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Study of Etiology and Prevalence of Non-Adherence to Treatment in Patients with Inflammatory Bowel Disease Referring to Gastroenterology Clinic of Imam Khomeini Hospital in Ahvaz and Private Gastroenterology Clinics in 2016

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Abstract: This study was conducted to determine etiology and prevalence of non-adherence to treatment in patients with inflammatory bowel disease referred to the gastroenterology clinic of Imam Khomeini Hospital in Ahvaz and private gastroenterology clinics in 2015. In this descriptive-analytical study, 233 patients with inflammatory bowel disease were studied. People aged 18 and over. These patients were selected among those referred to the gastroenterology clinic of Imam Khomeini Hospital in Ahvaz and those who were referred to private gastroenterology clinics. Data were analyzed by SPSS software version 20. Of 233 participants in this study, 147 people (63.1%) were female and 86 people (36.9%) were male. Regarding of non- adherence of 130 patients among our 233 patients, the percentage of non-adherence was 55.7%. The results of this study showed statistical significance and effectiveness of variables (P-value <0.05). Of the 26 people who had Crohn's disease, 3 had no medical care and 23 had medical care. All those who had non-care, their involvement site was colon. Of the people who had care, 65.5% of the cases were affected both large and small intestines, and frequency of involvement in each large and small intestines was separately 21.7%. The relationship between the site of intestinal involvement in Crohn's disease and non-adherence was statistically significant (P <0.05). In this part, people with ulcerative colitis were analyzed for medical care. Of the 233 participants in this study, 207 were suffering from ulcerative colitis that 127 of them had no medical care and 80 had care. The results showed a statistically significant relationship between the site of intestinal involvement in patients with ulcerative colitis and non-adherence (P <0.05). This study showed the effect of some factors on non- adherence to treatment in patients with inflammatory bowel disease.

Keywords: lack of medical care, lack of health care, inflammatory bowel disease, ulcerative colitis and Crohn's disease, adherence, non-adherence

INTRODUCTION

Inflammatory Bowel Disease (IBD) is a group of intestinal diseases, the most common of which is Crohn's Disease (CD) and ulcerative colitis (UC). CD can occur in any area of the gastrointestinal tract, but UC usually involves the colon. Full thickness of the intestinal wall is often affected by Crohn's disease, while ulcerative colitis only involved the mucous layer. Inflammatory bowel disease is a common disorder worldwide with a prevalence rate of 0.1 to 0.4 percent of the general population [1].

Ulcerative colitis is a mucosal disease that usually affects the rectum and progresses gradually towards the proximal to involve all or part of the colon, and in terms of location is divided into four forms of Proctitis, Proctosigmoiditis, Left-sided colitis, and Pancolitis. In proctitis form, the disease is limited to rectum. In proctosigmoiditis form, in addition to the rectum, sigmoid is involved. In the left-sided colitis, the disease starts from the rectum and affects the entire left side of the colon and in the pancolitis form the entire colon is involved, and regarding the severity of the disease is divided into mild, moderate, severe and fulminant forms [4, 3, 2]. Ulcerative colitis causes

prolonged inflammation in a part of gastrointestinal tract. Since ulcerative colitis is a chronic disease, its symptoms and severity become worse over time. Ulcerative colitis generally affects the mucosal surface of the large intestine and rectum [5, 6]. Complications of ulcerative colitis is megacolon, perforation of the colon, anemia and adenocarcinoma, and Crohn's complications include small and large intestinal stenosis, fistula, abscess, calcium oxalate stones and carcinoma [5]. The combination of some illnesses, manifestations and neurological complications with IBD has been suggested as a hypothesis. These include multiple sclerosis, peripheral neuropathy, optic neuritis, and a subclinical sensory loss in auditory hearing [7].

Crohn's disease is a pan-enteric inflammatory disease, which is commonly found throughout the gastrointestinal tract [8]. Several reports suggest that the Crohn's disease has increased in recent years in Asian countries [9]. In Crohn's disease, symptoms of disease depend on severity of inflammation, fibrosis, and the location of inflammation. Acute inflammation can cause diarrhea, abdominal cramps and fever. In Crohn's disease, weight loss is common, that is due to the loss of protein. The inflammation process in Crohn's disease is seen in one of two patterns: a Fibrostenotic-obstructing pattern or a penetrating-fistulous pattern. Each of these has different treatments and prognosis [10, 2].

