

Full Length Research paper

Severity of ulcerative colitis in the study population in Iran in correlation with cigarette consumption

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Despite many studies correlating smoking with later onset of ulcerative colitis and probable decreased severity of disease, controversies still exist. This study evaluates correlation between smoking status and severity of ulcerative colitis among Iranian patients. This was a cross-sectional retrospective study. Patients with ulcerative colitis attending the Amir Alam Hospital gastroenterology clinics in 2009 to 2010 were included. Smoking habits and severity of ulcerative colitis were evaluated depending on number of visits required to the clinic and related hospitalization in the past year, radiology results and pathology of patients. A total of 674 newly diagnosed and follow-up patients were included of which 304 (45.1%) individuals were men. Of these patients, 160 (23.7%) individuals were cigarette smokers. Nonsmokers on the average had 3.6 ± 1.8 and smokers 4.0 ± 1.4 visits per year ($p = 0.02$). Average number of hospitalizations per patient per year was 1.4 ± 1.1 for nonsmokers and 2.6 ± 0.7 for smokers ($p < 0.000$). Severity of illness in respect to pathology was stage 0 to 2 (mild) in 272 (40.4%) individuals and stages 3 and 4 (severe) in the remaining 402 (59.6%) individuals. Radiology showed mild disease in 270 (40.1%) and severe ulcerative colitis in 404 (59.9%) patients and the frequency was unrelated to gender or cigarette consumption. Unlike many studies from other countries severity of ulcerative colitis was not found to be correlated with smoking or nonsmoking status and average number of visits to physician or need for hospitalization were found to be higher in smokers which needs further studies for conclusions to be made.

Key words: Colitis, ulcerative, cigarette smoking, smoking cessation, severity of illness index.

INTRODUCTION

Ulcerative colitis is a chronic disease leading to inflammation of the colon and in more severe degrees even causing painful ulcers in the colon which can bleed, cause mucous production and infection. Symptoms can recur or be minimal for months and years. Common symptoms include bloody diarrhea, abdominal pain and weight loss which may be mild to severe and affect individual's quality of life (Lakatos et al., 2007). Disease etiology is relatively unknown. Yet, many studies have

shown influence of genetic and environmental factors. In a meta-analysis performed by Mayo Clinic, incidence of ulcerative colitis was reported as 2 to 14 per thousand person-years (Mahid et al., 2006). The incidence has been decreasing in the world.

According to one report, near 2000 patients have inflammatory bowel disease in Iran and in more than 95%, disease has been controlled with medications (http://www.irbme.ir/congress/p2_articleid/842). Reported cases in Tehran have been small in number. Between the years 1992 and 2002, 448 cases of inflammatory bowel disease have been diagnosed at two university centers and private gastroenterology clinics. Number of cases

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seems to be increasing in Iran (Lukas et al., 2006; Aghazadeh et al., 2004). Ulcerative colitis and crohn's disease rarely occur before the age of 15 years and after teenage years, it has a progressive nature. Age of disease onset is usually under 40 and it can present in elders. Selection for specific races, families and twin studies support genetic influence on disease manifestation. Genetic mutations associated with inflammatory bowel disease have been reported such as in the NOD2/CARD15 gene located on chromosomal region q12(1BD116). In Iranian patients, mutations have been associated only with the crohn's disease and were of the R70W type (Farnoud et al., 2010). Environmental factors implicated have been geographic region, nutrition, medical conditions in infancy and childhood infections, history of appendectomy, smoking, birth control pills and NSAIDs and antibiotics (Lakatos, 2006; Andersson et al., 2001). Many other studies have supported cigarette consumption to be protective of acquiring the disease and smoking cessation to aggravate illness. Risk of developing ulcerative colitis among smokers has been reported to be 0.58 times that of nonsmokers and among quitters, this risk is 1.79 times that of nonsmokers. Yet, second hand smoke exposure in childhood has been reported to increase risk of developing ulcerative colitis in adulthood. It seems that smoking does not influence severity of illness at diagnosis; yet, it increases age at diagnosis and improves course of illness. Course of illness can be evaluated by recurrences, need for hospitalization, need for colectomy and requiring steroid treatment (<http://forum.persianmobiles.com/health/1503-a.html>, 2008; Logan et al., 1984; Persson et al., 1990; Aldhous et al., 2007). A recent study including 401 patients with ulcerative colitis in Iran has shown that 15.5% of the patients are smokers and in comparison prevalence of smoking in society among individuals 15 to 69 years old is 11.7% (Lukas et al., 2006; Aghazadeh et al., 2004). Therefore, smoking may be associated with increased risk of developing ulcerative colitis which is different from studies done in countries of the Western world. Previous studies have overall not shown that age and gender have effect on epidemiology of disease as cofounders. Incidence of disease is less in Iran and course is milder and as a result, we found it valuable to study further any influence smoking may have on disease in this country. Therefore, smoking effect on severity and course of illness was evaluated in this study.

