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Obesity rates in renal stone formers from various countries

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Summary ***Objective: To collect evidence on the rate of obesity in renal stone formers (RSFs) living in different climatic areas and consuming different diets.***
Materials and methods: Data of adult renal stone formers were retrospectively collected by members of U-merge from 13 participant centers in Argentina, Brazil, Bulgaria (2), China, India, Iraq (2), Italy (2), Nigeria, Pakistan and Poland.
The following data were collected: age, gender, weight, height, stone analysis and procedure of stone removal.
Results: In total, 1689 renal stone formers (1032 males, 657 females) from 10 countries were considered. Average age was 48 (±14) years, male to female ratio was 1.57 (M/F 1032/657), the average body mass index (BMI) was 26.5 (±4.8) kg/m^2. The obesity rates of RSFs in different countries were significantly different from each other. The highest rates were observed in Pakistan (50%), Iraq (32%), and Brazil (32%), while the lowest rates were observed in China (2%), Nigeria (3%) and Italy (10%). Intermediate rates were observed in Argentina (17%), Bulgaria (17%), India (15%) and Poland (22%). The age-adjusted obesity rate of RSFs was higher than the age-adjusted obesity rate in the general population in Brazil, India, and Pakistan, whereas it was lower in Argentina, Bulgaria, China, Italy, and Nigeria, and similar in Iraq and Poland.
Conclusions: The age-adjusted obesity rate of RSFs was not higher than the age-adjusted obesity rate of the general population in most countries. The relationship between obesity and the risk of kidney stone formation should be reconsidered by further studies carried out in different populations.

KEY WORDS: Urinary calculi; Obesity; Diet, Body mass index.

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INTRODUCTION

Obesity is considered a risk factor for urinary stone formation. A recent meta-analysis based on 7 large cohorts in the *United States*, *China* and *Japan* computed a relative risk for kidney stone formation of 1.21 per 5 units of increment in *body mass index* (BMI) (1). This scientific evidence is robust although it is mainly dependent on observations collected from cohorts in the *United States*. For this reason, one might question the extension of these findings to other countries. In fact, the population of the *United States* is characterized by a dietary pattern that contains important risk factors for stone formation (a high animal protein load, a significant acid load due to lack of fruit and vegetable consumption).
Furthermore, morbid obesity (BMI ≥ 40) is much more prevalent in the population of the *United States* than in any other country excluding *Pacific Islands* (2). In fact, the prevalence of morbid obesity in the *United States* is high and is constantly increasing. From 2000 to 2010 the prevalence rate of a BMI > 40 increased by 70% (from 3.9% to 6.6%) and the prevalence of BMI > 50 has increased even more (from 0.27 to 0.55%) (3). Morbid obesity levels are also increasing in other countries but with much lower rates (< 2%) (4-6). Morbid obesity or type III obesity has a different impact on health than moderate obesity by increasing the risk and severity of many cardiovascular and non-cardiovascular comorbidities. Particularly, it was observed that 98% of subjects with morbid obesity have at least one lithogenic risk factor identified on 24-hour urine collection (7). The obese population of the *United States* is therefore a different popula-

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tion from obese populations observed in other countries in that it includes a higher percentage of morbid obese subjects. On the other hand, rates of overweight and obesity in a population consuming a Mediterranean diet were not different in renal stone formers with respect to a control population matched by age and gender (8) suggesting a prevalent role of the dietary pattern for the risk of stone formation (9).

The aim of the present study was to collect more evidence on the rate of obesity in renal stone formers living in different climatic areas and consuming different diets. Age and sex adjusted rates of obesity in stone formers from different countries were compared with already known obesity rates for each corresponding country.