Statistics show that 1.4 million Americans and 2.2 million people in Europe are affected with IBD [11]. The incidence of ulcerative colitis in North America is 2/2-14/3 per 100,000 population, and for Crohn's disease, it is 3/1-14/6 per 100,000 population [11]. The highest incidence of ulcerative colitis has been reported in Europe, Britain and North Americ [2]. The mean age of ulcerative colitis is between 15 and 35 years of age [2]. The incidence of Crohn's disease is increasing in Asia, especially in Iran. Crohn's disease has two age peaks, the first age peak is between 20-40 years of age and the second peak is between 55 and 65 years [12, 13]. The prevalence rate of IBD is higher in whites, with an almost identical prevalence of IBD in both genders [2].

Aghazadeh *et al*. in an article published in 2004, studied 457 IBD patients and showed that incidence of the disease is increasing, as in other countries. The mean age of Crohn's patients is 30.5 years and in cases of ulcerative colitis 31.9 [14].

In Iran, IBD epidemiology and exact prevalence have not yet been identified, and studies only have been conducted on a population of patients, mostly due to the absence of a national disease registration system in Iran. According to reports, these diseases are not rare in Iran [15]. The nature of the disease, the severity and frequency of relapses, the extra-intestinal symptoms, the effects of drug treatments, surgery and their side effects, the concern about the possibility of cancer and the need for surgery and other characteristics of IBD, affect the daily lives of patients, and significantly reduces the quality of life [16].Therefore, the purpose of this study is to determine frequency and causes of lack of medical care in patients with inflammatory bowel disease, referring to the gastroenterology clinic of Imam Khomeini Hospital in Ahvaz and private gastroenterology clinics in 2015.

MATERIALS AND METHODS

This research is a cross-sectional descriptive-analytic study. All patients enrolled in this study were people over 18 years of age who suffered from inflammatory bowel disease (IBD) and their disease was confirmed by a gastroenterologist based on the clinical and pathological signs and symptoms and had the criteria for entering the study. The patients were selected among the people referred to the gastroenterology clinic of Imam Khomeini Hospital in Ahvaz and those who are referred to the personal office of a gastroenterologist at this university

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To determine the sample size, referring to reference number [17], the sample size, based on following formula, was taken as 233 persons:

$$n = \frac{z^2 p(1-p)}{d^2}$$

D = 0.2P
P = 0.3
1-P = 0.7
$Z_{1-\alpha/2} = 1.96$

In this study, a researcher-made questionnaire was used. In order to assess the qualitative validity of the researcher-made questionnaire, comments of 6 expert and specialist gastroenterologist were used and their opinions were applied in the design of the questionnaire. In order to measure the reliability of the questionnaire, a pilot study was performed on 50 patients. Data were entered into SPSS version 20 and Cronbach's alpha was calculated. Cronbach's alpha test showed good reliability. Cronbach's alpha value was 0.82. The variables of this questionnaire include: age, gender, educational status, residency place, access to specialized care centers, quality of drugs and information about their habits and lifestyle including smoking and alcohol consumption, using of internet, and information about their disease including the type of disease (Crohn's disease or ulcerative colitis), location of intestinal involvement, extra intestinal disease manifestations and knowledge about nature of the disease. Finally, the relationship between this variables and lack of medical care was assessed and

evaluated. The "Cronbach Alpha Method" is used to measure reliability. This work is done using SPSS software. The credit number of 1/00 in this method is indication of full reliability of the measuring instrument and the credit number of 0/00 indicates complete unreliability.

Data were analyzed by SPSS software version 20. For qualitative variables, frequency and frequency percent, and for quantitative variables, mean and standard deviation were calculated. The normalization of quantitative variables is investigated by the Kolmogorov-Smirnov test. To test the assumptions in the case of normal data, two independent samples and one way analysis of variance are used. Also, for qualitative-qualitative variables, Chi-square and Fisher test will be used. The significance level was less than 0.05.

