, the intake of potassium, zinc and sugar was significantly higher in cases compared to controls; whilst among the women patients, cases had a higher intake of sodium, phosphorus, zinc and water as compared to controls (p < 0.05 for all parameters).

#### FOODS INTAKE

Table 6 shows the association of habitual foods intake with the risk of kidney stone formation among men and women. In an unadjusted analysis, the consumption of eggs, nuts and seafood was positively associated with KSD in both men and women. Dairy products and leafy vegetables intake were negatively associated with kidney stone formation in the unadjusted model for men. There was an association between the consumption of nuts ( $\geq 1$  time/week) and kidney stone formation for men and women according to the multivariate-adjusted model [Adjusted OR = 24.9 (95% OR = 1.12-54.9)] and [Adjusted OR = 31.4 (95% CI = 1.80-54.6)] (p < 0.05); while eggs (1-3 times/month) and beans

		Men	u			Women	u	
Variables	Case $(n = 45)$	Control $(n = 45)$	<i>p</i> value	OR (95% CI)	Case $(n = 36)$	Control $(n = 36)$	<i>p</i> value	OR (95% CI)
Ethnic Malay Chinese Indian	28(62.2) 15(33.3) 2(4.4)	28(62.2) 15(33.3) 2(4.4)			24(66.7) 8(22.2) 4(11.1)	24(66.7) 8(22.2) 4(11.1)	ı	
Religion Islam Buddha Hindu	28(62.2) 15(33.3) 2(4.4)	28(62.2) 15(33.3) 2(4.4)	ı	·	24(66.7) 8(22.2) 4(11.1)	24(66.7) 8(22.2) 4(11.1)	I	ı
Age (years) 19-29 30-39 40-49 50-59 60-69 ≥70	1(2.2)4(8.9)11(24.4)11(24.4)11(24.4)11(24.4)7(15.5)	$1(2.2) \\ 4(8.9) \\ 111(24.4) \\ 111(24.4) \\ 111(24.4) \\ 7(15.5) \\ 7(15.5) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 11(2.21) \\ 1$			$\begin{array}{c}1(2.8)\\0\\6(16.7)\\14(38.9)\\9(25)\\6(16.7)\end{array}$	$1(2.8) \\ 0 \\ 6(16.7) \\ 14(38.9) \\ 9(25.0) \\ 6(1.6.7) \\$	,	1
Age†	$55.6 \pm 12.5$	$58.4 \pm 12.5$	0.28		$58 \pm 10.3$	$57.8 \pm 9.7$	0.94	
Education level Low High	8(17.8) 37(82.2)	13(28.9) 32(71.1)	0.21	0.53 (0.19-1.45)	21(58.3) 15(41.7)	11(30.6) 25(69.4)	0.02*	3.18 (1.21-8.39)
Working status Working Not working	25(56.6) 20(44.4)	24(53.3) 21(46.7)	0.83	1.09 (0.48-2.51)	4(66.7) 12(33.3)	29(80.6) 7(19.4)	0.18	0.48 (0.16-1.42)
Working environment Office Outstation Field work Home	21(46.7) 22(48.9) 2(4.4) 0	23(51.1) 20(44.4) 2(4.4) 0	0.67	1.19 (0.52-2.73)	12(33.3)4(11.1)020(55.6)	14(38.9) 4(11.1) 0 18(50)	1.00	1.0 (0.23-4.35)
Family history of stone disease Yes No	18(40) 27(60)	8(17.8) 37(82.2)	0.02*	3.08 (1.17-8.13)	10(27.8) 26(72.2)	4(11.1) 32(88.9)	0.13	3.07 (0.86-10.9)
Diabetes Mellitus Yes No	16(35.6) 29(64.4)	11(24.4) 34(75.6)	0.25	1.70 (0.68-4.25)	17(47.2) 19(5.8)	8(22.2) 28(77.8)	0.02*	3.13 (1.12-8.71)

		Men	ue			Women	n	
Variables	Case $(n = 45)$	Control $(n = 45)$	<i>p</i> value	OR (95% CI)	Case $(n = 36)$	Control $(n = 36)$	<i>p</i> value	OR (95% CI)
Hypertension Yes No	20(44.4) 25(55.6)	19(42.2) 26(57.8)	0.83	1.09 (0.47-2.52)	21(58.3) 15(41.7)	15(41.7) 21(58.3)	0.15	1.96 (0.77-5.00)
Dyslipidemia Yes No	16(35.6) 29(64.4)	11(24.4) 34(75.6)	0.25	1.7 (0.68-4.25)	15(41.7) 21(58.3)	12(33.3) 24(66.7)	0.46	1.43 (0.55-3.73)
Heart Disease Yes No	4(8.9) 41(91.1)	3(6.7) 42(93.3)	0.69	1.36 (0.28-6.48)	2(5.6) 34(94.4)	4(11.1) 32(88.9)	0.39	0.47 (0.08-2.75)
Gout Yes No	6(13.3) 39(86.7)	4(8.9) 41(91.1)	0.71	1.58 (0.41-6.01)	3(8.3) 33(91.7)	1(2.8) 35(97.2)	0.61	3.18 (0.32-32.1)
Smoking habit Yes No	20(44.5) 25(55.6)	12(26.7) 33(73.4)	0.08	2.2 (0.91-5.33)			ı	
Amount of cigarettes ≤ 20 pieces >20 pieces	18(90) 2(10)	11(91.7) 1(8.3)	1.0	1.22 (0.09-15.1)			ı	
Alcohol consumption Yes No	10(22.3) 35(77.8)	6(13.4) 39(86.6)	0.27	1.86 (0.61-5.64)			I	
Supplement intake Yes No	29(64.4) 16(35.6)	20(44.4) 25(55.6)	0.06	2.26 (0.97-5.29)	26(72.2) 10(27.8)	16(44.4) 20(55.6)	0.02*	3.25 (1.22-8.67)
Physical activity level Low High	12(26.7) 3(73.3)	11(24.4) 34(75.6)	0.8 0.96	1.12 (0.44-1.21)	8(22.2) 28(77.8)	5(13.9) 31(86.1)	0.36 0.34	1.77 (0.52-6.05)
Total MET/min per week†	2126	2098	09.0	2339	2832	0.25		I