Materials and methods

Data were collected by 13 participating centers in *Argentina, Brazil, Bulgaria* (n = 2), *China, India, Iraq* (n = 2), *Italy* (n = 2), *Nigeria*, *Pakistan* and *Poland* under the umbrella of U-merge. Each participating center collected retrospectively data of consecutively observed adult (> 18 years) *renal stone former patients* (RSFs) by reviewing charts of patients who passed spontaneously a stone or had extracorporeal or endourological treatment for stone removal. For each patient, the following information was collected: age, gender, weight, height, stone analysis (optional), procedure of removal (spontaneous passage, SWL, PNL, URS, open surgery). Any method of stone analysis was accepted, but the methodology had to be known and registered. Excel files containing anonymised data from each patient and numbered consecutively were mailed to the coordinating center (*U-merge scientific office*). Each center retained the list of the corresponding names of the participants in their own original files at their institution. BMI was computed from weight and height of each subject. Obesity was defined as a *body mass index* (BMI) ≥ 30 kg/m^2. Tables reporting the number of subjects with obesity for each age and sex group were built. The obesity rates of RSFs in different countries were adjusted by the age distribution in the general population of each country, in order to compare them with age adjusted obesity rates in the general population of the corresponding country obtained from estimated worldwide trends in obesity by *NCD Risk Factor Collaboration* (NCD-RisC) (2). Briefly, RSFs of each country were grouped by sex and class age. Age and sex specific rate of obesity of RSFs of each subgroup was multiplied by the corresponding age and sex specific weight of that country. The weights used in the age-adjustment of obesity data are the proportion of the population of each country within each age and sex group according to the estimates prepared by the Population Division of the *Department of Economic and Social Affairs* (DESA) of the *United Nations Secretariat* (10). The weighted rates are then summed across the age and sex groups to give the age and sex adjusted rate of obesity for RSFs of each country (Table 1). Age adjusted obesity rates of male and female RSFs from each country were compared with age adjusted obesity rate of male and female general population obtained from estimated worldwide trends in obesity by NCD-RisC (2). Finally, obesity rates in RSFs with stones of different chemical composition were calculated. Statistical analysis was carried out using the *Statistical Package for the Social Sciences* (SPSS). Chi square analysis was used to compare rates of obesity in different groups. Mean values of age and BMI were compared by one-way ANOVA, and differences between groups were evaluated by post hoc Bonferroni analysis. A p-value < 0.05 was considered statistically significant.

Results

In total, 1689 renal stone formers (1032 males, 657 females) from 10 countries (*Argentina, Brazil, Bulgaria, China, India, Iraq, Italy, Nigeria, Pakistan, Poland*) were considered. Most of the cases were observed in the period 2016-2019. Only the series from *Argentina* included patients observed over a longer period from 2005 to 2017. Average age was 48 (±14) years, male to female ratio was 1.57 (M/F 1032/657), average BMI was 26.5 (±) 4.8 kg/m^2). Average age, M/F ratio and average BMI in series from different countries are shown in Table 2. The average age values in the different series were significantly different (p = 0.000).

The highest average age was observed in patients from

Table 1.
An example of computation of age-adjusted obesity rate (Italy-males).

Class age	Obesity rate in RSF	Weight of class ages in Italy (5)	Age adjusted
18-39	1/29 = 0.034	0.30	0.010
40-59	17/130 = 0.130	0.38	0.049
> 60	9/108 = 0.083	0.32	0.026
TOTAL	27/267 = 0.101	1.00	0.085
	10.1%		8.5%

Table 2.
Mean age, M/F ratio and mean BMI of RSFs from different countries.

	Argentina	Brazil	Bulgaria	China	India	Iraq	Italy	Nigeria	Pakistan	Poland
N°	300	216	183	90	33	246	428	31	50	112
M	179 (60%)	114 (53%)	112 (61%)	59 (66%)	26 (79%)	154 (63%)	267 (62%)	17 (55%)	41 (82%)	63 (56%)
F	121 (40%)	102 (47%)	71 (39%)	31 (34%)	7 (21%)	92 (37%)	161 (38%)	14 (45%)	9 (18%)	49 (44%)
Age	45 +/-11	42 +/-12	50 +/-13	51 +/-13	48 +/-11	46 +/-14	56 +/-14	44 +/-14	38 +/-8	48 +/-14
BMI	25.8 +/-4.4	28.3 +/-5.8	26.2 +/-3.8	24.2 +/-2.9	26.0 +/-4.2	28.3 +/-4.7	25.1 +/-4.3	26.2 +/-2.4	30.4 +/-6.7	26.7 +/- 4.6
UA %	11% §	-	29% *	6% *	34% *	-	16% §	-	25% *	33% *

*BMI = Body Mass Index; UA% = Rate of Uric Acid containing stones; § Present series; * Other series from the same institution.*

Table 3.
Crude and age-adjusted obesity rates in male and female RSFs from different countries in comparison of age-adjusted obesity rates in male and female general population.

