NONMODIFIABLE RISK FACTORS AND SOCIO-DEMOGRAPHIC STATUS IN HYPERURICEMIC SUBJECTS CONSUMING PURINE-RICH FOODS IN MAKKAH

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ABSTRACT

Gout is not the only complication resulting from hyperuricemia (HU). There are a variety of other pathological conditions where HU plays a role. The HU may occur in gastric cancer, ischemic colitis (IC) in young adult population, urinary stones in subjects with a permanent ileostomy, entero-arthrotic syndrome, obstructive uropathy associated with rotavirus gastroenteritis, laxative abuse syndrome and morbidly obese patients after jejunoileal intestinal bypass surgery etc. In the present study, the prevalence, role of nonmodifiable risk factors (age, gender), and socio-demographic status (education, family size and monthly income) in normouricemic subjects (NUS) and hyperuricemic subjects (HUS) (total randomly selected subjects=108; male: 83; female: 25; HUS: n= 21 men (25.30% of total subjects); mean±SD of age for HUS: 34.75±12.37 years that is significantly higher (p=0.009) than the control NUS: 27.76±8.54 years) in Makkah were studied. It was noticed that the HUS had habit of consuming purine- rich foods. The greater part of investigated subjects had graduate educational level for NUS (71.26%) and HUS (42.86 %). Education level, in general was found significantly different for the NUS and HUS (p<0.01). The highest percentage is of HUS (39.08%) and NUS (57.14%) for the family size of 5-10 persons. The income of total family subjects as <3500 SAR/month was found for the highest number of NU group as 33 subjects (37.8%), and HU group as 6 (28.57 %) receiving total family income 5000-<7000 SAR/month. In general, the value of p was found 0.09 for income levels in HUS compared with NUS. The present report is a cross-sectional design and also did not incorporate information on other factors that might be related to the prevalence of HP, and additionally considerable difficulty was faced for obtaining female HUS primarily due to religious and socio-cultural traditions. Hence, it is recommended for a comprehensive study in future with large sample size of hyperuricemic patients (HUP) with the inclusion of female subjects of various age groups.

Key words: Hyperuricemia, nonmodifiable risk factors, socio-demographic status, purine-rich foods

INTRODUCTION

Hyperuricemia may lead to gout (Al-Arfaj, 2001; Abdelrahman *et al.*, 2002; Bisht and Bist, 2011; Katsiki *et al.*, 2012; Torralba *et al.*, 2012). However, the gout is not the only complication resulting from hyperuricemia. There are a variety of other pathological conditions and disorders where hyperuricemia plays a role, e.g. cardiovascular, gastrointestinal, renal, metabolic etc (Katsiki *et al.*, 2012). Hyperuricemia may occur in gastric cancer (Ficarra, 1946), ischemic colitis (IC) in young adult population (Kimura *et al.*, 2012), urinary stones in subjects with a permanent ileostomy (Kennedy *et al.*, 1982), entero-arthrotic syndrome (Angeras, 1961), obstructive uropathy associated with rotavirus gastroenteritis (Ashida *et al.*, 2012), laxative abuse syndrome (Oster *et al.*, 1980), and morbidly obese patients after jejunoileal intestinal bypass surgery (Thomas and Madura, 1977).

It is quite established that the prevalence of hyperuricemia (HU) is much higher in some communities than others. In New Zealand (Klemp *et al.*, 1997), HU was more common in Maori (26.85%) than in European (10%). In Saudi Arabia (Al-Arfaj, 2001), the prevalence of HU was only 8.42%. Overall prevalence of HU in another report was 12.8% (Abreu *et al.*, 2011). One other recent study shows that 24.9 % of Arab subjects mainly men in Kuwait were hyperuricemic (Al-Meshaweh *et al.*, 2012). In Taiwan island of China (Huang and Chen, 1996), the prevalence of HU was high to 49.4% in Ayatals, but it was only 27.4% in non-aborigines. Total hyperuricemic prevalence in a large Chinese population was found as 12.89 % (Liu *et al.*, 2012) and 35.68% of the total subjects in Guangzhou (Ma *et al.*, 2012). Some studies indicate that the incidence and prevalence of HU have been increasing from 2.9 in 1960 to 5.2 in 1999 in the USA (Roddy and Doherty, 2010; Wallace *et al.*, 2004). In the UK the prevalence of HU increased during the period from 1975 to 1993. It was found that the prevalence of HU had increased from 2.6 to 9.5 in 1993 (Harris *et al.*, 1995). China reports an increase in HU prevalence from 3.6 in 2002 (Nan *et al.*, 2006) to 5.3 in 2004 (Miao *et al.*, 2008).