Types of supplement and herbs	Case $(n = 45)$	Control $(n = 45)$	p value	OR (95% CI)
Vitamin B				
Yes	5(11.1)	0	0.06	-
No	40(88.9)	45(100)		
Honey				
Yes	4(8.9)	1(2.2)	0.36	4.29(0.46-40.1)
No	41(91.1)	44(97.8)		
Vitamin C				
Yes	3(6.7)	6(13.3)	0.49	0.46(0.11-1.98)
No	42(93.3)	39(86.7)		
Calcium				
Yes	3(6.7)	3(6.7)	1.00	1.00(0.19-5.24)
No	42(93.3)	42(93.3)		· · · · · ·
Tongkat Ali				
Yes	3(6.7)	5(11.1)	0.71	0.57(0.19-2.55)
No	42(93.3)	40(88.9)		, ,
Multivitamin	. ,			
Yes	3(6.7)	4(8.9)	1.00	0.73(0.15-3.48)
No	42(93.3)	41(91.1)		· · · · · ·
Habatus sauda	. ,			
Yes	3(6.7)	0	0.24	-
No	42(93.3)	45(100)		
Ginger				
Yes	3(6.7)	0	0.24	-
No	42(93.3)	45(100)		
Jus delima		~ /		
Yes	1(2.2)	3(6.7)	0.62	0.31(0.32-3.18)
No	44(97.8)	42(93.3)		

Т	TABLE 2.	Compa	rison types o	f suppleme	ents intak	e betweer	n men ii	n cases an	d controls	[present as $n(\%)$ ]

\*Significant difference obtained by using Fisher Exact Test (p < 0.05)

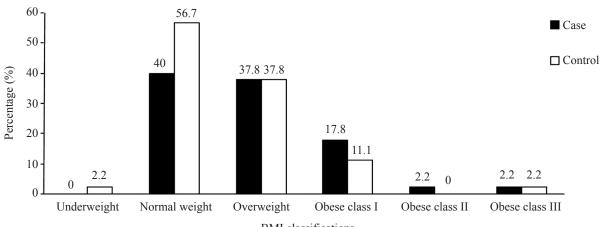
Types of supplement and herbs	Case $(n = 36)$	Control $(n = 36)$	p value	OR (95% CI)
Calcium				
Yes	11(30.6)	5(13.9)	0.10	2.64(0.81-8.62
No	25(69.4)	31(86.1)		
Vitamin C				
Yes	6(16.7)	4(11.1)	0.74	1.60(0.41-6.23
No	30(83.3)	32(88.9)		
Evening Primrose Oil				
Yes	4(11.1)	1(2.8)	0.36	4.37(0.46-41.2
No	32(88.9)	35(97.2)		× ×
Vitamin B				
Yes	4(11.1)	4(11.1)	1.00	1.00(0.23-4.34
No	32(88.9)	32(88.9)		×
Vitamin D				
Yes	1(2.8)	1(2.8)	1.00	1.00(0.06-16.2
No	35(97.3)	35(97.2)		× ×
Multivitamin				
Yes	2(5.6)	3(8.3)	1.00	0.65(0.10-1.20
No	34(94.4)	33(91.7)		× ×
Fish Oil				
Yes	2(5.6)	1(2.8)	1.00	2.05(0.18-23.8
No	34(94.4)	35(97.2)		× ×
Ginger				
Yes	2(5.6)	1(2.8)	1.00	2.05(0.18-23.8
No	34(94.4)	35(97.2)		<u></u>
Misai Kucing		× ,		
Yes	2(5.6)	2(5.6)	1.00	1.00(0.13-7.51
No	34(94.4)	34(94.4)		

\*Significant difference obtained by using Fisher Exact Test (p < 0.05)

Damanatan		Men			Women	
Parameter	Case $(n = 45)$	Control $(n = 45)$	<i>p</i> value	Case ( <i>n</i> = 36)	Control $(n = 36)$	<i>p</i> value
Weight (kg)	$74 \pm 13.1$	$68.9 \pm 12.7$	0.06	$66.1 \pm 14.1$	$60.4\pm11.3$	0.06
Height (cm)	$164 \pm 7.7$	$162\pm25.6$	0.35	$153\pm6.3$	$154 \pm 5.2$	0.51
BMI (kg/m <sup>2</sup> )	$27\pm4.8$	$24.9\pm4.4$	0.03*	$28.1\pm5.1$	$25.4\pm4.6$	0.01*
Waist circumference (cm)	$95.4\pm13.8$	$90.6\pm9.2$	0.06	$96.2\pm11.4$	$85.9\pm12.1$	<0.001**
Hip circumference (cm)	$101\pm8.7$	$94.7\pm15.1$	0.02*	$103\pm9.5$	$94.5\pm9.9$	< 0.001**
Waist/hip ratio	$0.94\pm0.08$	$0.93\pm0.05$	0.82	$0.93\pm0.07$	$0.91\pm0.07$	0.15
Fat percentage (%)	$27.0\pm4.7$	$26.0\pm4.5$	0.68	$35.0\pm5.9$	$34.2\pm4.9$	0.56
Total fat (kg)	19.7 ±5.3	$18.6\pm5.9$	0.34	$24.2\pm8.3$	$21.2 \pm 6.7$	0.09

TABLE 4. Anthropometry profiles of case and control subjects according to sex [present as mean ± standard deviation]

\*Significant difference obtained by using independent t-test (p < 0.05); \*\*Significant difference obtained by using independent t-test (p < 0.001)