Country	Gender	RSFs obese/total	RSFs obesity rate (crude)	RSFs obesity rate (adjusted)	General population obesity rate 2016
Argentina	T	51/300 (17%)	17%		
	M	32/179 (18%)	17.8%	15.9%	28.2%
	F	19/121 (16%)	15.7%	15%	30.1%
Brazil	T	70/216 (32%)			
	M	36/114 (31%)	31.5%	32.5%	19.2%
	F	34/102 (33%)	33.3%	31.9%	26.4%
Bulgaria	T	32/183 (17%)			
	M	18/112 (16%)	16.0%	15.3%	26.3%
	F	14/71 (19%)	19.7%	17.7%	25.2%
China	T	2/90 (2%)			
	M	1/59 (2%)	1.6%	1.5%	6.1%
	F	1/31 (3%)	3.2%	3.3%	6.8%
India	T	5/33 (15%)			
	M	3/26 (11%)	11.5%	11.0%	2.8%
	F	2/7 (28%)	28.5%	59.5%	5.3%
Iraq	T	78/246 (32%)			
	M	45/154 (29%)	29.2%	22.5%	24.3%
	F	33/92 (36%)	35.8%	32.3%	38.3%
Italy	T	43/428 (10%)			
	M	27/267 (10%)	10.1%	8.5%	20.9%
	F	16/161 (10%)	9.9%	9.5%	20.4%
Nigeria	T	1/31 (3%)			
	M	17	0	0	4.8%
	F	1/14 (7%)	7.1%	4.5%	13.6%
Pakistan	T	25/50 (50%)			
	M	20/41 (49%)	48.7%	20.7%	6.2%
	F	5/9 (55%)	55.5%	24.1%	11.7%
Poland	T	25/112 (22%)			
	M	18/63 (28%)	28.5%	27.9%	24.6%
	F	7/49 (14%)	14.2%	14.6%	23.2%
TOTAL	T	332/1689 (20%)			
	M	200/1032 (19%)			
	F	132/657 (20%)			

Italy, while the lowest average age was observed in patients from *Pakistan*.
The average age of patients from *Italy* was significantly higher than that of patients from *Bulgaria* (p = 0.000), *Iraq* (p = 0.000), *Pakistan* (p = 0.000), *Nigeria* (p = 0.000), *Poland* (p = 0.000), *Argentina* (p = 0.000) and *Brazil* (p = 0.000). The average age of patients from *Pakistan* was significantly lower than that of patients from *Bulgaria* (p = 0.000), *Iraq* (p = 0.003), *China* (p = 0.000), *India* (p = 0.039), *Italy* (p = 0.000), *Poland* (p = 0.000) and *Argentina* (p = 0.046). The average age of patients from *Bulgaria* and *China* was significantly higher than that of patients from *Pakistan* (p = 0.000 and p = 0.000), *Argentina* (p = 0.007 and p = 0.007) and *Brazil* (p = 0.000 and p = 0.000) and the average age of patients from *Brazil* was higher than that of patients from *Poland* (p = 0.002) and *Iraq* (p = 0.005).
Male to female ratio was in favor of men in all countries, with the percentage of men ranging from 53 to 63% in most countries except *Pakistan* and *India* where males accounted for 82 and 79%, respectively.

The average BMI values of patients in different countries were significantly different (p = 0.000). In particular, the average BMI was highest in patients from *Pakistan, Iraq* and *Brazil*. The average BMI of patients in *Pakistan* was significantly higher than that of patients in *Bulgaria* (p = 0.000), *China* (p = 0.000), *India* (p = 0.001), *Italy* (p = 0.000), *Nigeria* (p = 0.004), *Poland* (p = 0.000), *Argentina* (p = 0.000) and *Brazil* (p = 0.000). The average BMI of patients in *Iraq* was significantly higher than the average BMI of patients in *Bulgaria* (p = 0.000), *China* (p = 0.000), *Italy* (p = 0.000) and *Argentina* (p = 0.000). The average BMI of *Brazil*ian patients was intermediate, being higher than that of patients in *Bulgaria* (p = 0.001), *China* (p = 0.000), *Italy* (p = 0.000) and *Argentina* (p = 0.000). The lowest average BMI value was observed in patients from *China* being lower than that of *Bulgaria* (0.0024) and *Poland* (p = 0.007).
Crude and age-adjusted obesity rates in male and female RSFs from different countries in comparison of age-adjusted obesity rates in the male and female general population are shown in Table 3. In both, males and females, the age-adjusted rate of obesity in RSFs was higher than the age-adjusted rate of obesity in the general population in *Brazil, India,* and *Pakistan*, whereas it was lower in *Argentina, Bulgaria, China, Italy,* and *Nigeria*, and similar in *Iraq* and *Poland*.
The obesity rates of RSFs were significantly different from country to country. The highest rates were observed in *Pakistan* (50%), *Iraq* (32%), and *Brazil* (32%), while the lowest rates were observed in *China* (2%), *Italy* (10%), and *Nigeria* (3%). Intermediate rates were observed in *Argentina* (17%), *Bulgaria* (17%), *India* (15%), and *Poland* (22%). These differences were maintained when obesity rates were adjusted by age in reference to a pool of all series. In a sample of 666 patients (409 males and 257 females) with stone analysis, obesity rate was 13.3% (61/456) for calcium oxalate stones, 4.7% (1/21) for calcium phosphate, 8.5% (6/70) for mixed calcium phosphate/calcium oxalate, 18.8% (13/69) for uric acid, 20.8% (5/24) for mixed calcium oxalate/uric acid.
No obese patients were observed for infection (struvite) (0/21) and cystine stones (0/5).
Mean age (56±14 *vs* 50±14 years, p = 0.000), mean BMI (27.2±4.6 *vs* 25.0±4.2, p = 0.000) and obesity rates 18/86 (21%) *vs* 75/580 (13%) were higher in patients who formed uric acid-containing stones than in those of patients forming other type of stones.
In the present series, rate of uric acid containing stones was 16% in *Italy* and 11% in *Argentina* and, from data of other series collected in the same centers participating to the present study, 29% in *Bulgaria*, 6% in *China*, 34% in *India*, 25% in *Iraq*, 25% in *Pakistan* and 33%in *Poland*

