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Investigatıon of Inflammatory Marker Levels in Overactive Bladder Patients

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Abstract

***Aim**: To investigate whether inflammation plays a role in the pathogenesis of patients diagnosed with overactive bladder (OAB).*

***Material-Method**: Patients who applied to the urology outpatient clinic with a preliminary diagnosis of OAB between March 2022 and September 2023 and were diagnosed were prospectively included in the study. With the OAB V8 scores (0-40) and the anticholinergics used, the number of urgency attacks, pollakiuria and nocturia were also recorded. Blood group, complete blood count, inflammation markers and biochemical values recorded.*

Patients who presented to the outpatient clinic with non-OAB were included as the control group. Data recorded at baseline were compared between groups.

***Results**: A total of 198 patients were included in the study (OAB group n: 99, control group n: 99). No statistically significant difference was observed between the groups in terms of gender and blood group, hemoglobin, hematocrit, lymphocyte, platelet, AST, ALT, albumin, neutrophil-lymphocyte ratio (NLR), lymphocyte-monocyte ratio (LMR), platelet-lymphocyte ratio (PLR), Deritis, MLR and CRP/albumin ratio.*

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The mean age of the OAB group was found to be significantly higher than the control group (p<0.001). The mean WBC, neutrophil, monocyte and CRP values of the control group were found to be statistically significantly higher than the OAB group.

As a result of the multivariate analysis, only age was found to be a predictor for OAB.

***Conclusion**: According to the results of our study, inflammation markers used in our study were found to be low in OAB patients.*

***Key words**: Overactive bladder, inflammation, neutrophils*

Introduction

Overactive bladder is a syndrome characterised by urinary urgency, usually accompanied by frequency and nocturia, with or without UUI, in the absence of UTI or other obvious pathology (1). Diagnosis is based on symptoms. It is a chronic disease that significantly reduces quality of life.

Many theories have been proposed to explain the pathophysiology. The main known mechanism is detrussor hypersensitivity or imbalance in the inhibitory and excitatory pathways of the bladder. Many biomarkers have been identified that are thought to be effective in its pathogenesis (2). These include nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), prostoglandins, cytokines and CRP (3, 4).

Based on the assumption that inflammation plays an aetiological role in OAB, some authors have investigated the role of urinary cytokines in patients with OAB and whether they can be considered as a biomarker for the disease (5, 6). Biomarkers aim to aid diagnosis in OAB, monitor disease progression, and potentially assess response to treatment. However, there is no strong data on the usability of these biomarkers in the evaluation of diagnosis and response to treatment in the studies conducted so far.

In our study, we aimed to investigate whether inflammation markers play a role in the diagnosis of OAB patients.

Material-Method

Ethics committee approval dated 11.05.2023 and numbered 2023-10/1 was obtained from Erzincan Binali Yıldırım University Faculty of Medicine Ethics committee for the study.

Between May 2022 and September 2023, patients between the ages of 18 and 60 who were admitted to the urology outpatient clinic with a preliminary diagnosis of OAB and diagnosed with OAB were prospectively included in the study. OAB was diagnosed according to the criteria defined by the International Continence Society (7). The study was conducted in accordance with the principles of the 2008 Helsinki Declaration.

Demographic data including age, gender and BMI were recorded. Demographic data of the patients were recorded. With the OAB V8 scores (0-40) and the anticholinergics used, the number of urgency attacks, pollakiuria and nocturia were also recorded. The OAB-V8 form is a form consisting of 8 questions with each question being scored between 0-5 and a total score of 40 points. A total score above 8 is considered significant (8). Blood group, complete blood count and biochemical values, inflammation markers (NLR, PLR, LMR, CRP/Albumin ratio and De ritis ratios) were recorded from peripheral blood at outpatient clinic visits.

Patients with urinary tract infection, systemic inflammation, renal function test disorders, patients with a history of previous urological surgery, patients with a history of urological malignancy, patients with bladder stones, benign prostatic hyperplasia and urethral stricture were excluded from the study. Patients with haematological diseases that might affect haemogram parameters were also excluded from the study. As a control group, patients who were admitted to the outpatient clinic for other reasons and who did not have OAB symptoms were included. Haemogram and biochemical values of these patients were also recorded.

The data recorded at baseline were compared between the groups.

Statistical Analysis

Statistical analysis was performed using IBM SPSS version 21 (IBM Corp., Armonk, NY, USA). Variables were expressed as mean ± standard deviation and percentage. The Kolmogorov-Smirnov test was applied to examine normal distribution. Differences between 2 groups were analysed by Mann-Whitney U test. Chi-square test was used to compare qualitative data. Logistic regression analysis was used to identify predictors of

OAB. Predictive accuracy for diagnosis was assessed by area under the curve (AUC) of ROC analysis. G-Power 3.1.9.4 statistical power analysis programme was used to calculate the sample size of the study. $p < 0.05$ was considered statistically significant.

