ORIGINAL ARTICLES

ASSOCIATION OF TEA AND OTHER ADDICTIVE SUBSTANCES WITH GALLSTONE DISEASE IN SOUTHERN SINDH, PAKISTAN

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ABSTRACT

Objective: To evaluate any association of consumption and / or use of tea, paan, supari, naas, naswar, smoking, coffee and alcohol with gallstone disease.

Design: Case – Control study

Place and Duration of study: The study was carried out at different hospitals of Hyderabad and adjoining areas (Liaquat University Hospital, Jamshoro, Memon Charitable Hospital, Hyderabad, Wali Bhai Rajputana Hospital, Hyderabad, Naseem Medical Center, Hyderabad, and Isra University Hospital, Hyderabad) during January 1999 to December 2001.

Patients and Methods: 160 hospitalized gallstone patients and 112 patients admitted in eye wards were taken as controls (age, sex and locality matched with negative personal and family history). The justification of taking eye patients as controls lie in the fact that these patients have no gastrointestinal problem which could be associated with gallstones. All were interviewed through a standard questionnaire developed for that purpose.

Results: The consumption and / or use of tea, paan, naas / naswaar, alcohol and coffee were common among both the groups. Smoking was found to be the main risk factor for gallstone patients. Smokers as against non-smokers were however at risk 1.89 (95% CI, 0.68-5.26, p=0.105) to develop gallstones. Similarly consumers of more than 1 cup of tea per day were seen to be at higher risk (4.07, 95% CI; 1.71-9.64, p=0.001) for gallstone disease. No association of Supari, Naas and Naswar intake was found with the occurrence of gallstones. A significant inverse association (0.49 CI; 0.34-0.5, p=0.04) of paan, (0.39 CI; 0.11-0.52, p=0.00) alcohol, and (0.36 CI; 0.24-0.98, p=0.04) coffee was found with gallstone disease.

Conclusion: Tea consumption is positively and Paan, alcohol and coffee consumptions are negatively associated with gallstone disease in Southern Sindh, Pakistan.

Keywords: Gallstones, smoking, tea, paan, supari, naas, naswar, alcohol, coffee, cholelithiasis

INTRODUCTION

Gallstone disease is a common gastrointestinal problem in day to day practice. Cholesterol and bilirubin, either singly or together in various proportions, are the main constituents of human gallstones which are formed when these constituents precipitate in bile [1-4], possibly aided by certain promoting agents [5-8].

Recent epidemiologic studies have determined the factors favouring lithogenesis, in addition to those that are already well known, such as age, obesity, female gender, high blood triglyceride levels and multiparity; the risk is correlated with high, frequent variations in weight, with intake of certain drugs and with alimentary habits [9]. In

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addition, physical exercise plays a protective role against the development of symptomatic gallstone disease [10].

The gallstone disease is far more common at Hyderabad and its adjoining areas [11]. The intake of paan, naas, naswar, supari, alcohol, and coffee are common in the people of this area. Smoking is also a main addiction. Hence to see the epidemiological risk factors for gallstone disease, which have never been addressed as the risk factors, motivated us to undertake this study. For this purpose we surveyed different hospitals of Hyderabad and adjoining areas in Pakistan.

PATIENTS AND METHODS

Subjects

A case-control study was carried out in which one hundred and sixty gallstone patients and 112 control subjects (age, sex and locality matched patients of eye wards) from different hospitals of Hyderabad and adjoining areas (Liaquat University Hospital, Jamshoro, Memon Charitable Hospital, Hyderabad, Wali Bhai Rajputana Hospital, Hyderabad, Naseem Medical Center, Hyderabad, and Isra University Hospital, Hyderabad) were studied during January 1999 to December 2001. Eye patients having diabetes, hypertension, or obesity with positive personal or family history of gallstones were not included in the control group. As the eye patients have no gastrointestinal problem which could be associated with gallstone disease therefore, they are the best controls for present study. The gallstone patients with diabetes and or any other complication of gastrointestinal tract (except gallstone disease) were excluded from the study. In both groups, the presence/absence of gallstones was confirmed by ultrasound. All our patients resided in Southern Sindh, Pakistan.