BMI classifications

FIGURE 1. BMI classifications for men subjects

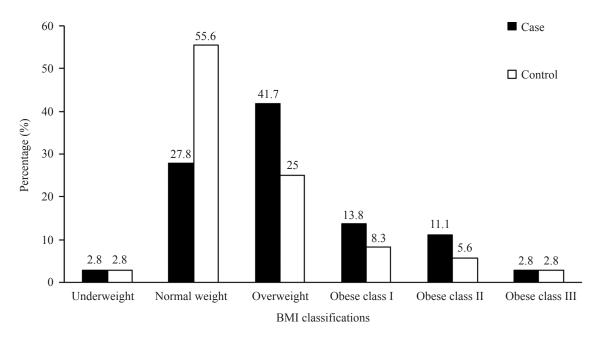


FIGURE 2. BMI classifications for women subjects

Description		Men			Women	
Parameter —	Case $(n = 45)$	Control $(n = 45)$	p value	Case ( <i>n</i> = 36)	Control $(n = 36)$	p value
Energy (kcal)	$2088\pm355$	$1731\pm244$	<0.001**	$1878\pm276$	$1633\pm203$	< 0.001**
Carbohydrate (g)	$340\pm192$	$274\pm40.6$	0.03*	$272\pm45.1$	$248\pm37.9$	0.02*
Percentage of carbohydrate (%)	$59.9 \pm 5.34$	$60.7\pm4.3$	0.41	$57.9\pm4.6$	$59.7\pm6.7$	0.21
Protein (g)	$74.2 \pm 12$	$67.8 \pm 10.9$	0.007*	$68.8\pm9.2$	$62.9\pm8.9$	0.008*
Percentage of protein (g)	$14.5\pm1.9$	$14.9\pm2.0$	0.45	$14.8\pm1.7$	$15.0\pm1.9$	0.56
Fat (g)	$62.3 \pm 19.9$	$48.5\pm12.7$	< 0.001**	$57.1 \pm 13.7$	$48.8\pm13.4$	0.01*
Percentage of fat (%)	$25.9\pm4.8$	$24.5\pm4.4$	0.15	$27.3\pm4.3$	$25.5\pm5.8$	0.18
Sodium (mg)	$2961 \pm 1182$	$2239\pm895$	0.17	$2660\pm995$	$1880\pm631$	< 0.001 **
Potassium(mg)	$1407\pm412$	$1138\pm289$	0.001*	$1281\pm304$	$1141\pm405$	0.10
Calcium (mg)	$439 \pm 150$	$515\pm294$	0.13	$468 \pm 156$	$429\pm166$	0.31
Oxalate (mg)	$266\pm221$	$222\pm135$	0.26	$237\pm138$	$217\pm121$	0.52
Magnesium (mg)	$134\pm42.2$	$150\pm18.9$	0.60	$197\pm378$	$103\pm36.6$	0.14
Phosphorus (mg)	$1016\pm379$	$892\pm349$	0.11	$925\pm248$	$807\pm212$	0.04*
Zinc (mg)	$3.5\pm1.8$	$2.4 \pm 1.8$	0.001*	$3.1 \pm 1.8$	$2.2\pm0.8$	0.01*
Vitamin C (mg)	$119\pm4.0$	$106\pm7.0$	0.43	$101\pm61.6$	$107\pm69.8$	0.70
Fibre (g)	$8.5\pm4.5$	$6.9\pm2.9$	0.05	$8.1\pm2.9$	$9.4 \pm 5.1$	0.21
Sugar (g)	$54.7\pm20.8$	$45.7\pm19.3$	0.04*	$49.9\pm24.7$	$45.4\pm25.9$	0.44
Water (ml)	$1771\pm637$	$2000\pm740$	0.12	$1737\pm531$	$2144 \pm 491$	0.001*

TABLE 5. Macro and micronutrients intake for case and control subjects according to sex [present as mean ± standard deviation]

\*Significant difference obtained by using independent t-test (p < 0.05); \*\*Significant difference obtained by using independent t-test (p < 0.001)

(1-6 times/week) showed positive association for women in the multivariate-adjusted model [Adjusted OR = 33.8 (95% CI = 2.24-40.7)] and [Adjusted OR = 80.8 (95% CI = 2.63-97.1)] (p < 0.05). Besides that, the consumption of leafy vegetables and fruits intake ( $\geq 1$  time/day) was negatively correlated with kidney stone formation for women in the multivariate-adjusted model [Adjusted OR = 0.06 (95% CI = 0.01-0.76)] and [Adjusted OR = 0.016 (95% CI = 0.5-0.98)] (p < 0.05). The consumption of grain and oil has not been analyzed since the consumption of that type of foods among all cases and controls were  $\geq 3$  times/day.

#### BEVERAGES INTAKE

Table 7 shows that six and eight glasses of plain water intake a day were able to reduce the risk of KSD for both men and women. Besides that, the consumption of cordial drinks of 1-3 times/month was found to increase the risk of KSD in men as compared to the intake of fewer than once per month. The intake of cordial drinks once or more daily was also found to increase the risk of KSD as compared to consumption of fewer than once a month, for both men and women. Furthermore, the consumption of carbonated drinks 1-3 times per month was found to increase the risk of KSD for both men and women subjects. The intake of carbonated drinks 1-6 times per week also showed a positive association with KSD for men subjects (p < 0.05for all parameters).

#### MULTIVARIATE ANALYSIS

All the risk factors that were found to be significant using the univariate test were considered independent parameters for multivariate tests, as shown in Table 8. The results indicated that for men, the consumption of tobacco products [Adjusted OR = 16.2 (95% CI = 1.29-203.5)] (p < 0.05), supplements [Adjusted OR = 24.4 (95% CI = (1.17-50.1) (p < 0.05) and the carbonated beverages of 1 to 6 times a week [Adjusted OR = 6.25 (95% CI = 1.04-40.7)] and more than once daily [Adjusted OR = 12.54(95% CI = 1.41-111.2)] (p < 0.05) were the risk factors for KSD. Whilst, among women, the risk factors for KSD were consumption of supplements [Adjusted OR = 57.83(95% CI = 2.1-157.57)] (*p* < 0.05) and diabetes mellitus [Adjusted OR = 27.55 (95% CI = 1.43-53.3)] (p < 0.05). On the other hand, the intake of plain water of at least six glasses [Adjusted OR = 0.001 (95% CI = 0.000 - 0.08)] (p < 0.05) and eight glasses daily [Adjusted OR = 0.001 (95%) CI = 0.000-0.02] (p < 0.05) were found to reduce the risk among women.