Results

According to the power analysis results (two-way correlation, type-1 error rate (α)=0.05, power of the study (1-β)=0.80 and effect size=0.52), a sufficient number of patients were included in each group (n=99). A total of 198 patients were included in the study. 99 patients were included in the OAB group and 99 patients were included in the control group.

The mean age of all patients was 52.3±15 years and the mean OAB-V8 score was 11.9±9.9. Male/female ratio was 101/98.

No statistically significant difference was observed between the groups in terms of gender and blood group (Table 1). No statistically significant difference was observed between the groups in terms of haemoglobin, haematocrit, lymphocyte, platelet, AST, ALT, albumin, LMR, PLR, De ritis, MLR and CRP/albumin ratio. The mean age of the OAB group was significantly higher than the control group ($p<0.001$). Mean WBC, neutrophil, monocyte and CRP values of the control group were significantly higher than those of the OAB group (p values were 0.007; 0.024; 0.010; 0.048, respectively) (Table 2).

In the multivariate analysis, only age was found to be a predictor for AAM (Table 3).

Table 1: Comparison of blood group and gender of the groups

	OAB group(n:99)	**Control group(n:99)**	**p value**
Gender (n/%)			0.394
Male	47 (47.4%)	54 (54.5%)	
Female	52 (52.6%)	45 (45.5%)	
Blood group (n/%)			0.761
A+	23 (23.2%)	21 (21.2%)	
A-	17 (17.2%)	21 (21.2%)	
B+	18 (18.1%)	13 (13.1%)	
B-	11 (11.1%)	13 (13.1%)	
AB+	5 (5.1%)	2 (2.2%)	
AB-	5 (5.1%)	3 (3%)	
0+	11 (11.1%)	16 (16.1%)	
0-	9 (9.1%)	10 (10.1%)	

Table 2: Comparison of inflammation markers between groups

Parameters (ort±SS)	OAB group (n:99)	Control group (n:99)	p value
Age (years)	57.5±13.7	47±14.5	**<0.001**
BMI (kg/m2)	25.2±1.4	25.4±1.5	0.393
OAB-V8 score	21.4±3.8	2.4±1.8	**<0.001**
Urgency attacks	2.7±0.7	0.05±0.22	**<0.001**
Hg (g/dL)	13.9±1.4	14.2±1.8	0.273
Hct	41.4±4	41.7±4.8	0.619
WBC (10^3/µL)	7.2±2.5	8.4±3.3	**0.007**
Neutrophils (10^3/µL)	4.5±2.3	6.1±6.3	**0.024**
Lymphocytes (10^3/µL)	2±0.6	2.1±0.8	0.173
Platelets (10^3/µL)	243±62	252±54	0.267
Monocyte (10^3/µL)	528±217	624±292	**0.010**
AST (U/L)	22.2±7.1	24.7±12.8	0.085
ALT (U/L)	23.9±23.9	24.4±17.3	0.884
CRP (mg/dL)	5.7±10.07	11.3±26.5	**0.048**
Albumin (g/dL)	41±5	41.9±4	0.163
NLR	2.9±3.9	3.6±4.7	0.28
PLR	139.7±102.2	152±156.8	0.513
LMR	4.6±4.4	3.9±1.7	0.145
De ritis rate	1.1±0.4	1.2±0.6	0.424
MLR	0.3±0.2	0.3±0.3	0.267
CRP/Albumin rate	0.1±0.2	0.2±0.7	0.056

BMI: Body mass index, OAB-V8: Overactive bladder form, Hg: Haemoglobin, HCT: Haematocrit, WBC: White blood cell, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C reactive protein, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet lymphocyte ratio, LMR: Lymphocyte monocyte ratio, MLR: Monocyte lymphocyte ratio De ritis: AST/ALT

Table 3. Multivariate analysis

Parameters	OR	95% CI	p value
Age	1.055	1.031-1.079	**<0.001**
Neutrophils	1.000	1.000-1.000	0.126
CRP	0.976	0.948-1.004	0.094

CRP: C reactive protein

According to ROC analysis, a cut-off value of 49.5 (years) for age had a sensitivity of 76% and a specificity of 57% for predicting AAM (AUC: 0.705, 95%CI=0.632-0.777, p<0.001) (Figure 1).