Discussion

In 2006, a prospective study of 3 large cohorts demonstrated that a BMI > 30 is associated with an increased risk of kidney stone formation for both, men and women (11). Some authors emphasized the presence of high rates of obesity in RSFs in some countries, whilst other authors did not confirm this finding in other countries (Table 4) (8, 12-20).

Table 4.
Obesity rates of RSFs of different countries (from the highest to the lowest).

Author, year	Country	N°	Obesity rate	Overweight
Semins, 2010	United States	1935 M+1322 F	49.9%-49.0%	34.1%-20%
Abu Ghazaleh and Budair, 2013	Jordan	8346	42.3 %	25.8%
Chou, 2011	Taiwan	907	38.8%	33.5%
Saenz, 2012	Spain	346	28.6%	43.6%
Funes, 2016	Paraguay	73	23.3	39.7%
Negri, 2008	Argentina	799	20.3%	40.6%
Siener, 2004	Germany	527	9.9%	44.6%
Daudon, 2006	France	1931 M+F	8.4%-13.5%	27.1%-19.6%
Trinchieri, 2016	Italy	1698	8.3%	31.9%
Oda, 2014	Japan	238 M+82 F	2.1%-0%	24.4%-12.2%

The assessment of the significance of the obesity rate in a given population on one hand, and the comparison of obesity rates in different populations on the other hand are complex because one must take into account the age and gender distribution of the population as well as the chemical composition of the stones.
Our study shows that obesity rates among RSFs in different countries range between 0 and 48.7% in men, and 7.1% and 55.5% in women. These differences are maintained after age adjustment according to the general population's age distribution, with rates ranging between 0 and 32.5% in men, and 3.3% and 59.5% in women, respectively.
These wide oscillations can be explained by the different age distributions in different countries, but also by different spectra of stone composition, dietary patterns and different climatic conditions.
In general, the rate of obesity tends to increase with increasing age, so it is possible that in populations with an older age distribution there may be a higher prevalence of obesity. To the contrary, in this study, series with higher average ages, such as those observed in *Italy*, *Bulgaria* and *China*, had the lowest obesity rates among both, men (1.6-16%) and women (3.2-15.7%), respectively.
On the other hand, the ranking of obesity rates in different countries does not vary after the rates have been adjusted by age taking as a reference the pooled population of all the series.
Another potential determinant of obesity rate among RSFs is the type of stone. Obesity tends to be more frequent in uric acid stone formers (21). Uric acid stones have a different prevalence in different countries.
In our series obesity rates were higher in *Pakistan, Iraq* and *Brazil*. The former two have reported a higher frequency of uric acid stones (22, 23), which was also observed in some parts of *Brazil* (24).
In contrast, the lowest obesity rates were observed in countries where the frequency of uric acid stones is low, such as *China*, *Nigeria* and, to a lesser extent, *Italy* (25-27).
One of the major determinants of the epidemiology of uric acid stones is climate, as higher environmental temperatures and humidity increase skin loss of fluids resulting in a reduction in urinary volumes, a decrease of pH values and, consequently, an increased urinary saturation for uric acid (28, 29). In fact, in our study, the countries with the highest rates of uric acid stones are characterized by higher environmental temperatures (30).
The finding of obesity rates in RSFs equal to or even lower than those observed in the general population of most countries can be explained by the interaction of several factors specific to each population.
Obesity is the result of the imbalance between dietary energy intake and energy expenditure that is modulated by the individual genetic characteristics that affect the absorption and metabolism of nutrients.
In Table 5 the different patterns of dietary energy intake, levels of physical activity and consumption of healthy and unhealthy foods in the general population of countries involved in the present study are summarized (31-33).
In countries with the lowest dietary energy intake, such as *India*, *Pakistan* and *Nigeria*, the lowest obesity rates were observed, but also in *China*, where dietary energy intake has an intermediate value, the obesity rate is low in view of the high levels of physical activity.
In other countries with intermediate energy intake values