# DISCUSSION

This study highlighted the contribution of a wide range of dietary intake and use of beverages to the risk factors of KSD according to sex since the variation in hormone

			Men				Women	
Variables	Case $(n = 45)$	Control $(n = 45)$	Crude OR (95% OR)	Adjusted OR <sup>‡</sup> (95% OR)	Case $(n = 36)$	Control $(n = 36)$	Crude OR (95% OR)	Adjusted OR‡ (95% OR)
Root stock								
<1 time/months	28	29			, 18	28		1
1-3 times/months 1-6 times/week	5 12	6 10	0.86(0.23 - 3.15) 1.24(0.46 - 3.33)	0.02(0.01-3.18) 0.37(0.05-2.63)	1 17	so m	0.34(0.04-3.17) 9.67(2.47-37.8)**	1.41(0.009-216) 9.38(1.09-80.3)
	ļ	9				3		
1 uuers <1 time/months	13	17			14	19	-	
1-3 times/months	12		2.24(0.68-7.28)	1.24(0.11-13.1)	7	ς ν	0.62(0.10-3.66)	0.46(0.019-11.3)
1-6 times/week	20	21	1.24(0.48-3.21)	0.14(0.01-1.55)	20	12	2.56(0.94-6.96)	5.45(0.78-37.9)
Leafy vegetables								
<1 time/months	11	5	1	1	5	5		1
1-6 time/week	20	10	1.05(0.28 - 3.89)	2.46(0.12-50.7)	10	13	1.26(0.33-4.79)	1.37(0.16-11.4)
≥1 time/day	14	30	0.23(0.06-0.81)*	0.10(0.01 - 1.63)	12	18	0.23(0.05-1.03)	$0.06(0.01 - 0.76)^{***}$
Bean								
<1 times/months	16	13	1	1	4	6	-	1
1-3 times/months	9	L	0.69(0.18 - 2.58)	3.07(0.23-40.1)	4	4	2.25(0.37 - 13.9)	13.8(0.15-26.7)
1-6 times/week	23	25	0.74(0.29 - 1.88)	0.42(0.06-2.77)	28	23	2.45(0.66-9.04)	80.8(2.63-97.1)***
Fruits								
<1 time/months	7	4	1	1	2	ę	-	1
1-3 times/months	ŝ	ς	0.57(0.07-4.29)	0.27(0.01-5.32)	б	1	4.50(0.25-60.6)	1.18(0.01 - 350)
1-6 times/week	28	26	0.61(0.16-2.34)	0.14(0.01 - 1.49)	9	18	2.17(0.33-14.3)	0.31(0.10-10.3)
≥1 time/day	7	12	0.33(0.07 - 1.55)	0.15(0.01-2.06)	5	14	0.40(0.05 - 3.27)	0.016(0.50-0.98)***
Eggs								
<1 time/months	11	8	1	1	5	15	1	1
1-3 times/months	7	21	0.24(0.06-0.84)*	0.33(0.03-3.83)	15	6	4.2(1.15 - 16.4)*	33.8(2.24-40.7)***
1-6 times/week	27	16	1.14(0.37 - 3.43)	2.54(0.31-20.5)	15	14	3.82(1.06-13.8)*	3.09(0.31 - 30.7)
Dairy products								
<1 time/months	40	34	1	1	19	17	1	
1-6 times/week	4	С	1.13(0.23-5.42)	5.16(0.28-93.3)	6	5	1.61(0.45 - 2.76)	0.24(0.015 - 4.08)
≥1 time/day	1	8	$0.10(0.01-0.89)^{**}$	0.14(0.01-2.55)	8	14	0.42(0.14-1.27)	0.16(0.02 - 1.28)
Meat								
1-6 times/week	14	18	1	1	16	14	1	1
≥1 time/day	31	27	1.47(0.61-3.51)	1.42(0.26-7.54)	20	22	0.72(0.28 - 1.85)	0.87(0.77 - 4.41)

			Men				Women	
Variables	Case $(n = 45)$	Control $(n = 45)$	Crude OR (95% OR)	Adjusted OR; (95% OR)	Case $(n = 36)$	Control $(n = 36)$	Crude OR (95% OR)	Adjusted OR; (95% OR)
Seafood								
<1 time/months	25	36			19	28	1	-
1-3 times/months	2	4	0.72(0.12-4.2)	2.34(0.09-58.4)	5	7	4.03(0.71-22.9)	21.4(0.40-1120)
1-6 times/week	18	5	4.89(1.59-15.0)*	13.75(1.03-183)	12	9	3.22(1.03-10.1)*	3.02(0.34-26.9)
Nuts								
< 1 time/month	23	39	1	1	12	24	1	1
2-3 times/month	7	2	5.93(1.13-31.0)**	17.7(0.71-44.9)	8	6	1.40(1.26-4.59)	4.25(0.43-41.6)
$\geq 1$ time/week	15	4	6.35(1.88-21.5)**	24.9(1.12-54.9)***	16	С	10.7(2.59-43.9)**	31.4(1.80-54.6)***
Others								
< 1 time/month	22	29		-	22	24	1	
2-3 times/month	7	7	1.31(0.40-4.31)	0.24(0.01 - 3.08)	6	6	2.87(0.99 - 8.31)	3.59(0.65 - 19.9)
$\geq$ 1 time/week	16	6	2.34(0.87-6.28)	3.57(0.54-23.5)	5	ŝ	1.15(0.26-4.59)	3.97(0.53-29.8)