RESULTS

In this study, among 233 patients and participants, 147 (63.1%) were female and 86 (36.9%) were male. The educational status of the participants in this study was reported and the highest number of participants had a diploma degree (34.8%). After diploma, the highest percentage was licentiate's degree (26.2%). Of the 233 participants 129 patients (55.4%) were live in Ahvaz, 9(3/9%) were smokers and 10 had a history of smoking. 225 (96.6%) patients had no history of alcohol consumption. 1 person consumed and 7 people left alcohol. The status of using the Internet indicated that the majority of participants used the Internet (76.8). 54 people did not use the Internet. Among 233 participants, 207 (88.4%) had ulcerative colitis and 26 cases (11.6%) had Crohn's disease. Based on drug use, patients were divided into three groups. Patients who used Iranian drugs (63.5%), foreign drug consumers (27.5%) and cases who have consumed the both type together (9%). As it was seen, maximum cases used Iranian drugs. Regarding drug use, more than 96% of patients took medication as ordered by their doctor and about 3% of them took medication arbitrarily. In this study, more than 80% of people knew that their disease control with drug use, 1.2% of them thought that their disease completely improve with drug use, and 17.2% of patients did not have any recognition about their disease.

Those who had pan colon involvement and passed for more than 8 years, were evaluated for colonoscopy. 198 people (85%) had no colonoscopy indication, 3 patients with colonoscopy indication did not do this, 13 people performed colonoscopy every two years, 19 people performed colonoscopy every 3 years or more. People with left colon involvement for 12 years and more, were evaluated for colonoscopy.178(76/4%) cases had no indication, 21 cases did not do this, 2 cases perfumed colonoscopy every 1 year, 5 cases every 2 years ,27 cases every 3 and more years. The subjects were evaluated about reasons for not performing colonoscopy. Based on the results, about 13 percent of people said that the reason for not using colonoscopy was the high cost of this test, which accounted for the highest percentage of people who did not use it. 4% of people expressed their fear for not doing this test. 4.7 percent of people mentioned lack of access to specialized centers as a reason for not using it. 6 percent of the participants noted that they did not know about the test. 168 people either did not have colonoscopy or did it on time.

Of those who did not test bone density (81 cases), 73 of them were unaware of a bone density test, 8 cases considered high cost of test and lack of access to specialized centers for not doing bone density testing. Of 233 patients, 69.5% of them had access to specialized care centers, and about 30% of them did not. The mean age of the adherence group was 36.17 and non-adherence group was 37.68 years. The difference in age of the two groups was not statistically significant. In other words, the age of the people did not affect the health care of individuals, but those with a lower age showed more importance to health care ($P > 0.05$). Chi-square test was used to examine the association between gender and marital status with health care. The results of this test showed that there was no significant statistical association between the gender and marital status of individuals and their lack of medical care at the level of 5% error ($P > 0.05$). The results of the Chi-square test indicated a significant association between the level of education and the lack of medical care ($P < 0.05$). According to the findings, the results of Chi-square test showed a statistically significant association between the place of residency and the lack of medical care ($P < 0.05$). The rural population was more likely to be looking for medical care. The results of the test of association between alcohol consumption and the lack of health care were reported statistically significant ($P < 0.05$) but There was no statistically significant correlation between smoking and using of internet with lack of medical care ($P > 0.05$).

Table-1: Location of intestinal involvement in patients with Crohn's disease

The location of intestinal involvement in patients with Crohn's disease	Frequency	Frequency percent
small intestine	5	19.20
large intestine	8	30.80
both cases	13	50.0
total	26	100

Of the 26 patients with Crohn's disease, in 5 cases (19.2%) site of involvement was small intestine, 8 (30.8%) cases was the large intestine, and 13 cases both small intestine and large intestine.

