

Gastroenterological disorders increase the prevalence of Overactive Bladder in females at various ages

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ABSTRACT

Objective: In this study we aimed to determine the coexistence of overactive bladder in patients with gastroenterological disorders including hepatitis, cirrhosis and IBD.

Materials and Methods: We prospectively collected the data of patients who admitted to the outpatient clinic of department of gastroenterology at Turkiye Yuksek Ihtisas Training and Research hospital between May 2017 and February 2019. All patients with chronic gastroenterological disorders such as hepatitis and irritable bowel syndrome willing to participate the study after the verbal consent were included the study

Results: A total of 289 female patients were included the study. The mean age of the patients was 49.9 ± 13 years. The mean BMI value was 27.9 ± 4.5 kg/m². Among 289 patients, 135 (46.7%) had Hepatitis B, 53 (18.3%) had ulcerative colitis, 35 (12.1%) had Crohn's disease, 22 (7.6%) had autoimmune hepatitis, 19 (6.6%) had primer biliary cirrhosis, 13 (4.5%) had Hepatitis C and 12(4.2%) had celiac disease. The mean age of patients was similar between patients having OAB-v8 higher and lower than 8 ($p=0.46$). However, patients having OAB score >8 had higher BMI compared to patients who had OAB score <8 , 29.1 ± 5 vs. 27.2 ± 4.1 kg/m², $p=0.001$. In multivariate regression analysis, BMI was the sole indicator of OAB ($p=0.001$) whereas age ($p=0.46$), menopause status ($p=0.33$), smoking status ($p=0.97$) were not.

Conclusion: The incidence of OAB in our patient cohort was higher than the reported incidence which might suggest evaluation patients with gastrointestinal disorders in terms of overactive bladder on routine follow-up.

WHAT'S KNOWN?

The etiology of overactive bladder (OAB) is still unknown. Atherosclerosis of pelvic vasculature and cross-organ sensitization are some of the theories suggested. Higher body mass index and smoking were reported to be associated with OAB.

WHAT'S NEW?

We found a significantly higher rate of OAB in our patient cohort including patients with inflammatory bowel disease and hepatitis. Body mass index was significantly higher in patients having OAB regardless of intraabdominal organ pathology.

INTRODUCTION

Overactive bladder (OAB) is defined as urinary urgency with or without incontinence, usually accompanied with frequency and nocturia. OAB affects 15% of the adult population with a slightly dominance in women. However, a few of people with OAB seek for medical care for this disorder. OAB might lead to several health problems such as depression, sleep disorder and worsen quality of life [1].

Ulcerative colitis and Chron's disease, known as 'inflammatory bowel disease (IBD)', constitutes a major health burden and have detrimental effects on quality of life of affected patients. As it is a chronic disease with unknown/ multifactorial etiology several attempts and investigations have been made to control these inflammatory processes [2]. Currently accepted treatments choices included antibiotics, probiotics, folic acid antagonists, aminosalicylates, corticosteroids, thiopurines, methotrexate and anti-TNF agents [2,3].

It has been estimated that approximately 2.5-3 million people are affected by IBD in Europe and there is a still tendency of increase in its incidence not only in Eastern Europe but also in Asia. The cumulative surgery rate 10 year after diagnosis was reported to vary between 37% and 61% and surgery rate was found to be declined in the last two decades [3]. Inflammatory bowel disease is not only a bowel limited disease but also has several extra-intestinal signs and symptoms. Extraintestinal manifestations include Joint manifestations (arthropathies), cutaneous manifestations (erythema nodosum, pyoderma gangrenosum), ocular manifestations which are found be frequent as high as 40% [3].

Furthermore, non-alcoholic fatty liver disease (NAFLD) was found to be associated with overactive bladder in women. The mechanism in this association was mainly based on NAFLD as being a component of metabolic syndrome. Thus, NAFLD might lead to atherosclerosis. However, mediators called hepatokines might also cause an inflammatory environment [4]. There is not much study showing the relation between hepatitis and overactive bladder.

To the best of our knowledge there is no study in the literature examining the bladder-related comorbidities of patients having gastroenterological diseases in Turkish population. Thus, in this study we aimed the determine the coexistence of bladder disorders in patients with gastroenterological disorders including hepatitis, cirrhosis and IBD.