MATERIALS AND METHODS

This study was cross-sectional and observational done at the Amir Alam Hospital. Patients attending gastroenterology clinic at this teaching hospital of Tehran University of Medical Sciences in the year 2009 to 2010 newly diagnosed or follow-up were included in the study. Prevalence of smoking in patients was assumed similar to general society to be 12%; at level of $\alpha = 0.05$ and power of 80%, sample size needed was estimated at 108 individuals to be able to show difference in smoking prevalence among ulcerative colitis patients and general society. Attendants during a complete year

were included. Participants were requested to complete two separate questionnaires one regarding smoking habits and one regarding history of illness. Severity of ulcerative colitis was obtained from patient charts ranked by the clinical presentation, radiology, sigmoidoscopic and histologic assessment during various stages of illness. Most patients were known to the center physicians and presented mostly for follow-up or recurrence of symptoms.

Demographic factors evaluated were age, gender, family members, occupation, marital status, tea and coffee and alcohol consumption as well as history of smoking. Patients had a thorough evaluation at diagnosis. Parameters evaluated in this study for severity and course of illness were number of symptom recurrences, clinic visits and need for hospitalization in a year, need for surgery, medications and change in regimen and family history of inflammatory bowel disease. Illness severity was defined using severe as stages 3 and 4 which show severe inflammatory infiltration and crypt abscess formation on pathology and toxic mega colon on radiology.

Patient exclusion criteria included dependency to alcohol or drugs of abuse, memory deficiencies, having other gastroenterological diseases or psychological disorders and inclusion criteria were all patients attending the clinic without the exclusion criteria. Ethical considerations were prevention of psychological or physical harm, confidentiality of patient information and obtaining consent from the patients. Data was entered into the computer and analyzed using SPSS 11 software. Chi-square and t-tests with level of significance of 0.05 were used for analysis.

RESULTS

A total of 674 patients were evaluated of which 304 (45.1%) were male. Mean age was 41.1 ± 17.3 years in women and 36.9 ± 15.4 years in men which was statistically different ($p < 0.001$). Tea and coffee consumption was significantly more frequent in women compared to men (100% versus 87.9%) ($p < 0.000$) and men consumed more alcohol than women (21.4% versus zero percent) ($p < 0.000$).

A total of 160 patients (23.7%) noted being smokers. Average age cigarette smoking had begun was 19.9 ± 5.4 years and not different between men and women ($p = 0.15$). Hundred and seven participants (66.9%) smoked occasionally and 53 (33.1%) on a daily basis. Occasionally being defined as not smoking one cigarette on a daily basis. Women smoked occasionally 100% of the times and men 59.2% ($p < 0.000$). Average number of cigarettes smoked was 8.5 ± 8.1 which was 5.1 ± 1.2 in women and 9.3 ± 8.9 in men ($p = 0.009$).

Average age of diagnosis for ulcerative colitis in study population was 34 ± 15.2 years not statistically different between men and women ($p = 0.082$). Average age of diagnosis for smokers was 35.8 ± 9.9 years and 33.5 ± 16.5 years in nonsmokers which also did not differ statistically ($p = 0.11$).

Most common symptom with illness was diarrhea (38.7%) followed by abdominal pain (34.7%) and blood in stool (9%) with diarrhea being significantly more present in men (44.7% versus 33.8%) and abdominal pain more common in women (42.4% compared to 25.3%) ($p < 0.000$). Also, diarrhea was more common among nonsmokers compared to smokers (40.3% compared to

Table 1. Distribution of ulcerative colitis severity based on clinics, pathology and radiology in Tehran, 2008.

Severity rating		Mild (Stage 0 - 2)	Severe (Stage 3 - 4)	Total
Total	Number	272	402	674
	Percent	40.4	59.6	100

P > 0.1.

Table 2. Distribution of ulcerative colitis patients based on gender and smoking status in Tehran in 2008.