Adjusted for education level, family history of kidney stone disease, diabetes mellitus, supplement intake, BMI, waist circumference, nutrients intake, plain water intake, cordial drink intake and carbonated drink intake; *Significant difference obtained using chi square test ( $p < 0.05$ ); **Significant difference obtained using chi square test ( $p < 0.05$ ); **Significant difference obtained using chi square test ( $p < 0.05$ ); **Significant difference obtained using chi square test ( $p < 0.05$ ); ***Significant difference obtained using logistic binary regression, enter method ( $p < 0.05$ ); Odts Ratio, Adjusted OR: Adjusted OR: Adjusted Odts Ratio, CI: Confidence Intervals
--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

TABLE 6. Continue

			Men Women			Women		
Water and drink consumption	Case $(n = 45)$	Control $(n = 45)$	<i>p</i> value	OR (95% CI) Adjusted OR‡ (95% CI)	Case $(n = 36)$	Control $(n = 36)$	<i>p</i> value	OR (95% CI) Adjusted OR‡ (95% CI)
Plain water intake		Ĩ,		-	11111			-
<pre></pre>	11(24.4)	5(0.7)	010		4(11.1)	1(2.8)		
4 glasses	1/(3/.8)	6(07)6	0.48 0.39	0.52(0.11-2.33) 0.40(0.03-3.16)	(8.20)61	4(11.1)	0.89 0.52	2.78(0.10-13.7) 2.78(0.13-61.1)
6 glasses	11(24.4)	17(37.8)	0.02**	0.17(0.04-0.78)	10(27.8)	20(55.6)	0.04**	0.13(0.01-1.27)
)		0.06	0.13(0.01-1.02)	~	~	0.09	0.09(0.05-1.44)	
8 glasses	6(13.3)	16(35.5)	$0.005^{**}$ $0.004^{***}$	0.10(0.02-0.49) 0.03(0.02-0.33)	3(8.3)	11(30.5)	$0.02^{**}$ 0.07	0.06(0.005 - 0.86) 0.05(0.002 - 1.28)
Tea								
<1 time/month	3(6.7)	5(11.1)		1	6(16.7)	8(22.2)		1
1-3 times/month	1(2.2)	2(4.4)	1.00	0.83(0.05 - 13.6)	3(8.3)	3(8.3)	1.00	1.33(0.19-9.08)
			0.83	0.69(0.03 - 18.2)			0.91	0.67(0.07 - 10.1)
1-6 times/week	8(17.8)	10(22.2)	1.00	1.33(0.24-7.34)	11(30.6)	5(13.9)	0.15	2.93(0.66-13.0)
			0.53	2.00(0.23 - 17.1)			0.78	1.41(0.13-14.9)
≥1 time/day	33(73.3)	28(62.2)	0.47	1.96(0.43-8.96)	16(44.4)	20(55.6)	0.92	1.01(0.31 - 3.71)
			0.35	2.41(0.38-15.4)			0.18	0.28(0.04-1.77)
Chocolate drink								
<1 time/month	12(26.7)	17(37.8)		1	11(30.6)	18(50)		1
1-3 times/month	3(6.7)	2(4.4)	0.45	2.13(0.31-14.7)	6(16.7)	4(11.1)	0.28	2.45(0.56-10.7)
			0.24	4.94(0.34-71.7)			0.37	2.38(0.35 - 16.2)
1-6 times/week	22(48.8)	15(33.3)	0.23	2.07(0.77-5.58)	12(33.3)	10(27.8)	0.24	1.96(0.64-6.05)
			0.15	2.64(0.69-9.96)			0.30	2.21(0.49-10.0)
≥1 time/day	8(17.8)	11(24.4)	0.96	1.03(0.32-3.29)	7(19.4)	4(11.1)	0.17	2.86(0.68-12.1)
			0.04	1.1/(0.23-3.444)			0.11	(0.76-17.0)60.4
Coffee				-				-
<1 ume/monut	14(51.1)	(1.15)41 1/0 0)1	1 00	1 75/0 79 5 65)	(0.00)	(/.14)(1)	0 71	T 1 1 1 2 201
	(1.11)c	4(0.7)	0.73	1.59(0.11-22.1)	4(11.1)	(4.61)6	0.29	0.0(0.14-2.02) 0.41(0.08-2.21)
1-6 times/week	15(33.3)	22(48.9)	0.45	0.68(0.25-1.83)	8(22.2)	8(22.2)	0.63	0.75(0.23-2.45)
	~		0.56	0.69(0.19-2.40)	~	~	0.38	0.54(0.13-2.16)
≥1 time/day	11(24.4)	5(11.1)	0.23	2.20(0.61-7.99)	4(11.1)	8(22.2)	0.19	0.38(0.09-1.48)
			0.43	1.85(0.39 - 8.58)			0.24	0.37(0.07-1.93)

imntion with kidney stone risk according to sex TABLE 7 Associations between fluid and her