The prevalence of HU according to age (Verdecchia *et al.*, 2000; Al-Arfaj, 2001; Krishnan *et al.*, 2006; Miao *et al.*, 2008; Vitoon *et al.*, 2008) and sex (Al-Arfaj, 2001; Annemans *et al.*, 2008; Doherty, 2009; Terkeltaub, 2010) did not show consistent findings though in general people with higher age and male gender were found afflicted more. Other studies provide information about the interrelationship of HU with education level (Liu *et al.*, 2012) family size and total income (Villegas *et al.*, 2010 ; Liu *et al.*, 2012).

The HU has often been found in the elderly (Lai *et al.*, 2001). Age, was significantly higher in hyperuric acid (HUA) patients than in the normal or normouricemic (NU) group (Yu *et al.*, 2010). It was further clarified that HU was noticed more common in elderly men than elderly women (Lai *et al.*, 2001). More information was provided that HU was found more common in men over age 30 years and in women over age 50 years (Miao *et al.*, 2008). A precise evaluation of the age related changes showed that age (1-year increase) was negatively associated with HU in men but positively associated with HU hyperuricemia in women (Yang *et al.*, 2012). One of the known risk factors for gout in USA is male sex (Roubenoff (1990). The HU was also found as significantly associated with male sex (Yang *et al.*, 2012).

Age of HU in men vs women showed more in men than women (Miao *et al.*, 2008). The increase in prevalence of HU occurred as according to age in women but not in men (Huang *et al.*, 2005) that showed that the processes that influence the UA metabolism and related parameters vary by gender and age. Significant negative correlation of HU with age and sex in male and female was noticed (Ma *et al.*, 2012).

A recent report (Liu *et al.*, 2012) shows higher incidence of HU in men than women. Hyperuricemia prevalence in men vs women was found almost equal in both sexes (Zimmet *et al.*, 1978 (64% vs 60%); higher in men than women (Lai *et al.*, 2001 (57.3% vs 40.9%); Miao *et al.*,2008 (18.32% vs 8.56%) ; Yu *et al.*, 2010 (19.90% vs 10.54%); Abreu *et al.*, 2011(17.8% vs 9.9%); Ma *et al.*, 2012 (46.83% vs 17.59%); Remedios *et al.*, 2012 (50% vs 21.7%) ; Yang *et al.*, 2012 (6.4% vs 2.1%) ; and in almost all men (Al-Meshaweh *et al.*, 2012) .

Urban areas had higher prevalence of HU (14.9%) while compared with the data of rural areas (10.1%) (Miao *et al.*, 2008). Higher prevalence of HU was investigated in developed city (18.02%) compared to less developed city (5.3%) (Miao *et al.*, 2008). These differences were found highly correlated with the economic development confirmed with the observation of increased daily consumption of meat and seafood (Miao *et al.*, 2008).

Steady increase in the HU prevalence was obtained while comparing the data with the previously published data (Miao *et al.*, 2008) that correlated with the economical developments considering the dietary and life style changes. Although the HU is probably genetic, the high prevalence of gout might be considered due to the environmental change from almost complete Westernized traditional island style of living (Zimmet *et al.*, 1978). The hyperuricemia in men was accompanied by a high prevalence of clinical gout (6.9%) (Zimmet *et al.*, 1978). Furthermore, one of the known risk factors for gout in USA is family history (Roubenoff (1990).

Demographic data, highest education degree, type of the work, commuting means and assessments of dietary factors influence the prevalence of HU (Liu *et al.*, 2012). Hyperuricemia was noted as significantly associated with urban residence than rural areas of Jinan, China (Yang *et al.*, 2012). It has been shown that serum urate in the most hyperuricemia relatives of gout can be changed by environmental factors, e.g. diet, and changes of life style etc. (Yu and Kaung, 1980).