		Number	Average	Std. Deviation	Significance
Number of daily cigarettes	Men	130	9.3	8.9	0.009
	Women	30	5	0	
Age of disease diagnosis	Men	304	32.9	9.2	0.08
	Women	370	34.9	18.7	
Episodes of hospitalization per year	Men	304	1.5	1.3	0.000
	Women	370	1.9	1	
Number of physician visits per year	Men	276	3.2	1.6	0.000
	Women	284	4.2	1.7	
Episodes of hospitalization per year	Nonsmoker	400	3.6	1.8	0.021
	Smoker	160	4	1.4	
Number of physician visits per year	Nonsmoker	514	1.4	1.1	0.000
	Smoker	160	2.6	0.7	
Cases requiring surgery	Nonsmoker	28	0.05	0.36	0.000
	Smoker	25	0.15	0.22	

33.8%) and abdominal pain was distributed equally independent of smoking status. Finally, blood in stool was more common in smokers compared to non smokers (13.1 versus 7.8%) which was statistically significant ($p = 0.01$).

Nonsmokers on the average had 3.6 ± 1.8 and smokers 4 ± 1.4 visits to physician per year ($p = 0.02$). Also, average episodes of hospitalizations occurred 1.4 ± 1.1 times per year for nonsmokers and 2.6 ± 0.7 times per year for smokers ($p < 0.000$).

Surgery was required for 28 nonsmokers (5.4%) and 25 smokers (15.6%) ($p < 0.000$). Medical treatment included steroids in 64.3%, Mesalamine in 63.5%, Sulfasalazine in 31.7%, Azathioprine in 22.9% and other medications in 27% of patients with combination therapy as needed.

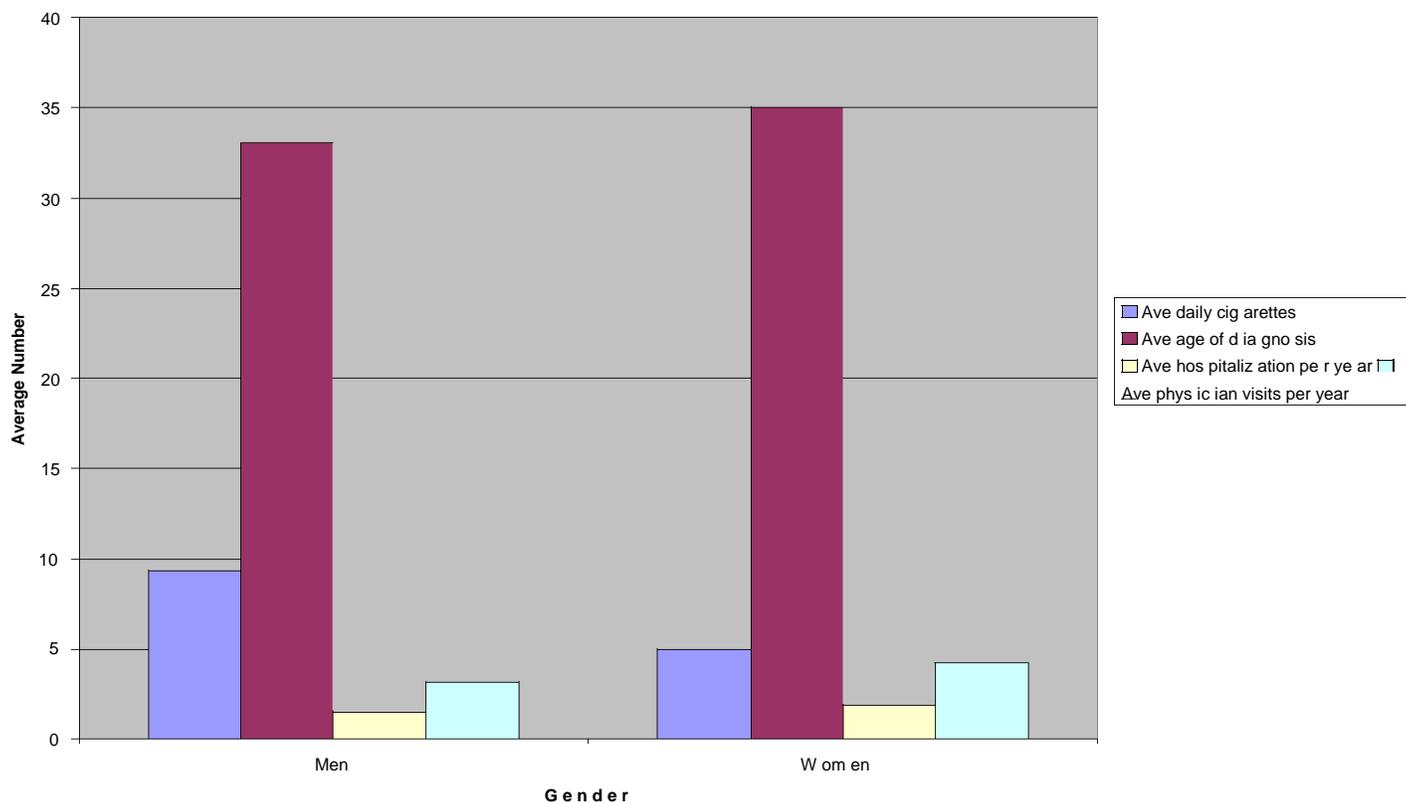
Of all patients, 577 (85.6%) noted no information on smoking affecting their illness, 79 (11.7%) considered it harmful and 18 (2.7%) thought it is useful.