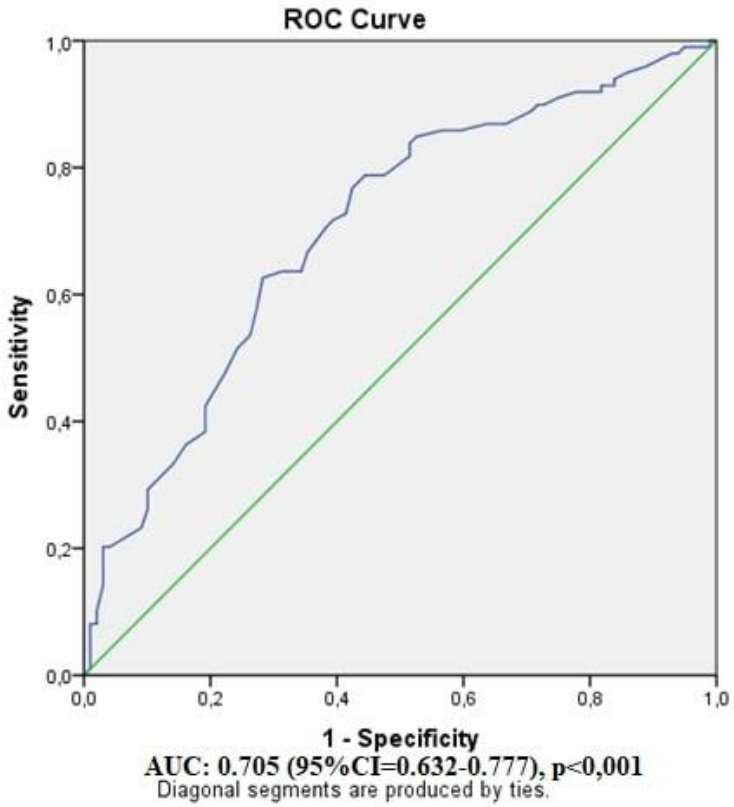

Figure 1: ROC curve for age in the diagnosis of AAM

Discussion

Overactive bladder is a pathology involving very complex processes involving the bladder urothelium, bladder nerves and central nervous system. The pathology causing this disease has not been elucidated so far. It is important to determine the underlying causes in order to provide safer and more effective treatment options (9). In our study, we investigated whether inflammation markers play a role in the pathogenesis of OAB. According to our results, inflammation markers were found to be lower in OAB patients than in the control group. In addition, the mean age of the patients in the OAB group was statistically significantly higher than that in the control group.

In our study, the mean age of the OAB group was 57.5 years, while the mean age of the control group was 47 years. Studies have shown that OAB symptoms increase with advancing age in both men and women (10). In the study conducted by Benli, the mean age of the OAB group was found to be significantly higher than that of the control group patients (11).

Involuntary contractions of detrussor muscle fibres play a role in the pathogenesis of overactive bladder. Although it is thought that stimuli originating from urothelium and suburothelium are the initiating factor of involuntary contractions, the cause has not been elucidated yet. Inflammation is one of the reasons to be emphasised. Kupelyan et al. in their study of 2301 male and 3202 female patients, showed a consistent association between increased CRP levels and OAB among both men and women. Among men, an increase in symptoms was observed above CRP>3 mg/L, whereas among women, an increase in symptoms was observed above CRP>1 mg/L (12).

In the present study, no correlation was found between NLR, LMR, PLR and LMR, which are well-known markers of inflammation, and OAB. There are contrary results to our findings in the literature. Çulha et al. 77 OAB and 80 control group patients, NLR and CRP values were found to be higher in the OAB group compared to the control group (13). In a study of 4394 South Korean women, the association of NLR with OAB was investigated. Among this group, 432 patients were diagnosed with OAB. In the analysis, the mean NLR value in the OAB group was found to be higher than the other group. In addition, NLR was found to be associated with the severity of OAB (14).

Similar to our findings in the literature, there are also studies supporting that inflammation does not play a role in OAB patients. Tyagi et al. concluded that PDGF, IL-1β, CCL2, CXCL1, CXCL8, and CXCL10 levels were not different in the OAB group compared to the control group (15). Similarly, Pennycuff et al. 38 OAB and 29 healthy volunteers concluded that NGF, BDNF, Substance p and CGRP levels were not different between the two groups and that NGF and BDNF levels increased with age (16). In a study investigating CRP levels in BPH patients, Inamura et al. showed that CRP was not associated with storage function. The authors emphasised that the cause of OAB exacerbation may be due to a cause other than elevated CRP levels (17). Considering that ischaemia plays an important role in the pathogenesis of OAB, tissue damage markers (NGF, BDGF) are expected to

increase as a result of denervation of bladder nerve fibres. Since the inflammation markers we analysed in our study are non-specific markers, variability in serum levels may be expected for many reasons. We can explain the discrepancies between our results and the literature with this situation.

One of the limitations of our study is that it was performed with a small number of patients. The second limitation is that we used non-specific inflammation markers. The study of more specific inflammation markers analysed from urine may provide more accurate results.

Conclusion

In conclusion, in our study, no elevated levels of inflammation markers were found in patients with OAB. In order to elucidate the relationship between OAB and inflammation, more specific markers analysed in urine and studies with a higher number of patients are needed.

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Conflict of Interest: Regarding this study, the authors and/or their family members do not have any relationship with scientific and medical committee membership or members, consultancy, expertise, employment status in any company, shareholding and similar situations that may have the potential for conflict of interest.

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