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Continued

			Men			women		
Water and drink consumption	Case $(n = 45)$	Control $(n = 45)$	<i>p</i> value	OR (95% CI) Adjusted OR‡ (95% CI)	Case $(n = 36)$	Control $(n = 36)$	<i>p</i> value	OR (95% CI) Adjusted OR‡ (95% CI)
Malted drink				-				-
<1 time/month	37(82.2)	39(7).60			24(66.7)	28(77.8)		_
1-3 times/month	3(6.7)	2(4.4)	0.68	1.58(0.25-10.0)	7(19.4)	3(8.3)	0.30	2.72(0.63-11.7)
			0.13	(1.) - 900.000			70.7	1.18(0.28-12.4)
1-6 times/week	2(4.4)	2(4.4)	1.00	1.05(0.14-7.87)	5(13.9)	5(13.9)	1.00	1.17(0.30-4.52)
	ĺ		0.99 0	1.01(0.21-4.75)			0.92	1.03(0.14-7.39)
≥l tıme/day	3(6.7)	2(4.424)	0.68 0.16	1.58(0.25-10.0) 7.36(0.56-97.1)	·		·	I
Fruit inice				~				
<pre></pre>	18(40)	26(57.8)		_	12(33 3)	15(417)		-
1-3 times/month	8(17.8)	3(6.7)	0.09	3.85(0.89-16.5)	6(16.6)	7(19.4)	0.92	1.07(0.28-4.05)
			0.19	2.87(0.59-14.1)			0.83	1.08(0.12-5.48)
1-6 times/week	18(40)	14(31.1)	0.18	1.86(0.74-4.67)	15(41.7)	11(30.6)	0.36	1.71(0.58-5.05)
			0.20	(01.C-20.0)6/.1			0.70	(10.0-67.0)
≥l time/day	1(2.2)	2(4.4)	1.00 0.88	0.72(0.06-8.58) 0.81(0.05-12-9)	3(8.3)	3(8.3)	0.19	1.25(0.21-7.35) 5.63(0.40-77.3)
			00.0				(1.0	
Cordial drink								
<1 time/month	22(48.9)	31(68.9)		1	15(41.7)	20(55.6)		1
1-3 times/month	9(20)	1(2.2)	0.006**	12.7(1.49-107)	7(19.4)	10(27.8)	0.91	0.93(0.29-3.02)
			$0.02^{***}$	14.1(1.56-126)			0.99	1.01(0.23-4.50)
1-6 times/week	7(15.6)	13(28.9)	0.61	0.76(0.26-2.21)	9(25)	6(16.7)	0.27	2.00(0.58-6.85)
		c	0.96	0.95(0.28-3.35)		¢	0.85	1.16(0.25-5.51)
≥1 time/day	(0.01)/	D	0.099	•	( <i>V</i> .51)c	D	0.04/*** 0.99	I
Carbonated drink					ĺ			
<1 time/month	10(22.2)	25(55.6)	$0.004^{*}$	1	15(41.7)	25(69.4)	0.04*	1
1-3 times/month	17(37.8)	9(20)	$0.007^{***}$	4.72(1.59-14.1)	13(36.1)	7(19.4)	0.22	3.09(1.01-9.48)
			$0.01^{*}$	7.59(1.74-33.1)			0.19	2.63(0.57-12.2)
1-6 times/week	17(37.8)	11(24.4)	$0.02^{***}$	3.86(1.35-11.1)	5(13.9)	3(8.3)	0.97	2.78(0.58-13.3)
			0.31	5.04(1.23-20.6)			0.29	1.05(0.07 - 15.1)
≥1 time/day	1(2.2)	0	1.00	I	3(8.3)	1(2.8)	0.23	5.00(0.48-52.5)
								6.96(0.29-165)

Variables –		Men	Women	
Variables –	p value	Adjusted OR <sup>‡</sup> (95% CI)	p value	Adjusted OR <sup>‡</sup> (95% CI)
Education level Low High	0.99	0.99(0.99-1.01)	0.59	2.52 (0.09-72.6)
Family history of kidney stone Yes No	0.32	4.95(0.22-112)	0.62	5.12(0.09-30.9)
Diabetes Mellitus Yes No	0.42	2.87(0.22-37.1)	0.02*	27.6(1.43-53.3)
Smoking Habits Yes No	0.03*	16.2(1.29-203)	-	-
Supplement intake Yes No	0.04*	24.7(1.17-50.1)	0.01*	57.8 (2.1-157)
BMI (kg/m <sup>2</sup> )	0.30	1.39(0.74-2.61)	0.56	1.21(0.64-2.29)
Waist circumference (cm)	0.43	0.92(0.75-1.13)	0.73	1.04(0.82-1.33)
Hip circumference (cm)	0.75	1.05(0.77-1.44)	0.39	1.11(0.88-1.41)
Energy (kcal)	0.20	1.01(0.99-1.01)	0.48	0.99(0.99-1.01)
Carbohydrate (g)	0.23	1.03(0.99-1.07)	0.55	0.98(0.91-1.05)
Protein (g)	0.54	1.05(0.90-1.21)	0.62	1.06(0.84-1.35)
Fat (g)	0.44	1.05(0.92-1.20)	0.15	1.20(0.96-1.32)
Sodium (mg)	0.43	1.00(0.99-1.01)	0.29	1.00(0.9-1.01)
Potassium (mg)	0.26	1.00(0.99-1.01)	0.08	0.99(0.99-1.00)
Zinc (mg)	0.12	3.35(0.74-15.2)	0.11	4.24(0.73-24.6)
Phosphorus (mg)	0.08	0.99(0.98-1.00)	0.88	1.00(0.99-1.01)
Sugar (g)	0.57	0.98(0.93-1.04)	0.13	0.86(0.72-1.04)
Water (ml)	0.11	0.99(0.99-1.00)	0.08	0.99(0.98-1.00)
BMR (kcal)	0.91	0.99(0.99-1.01)	0.15	0.96(0.92-1.01)
Plain water intake (daily) <2 glasses 4 glasses 6 glasses 8 glasses	1 0.42 0.69 0.38	1 4.14(0.14-128) 0.54(0.02-11.7) 0.18(0.004-8.6)	1 0.08 0.02* 0.01*	1 1.21(0.00-1.99) 0.001(0.00-0.08) 0.001(0.00-0.02)
Cordial drink intake <1 time/month 1-3 time/month 1-6 time/week ≥1 time/day	1 0.22 0.20 0.99	1 39.8(0.11-145) 0.21(0.02-2.31)	1 0.17 0.71 0.99	1 0.42(0.04-42.2) 9.05(0.38-21.8)
Carbonated drink intake <1 time/month 1-3 times/month 1-6 times/week ≥1 time/day	1 0.04* 0.02* 1.00	1 6.25(1.04-40.7) 12.5(1.41-111)	1 10.29 0.99 0.42	1 3.26(0.37-28.9) 1.02(0.07-15.6) 4.66 (0.11-19.8)

TABLE 8. Multivariate analyses of risk factors of kidney stone disease

Adjusted for education level, family history of kidney stone disease, diabetes mellitus, supplement intake, BMI, waist circumference, nutrients intake, plain water intake, cordial drink intake and carbonated drink intake; \*Significant difference obtained using binary logistic regression, enter method (p < 0.05); Adjusted OR: Adjusted Odds Ratio, (-): no value

levels will contribute to different factors in the prevalence of KSD (Liufang 2003). Nevertheless, regardless of sex, supplements such as vitamins and minerals and also herbs were found to increase the risk of kidney stone formation by 24% in men and 58% in women. As in par with the findings made from a study by Dai et al. (2013), it also could not differentiate the types of supplements with the risk of KSD. However, vitamin B, vitamin C, vitamin D and vitamin E are suggested to have protective effects on kidney stone formation in previous studies, although the findings are inconsistent (Goldfarb et al. 2005; Curhan et al. 1996). The effects of calcium intake on kidney stone formation are the most controversial part in previous reports. Some researchers believe that calcium can reduce the risk of kidney stone formation by decreasing the gastrointestinal oxalic acid salt intake (Curhan 1999), whereas other studies claimed contrasting conclusions (Curhan et al. 2004; Sowers et al. 1998).