Questionnaire

All subjects were interviewed through a standard questionnaire developed for the purpose to know about frequency of consumption and / or usage of tea, paan, naas, naswaar, supari, alcohol, coffee and smoking. Questions regarding frequency of consumption of tea, paan, supari (sweet areca nuts), smoking etc and about source of drinking water and of any previous illness were asked. From married females information about the age at the time of marriage, number and frequency of children and use of oral contraceptives, if any, was also obtained.

Statistical Analysis

Odds ratio with 95% confidence intervals were estimated to see the association of tea, paan, naas, naswaar, supari, alcohol, coffee and smoking with gallstone disease [12]. The odds ratio equal to 1.0 was considered as reference, <1.0 as protective factor, and >1.0 as risk factor for gallstone disease [13]. P-value was calculated by chi-squared test using Minitab software release 13.2.

RESULTS

Among 160 gallstone patients 29.37% were males and 70.63% were females. The age range for male gallstone patients was 41.2 to 60.8 years and for females 23.7 to 64.7 years. Whereas, the age range for female control patients was 24.1 to 65.2 and for males was 40.5 to 65.3 years. There was insignificant difference in age and gender distribution of both the groups ($p>0.05$) 87% of females among gallstone patients were married out of which 78% were married at the age of upto 19 years. The highest percentage of patients (81.25%) belong to low income group and majority (74.2%) of them were uneducated. In present study, odds ratio was used to see the association of frequency of tea, paan, naas, naswaar, supari, alcohol, coffee and smoking with gallstone disease. Amongst the studied factors some are not reported in the literature, as they are the specially consumed and / or used in this part of the world. Smoking is a well known addiction throughout the world [14-21]. The association of smoking with gallstone disease is depicted in (table-1). It revealed that smokers as against non-smokers were at higher risk 1.89 (95% CI, 0.68-5.26, $p=0.105$) to develop gallstones when non-

Table-1: Relationship between smoking and gallstone disease.

	Cases (n=160)	Controls (n=112)	Odds ratio (95% Confidence interval)	P value*
Smokers (>25 cigarettes/day)	25	10	1.89 (0.68-5.26)	
Non-smokers	135	102	1.0 (reference)	0.105

Table-2: Relationship between tea and gallstone disease.

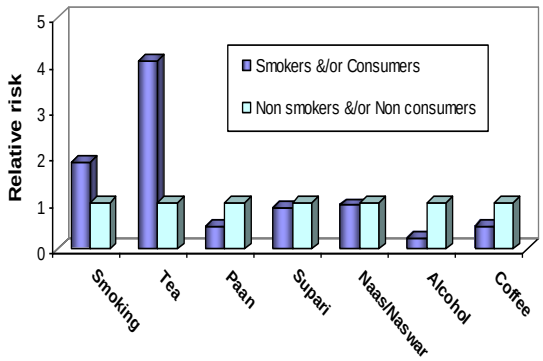
Tea	Cases (n=160)	Controls (n=112)	Odds ratio (95% Confidence interval)	P value*
1 cup/day				
Consumers	25	14	4.45 (0.54-12.45)	
Non-consumers	8	20	1.0 (reference)	0.004
More than 1 cup/day				
Consumers	127	78	4.07 (1.71-9.64)	
Non-consumers	8	20	1.0 (reference)	0.001

Table-3: Association of Paan/Supari/Naas/ Naswar with gallstone disease.

	Cases (n=160)	Controls (n=112)	Odds ratio (95% Confidence interval)	P value*
PAAN				
Consumers (>3/day)	17	22	0.49 (0.34-0.5)	
Non-consumers	143	90	1.0 (reference)	0.037
SUPARI				
Consumers	27	20	0.9 (0.41-2.47)	
Non-consumers	133	92	1.0 (reference)	0.833
NAAS/NASWAR				
Users	11	8	0.95 (0.29 – 3.09)	
Non-users	149	104	1.0 (reference)	0.932

Table-4: Association of alcohol and coffee with gallstone disease.