Tables 1 and 2, Graphs 1 and 2 illustrates the illness severity distribution and characteristics.

DISCUSSION

Foreign studies have supported cigarette consumption can be protective against acquiring ulcerative colitis (UC) and smoking cessation can lead to exacerbation (Tuvlin et al., 2007). Risk of developing UC in smokers has been shown to be 0.58 times that of nonsmokers. Also, quitters develop UC 1.79 times that of nonsmokers. Yet, second hand smoke exposure during childhood increases risk of UC in adulthood. Cigarette consumption does not appear to affect severity of illness at diagnosis but delays age of diagnosis and is associated with milder course of illness. Course of illness has been evaluated by measures such as need for hospitalization, colectomy and steroid treatment (Karban and Eliakim, 2007).

Studies in Iran have shown that 15.5% of patients are smokers, while smoking prevalence among 15 to 69 year olds is 11.7% (Aghazadeh et al., 2004). Therefore, smoking can be associated with increased risk of UC which is different from observations in Western countries.



Graph 1. Distribution of illness characteristics based on gender.

Association between UC and smoking was first described in 1982 by Logan and colleagues. They noticed 8% of the patients are smokers compared to 44% of control patients in a fracture clinic (Logan et al., 1984).

In a met analysis at Mayo Clinic, association between UC and cigarette consumption was evaluated. Nine case-control studies were reviewed. Quitters developed UC 1.79 times nonsmokers and smokers 0.58 times nonsmokers. Risk of UC in previous smokers was 0.98 times nonsmokers (Mahid et al., 2006).

In a case-control study, smoking history was obtained from patient charts and postal questionnaire and the Lennard Jones criteria was used at time of diagnosis for determination of severity of illness. Risk of UC in smokers compared to nonsmokers was 0.96 among men and 0.72 among women. Recent quitters had 2.18 times the risk of nonsmokers in developing UC. Previous smokers were 0.6 times as likely as nonsmokers to acquire UC. Five years after quitting, men had 1.2 times and women 1.5 times the risk of developing UC compared to nonsmokers. Therefore, after quitting, passage of time is considered to normalize risk of developing UC in relation to smoking. In the mentioned study, prevalence of smoking in control group was like general society and 36% (Pullan et al., 1994).