The explanation of the null association in this study may be partly because of the low exposure rate of dietary supplements. Alternatively, dietary supplements might take a long time to produce effects on kidney stone formation (Dai et al. 2013). However, studies have showed that supplements such as vitamin C can increase the risk of stone formation (Chamers et al. 1986). Vitamin C can be metabolized to form oxalate, which can increase oxalate excretion and hence trigger the risk of calcium oxalate stone formation (Curhan et al. 1999; Gerster 1997). Most of the oxalate found in urine is usually formed endogenously as a metabolic end product of glycoxylic (50% to 70%) and ascorbic acid (30% to 50%), with minor contributions by gelatin, tryptophan, phenylalanine, tyrosine, aspartic acid, creatinine and purines (Urivetzky et al. 1992). A few of previous studies have been focused on the effects of vitamin C and oxalate excretion on calcium stone forming patients (Tiselius & Almgard 2001; Heckes et al. 1993). Three studies have reported a significant increase from 31% to 100% in urinary oxalate after vitamin C was supplemented at doses from 0.5 to 2 g per day (Chalmers et al. 1986, Urivetzky et al. 1992; Tiselius & Almgard 2001).

This study also found that smoking habits among men increased the risk of KSD by 16%, as reported by a casecontrol study on 102 cases diagnosed with nephrolithiasis and 121 age-matched healthy controls in the Iranian population (Tamadon et al. 2013). Tobacco consumption will increase serum levels of cadmium and thus increase the risk of KSD (Scott et al. 1982). Furthermore, Mooser et al. (1989) found that there were significant changes in the plasma arginine vasopressin (AVP) ( $0.8 \pm 0.3$  pg/ mL) before and  $(4.2 \pm 4.1 \text{ pg/mL})$  after smoking (p = 0.001). Arginine vasopressin acts as an anti-diuretic agent which will reduce urine output. In addition, smoking also increases the production of reactive oxygen species and causes oxidative stress in kidneys, leading to kidney injury (Obatta et al. 2000). This injury increases nucleation, crystal accumulation and retention in the kidneys (Khan 2006).

Diabetes mellitus was found to increase the risk of KSD among women by 27%. Diabetes mellitus is associated with insulin resistance and changes in renal ammonium production which will increase the acidity of urine, reduce citrate in the urine and can further lead to high amount of calcium in the urine (Weinberg et al. 2014). This condition can contribute to the formation of uric acid stones and calcium stones (Cameron et al. 2006). In addition, the simultaneous occurrence of the metabolic syndrome, hyperglycaemia, hyperlipidaemia, hypertension and obesity show a high-risk ratio for the prevalence of kidney stone disease (Jeong et al. 2011). This study also revealed that obesity indices including high BMI, waist and hip circumferences increased the risk of KSD in univariate analysis but the findings were not significant in the multivariate model, probably due to the small sample size. Other larger prospective studies have proved that obesity as a predictor of KSD (Sorenson et al. 2012; Taylor et al. 2005; Semins et al. 2010). Obesity is associated with insulin resistance, hyperinsulinemia and metabolic syndrome that can lead to the formation of calcium kidney stones. A metabolic trial has demonstrated that insulin resistance is associated with the production of ammonium kidney (Abate et al. 2004). Changes in acid excretion in the kidneys can lead to hypocitraturia, an important risk factor for calcium nephrolithiasis (Coe et al. 1992). Hyperinsulinemia may contribute to the formation of calcium kidney stones by increasing the excretion of calcium in the urine (Nowicki et al. 1998). A large body size can also increase the excretion of uric acid and oxalate in urine and it is a risk factor for renal calcium stone formation (Coe et al. 1980).

Higher energy and macronutrients intake have shown to be associated with KSD as reported by Meschi et al. (2012) in a case-control study among 143 women with recurrent idiopathic calcium nephrolithiasis and 170 healthy women. This study was not able to show the contribution of macro and micronutrients in the multivariate analysis model. However, a high intake of carbonated drinks, which are usually rich in sugar, was found to increase the risk of KSD in men by 6% for consumption of one to six times per week and up to 12% for intake of more than once daily. Ferraro et al. (2013) also found that the intake of carbonated drinks can increase the formation of kidney stones by 23%. The consumption of carbonated drinks and cordials was associated with KSD due to the high fructose content. Fructose increases the excretion of calcium oxalate and high uric acid in the urine (Taylor & Curhan 2007). In addition, Saldana et al. (2007) have also reported that taking two or more carbonated drinks a day is associated with diabetes, high blood pressure and KSD.

Calcium intake and the risk of KSD have been widely studied. In this study, there were no significant differences between the case subjects and control subjects (p > 0.05). These findings coincide with the results of the case-control study by Meschi et al. (2012). Furthermore, some studies also showed that individuals with calcium kidney stones

have lower calcium intake compared to control subjects (Al Zahrani et al. 2000). A low dietary intake of calcium has been known to be a risk factor for the formation of calcium nephrolithiasis because it tends to increase the absorption of oxalate in the digestive system (Curhan et al. 1993). Calcium in the digestive tract will bind oxalate from food and avoid the oxalate from entering the blood or urinary tract, where it can form kidney stones (Holmes & Assimos 2004). Among the women in this study, phosphorus intake was also higher for cases as compared to controls (p < 0.05). High phosphorus intake is associated with the reduction of calcium absorption in the intestinal tract and this will increase the absorption of oxalate (Taylor & Curhan 2007).