Table-2: Location of intestinal involvement in patients with ulcerative colitis

The location of intestinal involvement in patients with ulcerative colitis	Frequency	Frequency percent
left part of colon	114	55.30
Pancolonic involvement	51	24.80
rectum	23	11.20
rectosigmoid	18	8.70
Total	206	100

Of the 206 people with ulcerative colitis, there has been more involvement in the left part of colon (55.3%). 51 cases had pancolon involvment. The involvement of rectum and rectosigmoid was 11.2% and 8.7%, respectively.

Table-3 :Association between lack of therapeutic health care and drug quality

variable	non health care		health care		significance
drug quality	frequency	percent	frequency	percent	
Iranian	93	71.50	55	53.40	0.002
foreign	32	24.60	32	31.10	
both cases	5	3.80	16	15.50	
Total	130	100	103	100	

The association between the quality of drug and lack of therapeutic health care was statistically significant (P <0.05). People who did not have health care mostly used Iranian drugs, and in the group who had health care, they tended to use foreign drugs or foreign and Iranian compounds more than those who did not have health care.

Table-4: Association between lack of therapeutic health care and type of disease

variable	non health care		health care		significance
type of disease	frequency	percent	frequency	percent	
Crohn	3	2.30	23	22.30	P < 0.002
ulcerative colitis	127	97.70	80	77.70	
Total	130	100	103	100	

In this study, there was a significant association between type of inflammatory bowel disease and lack of therapeutic health care (P <0.05). Majority of patients with U.C are in non-adherant group and majority of patients with C.D are in adherant group.

Table-5: The association between non-therapeutic health care and site of involvement in crohn's patients

variable	non health care		health care		significance
intestinal involvement	frequency	percent	frequency	percent	
small intestin	0	0	5	21.70	0.022
large intestin	3	100	5	21.70	
both cases	0	0	163	65.50	
Total	3	100	23	100	

Of the 26 people who had Crohn's disease, 3 had no health care and 23 had health care. All those who had non-health care their involvement site was large intestine. Among the people who had health care, 65.5% of them the site of involvement was large and small intestines and abundance of involvement in each of the large and small intestines was reported 21.7% separately.

There was a significant association between site of intestinal involvement in Crohn's disease and lack of health care (P <0.05). In other words, in patients

with Crohn's disease, site of intestinal involvement affect health care.

People with ulcerative colitis have been analyzed for health care. Of the 233 participants in the study, 207 were suffering from ulcerative colitis, 127 of them had no health care and 80 had health care. The results showed a significant statistical association between the site of involvement in patients with ulcerative colitis and lack of medical care (P <0.05).

No significant correlation was found between the knowledge about nature of the inflammatory bowel disease and its association with the lack of therapeutic care (P >0.05). In other words, the knowledge about the nature and the process of the disease did not affect the patients' health care.

In this research, extra intestinal disease manifestations did not have any effect on patient health care (P >0.05). In other words, other areas of manifestation did not affect the patients' health care. In this research, the hypothesis of correlation between the access to specialized care centers and the lack of therapeutic care at a 5% error rate was not rejected. There was a significant statistical relationship between them (P<0.05).

DISCUSSION

Due to the lack of a control and reporting center for non-contagious diseases, the pattern of many non-contagious diseases, especially IBD in Iran is unclear, and there are limited studies in this field [18]. This study was conducted to determine etiology and prevalence of non-adherence to treatment in patients with inflammatory bowel disease referred to gastroenterology clinic of Imam Khomeini Hospital in Ahvaz and private gastroenterology clinics in 2016. In this research, in order to investigate the causes of lack of medical care, following factors such as age, gender, education, marital status, place of residency, access to treatment centers, alcohol consumption, smoking, internet use, quality of drug use, the type of disease (Crohn's disease and ulcerative colitis), location of the involvement of Crohn's disease, location of the involvement of patients with ulcerative colitis, knowledge about the nature and the course of the disease, extra intestinal disease manifestations were analyzed. The results of this study indicate significant statistical association between variables of education, place of residency, access to treatment centers, alcohol consumption, drug quality, type of disease (Crohn's disease and ulcerative colitis), site of involvement of Crohn's patients, the site of involvement of ulcerative colitis and non-adherence to treatment (P-value <0.05). Others factors mentioned in this study did not have a significant statistical effect on the non-adherence to treatment (P-value <0.05).