Although the above mentioned literature provides information of HU through various perspectives, a quite clear idea of the nonmodifiable risk factors and role of age, gender and life style of the patients with HU are controversial. Hence, the need of conducting the current study to find the involvement of age, sex and socio-demographic status in subjects using purine-rich diets and showing hyperuricemia in Makkah, Saudi Arabia was essentially required.

MATERIALS AND METHODS

Subjects:

A cross-sectional study was conducted during the academic year 1432-1433H (2011-2012). The total subjects in the present study were one hundred and eight (108) (83 male & 25 female). The control subjects without HU were 87 and those with HU were 21 in number. A random sampling was carried out and the patients were chosen from orthopedic outpatient clinics and labs at public and central hospitals and other labs from Makkah, Saudi Arabia. The age of the subjects was in the range of 18-65 years. The control subjects were those having habit of moderate consumption of purine diets, but those having HU were found those using too much Shoor fish, Hamoor fish, Najel fish, Mussel, Lentil, Beans, Goats/Sheep meat and Liver compared to controls. This was confirmed further by estimating the serm uric acid (SUA) levels that must had to be significantly higher for HUS compared to that in NUS.

Study Design:

Hospitals were randomly selected to participate, and the patients were from the selected hospitals. A specified quota of the patients was assigned for each hospital. If the quota was not achieved, over sampling from other hospitals was sought to be the solution. At the commencement, a letter was submitted to every hospital indicating our objectives for conducting the research. Patients were provided with the study questionnaire stating their health, nutritional and social conditions. The data of the anthropometric assessment was also collected from the patients and control subjects.

Population:

The study was conducted in the holy city of Makkah at different areas/ districts and the community had varied socio-economic and cultural backgrounds. Five hospitals were visited and contribution to the study was discussed with the administration and staff in hospitals. All hospitals followed the Ministry of Health.

Data and methods:

Data was collected through an interview with HUS by using socioeconomic level questionnaire and food frequency questionnaire. Same questionnaire with the interview was carried out for collecting the data of the randomly selected control subjects (NUS). A socioeconomic level questionnaire was used to collect data on age, sex, educational level, family size, income etc. A food frequency questionnaire was used to illustrate the consumption rate of purine foods. (Yeomans, 1991). Uric acid was determined according to the enzymatic colorimetric test of Fossatti and Prencipe (1980). Estimation of uric acid was employed to categorize the subjects into those with and others without HP. Whether a subject be included in the HU group or not based on their consumption of purine-rich diets and confirmed by estimating the SUA levels. The subjects showing SUA level above 420 micromol/l for males and above 360 micromol/l for females were considered to be included in HU group (Al-Arfaj, 2001).

Statistical Analysis:

The statistical analysis was carried out using windows version of SPSS 16 (SPSS, 2008). Frequencies, relative and cumulative percentages, means, standard deviation (SD), and range were computed. Quantitative data are presented as mean±standard deviation. Qualitative data were expressed as percentages. For the quantitative variables, compliance with the normal distribution was assessed using the Kolmogorov-Smirnoff test, as appropriate. For comparing the groups, the chi-square test or Fisher's exact test were used for qualitative variables as well as the t-test or Mann-Whitney U test for quantitative variables.

RESULTS AND DISCUSSION

Table 1 shows the frequency distribution of subjects according to gender. The present results revealed that the majority of studied subjects were male. It was found that 21 out of 83 male subjects (25.30 %) were hyperuricemic patients (HUP). However, HU was not found in any of randomly selected female subjects. It was noticed that the mean±SD of age for HUS as 34.75±12.37 years was significantly higher (P=0.009) than that in NUS (27.76±8.54 years).

Table 1. Influence of age and gender in hyperuricemic subjects consuming high purine diets.