	Cases (n=160)	Controls (n=112)	Odds ratio (95% Confidence interval)	P value*
Alcohol				
Consumers	10	24	0.24 (0.11-0.52)	
Non-consumers	150	88	1.0 (reference)	0.000
Coffee				
consumers	15	20	0.48 (0.24-0.98)	
Non-consumers	145	92	1.0 (reference)	0.04



**Reference = 1, <1 are protective factors, >1 are risk factors for gallstone disease.*

Figure: Comparison between smokers &/or consumers and Non smokers &/or non consumers (reference) with respect to their odds ratio.

smokers were taken as reference (1.00). Hence a positive association of smoking with gallstone disease is seen in present study, although the p value did not approach to significance. A typical Southern Pakistani consumes more tea as compared to other beverages. In this study consumers of more than 1 cup of tea per day were seen to be at higher risk (4.07, 95% CI; 1.71-9.64, p=0.001) for gallstone disease when non-consumers were taken as reference (table-2).

No association of Supari (areca nuts), Naas and Naswar intake was found with the occurrence of gallstones (table-3). However, Paan seemed to be a protective factor owing to its significant inverse association (0.49 CI; 0.34-0.5, p=0.037) with gallstone disease.

A closer look to the (table-4) reveals that both coffee and alcohol have a protective effect on gallstone disease, as their odds ratio was found to be 0.24 and 0.48 respectively. Both showed significant inverse association (p=0.00 and 0.04) with gallstone disease.

Figure depicts the highest odds ratio for tea consumption as compared to all the other things consumed and / or used in Southern Sindh, Pakistan, when non consumers and / or users were taken as reference.

DISCUSSION

Besides other epidemiological risk factors, several prospective studies of clinical gallbladder disease have suggested that cigarette smoking may increase the gallstone risk in men and women [14-18], while the Framingham Study [19] failed to find a positive association between smoking and clinical gallbladder disease. A population-based prospective study using ultrasonography reported a moderate increase in the incidence of gallstones among cigarette smokers as compared with nonsmokers [20]. Our results (table-1) are comparable with Misciagna et al. [20].

Biological mechanisms are unclear even if cigarette smoking may increase a predis-position to gallstones. Lower concentrations of plasma high density lipoprotein cholesterol associated with cigarette smoking [21] may be relevant to the positive association between smoking and gallstones. Lower levels of high-density lipoprotein cholesterol may increase the risk of gallstones due to decreased hepatic excretion of bile acids [22]. While estrogens are implicated as being etiologically linked with gallstone formation because of female predominance of the disease [23, 24], it is unlikely that estrogens explain the relation between cigarette smoking and gallstones. Cigarette smoking is associated with increased hepatic degradation of estrogens [25] and cholesterol levels of urinary estrogens [26] in premenopausal women, and there is no difference in plasma estrogen levels between smokers and nonsmokers in post-menopausal women [27]. In men, cigarette smoking is associated with higher levels of endogenous estrogens in some studies [20], but not in others [28, 29].

Other studies suggested that gallstones recovered from smokers contain high concentrations of mercury [30], whereas reverse was true for the concentrations of barium and strontium [31].

Tea consumption was seen positively associated with gallstone disease in this study (table-2). Other studies show that consumption of tea or green tea is associated with lower risk of gallstones [32-34], possibly due to the lower amount of caffeine in these beverages [35]. Our study suggests that there is a positive association of tea with gallstone disease. It might be due to difference in the method of making tea, as the people of Southern Sindh like to take strong tea with more sugar. It is not yet clear; to clarify the results we need to know the use of sugar in tea and milk, as there is a positive association of carbohydrates and caloric intake with gallstone disease [36].

A significant inverse association of Paan (paan or betel-quid is a roll of betel leaf containing areca nut, catechu, lime, tobacco – optional, sometimes including additives and flavouring agents) with gallstone disease (table-3) indicates that Paan has a protective role in gallstone disease. We could not identify other studies with which our data on this basis can be compared. Although, it has been recently reported that Helicobacter Pylori is detected in significant numbers in the oral cavities of paan chewers, most of whom have developed periodontal disease and also suffer B type gastritis [37]. In agreement with literature the gallstone disease is associated with atrophic gastritis, but the difference was not statistically significant [38]. Thus, additional studies are needed to evaluate the inverse association between paan consumption and gallstone disease, particularly with respect to biological mechanism.