The exact cause of IBD (CD, UC) is unknown. But risk factors such as family history, smoking, air pollution, the use of pregnancy pills and the type of diet can contribute to the disease. It is likely that a combination of factors such as genetic defect, inaccurate mucosal immune response, intestinal mucus membrane dysfunction, and deficiency in host interaction with intestinal microorganism can play a significant role in Crohn's disease and ulcerative colitis [19-21].

In the study of Rahim Aghazadeh *et al*. the most U.C patients 95.9% were urban and 4.1% rural and in patients with C.D 97% were urban and 3% rural. The study also found that majority of IBD patients had high school diploma degree [22]. Also in the present study, majority of IBD patients had a diploma degree and 94% were urben and 6% were rural.

A study in 2007 by Cerveny *et al.* Entitled "non-adherence in inflammatory bowel disease in the Czech Republic," was performed on 396 patients, 186 patient with ulcerative colitis and 210 patients with Crohn's disease. The results showed that non-adherence with treatment in inflammatory bowel disease were observed in 32% of patients, that 12% of them reported at least one treatment discontinuation. The use of arbitrary doses of drugs was observed in 19% of patients. Also, in 11% of patients after drug discontinuation, the drug was not re-administered. Finally, there was no statistically significant association between non-adherance and smoking habits, educational level, type of inflammatory bowel disease, type of previous surgery, and other variables [23].unlike Carvery's study that educational status and type of disease did not have statistically significant association with non-adherence, in the present study this two variables statistically had significant association with non-adherence.

In a study done in 2014 by joana magalhaes in cohort on 138 patients with inflammatory bowel disease with 55.8% crohn,s and 44.2% ulcerative colitis, the following results were obtained: non adherence in general was reported in 29.7% of patients. Non-adherence value was statistically associated with the following: shorter disease duration (p <0.001), age (p = 0.001), topical aminosalicylates use (p = 0.005), social status, and high education (p = 0.011) [17].like joana magalhaes's study, in the present study, Ejucational status statistically had significant association with non-adherance.

The following results were obtained in a cross-sectional study on the awareness, knowledge and insights of patients with IBD about their disease in 2014 by Daniela Simian *et al.* on 203 patients in Singapore. The results showed that the patients included in the

study, such as developed countries, have little knowledge and insight into their illness [24]. In the present study, more than 80% of people knew that their disease control with drug use.

In a study conducted in 2008 on 485 patients with IBD with regard to drug adherence risk factors by DInca et al., following results were obtained: 39% of patients were reported in the non-adherence group. The mean age of the non-adherent group was 38 years (range: 17-82). While the average age of the Adherent group was 42 years with a range of 15-83. Variables such as the age below 40, the use and administration of multiple doses of drug, and prolonged exposure to the disease were associated with non- adherence to drug use [25]. In present study, age did not have significant association with non-adherance.

In a study conducted by Dr. Hajiani *et al*. in 2007, prevalence of ulcerative colitis in Khuzestan province, is more than Crohn's disease. The incidence of ulcerative colitis in women is higher than that of men. The complications of colon and colon cancer are lower in patients with inflammatory bowel disease in Khuzestan. Family history of the disease and its relation to smoking in Khuzestan are similar to other reports in other areas [26].also in the present study, prevalence of ulcerative colitis, is more than Crohn's disease and the incidence of ulcerative colitis in women is higher than that of men. Regarding other variables studied in this research, we did not find a similar study to compare the results.

CONCLUSION

In general, the results of this study indicate the effect of factors on non-adherence to treatment in patients with IBD. factors including education, residency, access to treatment centers, alcohol consumption, drug quality, type of disease (Crohn's disease and colitis ulcerative), the location of involvement of Crohn's disease, the location of involvement of patients with ulcerative colitis. by creating specialized centers in the cities and paying attention to the income of patients and improving the quality of medications and informing patients about their disease, can help them in health care and prevent the occurrence of irreparable conditions for patients.

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