Table 5.
Rates of obesity, estimated energy intake, levels of physical inactivity and quality of dietary pattern of the general population in countries involved in this surveycomparison of age-adjusted obesity rates in male and female general population.

Country	Obesity (NCD-RiskCo) M-F Kcal/day	Energy intake (FAO) *	Physical inactivity (WHO)	Quality of dietary pattern (NutriCoDE)
Argentina	28.2-30.1 37.6% (M) 45.3% (F)	3030	41.6% (T)	Healthy foods very low Unhealthy foods low/mod
Brazil	19.2-26.4 40.4% (M) 53.3% (F)	3120	47.9% (T)	Healthy foods moderate Unhealthy foods high
Bulgaria	26.3-25.2 35.6% (M) 41.4% (F)	2760	38.6% (T)	Healthy foods moderate Unhealthy foods low/moderate
China	6.1-6.8 16.0% (M) 12.2% (F)	2990	14.1% (T)	Healthy foods low Unhealthy foods low
India	2.8-5.3 24.7% (M) 43.9% (F)	2360	34.0% (T)	Healthy foods low Unhealthy foods very low
Iraq	24.3-38.3 39.5% (M) 64.6% (F)	-	52.0%(T)	Healthy foods moderate Unhealthy foods low/moderate
Italy	20.9-20.4 36.2% (M) 46.2% (F)	3650	41.4% (T)	Healthy foods low/mododrate Unhealthy foods moderate
Nigeria	4.8-13.6 24.7% (M) 29.6% (F)	2710	27.1% (T)	Healthy foods moderate Unhealthy foods low
Pakistan	6.2-11.7 24.4% (M) 43.3% (F)	2280	33.7% (T)	Healthy foods very low Unhealthy foods low
Poland	24.6-23.3 31.5% (M) 33.4% (F)	3410	32.5% (T)	Healthy foods low/moderate Unhealthy foods high/moderate

but reduced levels of physical activity, such as *Brazil* and *Argentina*, high obesity rates are observed similarly to those of countries with higher energy intakes, such as *Italy* and *Poland*. Finally, the highest levels of obesity were observed in *Iraq* where lowest levels of physical activity were reported.

Obesity rate in RSFs was higher than in the general population in *Brazil*, which is, a country with a high consumption of unhealthy foods (34, 35).

The other two countries where obesity rates were increased in RSFs, namely *Pakistan* and *India*, are not characterized by a high consumption of unhealthy foods, but have a low consumption of healthy foods such as fruits, vegetables, beans and legumes, nuts and seeds, whole grains, milk, total polyunsaturated fatty acids, fish, plant omega-3s, and dietary fibers (33).

Admittedly, our study has some limitations such as the retrospective study format, the small number of subjects observed in some countries, the heterogeneous nature of data, the variability in the population pattern and nature of cohorts and the availability of the chemical examination of the stones only in some series

Particularly, series observed in some areas of large countries are representative only for those specific areas, notably *Shanghai* (*China*), *Lagos* (*Nigeria*), *Pakpattan* (*Pakistan*) and *Manipal* (Karnataka-*India*) and obesity rates cannot be translated to populations of countries with several million inhabitants. In fact, the populations of these countries are made up of different ethnicities with different genetic characteristics and different culture and religion influencing eating habits and lifestyle.

In conclusion, obesity rates among patients with urinary stones are variable in different countries. Higher obesity rates were observed in countries with a high prevalence of uric acid stones. On the other hand, obesity rates observed in RSFs tend to overlap with the rates observed in the general population, with equal or lower values even after adjustment by age. Accordingly, the role of obesity on the risk of kidney stones formation should be confirmed by further studies carried out in different populations.

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