	NUS (n=87)		HUS (n=21)		p value by X2	Mann-Whitney test
	Frequency	Percent	Frequency	Percent		
Male	62	71.26	21	100.0		
Female	25	28.74	0	0	0.01	
Total	87	100.0	21	100		
Age						
Mean	27.76		34.75			0.009
SD	8.54		12.37			

HUS= hyperuricemic subjects; NUS= normouricemic subjects; X²: Chi-Square

Table 2 illustrated the distribution of subjects according to socio-demographic status. The greater part of investigated subjects had graduate educational level for NUS (71.26%) and HUS (42.86 %). Education level, in general was found significantly different for the NUS and HUS (p<0.01). The highest percentage is of HUP (39.08%) and NUS (57.14%) for the family size of 5-10 persons. The income for total family subjects as <3500 SAR/month was found for the highest number of NUS as 33 subjects (37.8%). Whereas, the HUS group showed the maximum number of subjects as 6 (28.57 %) receiving total family income as 5000-<7000RS/month. In general, the value of p was found 0.09 for income levels in HUS compared with NUS as shown in Table 2.

Table 2. Influence of socio-demographic status in hyperuricemic subjects consuming high purine diets.

	NUS (n=87)		HUS (n=21)		p value by X2
	No.	%	No.	%	
Education level					
Primary	4	4.60	3	14.29	
Intermediate	5	5.75	3	14.29	
Secondary	13	14.94	3	14.29	0.01
Graduate	62	71.26	9	42.86	
Postgraduate	3	3.45	3	14.29	
Family size					
<5	26	29.89	5	23.81	
5-10	34	39.08	12	57.14	0.18
>10	27	31.03	4	19.05	
Total income					
<3500 SAR	33	37.93	3	14.29	
3500-<5000 SAR	14	16.09	2	9.52	
5000-<7000 SAR	6	6.90	6	28.57	0.09
7000-<10000 SAR	20	22.99	5	23.81	
>=10000 SAR	14	16.09	5	23.81	

HUS= hyperuricemic subjects; NUS= normouricemic subjects; X^2: Chi-Square

The literature shows that the patients with HU are mostly with age range higher than the one currently obtained. The present study comprises the subjects with HU and those without HU all in a wide range of age. Inspite of that, most of the patients in this study are not above 40 years. Hence, the results obtained here vary from those reports where age of the patients and controls is quite high or with wide range containing low and high age. Whether men or women, aging seems a key factor for higher risk of HP, that is evident in the current study where age of HUS was found higher than the age in those NUS. This investigation is similar as found by Al-Arfaj (2001) in Saudi Arabia though the mean age of the HUS found in Al-Arfaj (2001) study was higher than the present study. The present study had not HUP of higher average age as were in other studies (Verdecchia *et al.*, 2000; Al-Arfaj, 2001; Krishnan *et al.*, 2006; Vitoon *et al.*, 2008) and where prevalence decreased from the age range of 65 – 69 years to age above 80 years (Verdecchia *et al.*, 2000). In view of small sample size in the present study, it was difficult to predict changes in the prevalence of HUP at lower and higher range of age as were found by Krishnan *et al.* (2006) and Vitoon *et al.* (2008).

It is not a precise view to predict about the prevalence of hyperuricemia with the help of current small sized data of subjects with and without HU in male and female. There are several aspects to be uncovered. In contrary, this is evident in the investigations where more number of male subjects with HU were found more common in elderly men than women (Lai *et al.*, 2001), though it is also mentioned that HU is more common in men over age 30 years and in women over age 50 years (Miao *et al.*, 2008). The mean Age in the current report is higher in HUP compared to controls with NU as was found by Yu *et al.* (2010). Similarly, age of men patients was noticed as higher than that in women patients and this is exactly what has been reported (Miao *et al.*, 2008). The female HUS could not be collected and it is thought that it might had been due to less cooperation where the data was collected and the possibility of religious and socio-cultural boundations, but in fact there are other reports that suggest the male sex as one known risk factor for gout and HU (Roubenoff, 1990; Yang *et al.*, 2012). On the basis of this current report, it might be planned to search and study the HUP of various age groups e.g. in the patients with higher age groups in men. However, existing information shows that the age (1-year increase) was negatively associated with HU in men but positively associated with HU in women (Yang *et al.*, 2012), though the controversial results were obtained by various workers (the increase in prevalence of HU occurred as according to age in women but not in men by Huang *et al.* (2005) that showed that the processes that influence the UA metabolism and related parameters vary by gender

and age, and hence, significant negative correlation of HU with age and sex in male and female was noticed by Ma *et al.* (2012).