The results of most [39-59], but not all [60 -68], epidemiologic investigations that addressed the relation between alcohol intake

and gallstone disease suggest that alcohol confers protection against gallstone development. However, controversy exists regarding the magnitude of the inverse association between alcohol intake and gallstone disease. Our findings regarding alcohol intake confirm those reports that indicate that alcohol consumption is inversely related to the risk of gallstone disease [17, 19, 39-58]. A French case-control study [58] found that, relative to alcohol abstainers, subjects who had an alcohol intake of 30 g/d had an odds ratio for ultrasound-detected gallstones of 0.28 (95% CI: 0.08, 0.95). In the Framingham study [41], women who consumed ≥ 30 g alcohol/d had an RR of gallbladder disease of 0.63 (95% CI: 0.39, 1.01). Similarly, a case-control study from Greece [45] observed that, relative to alcohol abstainers, subjects who consumed alcohol 3–4 d/wk had an odds ratio of gallstone disease of 0.7(95% CI:0.5,0.9)

Alcohol consumption may decrease the risk of gallstone disease by affecting bile lithogenicity. The decrease in cholesterol saturation index observed with moderate alcohol intakes [22] may be due to an increased conversion of cholesterol to bile acids [70] and a decreased ratio of trihydroxy to dihydroxy bile acids [71]. Serum HDL-cholesterol concentrations, which correlate directly with total biliary bile acids [72], are elevated in persons who regularly consume alcohol [73] and are inversely associated with bile lithogenicity [74] and the prevalence of gallstones [44]. Whereas regular alcohol intake increases serum HDL, binge drinking has little effect on serum HDL concentrations [75].

Alternatively, alcohol consumption may confer protection against gallstone development by stimulating gallbladder emptying and accelerating gallbladder filling [76]. These effects could be mediated by the effect of alcohol on gallbladder membrane transport properties. Alcohol reduces bile concentrations by inhibiting the absorption of water and electrolytes by the gallbladder mucosa [77]. These mechanisms are likely to operate better with frequent than with infrequent alcohol consumption. Another possibility is that alcohol exerts a prokinetic effect on the gut [78]. Gallstone formation is favoured by decreased intestinal transit mainly because of increased colonic absorption of deoxycholic acid [79], which is known to promote cholesterol nucleation [80].

Most [18,32-35,40,63,81,82] but not all, epidemiologic studies [45,83] report the association between coffee consumption and reduced risk of gallstone disease. Statistically significant findings are limited to 2 prospective studies [20, 84] and 1 cross-sectional study [81]. The odds ratio estimates of gallstone disease in the present study are consistent with these reports. One study in both genders reported an odds ratio of 0.62 for dinking vs. no coffee drinking [20]. Leitzmann et al. reported an odds ratio of 0.67 comparing ≥4 cups of coffee per day [84], and Ruhl et al. found a decreased trend of prevalent gallbladder disease with increasing coffee consumption (p value of test for trend, 0.027) in women [81].

The inverse association between coffee intake and gallstone disease is supported by laboratory studies showing that coffee or individual coffee constituents enhance gallbladder motility [85, 86], improve gallbladder mucosal function [87, 88], and may increase intestinal motility [89], factors related to reduced cholesterol lithogenesis. Effects of caffeine may contribute as protective influence of coffee on gallstone formation. Caffeine and other methylxanthines may prevent bile cholesterol supersaturation by stimulating ileal bile acid absorption [90], increasing hepatic bile acid uptake [91], decreasing serum estrogen levels [92], increasing sex hormone–binding globulin concentrations [93], and increasing thermogenesis and reducing body fat stores [94].

Other ingredients such as magnesium, potassium, or niacin in coffee might contribute to the inverse relation [95,96]. Coffee also contains an insoluble hemicellulose fiber [97] that may decrease the colonic absorption of deoxycholic acid. In

addition, coffee contains antioxidants, such as tocopherols [98] and caffeic acid [96], capable of inhibiting reactive oxygen metabolites [99], which appear to enhance cholesterol crystallization [101]. Coffee may also exert a protective influence on gallstone development through the effect of diterpines, which are removed by filtering [102] and may modulate hepatic cholesterol metabolism, possibly by down-regulating the activity of sterol regulatory element-binding proteins [103].

CONCLUSION

Tea consumption is positively and Paan, alcohol and coffee consumptions are negatively associated with gallstone disease in Southern Sindh, Pakistan.

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