MATERIAL AND METHODS

After obtaining the approval from the institutional review board (IRB number:29620911-929-65), we prospectively collected the data of patients who admitted to the outpatient clinic of department of gastroenterology at Turkiye Yuksek Ihtisas Training and Research hospital between May 2017 and February 2019. All patients with chronic gastroenterological disorders

such as hepatitis and irritable bowel syndrome willing to participate the study after the verbal consent were included the study. The inclusion criteria were as follow:

1. Both male and female patients older than age of 18
2. Having chronic gastroenterological disorders
3. Willing to participate the study and fulfill the questionnaire
4. Having regular follow-up.

The exclusion criteria included:

1. Being younger than 18 years of old.
2. Having a history of cancer
3. Receiving any chemo-radiotherapy for any reasons.
4. Being on medications like opioids or analgesics.
5. Having psychiatric disorders impairing or aggregating pain perception.

All patients were requested to fulfill the Overactive bladder V8 questionnaire which is a validated questionnaire in Turkish [5]. The recorded parameters also included patient demographics, medical history and medications, complete blood count, urinalysis, serum urea and creatinine. The patients were divided into three groups according to symptom severity as in previous studies: Group 1- having OAB v8 score= 0-7, Group 2- having OAB v8 score=8-16, Group 3- having OAB-v8 >16 [6]. Patients having OAB v8 score>7 assumed to have OAB.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows v.21.0 (IBM Corp., Armonk, NY). Quantitative values are shown as mean \pm SD (range) and qualitative values are shown as number and percentage. One-way ANOVA and the chi-squared test were used to

compare dichotomous variables between groups. Student's t-test and the Mann-Whitney U-test were used to compare groups with normally and non-normally distributed continuous data, respectively. The level of statistical significance was set at $P < .05$.

RESULTS

A total of 289 female patients were included the study. The mean age of the patients was 49.9 ± 13 years. The mean BMI value was 27.9 ± 4.5 kg/m². Among 289 patients, 135 (46.7%) had Hepatitis B, 53 (18.3%) had ulcerative colitis, 35 (12.1%) had Crohn's disease, 22 (7.6%) had autoimmune hepatitis, 19 (6.6%) had primer biliary cirrhosis, 13 (4.5%) had Hepatitis C and 12(4.2%) had celiac disease. 115 (39.8%) of the patients were in menopause. 31 (10.7%) were active smokers. Six patients (2.1%) had psychiatric disease including depression (n=3), anxiety (n=2) and panic attack (n=1). 78 patients (22.8%) had a OAB-v8 score higher than 8.

There was no statistically difference between patients having different gastroenterological pathologies in terms of OAB ($p= 0.34$). The mean age of patients was similar between patients having OAB-v8 higher and lower than 8 ($p=0.46$). However, patients having OAB score>8 had higher BMI compared to patients who had OAB score <8, 29.1 ± 5 vs. 27.2 ± 4.1 kg/m², $p=0.001$. There was no difference between patients who had menopause and who had not in terms of OAB score, $p=0.37$. OAB frequency was similar between patients who were active smoker and who were not active smokers ($p= .11$). In multivariate regression analysis, BMI was the sole indicator of OAB ($p=0.001$) whereas age ($p=0.46$), menopause status ($p=0.33$), smoking status ($p=0.97$) were not.

DISCUSSION

Over active bladder (OAB) is defined as urgency with or without incontinence, often accompanied with frequency or nocturia. OAB may be idiopathic or related to neurologic

disorders. The reported prevalence of OAB varies between 5.9 and 15.6% and strongly correlated with aging. OAB severity tends to increase in post-menopausal women which might be associated with decreased levels of estrogen [7]. In our patient cohort, the prevalence of OAB was 22.8% which might indicate the high prevalence of OAB related to gastrointestinal disorders.

Etiology of OAB is considered multifactorial and ischemia related bladder dysfunction is one of the suggested mechanisms. It has been reported that atherosclerosis causes bladder ischemia. Smoking is one of the leading factors of atherosclerosis. In previous studies, OAB symptoms have shown to strongly correlated with aging and smoking status [8].

Increased body mass index (BMI) was also reported to be associated with OAB symptoms [9]. In the present study, the mean age of the patients and smoking status of the patient who had OAB symptoms and who had not, were similar. This might due to the confounder effect of gastrointestinal disorders.