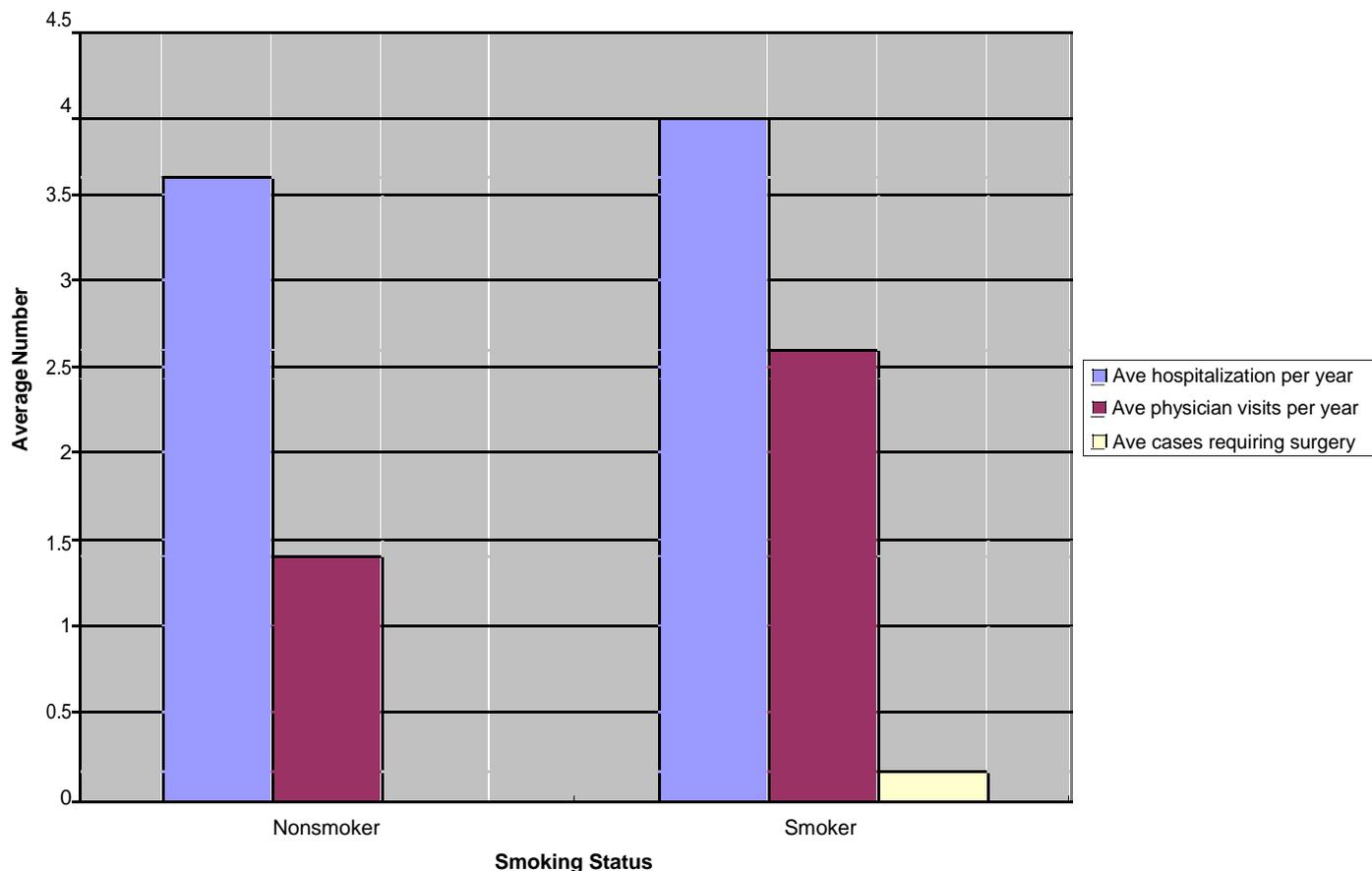
As previously noted, association between UC and smoking has not been consistently shown and

international studies have not reached definite conclusions and need for further research has been supported. This study was done to evaluate influence of cigarette consumption on illness in this country.

Results of this study show that 23.7% of patients are smokers which are higher than that reported in other studies (Achkar, 2007). Prevalence of smoking in the study population is 8.1 and 42.8% for women and men respectively and 2.5 and 25% in general society as per other studies (Makhlough and Fakheri, 2008). The latter supports increased smoking prevalence among patients which needs further investigation and careful methodology. Of importance was that few (3%) patients believed smoking is protective and therefore, we could not explain the high prevalence of smoking in the study population. The above findings were not statistically significant. Age of disease diagnosis in nonsmokers was about 33 years and in smokers near 36 which was not statistically significant ($p = 0.11$).

Need for surgery was observed among men only which was 5.4% in nonsmokers and 15.6% among smokers and statistically significant which has not been reported in other studies (17 to 22).

Incidence of severe illness defined as grades 3 and 4 by pathology (severe crypt abscess infiltration) and radiology (toxic mega colon) was 60% and not different depending on gender or smoking status.



Graph 2. Disease characteristics based on smoking status.

This study did not support cigarette consumption decreases symptoms or disease severity. Need for hospitalization was higher among smokers compared to nonsmokers and further studies are recommended.

Conclusions

1. Prevalence of smoking is higher in patient population compared to national levels.
2. Age of disease diagnosis is a few years higher in smokers compared to nonsmokers but not statistically significant.
3. Smokers had higher rates of physician visits and hospitalization in the year of study.
4. Need for surgery was observed in men and smokers significantly had higher rates compared to nonsmokers.
5. Illness severity based on clinics and radiology and or pathology was not different based on gender or smoking status.

Points of strength

1. Information was collected carefully from patient charts

and questionnaires.

2. Sample size was acceptable compared to other studies.
3. We are able to follow-up with patients.

Points of weakness

1. Nutritional assessment was not done.
2. Ethnicity was not considered.

Suggestions

1. Nicotine treatment study for patients and follow-up as well as follow-up of course of illness in patients who quit smoking.
2. Similar study including points of weakness at national level in the next 5 years.
3. Evaluation of health, ethnics and regions.
4. Evaluation of effect of second hand smoke.

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