In the present study, only male subjects suffering from HU could be obtained. Though apparently this indicates that the men in the region where the study was performed are more prone than women for HU, but it might partly had been due to the reason that the current study was a cross sectional and it dealt with the small sample size. Furthermore, that might had been partly due to social and cultural barrier and lack of cooperation from most of the visited places for collecting the data of women suffering from HU. However, Wang *et al.* (2011) found higher prevalence of HU in men than women in China that provides evidence that men suffer more in HU than women. The description of HU as a disease of men (Terkeltaub, 2010); investigation of HUS as 3-4:1 as male to female ratio (Doherty, 2009); and men as 80% of the HUP are the other verifications for the explaination of the current investigation. However, the current study is not in accordance with the results obtained by a local group of researcher in Saudi Arabia (Al-Arfaj, 2001) where a little variation in the number and age of male and female HP subjects was obtained.

No doubt, female subjects could not be studied in the present investigation but it might also partly be due to less prevalence of HU in women as a recent report (Liu *et al.*, 2012) shows higher incidence of HU in men than women, and other reports where HU was higher in men than women (Lai *et al.*, 2001; Miao *et al.*, 2008; Yu *et al.*, 2010; Abreu *et al.*, 2011; Ma *et al.*, 2012; Remedios *et al.*, 2012; Yang *et al.*, 2012). Hence, an important precaution to clarify the currently obtained results might be to establish a procedure to observe more women afflicted with HU in Makkah, as a report provides such evidence (HU prevalence in men vs women almost equal in both sexes reported by Zimmet *et al.* (1978). This approach proves the current results. (only men were reported by Al-Meshaweh *et al.* (2012) to have HU).

The current study provides information about the influence of less education and absence of awareness about general knowledge of life style and especially food habits and the data manifests the existence of correlation between educational background and HU. The highest percent of HU was in patients with primary and intermediate levels of education. But opposite of that might be possible, as urban areas showed higher prevalence of HU while comparing with the data of rural areas (Miao *et al.*, 2008) and higher prevalence of HU was investigated in a developed city compared to less developed city (Miao *et al.*, 2008). These differences were found highly correlated with the economic development confirmed with the observation of increased daily consumption of meat and seafood (Miao *et al.*, 2008). These might be the reasons that the data of patients with much higher educational background in the present study showed that the post-graduate degree holders suffer from elevated SUA than normal subjects which needs further investigations, but primarily it could be explained by the fact that higher income might be associated with the facility to have higher quantity of sea food and meat as it is explained in above lines. Furthermore, modernization and modern civilization has provided ways and opportunities for rich and highly skilled and educated people to increase their income and luxuries and this might had been a main reason that the steady increase in the HU prevalence was obtained while comparing with the previously published data (Miao *et al.*, 2008) that correlated with the economical developments considering the dietry and life style changes. Although the HU is probably genetic, the high prevalence of gout might be considered due to the environmental change from almost complete Westernized traditional island style of living (Zimmet *et al.*, 1978). The results for the post-graduate degree holders in the present investigation are in accordance with a report where HP was noted as significantly associated with urban residence than rural areas of Jinan, China (Yang *et al.*, 2012). Moreover, the demographic data, highest educational degree, type of the work, and commuting means and assessments of dietary factors has been found to influence the prevalence of HU (Liu *et al.*, 2012).

The consumption of high purine-rich diet in the daily food habit is not accessible to all because of higher price. An indirect indicator of food pattern and consumption type and level could be referred to family size and income. It can be hypothesized that if total income is higher, the rich people can purchase purine- rich food sources. That hypothesis stands correct for the present study, where HU is more common in people having family size of 5-10 persons; and those having income of SAR 5000 to 7000 compared to those who had less monthly income that is in accordance with the report of Villegas *et al.* (2010).

The major limitation of the present report is that it is a cross-sectional design, which prevented from making any causal inferences based on the presently obtained results. Another limitation of the study is that information on other factors related to HU prevalence was not incorporated, such as gastrointestinal disorders, kidney disease, skin psoriasis, metabolic syndrome, or family history of gout or HU; role of various diets; and pathophysiological alterations (will be published later), and considerable difficulty was faced in obtaining data where the subjects were consulted. Another reason concerning less number of female subjects in our study was due to religious and socio-cultural traditions. Hence, it is recommended for a comprehensive future study with large sample size of HU and gout patients with the inclusion of female subjects of various age groups.

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