Cross organ sensitization has been widely studied and suggested in various conditions including trochal and abdominal organs. The organs reported to involve cross organ sensitization phenomena included pelvic and lower abdominal organs: colon, rectum, urinary bladder, urethra, uterus and the prostate. It has been also suggested that urinary bladder is more vulnerable to cross-sensitization than other pelvic organs [10]. In an ancient study in 1980's Whoewel et al. reported that patient with irritable bowel syndrome may represent symptoms related to urinary bladder such as nocturia, frequency, urgency and sense of incomplete bladder emptying [11]. Gastrointestinal disorders generally classified under two groups as organic and functional. Inflammatory bowel disease (IBD) consists of Crohn's disease and ulcerative colitis is an organic digestive tract disease characterized with chronic relapse and remittance of intestinal

inflammation. The most frequent symptoms of IBD are abdominal pain, diarrhea, gastrointestinal bleeding as well as malnutrition [12]. Although there have been several studies regarding to relationship between various gastroenterological disease and urological problems, there is not a study examining overactive bladder in a gastroenterological disease spectrum.

In a study by Haim et al. the researchers found that 24.7% of the patients with Crohn's disease have urological symptoms which included cystitis, hydronephrosis, urolithiasis, enterovesical fistulas and retroperitoneal abscess [13]. In a recent study by Xia et al. [14] authors investigate the mechanism of bladder hypersensitivity in patients with colonic inflammation. In their experimental study with rats, authors found that colon to bladder cross-sensitization exists with the upregulation of brain-derived neutrophic factor (BDNF) in dorsal the dorsal root ganglia.

Experimental animal studies have shown that chemically induced OAB might result in a hypersensitized colon and conversely induced colitis might alter urinary bladder functioning bladder [15]. There have been several studies evaluating the association between irritable bowel syndrome and overactive bladder [16,17]. Matsumoto et al. [16] found that 33.3% of patients with OAB had concurrent IBS. And they concluded that assessing the defecation habits of patients is of important when diagnosing or treating OAB. In contrast with Matsumoto et al., Kim et al. [17] reported no association between IBS and OAB. In our study, OAB was found to be present at 21.6% of our patient cohort which indicates the increased frequency of OAB compared to healthy population. These results might reflect the aforementioned mechanisms of cross-sensitization between abdominal organs. In concordance with the aforementioned studies, we found a high incidence of OAB in our patient cohort having gastrointestinal disorders. Although, the relationship between bowel diseases and OAB have been frequently studied, there

is a lack of data assessing the possible relation between hepatic diseases and OAB. Almost all studies, reported a possible relationship based on the similar etiological risk factors for fatty liver and atherosclerosis.

Our study is not without limitations. The main limitation of the present study is that the heterogenous nature of the study population like some were in menopause and some were active smoker which might affect bladder habitus. Also, there was no so much patient in gastroenterological disease's subgroups that might cause statistical weakness.

CONCLUSION

We found a similar overactive bladder frequency in patients having various gastroenterological disease such as hepatitis, inflammatory bowel disease, celiac and autoimmune hepatitis. The incidence of OAB in our patient cohort was higher than the reported incidence which might suggest evaluation patients with gastrointestinal disorders in terms of overactive bladder on routine follow-up.

Table 1. Comparison of patients according to OAB-v8 score

Variable		OAB-v8 score <8 (n=188)	OAB-v8 score>7 (n=101)	P value
Age (yr)		49.5±12.5	50.7±13.5	.46
BMI (kg/m ²)		27.2±4.1	29.1±5	.001
Crohn's disease		22 (62.9%)	13(37.1%)	.62
Ulcerative colitis		35(66%)	18(34%)	
Autoimmune hepatitis		12(54.5%)	10(45.5%)	
Hepatitis B		94(80.7%)	41(19.3%)	
Primer biliary cirrhosis		12(63.2%)	7(36.8%)	
Hepatitis C		7(53.8%)	6(46.2%)	
Celiac disease		6(50%)	6(50%)	
On Menopause	Yes	71(37.8%)	44(43.6%)	.37
	No	117(62.2%)	52(56.4%)	
Active smoker	Yes	16(8.5%)	15(14.9%)	.11
	No	172(91.5%)	86(85.1%)	
Hypertension	Yes	14(7.4%)	6(5.9%)	.80
	No	174(92.6%)	95(94.1%)	

BMI: Body Mass Index

Conflict of interest statement

The authors have no conflicts of interest.

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