Oxalate is a factor that is known to be associated with triggering the risk of KSD. However, this study found that the average intake of oxalate was not significantly different between case and control subjects. The foods high in oxalate resources taken by the subjects were tea, beans, spinach, chocolate sourced food, tempeh and tofu. The results of oxalate were similar to the study by Meschi et al. (2012). Oxalate was not the main factor for the formation of kidney stones in these studies. This is probably due to the fact that the absorption of oxalate when taken together with other foods was only 6% for each person and increased slightly when oxalate intake increased (Holmes et al. 2001). This is due to the regression of process of oxalate absorption because of the saturation of oxalate carrier or saturation of calcium oxalate in the intestinal lumen, which can cause crystallization (Holmes et al. 1994). Therefore, it can be concluded that the absorption of oxalate is also influenced by the intake of calcium food sources (Borghi et al. 2002). The findings were in contrast to the study by Krishna (2011) in which the study found a relationship between the resource consumption and the incidence of calcium oxalate KSD in Indonesia. This is consistent with the theory that the origin of oxalate in the body (endogenous) is from the food that we eat and in general, the metabolism of vitamin C will form crystals with the calcium which can cause KSD (Penniston 2014). Future studies need to be considered with a more specific dietary methodology such as using a food frequency questionnaire (FFQ) of calcium or oxalate in order to investigate the role of these elements or other nutrients related to KSD.

Previous studies reported that vegetables and fruits with high fibre are beneficial in preventing stone formation (Rotily et al. 2000) whereas others claimed that the excessive consumption of oxalate in vegetables and fruits is directly related to kidney stones (Meschi et al. 2004). In this study, root-stock food, tubers and fruits were not associated with kidney stones. An intriguing finding in this study was that the bean products played a significant risk effect on kidney stone formation among the women. Besides that, Massey et al. (2001) reported that soybean seeds have a high level of oxalate which might cause phytic acid salt stone formation. However, the association of eggs with kidney stone formation was contradicted by the study conducted by Dai et al. (2013). The consumption of eggs, oil, dairy products, meat and fish had no association with kidney stones in a multivariate analysis for both men and women.

Intake of water for at least six to eight glasses a day was found to reduce the risk of KSD among women by 99.9%. Dai et al. (2013) also showed that water intake of 2000 ml/day was able to reduce the risk of KSD compared to subjects with water intake of 500 ml/day [OR = 0.57 (95% CI = 0.36-0.88)]. Drinking less than six to eight glasses a day can reduce the amount of urine and thus increase the concentration of salt-forming stones such as calcium, oxalate and uric acid; and reduce absorption of inhibitors such as citrate, glycosaminoglycans and nephrocalcin (Awasthi et al. 2011).

Fluid intake has an association with climate change. It has been well documented that the occurrence of urinary stones is higher in countries with warm or hot climates, probably due to low urinary output and scant fluid intake (López & Hoppe 2010). These are some of the factors that contribute to the geographical pattern that has characterized the North American and Afro-Asian stone belts. Also, in a given population, stone recurrence is higher in summer and fall than in winter and spring (Sternberg et al. 2005). In a North American study, the prevalence of stones tends to increase in line with the average annual temperature (5.2°C in North Dakota to 22°C in Florida) and sunlight index (14.6 in Washington state to 39.7 in Florida) (Soucie et al. 1996).

Besides that, the debate on the relationship between the nature of work and urinary stone disease is still continuous. Fatemeh et al. (2009) found that workers who are chronically exposed to the hot environment and significantly sweat are at greater risk of urinary stones. In our subjects, there were no significant differences of KSD between office and manual workers. A similar finding has been reported by Hussein et al. (2013), stating that there were no significant differences in the prevalence of urinary stone between those two groups of workers with urinary biochemical parameters.

Other beverages such as tea and coffee showed no effect on KSD in the present study and also another prospective study by Ferraro et al. (2013). However, a cross-sectional study by Awasthi et al. (2000) have revealed that the daily consumption of tea and coffee may increase the risk of kidney stones formation as tea and coffee are a source rich in calcium oxalate and act as a diuretic (Liebman & Murphy 2007). However, the phytochemical content and antioxidant properties such as chlorogenic properties found in coffee and tea can reduce the risk of KSD (Stalmach et al. 2010; Samanidou et al. 2012).

This study highlighted the role of dietary and lifestyles factors on KSD among the multi-ethnic Malaysian adult population in the Klang Valley. It is one of the very few studies that include both sex in examining the risk factors of KSD. However, it should be kept in mind that this study is a case-control study, thus the results should be treated with caution. Recall bias might exist and residual confounding by imprecisely measured or unmeasured factors remain possible for our findings. There is a need to conduct a larger prospective study in order to investigate the roles of dietary and lifestyles in KSD. Another limitation of this study was the uneven distribution of races among the subjects, especially the number of Indian subjects in this study which was very low. In addition, the types of kidney stone diseases suffered by patients in this study were not known as the detection for types of kidney stones after the surgery was not a routine at the study location. The use of the diet history also caused underreported and overreported diet intake and affected the results of the study. Future studies should combine the diet history with other dietary methodology such as FFQ.

# CONCLUSION

In conclusion, unhealthy dietary intake, excessive intake of carbonated drinks and inadequate intake of plain water, together with smoking habits, supplement consumption and the presence of diabetes were found to increase the risk of KSD among the subjects in this study. Thus, it is essential for individuals to adhere to healthy lifestyles in order to reduce the risk of KSD. There is a need for a healthy lifestyles promotions in order to reduce the risk of occurrence and recurrence of KSD.

#### ACKNOWLEDGEMENT

The authors wish to acknowledge the Urology Unit of University Kebangsaan Malaysia Medical Center for the assistance in obtaining subjects for this study and to all subjects involved in this study. This study was funded by PPP-2015-115.

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Received: April 2016 Accepted for publication: November 2016

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